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Massimiliano Visocchi *Editor*

The Funnel: From the Skull Base to the Sacrum

New Trends, Technologies and Strategies

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Contents

Why the Funnel in Neurosurgery?

Massimiliano Visocchi

1 Editorial

According to the Cambridge Dictionary, a **Funnel** is an object that has a wide round opening at the top, sloping sides, and a narrow tube at the bottom, used for pouring liquids or powders into containers with narrow necks.

From a simplified anatomic point of view, the skull base along with its offshoot, the spine, replicate a bone funnel as a vessel sustaining the brain, the cerebellum and the spinal cord along with cranial and radicular nerves. There is no doubt at all that the knowledge of the embryology, anatomy, physiology, pathophysiology, and the more effective surgical pathways to engage and remove surgical diseases is of paramount importance in the surgical cultural heritage and should be strongly encouraged and supported in young neurosurgeons (Fig. 1).

Moreover, the Funnel is also a scientific philosophy (epistemology?) aimed at progressively focusing a scientific investigation on the core of the problem, etiology, basic pathophysiological mechanisms, strategic radical minimally invasive and maximally effective surgical principles. The Funnel is a general philosophic concept starting and ending also in religious principles.

The **Funnel** is also a technique that involves starting with general questions, and then drilling down to a more specific point in each. Usually, this will involve asking for more and more detail at each level. It is often used by detectives taking a statement from a witness.

The purchase funnel, or purchasing funnel, is a consumer-focused marketing model that illustrates the theoretical customer journey toward the purchase of a good or service. In 1898, E. St. Elmo Lewis developed a model that mapped a theoretical customer journey from the moment a brand or product attracted consumer attention to the point of action or purchase [1]. St. Elmo Lewis' idea is often referred to as the AIDA-model, an acronym that stands for Awareness, Interest, Desire, and Action. This staged process is summarized below: Awareness—the customer is aware of the existence of a product or service; Interest—actively expressing an interest in a product group; Desire—aspiring to a particular brand or product; Action—taking the next step toward purchasing the chosen product. The purchase funnel is also often referred to as the "customer funnel," "marketing funnel," "sales funnel," or "conversion funnel." The association of the funnel model with the AIDA concept was first proposed in Bond Salesmanship by William W. Townsend in 1924 [2] (Fig. 2).

When I learned these original and interesting concepts from the *Internet*, so far from the sensitivity of a "simple" Neurosurgeon, I remained impressed and emotional. The spirit of this Issue of Acta Neurochirurgica appears to me quite the same.

To bring attention to new trends and developments of the modern neurosurgical practice and, at the same time, to offer different and new points of suggestions and scientific speculation. Finally, to drive the practical interests of the neurosurgeons to further investigate and implement such blooming new trends in technologies both in research and in surgical practice.

So, the steps that seem to emerge from this Issue of Acta Neurochirurgica Suppl are exploratory, strategic, tactical, and, finally, operational. From the skull base to the sacrum, we meet a macrosystem of anatomically and functionally complex networks with a common embryological history as well as contiguity. Different skills are necessary to face a 360° universe of functions and diseases. Intelligence and culture as knowledge of both anatomy and pathology help to elaborate the STRATEGY while technical and manual supports are part of the TACTIC armamentarium which is proactive and determinant to the final OPERATIONAL step (Fig. 3).

In conclusion the Funnel is an anatomic concept, is a philosophy, is the prerequisite of all operational performances, is a creed.

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Fig. 1 The skull base and spine resemble a funnel

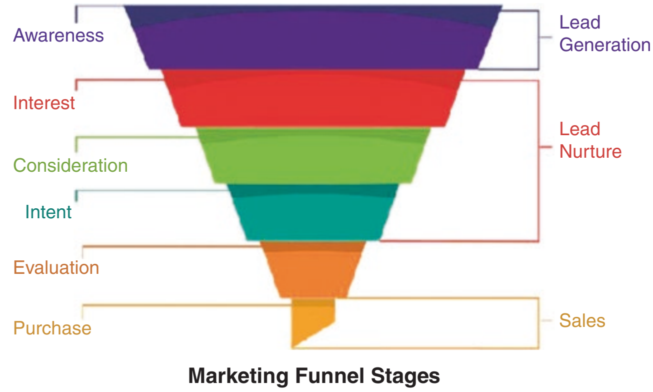
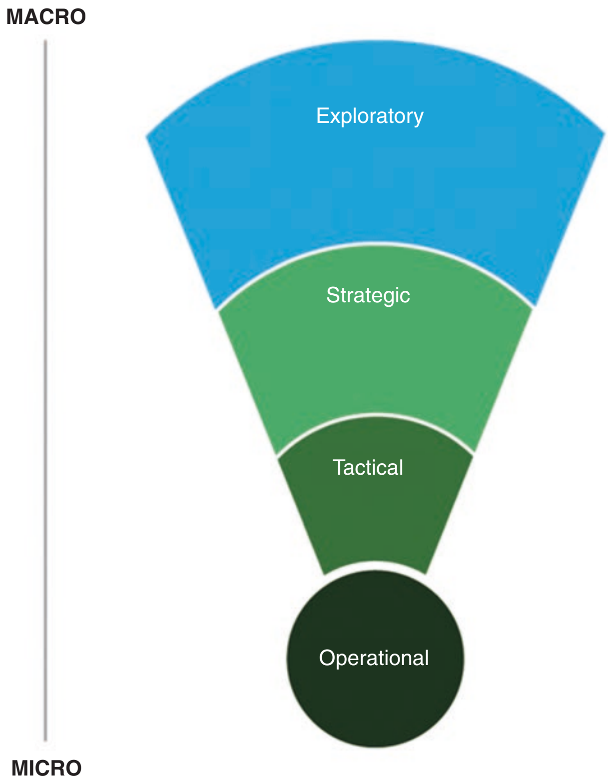


Fig. 2 Marketing funnel stages representation



Phase detail	Example
Exploratory Big picture Defining the problems	Ecosystem analysis Market survey
Strategic The problem is known Defining a customer/audience strategy	Stakeholder facilitated workshops Customer segmentation
Tactical Ad-hoc research Planning operational research	User depth interviewing Customer focus groups
Operational Day-to day research reporting	Web analytics reporting Customer satisfaction ratings

Fig. 3 Operational funnel stages representation

References

1. Strong EK Jr. The psychology of selling and advertising. New York, NY: McGraw-Hill; 1925, p. 349 and p. 9. “The salesman should visualize his whole problem of developing the sales steps as the forcing by compression of a broad and general concept of facts through a funnel which produces the specific and favorable consideration of one fact. The process is continually from the general to the specific, and the visualizing of the funnel has helped many salesmen to lead a customer from Attention to Interest, and beyond” (p. 109).
2. William W. Townsend: bond salesmanship. New York, NY: H. Holt; 1924. 468 p.

Surgeon's Eyes on the Relevant Surgical Target

Oreste de Divitiis, Elena d'Avella,
Gianluca Lorenzo Fabozzi, Luigi Maria Cavallo,
and Domenico Solari

1 Introduction

The discipline of neurosurgery has faced various stages of development, featuring over time periods of prolonged immobilism followed by rapid advancements [1]. The ultimate challenge of the neurosurgical endeavor was the possibility of overcoming the resolution of the human eye; therefore, the operating microscope is considered the major milestone in the recent history of neurosurgery [2].

The innovation and technological contributions by the neurosurgical discipline raises the question about the need for scientific validation of emerging technological advancement, especially during recent years, when the promotion and diffusion of ideas and methods has been more efficient and global than ever [3, 4]. Surgeons may not always have the benefit of level I evidence in support of the technology or approaches available and at any given time need to make the best decisions for their patients. In fact, while Yasargil presented at the Giessen Congress in 1997 at the dawn of modern microsurgery for cerebral aneurysms [5], Suzuki in 1979 kept reporting excellent results in over 1000 aneurysms patients undergoing operation without microsurgical techniques [6]. However, Yasargil concluded that: "while there is no question that a few accomplished neurosurgeons with a wealth of clinical material can achieve a high standard of operative results with classical or other sophisticated approaches to aneurysm surgery, for most neurosurgeons there nevertheless remains the need for a comprehensive plan of operation fully utilizing the benefits of the microsurgical technique; a plan that incorporates microsurgical principles into the entire procedure from craniotomy to closure" [5].

The flourishing of microsurgical techniques and advances in the quality of surgical microscopes relegated the endoscope to a role supporting the visualization obtained with the microscope [7]. Tremendous improvements in the overall quality of the endoscopic equipment allowed for the expansion of endoscopic surgery and permitted the evolution of the "pure" endoscopic transsphenoidal technique in the late 1990s [8–10]. Further enhancement of image quality, such as the recent introduction of 4K technology, along with the increased surgical experience, allowed for the expansion of indications of the endoscopic technique, defining new routes beyond the sella and playing a key role in its widespread clinical application [11–16]. As with many advances in medical technology, the development of functional surgical visualization systems did not occur at one defined moment or as a result of any major paradigm shift, but rather as a process of ongoing refinement and stepwise progression resulting from the conceptualization, deliberation, and innovation of numerous scientists and physicians over a span of more than two centuries [17, 18]. Many of these improvements occurred as a direct result of the introduction and application of emerging technology into the surgical environment. With major advancement in illumination and magnification, innovations in digital imaging, and robotics, all occurring nearly simultaneously, the neurosurgeon must confront a series of issues, including which system to utilize and in which device to invest, relying on the judgment of the operator to determine specific surgical indications. The continuous evolution of visualization tools in neurosurgery has been driven by the need of magnification and precision, with the aim of maximizing benefits while decreasing morbidity: this synergism between refinement of the surgical technique and technological innovations represents the natural evolution of this discipline.

Herein we present a review of the evolution of visualization tools in neurosurgery, with a special glimpse into the future perspectives, analyzing in detail the current technology development from the neurosurgeon's eye perspective.

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2 Loupes

Spectacles, invented in the thirteenth century, represented the first widespread practical use of magnification. The modification of lenses by manufacturers and scientists led to the development of telescopes, loupes, and early compound microscopes [19]. Historically, loupes became an essential tool for watchmakers, who took advantage of the opportunity of magnifying extremely miniaturized mechanisms, to improve their precision and ability. In 1876, the ophthalmologist Edwin Theodore Saemisch of Bonn developed the first simple loupe for surgical use [20]. The German Ernst Abbé (1840–1905), collaborating with Carl Zeiss, derived the theoretical formulas that governed the optical properties of lenses, allowing the performance of new lenses to be predicted and systematically designed [21]. At approximately the same time, surgeons had already recognized the potential benefit of magnification and had adopted single lens magnifying loupes [22, 23]. However, the challenge of improving visualization runs parallel with the need for providing safe and adequate illumination. Initial light sources, such as ambient light, candles, and bulbs, were inadequate for bringing light into the surgical field. The discovery that light could be transmitted in through various conductors from an external source improved the neurosurgeon's vision [24].

Many surgical fields have adopted using surgical loupes when high-demand visual performance is needed during macroscopic procedures [25]: hand surgery as well as in plastic, maxillofacial, otorhinolaryngologic, ophthalmic, cardiothoracic, and pediatric surgery. In neurosurgery, after an initial widespread application, loupes began to overcome microscope use and, nowadays, they find their application in peripheral nerves and spine surgery. Loupes allow magnification from 2 to 8 times and for every 30% increase in magnification, the depth and width of the field are decreased by approximately 2.5 cm [22, 26]. The main advantages are portability, lower cost, and maneuverability; on the other hand, all loupes are limited by their nonadjustable focus, low magnification, ring of blindness peripherally (3–4 cm wide), and problems with slippage and pressure on the nose [23]. Building on ergonomics, loupes require a flexed head-neck posture for prolonged periods of time, with a potential increased biomechanical risk for cervical musculoskeletal disorders among surgeons who routinely use this device [27, 28].

3 Microscope

The introduction of the operating microscope in the 1960s opened the era of modern neurosurgery, along with an escalation in diagnostic and therapeutic capabilities [2, 19, 29]. During this time, the refinement of medical imaging, the minimization of operative corridors and reduction of operative trauma through the adoption of the microsurgical technique, and the incorporation of technical tools into the operative environment produced an evolution in neurosurgery, which offered higher precision of orientation and brain manipulation, resulting in decreased morbidity, and improved clinical outcomes. Over the past half century, perhaps, no other innovation has uniquely characterized the surgical technique and operating room spatial organization as much as the operating microscope.

During the early part of the twentieth century, technical advances in lighting and microscope design by manufacturers such as Carl Zeiss (1816–1888) brought improvement in operative visualization [19]. The first use of the microscope in a neurosurgical setting took place in 1957 by Theodore Kurze (1922–2002) of the University of Southern California, who adapted the otological microscope for use in the neurosurgical operating room [30]. However, history changed when Raymond MP Donaghy (1910–1979) presented the first course on microsurgery at the University of Vermont in 1966 [31]. M. Gazi Yasargil (1925–), who arrived at the University of Vermont in 1965, under the mentoring of Donaghy, was able to perform anastomosis of small blood vessels in the limbs of animals. Building on these initial efforts, he would firmly establish the microneurosurgical revolution [32, 33]. Yasargil's chief in Zurich, Hugo Krayenbuhl, prophesied such a revolution in surgery when, visiting Donaghy's microsurgical laboratory he pronounced: "Gentlemen, I give you the surgery of the future." Operating microscopes have improved impressively since they first entered the operating room [18, 20, 29]. Today, they offer good magnification without significant aberrations, adequate illumination without excessive heat, and good stability without sacrificing operational ergonomics. The cameras attached to modern microscopes allow surgical procedures to be recorded in high-definition quality. Sophisticated imaging capabilities have been developed for today's operating microscopes: in patients who have been given ionophores, they allow visualizing malignant glioma or intraoperative angiography; they might display and overlap MR images, angiograms, and CT scans simultaneously to the intraoperative information, thus boosting the real-time access decision making of the surgeon in the operating room. Nowadays, optical microscopes working with the near field imaging systems are already generating images of sub micrometer resolution: further magnification beyond the limits of near-field optical microscopes and electron microscopes might be expected to enlighten the cellular and ultrastructural environments during the procedures.

4 Endoscope

In 1805, the Alert Faculty in Vienna heard Philippe Bozzini (1773–1809) reporting on an instrument he had developed, the "Lichtleiter," which used candlelight reflected by a concave mirror for the inspection of the abdominal visceral organs [34]. Seventy years later, Max Nitze (1849–1906) described the first system that contained a series of lenses: i.e., a scope [35]. The German urologist definitely guessed two crucial ideas: the need of magnifying the images through a series of lenses and illumination through internal lights rather than external ones. By the turn of the century, the promise of endoscopy had been demonstrated, but its acceptance was slowed because of the poor illumination. Harold Hopkins (1918–1994), a British optical physicist, built a new endoscope designed to improve on light conduction [36, 37]: he interchanged glass for air and vice versa, resulting in a series of "air lens" housed in a glass tube (SELFOC lens, 1966). In the same period, Basil Hirschowitz, an American gastroenterologist, developed an endoscope with flexible glass-coated fibers (fiberoptics) illuminated by a simple light bulb at the distal end. He called this system a fiberscope and presented it at a meeting of the American Gastroscopic Society in 1957 [36, 38]. Later on, the advent of charge-coupling devices (CCDs) marked another technological breakthrough [39, 40]: the CCDs are solid-state devices, which can convert optical data into electrical current. The endoscope's earliest application in neurosurgery was its use within the ventricular system [16, 40]: although Victor Darwin Lespinasse (1878–1946), a urologist from Chicago, was the first to use a cystoscope to coagulate the choroid plexus, the father of neuroendoscopy is recognized as Walter Dandy [36]. In 1922, he reported in the *Annals of Surgery* using endoscopic ventriculostomy to remove the choroid plexus for the treatment of hydrocephalus [41]. Endoscopy was initially used as an adjunct to microneurosurgical techniques, above all in tumor and aneurysm surgery, to provide views in blind corners that surgeons had achieved with angled mirrors [42]. Axel Perneczky and George Fries, who pioneered using the endoscope in intracranial neurosurgery, emphasized that endoscopy "improved appreciation of micro-anatomy not apparent with the microscope" and introduced the concept of "minimally invasive neurosurgery" [43, 44].

Based on otorhinolaryngologists experience with functional endoscopy in the nasal cavity, the endoscope has been progressively adopted for the treatment of sellar lesions [16]. Roger Jankowski and his group [45] published the first use of the pure endoscopic sublabial transsphenoidal approach. Three years later, Drahambir Sethi and Prem Pillay [46], from Singapore, reported their experience using a pure endoscopic endonasal approach. Finally, Carrau and Jho, working at the University of Pittsburgh Medical Center started to apply endoscopy to the removal of pituitary adenomas and established guidelines for fully endoscopic skull base procedures [9, 47]. Owing to the introduction of other technical adjuncts, endoscopic endonasal surgery has been extended to the treatment of lesions outside the sella, introducing the concept of "endoscopic extended endonasal" skull base surgery [13, 14, 48–61].

Expansion of indications moved along with visualization technical improvements, such as 3-CCD xenon light source, high-definition filters, ultra-high-definition television, the 4K and three-dimensional (3D) technologies.

5 Exoscope

Exoscopes are telescopic optical systems attached to a high-quality television camera. The surgeon looks away from the surgical field over a video monitor screen, and so it requires eye-hand coordination that is quite different from the operating microscope [62]. The exoscope differs from endoscopes presenting a long focal distance (therefore it is positioned outside the surgical cavity), and the wide field of view that parallels those seen with the operating microscope, as well as the excellent optical quality without spherical aberration.

During the past three decades, telescopes have been recognized as valid visualization tools in many surgical fields. In 2008, Mamelak et al. reported on preliminary experiences using this novel tool in neurosurgery [63]. Following many clinical reports and multiple technical improvements, high definition exoscope systems have entered the field of contemporary neurosurgery [64–71]. Initial considerations were that the most relevant benefits are related to working environment ergonomics (easiness of operating room setup, instruments handling, and surgeons' comfort) and trainees learning experience [72–74].

Along with the definition of advantages and disadvantages of the exoscope over the operating microscope or endoscope [75–78], the increased experience has been lightening on the surgical setting in which using exoscopes could be best indicated. In general, the exoscope has proven extremely useful in spinal procedures [79–83]: the visual property of delivering light and magnification uniformly across a wide field quite homogeneously deep, allows for a reduced need of zooming and refocusing during spinal procedures; the working distance offers enough space for the surgeon to bring spinal instrumentation into the operating field under a direct high-definition magnified view without needing to move the scope out of the field; the exoscope does not need to be transitioned in and out of the operative field during placement of fluoroscopy, which may potentially contribute to increased efficiency.

More recently, the exoscope visualization system has been integrated into surgical robotic devices that enhance optical visualization, i.e., ROVOT-m, a robotically operated video optical telescopic-microscope [84, 85]. This is a three-element optical chain combining exoscope, navigation system, and an automated holding robotic arm. The benefits of the ROVOT include maneuverability, ergonomics, and increased volume of view, while the inherent disadvantages include the lack of stereoscopy and 3D perception and proprioception.

6 A Glimpse into the Future

Augmented reality (AR) and virtual reality (VR) represent some of the newest visualization modalities being integrated into neurosurgical practice [86, 87]. VR offers the opportunity to interact with a virtual environment and objects within it. The concept of AR is to overlay artificial images onto the current visual field, with users able to interact simultaneously with the real world and the virtual objects. In AR and VR systems, the user wears glasses that display holographic images onto the real world and interactions occur either through voice commands or by hand gestures. Since the 1990s, pioneer contributions came from the field of video games production and the U.S. military for training and rehabilitation of soldiers, but the available technology was not ready to bring it into everyday application [88–90]. It was not until the year 2010 that computer technology advanced enough to support the development of truly immersive VR and AR systems, that are progressively finding their application also in the realms of surgery [86]. In neurosurgery, VR may become an extremely valuable tool for education and surgical planning [87, 91–93]. Trainees and residents can virtually experience a surgical procedure, getting familiar with anatomical orientation and assessing technical skills, away from the risk of morbidity inherent to the intricate and complex nature of neurosurgical practice. VR has the potential for a shift in the current paradigm of learning neurosurgery, which still relies on mentorship, volume of operations performed, and time spent in hospital, as it has been during the past three centuries. Utilizing VR to aid in preoperative planning is another area of interest. Using traditional planning algorithms, the neurosurgeon uses 2D information from computed tomography and/or magnetic resonance imaging to build his or her own mental 3D model of the patient's anatomy and pathology. A VR system can allow the surgeon to pre-operatively rehearse an upcoming procedure using VR simulation loaded with patient-specific imaging. Several AR systems have been shown to have specific uses in the field of neurosurgery [94–96]. The projection of planned 3D diagnostic images directly to the surgeon's optical view onto the patient in the surgical field can aid in orientation, anatomical delineation, and development of the surgical approach. Specific software allows the surgeon to sample surgical instruments prior to use, i.e., sample various clips size before aneurysm exclusion. Nevertheless, they should be adaptable to the surgical endeavor, in terms of ergonomic, versatility, wear-ability, learning-curve, and affordability. Lastly, the discussion of whether virtual reality applications in neurosurgery are ethically just an evolving landscape that changes with the technology in question.

Recently, radiomics methods are being adopted to retrieve advanced data off radiological images and define eventual predictive factors to support the management decision process and better understand disease prognosis [97–99]. This branch of artificial intelligence is bringing the eye of the neurosurgeon beyond a qualitative and subjective description of individual patient's images, focusing instead on deep learning software to be applied on a large scale so that "images are more than pictures, they are data" [100].

Another recent paradigm shift in approaching neuroscience relies on the possibility of mapping the connectivity architecture of the brain—a connectome—and the neural network organization [101–103]. Magnetic resonance imaging is the tool used to map structural and functional properties of the human connectome. Connectomic offers a powerful analytic framework for localizing pathology, tracking patterns of disease spread and predicting which areas will be affected next, thus modifying the neurosurgeon's vision of the phenotypic expression of the disease.

Nowadays, we are see the possibilities of looking beyond the anatomy and intra-operatively investigating the ultrastructural texture and neural network to modulate the proper treatment and address prognostic aspects of pathology.

There is no chance that this will replace the surgeon's eye, but we do hope that this will be the magic looking glass that will boost surgical treatment paradigms.

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Liu CY, Spicer M, Apuzzo ML. The genesis of neurosurgery and the evolution of the neurosurgical operative environment: Part II--concepts for future development, 2003 and beyond. Neurosurgery. 2003;52:20–33. https://doi.org/10.1097/00006123-200301000-00002; discussion 33–25.
2. Yaşargil MG, Krayenbühl H. The use of the binocular microscope in neurosurgery. Bibl Ophthalmol. 1970;81:62–5.
3. Cappabianca P, Zada G. "IDEAL", the operating microscope, and the parachute. Acta Neurochir. 2018;160:367–8. https://doi.org/10.1007/s00701-017-3425-4.
4. Muskens IS, Diederen SJH, Senders JT, Zamanipoor Najafabadi AH, van Furth WR, May AM, Smith TR, Bredenoord AL,

Broekman MLD. Innovation in neurosurgery: less than IDEAL? A systematic review. Acta Neurochir. 2017;159:1957–66. https://doi.org/10.1007/s00701-017-3280-3.

5. Yasargil M. Microsurgical anatomy of the basal cistern and vessels of the brain, diagnostic studies, general operative techniques and pathological considerations of the intracranial aneurysms. In: Yasargil M, editor. Microsurgery, vol. 1. Stuttgart: Thieme; 1984.
6. Suzuki J. Cerebral aneurysms: experience with 1,000 directly operated cases. Tokyo: Neuron; 1979.
7. Prevedello DM, Doglietto F, Jane JA, Jagannathan J, Han J, Laws ER. History of endoscopic skull base surgery: its evolution and current reality. J Neurosurg. 2007;107:206–13. https://doi.org/10.3171/JNS-07/07/0206.
8. Wang AJ, Zaidi HA, Laws ED. History of endonasal skull base surgery. J Neurosurg Sci. 2016;60:441–53.
9. Jho H-D, Carrau RL, Ko Y. Endoscopic pituitary surgery. In: Wilkins RH, Rengachary SS, editors. Neurosurgical operative atlas, vol. 5. Park Ridge, IL: American Association of Neurological Surgeons; 1999. p. 1–12.
10. Cappabianca P, Alfieri A, de Divitiis E. Endoscopic endonasal transsphenoidal approach to the sella: towards functional endoscopic pituitary surgery (FEPS). Minim Invasive Neurosurg. 1998;41:66–73.
11. Di Somma A, Andaluz N, Cavallo LM, de Notaris M, Dallan I, Solari D, Zimmer LA, Keller JT, Zuccarello M, Prats-Galino A, Cappabianca P. Endoscopic transorbital superior eyelid approach: anatomical study from a neurosurgical perspective. J Neurosurg. 2018;129:1203–16. https://doi.org/10.3171/2017.4.JNS162749.
12. Cavallo LM, de Divitiis O, Aydin S, Messina A, Esposito F, Iaconetta G, Talat K, Cappabianca P, Tschabitscher M. Extended endoscopic endonasal transsphenoidal approach to the suprasellar area: anatomic considerations--Part 1. Neurosurgery. 2008;62:1202–12. https://doi.org/10.1227/01.neu.0000333786.98596.33.
13. Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A, De Divitiis E. Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. Adv Tech Stand Neurosurg. 2008;33:151–99.
14. Frank G, Pasquini E, Mazzatenta D. Extended transsphenoidal approach. J Neurosurg. 2001;95:917–8.
15. Kassam AB, Gardner P, Snyderman C, Mintz A, Carrau R. Expanded endonasal approach: fully endoscopic, completely transnasal approach to the middle third of the clivus, petrous bone, middle cranial fossa, and infratemporal fossa. Neurosurg Focus. 2005;19:E6.
16. Cavallo LM, Somma T, Solari D, Iannuzzo G, Frio F, Baiano C, Cappabianca P. Endoscopic endonasal transsphenoidal surgery: history and evolution. World Neurosurg. 2019;127:686–94. https://doi.org/10.1016/j.wneu.2019.03.048.
17. Apuzzo ML. Modernity and the emerging futurism in neurosurgery. J Clin Neurosci. 2000;7:85–7. https://doi.org/10.1054/jocn.1999.0182.
18. Apuzzo ML, Liu CY. 2001: Things to come. Neurosurgery. 2001;49:765–78. https://doi.org/10.1097/00006123-200110000-00002.
19. Kriss TC, Kriss VM. History of the operating microscope: from magnifying glass to microneurosurgery. Neurosurgery. 1998;42:899–907. https://doi.org/10.1097/00006123-199804000-00116; discussion 907–898.
20. Uluç K, Kujoth GC, Başkaya MK. Operating microscopes: past, present, and future. Neurosurg Focus. 2009;27:E4. https://doi.org/10.3171/2009.6.FOCUS09120.
21. Volkmann H. Ernst abbe and his work. Appl Opt. 1966;5:1720–31. https://doi.org/10.1364/AO.5.001720.
22. Ilie VI, Ilie VG, Lefter M. Loupes in surgical training. ANZ J Surg. 2011;81:580–1. https://doi.org/10.1111/j.1445-2197.2011.05832.x.
23. Stanbury SJ, Elfar J. The use of surgical loupes in microsurgery. J Hand Surg [Am]. 2011;36:154–6. https://doi.org/10.1016/j.jhsa.2010.09.016.
24. Zada G, Liu C, Apuzzo ML. "Through the looking glass": optical physics, issues, and the evolution of neuroendoscopy. World Neurosurg. 2013;79:S3–13. https://doi.org/10.1016/j.wneu.2013.02.001.
25. Jarrett PM. Intraoperative magnification: who uses it? Microsurgery. 2004;24:420–2. https://doi.org/10.1002/micr.20066.
26. Baker JM, Meals RA. A practical guide to surgical loupes. J Hand Surg [Am]. 1997;22:967–74. https://doi.org/10.1016/S0363-5023(97)80034-2.
27. Demetriades AK, Meling TR, Ringel FA, Schaller K. Postural ergonomics and micro-neurosurgery: microscope has an edge over loupes. J Am Coll Surg. 2020;231:300–1. https://doi.org/10.1016/j.jamcollsurg.2020.04.026.
28. Kumar SS, Mourkus H, Farrar G, Yellu S, Bommireddy R. Magnifying loupes versus microscope for microdiscectomy and microdecompression. J Spinal Disord Tech. 2012;25:E235–9. https://doi.org/10.1097/BSD.0b013e31825010ae.
29. Liu CY, Apuzzo ML. The genesis of neurosurgery and the evolution of the neurosurgical operative environment: part I-prehistory to 2003. Neurosurgery. 2003;52:3–19. https://doi.org/10.1097/00006123-200301000-00001; discussion 19.
30. Kurze T, Doyle JB. Extradural intracranial (middle fossa) approach to the internal auditory canal. J Neurosurg. 1962;19:1033–7. https://doi.org/10.3171/jns.1962.19.12.1033.
31. Donaghy RM. The history of microsurgery in neurosurgery. Clin Neurosurg. 1979;26:619–25. https://doi.org/10.1093/neurosurgery/26.cn_suppl_1.619.
32. Yasargil M. Microneurosurgery, vol. 1. New York, NY: Thieme; 1984.
33. Donaghy RM. Neurosurgeon of the year: Mahmut Gazi Yasargil. Surg Neurol. 1980;13:1–3.
34. Doglietto F, Prevedello DM, Jane JA, Han J, Laws ER. Brief history of endoscopic transsphenoidal surgery--from Philipp Bozzini to the First World Congress of Endoscopic Skull Base Surgery. Neurosurg Focus. 2005;19:E3. https://doi.org/10.3171/foc.2005.19.6.4.
35. Mouton WG, Bessell JR, Maddern GJ. Looking back to the advent of modern endoscopy: 150th birthday of Maximilian Nitze. World J Surg. 1998;22:1256–8.
36. Abbott R. History of neuroendoscopy. Neurosurg Clin N Am. 2004;15:1–7.
37. Liu CY, Wang MY, Apuzzo ML. The physics of image formation in the neuroendoscope. Childs Nerv Syst. 2004;20:777–82. https://doi.org/10.1007/s00381-004-0930-6.
38. Hirschowitz BI. The development and application of fiberoptic endoscopy. Cancer. 1988;61:1935–41. https://doi.org/10.1002/1097-0142(19880515)61:10<1935::aid-cncr2820611002>3.0.co;2-e.
39. Di Ieva A, Tam M, Tschabitscher M, Cusimano MD. A journey into the technical evolution of neuroendoscopy. World Neurosurg. 2014;82:e777–89. https://doi.org/10.1016/j.wneu.2014.09.005.
40. Li KW, Nelson C, Suk I, Jallo GI. Neuroendoscopy: past, present, and future. Neurosurg Focus. 2005;19:E1.
41. Dandy W. Cerebral ventriculostomy. Johns Hopkins Hosp Bull. 1922;189
42. Apuzzo ML, Heifetz MD, Weiss MH, Kurze T. Neurosurgical endoscopy using the side-viewing telescope. J Neurosurg. 1977;46:398–400.
43. Perneczky A, Fries G. Endoscope-assisted brain surgery: Part 1--evolution, basic concept, and current technique. Neurosurgery. 1998;42:219–24; discussion 224–215.

44. Fries G, Perneczky A. Endoscope-assisted brain surgery: Part 2--analysis of 380 procedures. Neurosurgery. 1998;42:226–31; discussion 231–222.
45. Jankowski R, Auque J, Simon C, Marchal JC, Hepner H, Wayoff M. Endoscopic pituitary tumor surgery. Laryngoscope. 1992;102:198–202. https://doi.org/10.1288/00005537-199202000-00016.
46. Sethi DS, Pillay PK. Endoscopic management of lesions of the sella turcica. J Laryngol Otol. 1995;109:956–62. https://doi.org/10.1017/s0022215100131755.
47. Carrau RL, Jho HD, Ko Y. Transnasal-transsphenoidal endoscopic surgery of the pituitary gland. Laryngoscope. 1996;106:914–8.
48. Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL. Expanded endonasal approach: the rostrocaudal axis. Part I. Crista galli to the sella turcica. Neurosurg Focus. 2005;19:E3.
49. Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL. Expanded endonasal approach: the rostrocaudal axis. Part II. Posterior clinoids to the foramen magnum. Neurosurg Focus. 2005;19:E4.
50. Schwartz TH, Fraser JF, Brown S, Tabaee A, Kacker A, Anand VK. Endoscopic cranial base surgery: classification of operative approaches. Neurosurgery. 2008;62:991–1002. https://doi.org/10.1227/01.neu.0000325861.06832.06; discussion 1002-1005.
51. de Divitiis E, Cappabianca P, Cavallo LM. Endoscopic transsphenoidal approach: adaptability of the procedure to different sellar lesions. Neurosurgery. 2002;51:699–705; discussion 705–697.
52. Cavallo LM, Mazzatenta D, d'Avella E, Catapano D, Fontanella MM, Locatelli D, Luglietto D, Milani D, Solari D, Vindigni M, Zenga F, Zona G, Cappabianca P. The management of clival chordomas: an Italian multicentric study. J Neurosurg. 2020;135:93–102. https://doi.org/10.3171/2020.5.JNS20925.
53. Stippler M, Gardner PA, Snyderman CH, Carrau RL, Prevedello DM, Kassam AB. Endoscopic endonasal approach for clival chordomas. Neurosurgery. 2009;64:268–77. https://doi.org/10.1227/01.NEU.0000338071.01241.E2, 00006123-200902000-00008 [pii]; discussion 277–268.
54. Koutourousiou M, Fernandez-Miranda JC, Stefko ST, Wang EW, Snyderman CH, Gardner PA. Endoscopic endonasal surgery for suprasellar meningiomas: experience with 75 patients. J Neurosurg. 2014;120:1326–39. https://doi.org/10.3171/2014.2.JNS13767.
55. Koutourousiou M, Gardner PA, Fernandez-Miranda JC, Tyler-Kabara EC, Wang EW, Snyderman CH. Endoscopic endonasal surgery for craniopharyngiomas: surgical outcome in 64 patients. J Neurosurg. 2013;119:1194–207. https://doi.org/10.3171/2013.6.JNS122259.
56. Koutourousiou M, Gardner PA, Tormenti MJ, Henry SL, Stefko ST, Kassam AB, Fernandez-Miranda JC, Snyderman CH. Endoscopic endonasal approach for resection of cranial base chordomas: outcomes and learning curve. Neurosurgery. 2012;71:614–24. https://doi.org/10.1227/NEU.0b013e31825ea3e0; discussion 624–615.
57. Cavallo LM, Frank G, Cappabianca P, Solari D, Mazzatenta D, Villa A, Zoli M, D'Enza AI, Esposito F, Pasquini E. The endoscopic endonasal approach for the management of craniopharyngiomas: a series of 103 patients. J Neurosurg. 2014;121:100–13. https://doi.org/10.3171/2014.3.JNS131521.
58. Jeswani S, Nuno M, Wu A, Bonert V, Carmichael JD, Black KL, Chu R, King W, Mamelak AN. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study. J Neurosurg. 2016;124:627–38. https://doi.org/10.3171/2015.3.JNS142254.
59. Fraser JF, Nyquist GG, Moore N, Anand VK, Schwartz TH. Endoscopic endonasal transclival resection of chordomas: operative technique, clinical outcome, and review of the literature. J Neurosurg. 2010;112:1061–9. https://doi.org/10.3171/2009.7.JNS081504.
60. Castelnuovo P, Battaglia P, Turri-Zanoni M, Tomei G, Locatelli D, Bignami M, Villaret AB, Nicolai P. Endoscopic endonasal surgery for malignancies of the anterior cranial base. World Neurosurg. 2014;82:S22–31. https://doi.org/10.1016/j.wneu.2014.07.021.
61. Turri-Zanoni M, Lambertoni A, Margherini S, Giovannardi M, Ferrari M, Rampinelli V, Schreiber A, Cherubino M, Antognoni P, Locatelli D, Battaglia P, Castelnuovo P, Nicolai P. Multidisciplinary treatment algorithm for the management of sinonasal cancers with orbital invasion: a retrospective study. Head Neck. 2019;41:2777–88. https://doi.org/10.1002/hed.25759.
62. Langer DJ, White TG, Schulder M, Boockvar JA, Labib M, Lawton MT. Advances in intraoperative optics: a brief review of current exoscope platforms. Oper Neurosurg. 2020;19:84–93. https://doi.org/10.1093/ons/opz276.
63. Mamelak AN, Danielpour M, Black KL, Hagike M, Berci G. A high-definition exoscope system for neurosurgery and other microsurgical disciplines: preliminary report. Surg Innov. 2008;15:38–46. https://doi.org/10.1177/1553350608315954.
64. Mamelak AN, Drazin D, Shirzadi A, Black KL, Berci G. Infratentorial supracerebellar resection of a pineal tumor using a high definition video exoscope (VITOM®). J Clin Neurosci. 2012;19:306–9. https://doi.org/10.1016/j.jocn.2011.07.014.
65. Birch K, Drazin D, Black KL, Williams J, Berci G, Mamelak AN. Clinical experience with a high definition exoscope system for surgery of pineal region lesions. J Clin Neurosci. 2014;21:1245–9. https://doi.org/10.1016/j.jocn.2013.10.026.
66. Belloch JP, Rovira V, Llácer JL, Riesgo PA, Cremades A. Fluorescence-guided surgery in high grade gliomas using an exoscope system. Acta Neurochir. 2014;156:653–60. https://doi.org/10.1007/s00701-013-1976-6.
67. Krishnan KG, Schöller K, Uhl E. Application of a compact high-definition exoscope for illumination and magnification in high-precision surgical procedures. World Neurosurg. 2017;97:652–60. https://doi.org/10.1016/j.wneu.2016.09.037.
68. Oertel JM, Burkhardt BW. Vitom-3D for exoscopic neurosurgery: initial experience in cranial and spinal procedures. World Neurosurg. 2017;105:153–62. https://doi.org/10.1016/j.wneu.2017.05.109.
69. Rossini Z, Cardia A, Milani D, Lasio GB, Fornari M, D'Angelo V. VITOM 3D: preliminary experience in cranial surgery. World Neurosurg. 2017;107:663–8. https://doi.org/10.1016/j.wneu.2017.08.083.
70. De Divitiis O, D'Avella E, Denaro L, Somma T, Sacco M, D'Avella D. Vitom 3D: preliminary experience with intradural extramedullary spinal tumors. J Neurosurg Sci. 2019;66:356. https://doi.org/10.23736/S0390-5616.19.04666-6.
71. Angileri FF, Esposito F, Scibilia A, Priola SM, Raffa G, Germano A. Exoscope-guided (VITOM 3D) single-stage removal of supratentorial cavernous angioma and hemangioblastoma: 3-dimensional operative video. Oper Neurosurg. 2019;17:E164–5. https://doi.org/10.1093/ons/opz010.
72. Moisi M, Tubbs RS, Page J, Chapman A, Burgess B, Laws T, Warren H, Oskouian RJ. Training medical novices in spinal microsurgery: does the modality matter? A pilot study comparing traditional microscopic surgery and a novel robotic optoelectronic visualization tool. Cureus. 2016;8:e469. https://doi.org/10.7759/cureus.469.
73. De Virgilio A, Costantino A, Ebm C, Conti V, Mondello T, Di Bari M, Cugini G, Mercante G, Spriano G. High definition three-dimensional exoscope (VITOM 3D) for microsurgery training: a preliminary experience. Eur Arch Otorhinolaryngol. 2020;277:2589–95. https://doi.org/10.1007/s00405-020-06014-7.

74. Garneau JC, Laitman BM, Cosetti MK, Hadjipanayis C, Wanna G. The use of the exoscope in lateral skull base surgery: advantages and limitations. Otol Neurotol. 2019;40:236–40. https://doi.org/10.1097/MAO.0000000000002095.
75. Hafez A, Elsharkawy A, Schwartz C, Muhammad S, Laakso A, Niemela M, Lehecka M. Comparison of conventional microscopic and exoscopic experimental bypass anastomosis: a technical analysis. World Neurosurg. 2020;135:e293–9. https://doi.org/10.1016/j.wneu.2019.11.154.
76. Herlan S, Marquardt JS, Hirt B, Tatagiba M, Ebner FH. 3D exoscope system in neurosurgery-comparison of a standard operating microscope with a new 3D exoscope in the cadaver lab. Oper Neurosurg. 2019;17:518–24. https://doi.org/10.1093/ons/opz081.
77. Ricciardi L, Mattogno PP, Olivi A, Sturiale CL. Exoscope era: next technical and educational step in microneurosurgery. World Neurosurg. 2019;128:371–3. https://doi.org/10.1016/j.wneu.2019.05.162.
78. Ricciardi L, Chaichana KL, Cardia A, Stifano V, Rossini Z, Olivi A, Sturiale CL. The exoscope in neurosurgery: an innovative "point of view". A systematic review of the technical, surgical and educational aspects. World Neurosurg. 2019;124:136. https://doi.org/10.1016/j.wneu.2018.12.202.
79. Shirzadi A, Mukherjee D, Drazin DG, Paff M, Perri B, Mamelak AN, Siddique K. Use of the video telescope operating monitor (VITOM) as an alternative to the operating microscope in spine surgery. Spine (Phila Pa 1976). 2012;37:E1517–23. https://doi.org/10.1097/BRS.0b013e3182709cef.
80. Barbagallo GMV, Certo F. Three-dimensional, high-definition exoscopic anterior cervical discectomy and fusion: a valid alternative to microscope-assisted surgery. World Neurosurg. 2019;130:e244–50. https://doi.org/10.1016/j.wneu.2019.06.049.
81. de Divitiis O, d'Avella E, Sacco M, Somma T, Turgut M, Baro V, Denaro L. The role of Vitom-3D in the management of spinal meningiomas: review of the literature and illustrative case. Minim Invasive Surg. 2020;4:75.
82. Kwan K, Schneider JR, Du V, Falting L, Boockvar JA, Oren J, Levine M, Langer DJ. Lessons learned using a high-definition 3-dimensional exoscope for spinal surgery. Oper Neurosurg. 2019;16:619–25. https://doi.org/10.1093/ons/opy196.
83. de Divitiis O, Sacco M, d'Avella E, Guizzardi G, et al. VITOM-3D in lumbar disc herniation: preliminary experience. Interdiscipl Neurosurg. 2019;18:47–51.
84. Nishiyama K. From exoscope into the next generation. J Kor Neurosurg Soc. 2017;60:289–93. https://doi.org/10.3340/jkns.2017.0202.003.
85. Gonen L, Chakravarthi SS, Monroy-Sosa A, Celix JM, Kojis N, Singh M, Jennings J, Fukui MB, Rovin RA, Kassam AB. Initial experience with a robotically operated video optical telescopic-microscope in cranial neurosurgery: feasibility, safety, and clinical applications. Neurosurg Focus. 2017;42:E9. https://doi.org/10.3171/2017.3.FOCUS1712.
86. Chan S, Conti F, Salisbury K, Blevins NH. Virtual reality simulation in neurosurgery: technologies and evolution. Neurosurgery. 2013;72(Suppl 1):154–64. https://doi.org/10.1227/NEU.0b013e3182750d26.
87. Spicer MA, Apuzzo ML. Virtual reality surgery: neurosurgery and the contemporary landscape. Neurosurgery. 2003;52:489–97; discussion 496–487.
88. Satava RM. Virtual reality and telepresence for military medicine. Comput Biol Med. 1995;25:229–36. https://doi.org/10.1016/0010-4825(94)00006-c.
89. McCloy R, Stone R. Science, medicine, and the future. Virtual reality in surgery. BMJ. 2001;323:912–5. https://doi.org/10.1136/bmj.323.7318.912.
90. Kolga Schlickum M, Hedman L, Enochsson L, Kjellin A, Felländer-Tsai L. Transfer of systematic computer game training in surgical novices on performance in virtual reality image guided surgical simulators. Stud Health Technol Inform. 2008;132:210–5.
91. Pelargos PE, Nagasawa DT, Lagman C, Tenn S, Demos JV, Lee SJ, Bui TT, Barnette NE, Bhatt NS, Ung N, Bari A, Martin NA, Yang I. Utilizing virtual and augmented reality for educational and clinical enhancements in neurosurgery. J Clin Neurosci. 2017;35:1–4. https://doi.org/10.1016/j.jocn.2016.09.002.
92. Fiani B, De Stefano F, Kondilis A, Covarrubias C, Reier L, Sarhadi K. Virtual reality in neurosurgery: "can you see it?"-a review of the current applications and future potential. World Neurosurg. 2020;141:291–8. https://doi.org/10.1016/j.wneu.2020.06.066.
93. Bernardo A, Preul MC, Zabramski JM, Spetzler RF. A three-dimensional interactive virtual dissection model to simulate transpetrous surgical avenues. Neurosurgery. 2003;52:499–505; discussion 504–495.
94. Meola A, Cutolo F, Carbone M, Cagnazzo F, Ferrari M, Ferrari V. Augmented reality in neurosurgery: a systematic review. Neurosurg Rev. 2017;40:537–48. https://doi.org/10.1007/s10143-016-0732-9.
95. Tagaytayan R, Kelemen A, Sik-Lanyi C. Augmented reality in neurosurgery. Arch Med Sci. 2018;14:572–8. https://doi.org/10.5114/aoms.2016.58690.
96. Lee C, Wong GKC. Virtual reality and augmented reality in the management of intracranial tumors: a review. J Clin Neurosci. 2019;62:14–20. https://doi.org/10.1016/j.jocn.2018.12.036.
97. Gu H, Zhang X, di Russo P, Zhao X, Xu T. The current state of radiomics for meningiomas: promises and challenges. Front Oncol. 2020;10:567736. https://doi.org/10.3389/fonc.2020.567736.
98. Lohmann P, Galldiks N, Kocher M, Heinzel A, Filss CP, Stegmayr C, Mottaghy FM, Fink GR, Jon Shah N, Langen KJ. Radiomics in neuro-oncology: basics, workflow, and applications. Methods. 2021;188:112–21. https://doi.org/10.1016/j.ymeth.2020.06.003.
99. Cuocolo R, Ugga L, Solari D, Corvino S, D'Amico A, Russo D, Cappabianca P, Cavallo LM, Elefante A. Prediction of pituitary adenoma surgical consistency: radiomic data mining and machine learning on T2-weighted MRI. Neuroradiology. 2020;62:1649–56. https://doi.org/10.1007/s00234-020-02502-z.
100. Gillies RJ, Kinahan PE, Hricak H. Radiomics: images are more than pictures, they are data. Radiology. 2016;278:563–77. https://doi.org/10.1148/radiol.2015151169.
101. Hart MG, Romero-Garcia R, Price SJ, Santarius T, Suckling J. Connections, tracts, fractals, and the rest: a working guide to network and connectivity studies in neurosurgery. World Neurosurg. 2020;140:389–400. https://doi.org/10.1016/j.wneu.2020.03.116.
102. Henderson F, Abdullah KG, Verma R, Brem S. Tractography and the connectome in neurosurgical treatment of gliomas: the premise, the progress, and the potential. Neurosurg Focus. 2020;48:E6. https://doi.org/10.3171/2019.11.FOCUS19785.
103. Herbet G, Duffau H. Revisiting the functional anatomy of the human brain: toward a meta-networking theory of cerebral functions. Physiol Rev. 2020;100:1181–228. https://doi.org/10.1152/physrev.00033.2019.

New Trends in Neurosurgery: Toward a Future of Integration and Equity Among Male and Female Neurosurgeons

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Over the past few decades, the female presence in medical schools and residency programs has progressively increased; in the United States, for instance, in the past 5 years, women have come to exceed men in the number of medical school applications and matriculation [1].

Despite the rising percentage of women accessing the medical profession, surgical specialties remain largely male-dominated; in particular, only approximately 18% of neurosurgeons are females [2]. Several factors may be posited to explain this remarkable gender disparity in neurosurgery [3, 4]. In the first place, many women have been reluctant to choose neurosurgery, being concerned about how to balance family and career. Especially in countries where the burden of children's upbringing is traditionally placed on females only, many women eventually give up or are encouraged to switch track to less demanding subspecialties. On the other hand, prejudices against women neurosurgeons have long been deeply rooted and may still be present nowadays. Besides the fear that embracing motherhood might impact their work performance, female neurosurgeons have often been considered less "suitable" for this profession, as traits of weakness and lack of physical resistance are attributed to them. Consequently, many female neurosurgeons have experienced difficulties in career progression and have received unequal treatment in comparison with their male counterparts; such barriers might well exist even today.

In 1989 a group of eight female neurosurgeons founded Women in Neurosurgery (WINs), an organization aiming to "educate, inspire, and encourage women neurosurgeons to realize their professional and personal goals, and to serve neurosurgery in addressing the issues inherent to training and maintaining a diverse and balanced workforce." Thus, the original intentions of WINs founders were undoubtedly praiseworthy. Their purpose was to guarantee inclusivity in neurosurgery, promoting a better and egalitarian working environment, free of gender discrimination [5]. Thereafter, WINs' sessions were regularly organized in international conferences in order to offer female neurosurgeons a platform in which to report issues related to gender discrimination and promote a new culture against any form of prejudice.

With regret, we must admit that in the past several years, the original scope has been lost along the way and the mission of WINs sessions in national and international conferences has taken an unexpected deviation. WINs sessions have progressively become supplementary scientific sessions with only female neurosurgeons as speakers, thus paving the road to a form of self-segregation. This dangerous tendency has also been demonstrated by the foundation of sections of only-female neurosurgeons within some national societies [5].

Thus, the current situation is diametrically opposed to WINs' original intention: it only results in an unproductive separation, unfair to all neurosurgeons. We find women relegated into neurosurgical "pink rooms." Labels of male chauvinism are implicitly fixed onto those men who have always interacted with their female colleagues in a peer-to-peer relationship.

Although there remains a non-negligible faction that fiercely supports the WINs mindset of reserved spaces for women, a growing part of the global community believes that the conception of a "female neurosurgery" and a "male

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neurosurgery" is misguided and counterproductive. Such segregation is an upsetting prospect for all those who deeply believe that science and professionalism have no gender [6].

WFNS will soon have a female president, who has been elected by both male and female neurosurgeons around the world. This election represents a clear indicator of the revolutionary changes in the mindset of most neurosurgeons and should advocate for the abolition of a cumbersome organization that nowadays merely contributes to gender discrimination instead of favoring integration; if any form of discrimination still persists, the boards of each society (in particular WFNS) should supervise and enforce measures that establish equity. Finally, the Covid-19 pandemic further improved the natural trend of this progressive women inclusive process in neurosurgery as well as in neurosurgical meetings. In fact, due to the surprising implementation of virtual workshops (webinars) in the most attractive World Neurosurgical Societies Meetings (included WFNS) and the need to reverberating neurosurgical activities worldwide in such a critical and unique time, the impressive role and merit of the women's neurosurgical community was newly further found out both in research and surgical practice. So far, the number of women as invited speakers recently increased up to 50% compared to the men, as confirmed by the Co-Chair of the WFNS Neurorehabilitation and Reconstructive Committee (MV) who recently co-organized around 30 webinars. Moreover, noteworthy, in the recent Italian Society of Neurosurgery (October 15, 2020), the very first voted candidate who became Society Board Member (Società Italiana di Neurochirurgia) was a young female neurosurgeon (TS), overcoming an experienced worldwide known chairman of a Neurosurgical Dept in a prestigious Italian University.

The best possible future of neurosurgery can be achieved only through promotion of professionalism, commitment, and dedication to the profession, regardless of the gender of those that practice this challenging surgical specialty. Nowadays, the existence of the WINs is anachronistic and should no longer be necessary in a new era, open to integration, inclusivity, and equality.

References

1. Yaeger KA, Munich SA, Byrne RW, Germano IM. Trends in United States neurosurgery residency education and training over the last decade (2009-2019). Neurosurgery. 2020;48:E6.
2. World Health Organization. Global atlas of the health workforce: gender distribution of selected health professions. Geneva: World Health Organization; 2006.
3. Benzil DL, Abosch A, Germano I, Gilmer H, Maraire JN, Muraszko K, et al. The future of neurosurgery: a white paper on the recruitment and retention of women in neurosurgery. J Neurosurg. 2008;109(3):378–86.
4. Graziano F, Gerardi RM, Scalia G, Cammarata G, Nicoletti GF, Chaurasia B, Umana GE. Women in neurosurgery: from a matter of fortuitous occasions toward a conscious choice. World Neurosurg. 2021;148:129–35. https://doi.org/10.1016/j.wneu.2021.01.049. Epub 2021 Jan 28. PMID: 33515798.
5. Jung T-Y, Kim E-Y, Park M-S. Herstory of the Korean Women Neurosurgical Society since 2008. J Kor Neurosurg Soc. 2019;62:619–25.
6. Grotenhuis A. Women in neurosurgery: a personal contemplation. Letter to WFNS. 2020.

Tools and Modalities for Postural Ergonomics Research in Surgery and Neurosurgery

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Abbreviations

BPD	Body Part Discomfort
EMG	Electromyography
IMUs	Inertial measurement units
NASA-TLX	National Aeronautics and Space Administration Task Load Index
NIOSH	National Institute for Occupational Safety and Health
REBA	Rapid entire body assessment
RULA	Rapid Upper Limb Assessment
sEMG	Surface electromyography
SURG-TLX	Surgery task load index
WMSDs	Work-related musculoskeletal disorders

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1 Introduction

Ergonomics is defined by the International Ergonomics Association as ‘the scientific discipline concerned with the understanding of interactions among humans and other elements of a system. It also encompasses the application of theory, principles, data, and methods to optimize human well-being and overall system performance’ [1]. Ergonomics brings knowledge from anatomy and physiology, psychology, engineering and statistics to ensure that a product, workplace or system are designed to suit the user, rather than expecting people to adapt to a design that forces them to work in an uncomfortable, stressful or dangerous way.

Work-related musculoskeletal disorders (WMSDs) lead to suboptimal performance, affecting the surgeons’ ability to operate and as a result patient outcome. In recent studies, up to 88% of neurosurgeons reported having experienced work-related fatigue or pain at least once in their career [2, 3]. Consequently, performing surgical ergonomics research is important to reduce the prevalence and effect of WMSDs and to establish preferable techniques and surgical tools to perform an operation [3, 4].

The aim of the current short review is to present the available tools to perform ergonomics research in the surgical specialties and, specifically, in neurosurgery. We also aim to highlight some important future considerations specific to the neurosurgical specialty.

2 Tools for Surgical Ergonomics Research

The tools and technologies available for ergonomics research in the surgical specialties can be broadly divided into subjective and objective. Figure 1 presents a summary of the available subjective and objective tools for ergonomics research.

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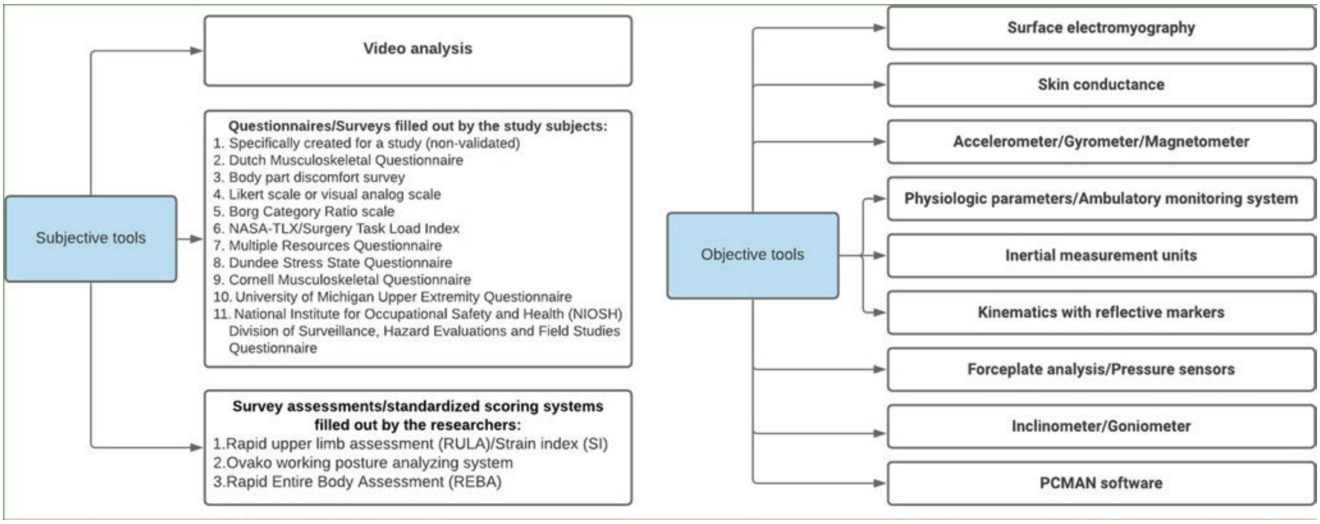

Fig. 1 Summary of the available subjective and objective tools to perform ergonomics research

2.1 Subjective Tools

The subjective tools can be further divided into three subcategories: (1) questionnaires filled out by the participants, (2) survey assessments/standardized scoring systems filled out by the researchers and (3) video analysis. Even though subjective tools are important in ergonomics research, it should be noted that their use is hindered by the presence of recall bias, and intra-rater and inter-rater variability [5].

A plethora of validated questionnaires are available [5], and some of them have been used in craniofacial and spine ergonomics studies [6]. The National Aeronautics and Space Administration Task Load Index (NASA-TLX) evaluates the physical and mental workload required for the execution of a specific task and was initially developed for use in the aeronautical industry [7]. It consists of six subscales (mental demand, physical demand, temporal demand, effort, performance, frustration levels) that are combined to provide an estimate of the required workload to perform a task. In a recent study, Ramakrishnan et al. [8] used the NASA-TLX to compare the standing and sitting positions in a cadaveric study of endoscopic sinus surgery. Notably, the surgery task load index (SURG-TLX) is a modified version of the NASA-TLX, validated for use in surgical ergonomics research [9]. Other validated questionnaires that have been previously used in surgery and neurosurgery ergonomics research include: (1) the University of Michigan Upper Extremity Questionnaire, (2) the National Institute for Occupational Safety and Health (NIOSH) Division of Surveillance, Hazard Evaluations and Field Studies Questionnaire, (3) the Body Part Discomfort (BPD) survey and (4) the Dutch Musculoskeletal Questionnaire [10–12].

It is important to note that non-validated questionnaires are often used by researchers who are investigating the prevalence of WMSDs amongst a specific population. This was also the case in two recent cross-sectional questionnaire-based ergonomics studies amongst neurosurgeons [2, 3]. Although it can be argued that, when possible, researchers should avoid using non-validated questionnaires, these studies are important because they can ask specialty-specific questions that usually cannot be found in validated questionnaires.

Video recording and analysis is another tool available for ergonomics research and posture analysis. Single or multiple-camera systems are used to record the surgeons while they perform a specific task, either in the operating theatre or in a simulation laboratory. The researchers then analyse and score the ergonomic performance of the surgeons, usually using standardized scoring systems. The most commonly used scoring system is the Rapid Upper Limb Assessment (RULA) [5]. Researchers assess upper limb, neck, trunk and leg posture alongside muscle use and force rates, leading to a total score of 1–7. Scores of 3 or higher imply possible ergonomic risk, while a score of 7 suggests high ergonomic risk necessitating change [13]. The Rapid Entire Body Assessment (REBA) is a scoring system that has been specifically developed to assess the unpredictable static-dynamic changes in the posture of healthcare workers [14]. A recent study by Aaron et al. [15] used the REBA tool to assess the ergonomic injury risk intraoperatively and reported that neurosurgeons had the highest REBA scores amongst surgeons from ten different surgical specialties. It should be pointed out that the standardized scoring systems can be either used in conjunction with video recording or as a stand-alone tool for intraoperative, real-time posture assessment, as was the case for the study by Aaron et al.

2.2 Objective Tools

Surface electromyography (sEMG) is a type of electromyography (EMG) that uses non-invasive electrodes attached to the skin of the study participant and provides information regarding the time and intensity of muscle activation [16]. It has been extensively used in ergonomics research in various fields, and it is probably the most commonly used objective tool in surgery ergonomics research [5, 16]. By using sEMG readings alongside various analysis tools, researchers can identify excessive muscle activity and fatigue [5]. In neurosurgery-related studies, sEMG has been used to assess novel ergonomic body supports for spine surgeons [17, 18] and to compare the sitting versus the standing position in endoscopic sinus surgery [8]. The use of sEMG in the operating theatre is currently complicated by the cumbersome wiring that might contaminate the sterile surgical field and could affect surgeons' performance [19]. However, in recent years, engineers have managed to create wearable sEMG acquisition systems that can be used in surgery ergonomics research [20]. Figure 2 shows an example of the set-up needed for sEMG recordings [21].

Systems for kinematic data capturing using reflective markers and cameras are also commonly used in surgery ergonomics research [22, 23]. High-speed, high-resolution motion capture systems, consisting of multiple digital cameras, are used to track the reflective markers that are attached to specific anatomical landmarks. The researchers are then able to use the data to reconstruct the movement of selected body segments in three-dimensional space. Park et al. [23, 24] used this modality to compare different operating table heights and various visualization methods while performing spine surgery, in a simulated environment. Notably, this research tool is completely wireless, thus minimizing the risk of compromising sterility. However, its limitations are associated with the application of the non-sterile markers on the sterile surgical gown [5]. Furthermore, objects or personnel in the operating theatre who cause reflections or block the direct visualization of the reflective markers from the camera can interfere with measurements [25]. Figures 3 and 4 present examples of the elaborate camera system needed for kinematic data capturing and the placement of the reflective markers, respectively [26, 27].

Inertial measurement units (IMUs) are sensors that are comprised of accelerometers, magnetometers and gyroscopes creating a wearable device that can be used for motion tracking [28]. They have the advantage of being entirely wireless and they can be placed underneath the surgical gown, thus avoiding interference with the surgical sterile field. They are also lightweight and small, ensuring minimal effect on a surgeon's ability to operate. Yang et al. [29] used IMUs in the operating theatres to evaluate the impact of procedure type, operation duration and adjunctive equipment on intraoperative discomfort, across surgical specialties including neurosurgery. Figure 5a, b presents the IMUs used in the study. Another study used IMUs to assess neck postures and cervical spine loading in microsurgeons using loupes and a headlamp [30]. In the future, wearable technology might be used to enable the adjustment of a surgeon's

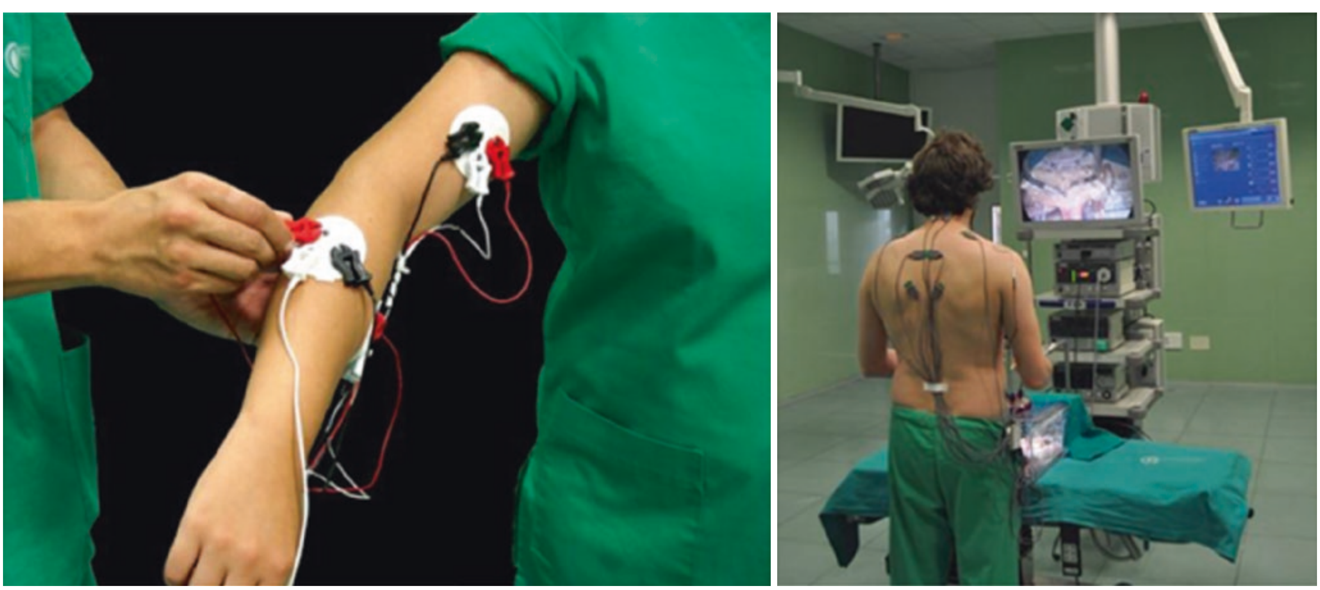

Fig. 2 The set-up and wiring during an ergonomic study using surface electromyography [Reproduced from [21] (License: Creative Commons Attribution 3.0 License)]

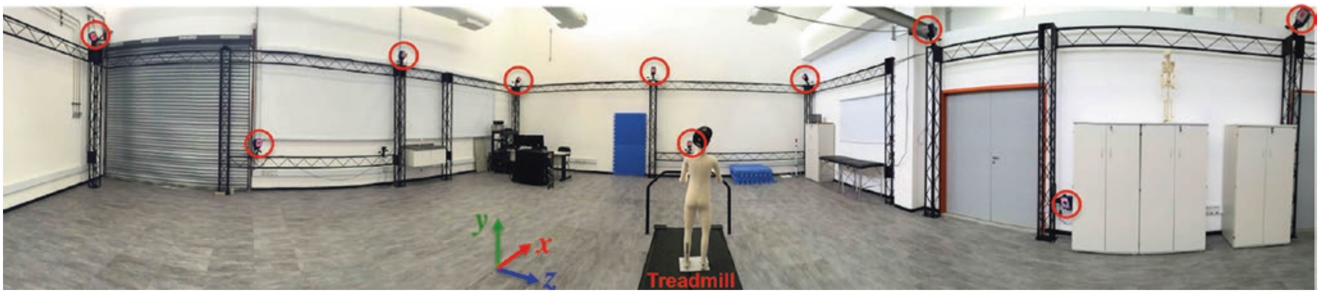

Fig. 3 The elaborate camera system needed to perform kinetic data capturing [Reproduced from [27] (License: Creative Commons Attribution License)]

Fig. 4 (**a**–**c**) The reflective markers used during kinetic data capturing [Reproduced from [26] (License: Creative Commons Attribution License)]

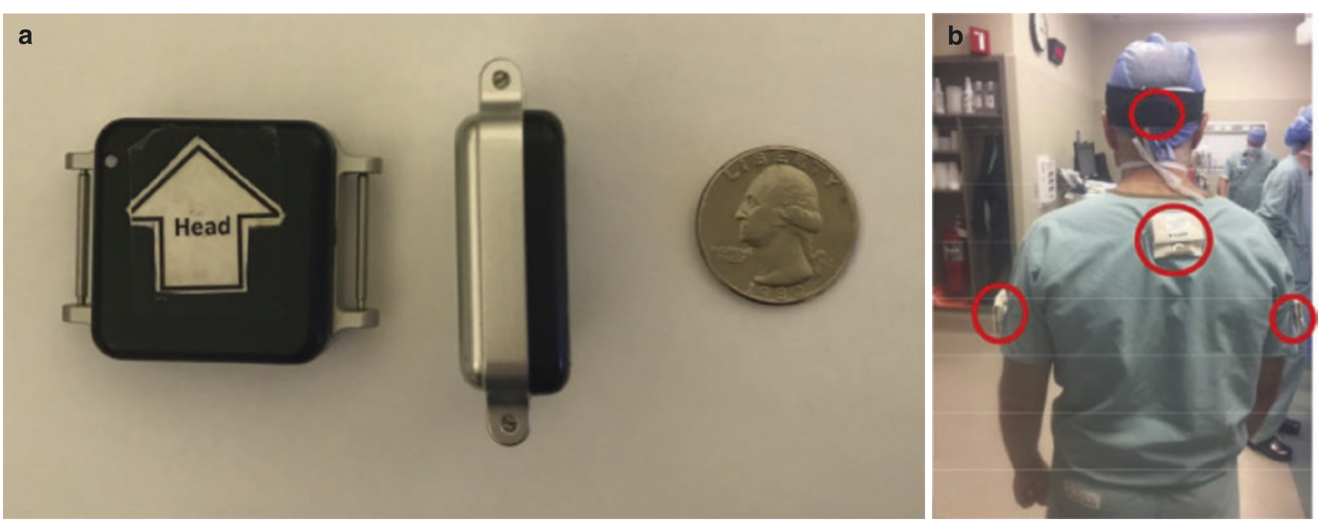

Fig. 5 The (**a**) size and (**b**) placement of inertial measurement units (Reproduced from [29] [License: Creative Commons Attribution—NonCommercial—NoDerivs (CC BY-NC-ND 4.0)])

posture by broadcasting real time data on a screen that the surgeon can observe while operating.

Force plates are mechanical systems that measure the ground reaction forces created by someone standing or moving on them [31]. They can be used in surgical ergonomics research to quantify the weight distribution between the two legs while operating [22]. In neurosurgery, a possible application is the assessment of the effect of using the foot pedal of the craniotome or the bipolar cautery on posture. They can also be used not only to evaluate the posture of the primary surgeon but the assistant surgeon as well. In similar fashion, pressure sensors have been used to map and evaluate the pressure on the seat of the surgical chair, in a study comparing four different types of chairs [32].

2.3 Future Perspectives

Ergonomics research can help in the assessment and comparison between novel and existing tools, and between surgical approaches. It can also enable the establishment of guidelines and policies regarding the use of specific surgical tools, the neurosurgical microscope, and surgical chairs. Important projects specific to neurosurgery include, but are not limited, to: (1) the comparison of loupes, microscope and exoscope in various types of operations and different approaches, (2) the evaluation of the burden of assisting in cranial and spine surgery, (3) the comparison between performing specific tasks while standing versus while sitting and (4) the individualization of choosing a surgical chair/surgical shoes/surgical tools based on a surgeon's discrete body characteristics.

3 Conclusion

It is imperative that ergonomics research becomes an important part of the research output in all surgical specialties, including neurosurgery, as it can help in alleviating the burden of WMSDs. In doing that, surgeons can become more productive and healthier resulting in better outcomes and optimal patient care. As the current technology evolves into wireless designs, ergonomics research will become easier to perform in the sterile environment of the operating theatre.

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References

1. The International Ergonomics Association. What Is Ergonomics? The International Ergonomics Association is a global federation of human factors/ergonomics societies, registered as a nonprofit organization in Geneva, Switzerland.
2. Gadjradj PS, Ogenio K, Voigt I, Harhangi BS. Ergonomics and related physical symptoms among neurosurgeons. World Neurosurg. 2020;134:e432–41.
3. Mavrovounis G, Meling TR, Lafuente J, Fountas KN, Demetriades AK. Postural ergonomics and work-related musculoskeletal disorders in neurosurgery: lessons from an international survey. Acta Neurochir. 2021;163(6):1541–52.
4. Demetriades AK, Meling TR, Ringel FA, Schaller K. Postural ergonomics and micro-neurosurgery: microscope has an edge over loupes. J Am Coll Surg. 2020;231(2):300–1.
5. Catanzarite T, Tan-Kim J, Whitcomb EL, Menefee S. Ergonomics in surgery: a review. Fem Pel Med Reconstr Surg. 2018;24(1):1–12.
6. Lavé A, Gondar R, Demetriades AK, Meling TR. Ergonomics and musculoskeletal disorders in neurosurgery: a systematic review. Acta Neurochir. 2020;162(9):2213–20.
7. Hart SG, Staveland LE. Development of NASA-TLX (Task Load Index): results of empirical and theoretical research. Adv Psychol. 1988;52:139–83.
8. Ramakrishnan VR, Milam BM. Ergonomic analysis of the surgical position in functional endoscopic sinus surgery. Int Forum Allergy Rhinol. 2017;7(6):570–5.
9. Wilson MR, Poolton JM, Malhotra N, Ngo K, Bright E, Masters RSW. Development and validation of a surgical workload measure: the surgery task load index (SURG-TLX). World J Surg. 2011;35(9):1961–9.
10. Alleblas CCJ, Formanoy MAG, Könemann R, Radder CM, Huirne JA, Nieboer TE. Ergonomics in gynecologists' daily practice: a nationwide survey in The Netherlands. Work. 2016;55(4):841–8.
11. Forst L, Friedman L, Shapiro D. Carpal tunnel syndrome in spine surgeons: a pilot study. Arch Environ Occup Health. 2006;61(6):259–62.
12. Lawson EH, Curet MJ, Sanchez BR, Schuster R, Berguer R. Postural ergonomics during robotic and laparoscopic gastric bypass surgery: a pilot project. J Robot Surg. 2007;1(1):61–7.
13. McAtamney L, Nigel Corlett E. RULA: a survey method for the investigation of work-related upper limb disorders. Appl Ergon. 1993;24(2):91–9.
14. Hignett S, McAtamney L. Rapid entire body assessment (REBA). Appl Ergon. 2000;31(2):201–5.
15. Aaron KA, Vaughan J, Gupta R, Ali N-E-S, Beth AH, Moore JM, Ma Y, Ahmad I, Jackler RK, Vaisbuch Y. The risk of ergonomic injury across surgical specialties. PLoS One. 2021;16(2):e0244868.
16. Chowdhury RH, Reaz MBI, Ali MABM, Bakar AAA, Chellappan K, Chang Tae G. Surface electromyography signal processing and classification techniques. Sensors. 2013;13(9):12431–66.
17. Albayrak A, van Veelen MA, Prins JF, Snijders CJ, de Ridder H, Kazemier G. A newly designed ergonomic body support for surgeons. Surg Endosc. 2007;21(10):1835–40.

18. Ito K, Horiuchi T, Seguchi T, Hongo K. Usefulness of a device for body support during operations performed while standing. Neurosurg Rev. 2015;38(4):731–7.
19. Koneczny S, Matern U. Instruments for the evaluation of ergonomics in surgery. Minim Invasive Ther Allied Technol. 2004;13(3):167–77.
20. Cerone GL, Botter A, Gazzoni M. A modular, smart, and wearable system for high density sEMG detection. IEEE Trans Biomed Eng. 2019;66(12):3371–80.
21. Sánchez-Margallo FM, Sánchez-Margallo JA. Ergonomics in laparoscopic surgery. In: Laparoscopic surgery. London: IntechOpen; 2017. https://doi.org/10.5772/66170.
22. Lee G, Lee T, Dexter D, Godinez C, Meenaghan N, Catania R, Park A. Ergonomic risk associated with assisting in minimally invasive surgery. Surg Endosc. 2009;23(1):182–8.
23. Park JY, Kim KH, Kuh SU, Chin DK, Kim KS, Cho YE. Spine surgeon's kinematics during discectomy according to operating table height and the methods to visualize the surgical field. Eur Spine J. 2012;21(12):2704–12.
24. Park JY, Kim KH, Kuh SU, Chin DK, Kim KS, Cho YE. Spine surgeon's kinematics during discectomy, part II: operating table height and visualization methods, including microscope. Eur Spine J. 2014;23(5):1067–76.
25. Lee G, Lee T, Dexter D, Klein R, Park A. Methodological infrastructure in surgical ergonomics: a review of tasks, models, and measurement systems. Surg Innov. 2007;14(3):153–67.
26. Fukuchi RK, Fukuchi CA, Duarte M. A public dataset of running biomechanics and the effects of running speed on lower extremity kinematics and kinetics. PeerJ. 2017;5:e3298, figure 2.
27. Fukuchi RK, Fukuchi CA, Duarte M. A public dataset of running biomechanics and the effects of running speed on lower extremity kinematics and kinetics. PeerJ. 2017;5:e3298, figure 1.
28. Yu D, Dural C, Morrow MMB, Yang L, Collins JW, Hallbeck S, Kjellman M, Forsman M. Intraoperative workload in robotic surgery assessed by wearable motion tracking sensors and questionnaires. Surg Endosc. 2017;31(2):877–86.
29. Yang L, Money SR, Morrow MM, Lowndes BR, Weidner TK, Fortune E, Davila VJ, Meltzer AJ, Stone WM, Hallbeck MS. Impact of procedure type, case duration, and adjunctive equipment on surgeon intraoperative musculoskeletal discomfort. J Am Coll Surg. 2020;230(4):554–60.
30. Nimbarte AD, Sivak-Callcott JA, Zreiqat M, Chapman M. Neck postures and cervical spine loading among microsurgeons operating with loupes and headlamp. IIE Trans Occup Ergon Hum Fact. 2013;1(4):215–23.
31. Lamkin-Kennard K, Popovic MB. Sensors: natural and synthetic sensors. In: Biomechatronics. London: Academic Press; 2019. https://doi.org/10.1016/B978-0-12-812939-5.00004-5.
32. Singh R, Carranza Leon DA, Morrow MM, Vos-Draper TL, McGree ME, Weaver AL, Woolley SM, Hallbeck S, Gebhart JB. Effect of chair types on work-related musculoskeletal discomfort during vaginal surgery. Am J Obstet Gynecol. 2016;215(5):648.e1–9.

The Impact of a Robotic Digital Microscope on the Ergonomics in a Neurosurgical Operating Theatre (A Single-Centre Experience)

N. Gabrovsky and M. Petrov

1 Introduction

The operative microscope (OPMI) is established as a pillar of surgical precision and by enabling better visualization and dissection of the neural structures has marked the beginning of the microneurosurgical era.

A new class of intraoperative visualization tools, the operative exoscopes, has been introduced recently. They have proven to have some important advantages, such as better magnification, brightness and mobility, compared to the conventional operative microscope [1–6]. Moreover, the exoscope brings better ergonomics to the neurosurgical operating theatre, which is considered as a great asset given the fact that work-related musculoskeletal disorders (WMSD) are becoming widespread in the neurosurgical community [2, 5, 7]. WMSD have been proven to negatively impact surgical performance and decrease the surgeons' quality of life [7, 8]. The operative exoscope could play a substantial role for the resolution of these problems of ergonomics by reducing the continuous neck flexion and uncomfortable position of the neurosurgeon. In a comparative study, 84% of the participants found the exoscope more ergonomic than the OPMI [5].

The purpose of the present study is to compare the ergonomics in similar neurosurgical cases while using a conventional operative microscope (OPMI) and a Robotic Digital Microscope (RDM) measured by the REBA scores [9].

2 Materials and Methods

For the period 01.04.2021–01.06.2021 at the Department of Neurosurgery of the University Hospital Pirogov, Sofia, Bulgaria, 41 consecutive patients (23 female and 18 male) were operated on using the Aesculap AEOS® Robotic Digital Microscope. Sixteen of the operations were cranial and 25 spinal. The mean age of the patients was 59 years. This comprised Group A. The control, Group B, included patients with similar pathologies to Group A but operated on with OPMI. REBA Employee Assessment Worksheets (Fig. 1) were filled in prospectively based on the position of the senior author on intraoperative photos [9].

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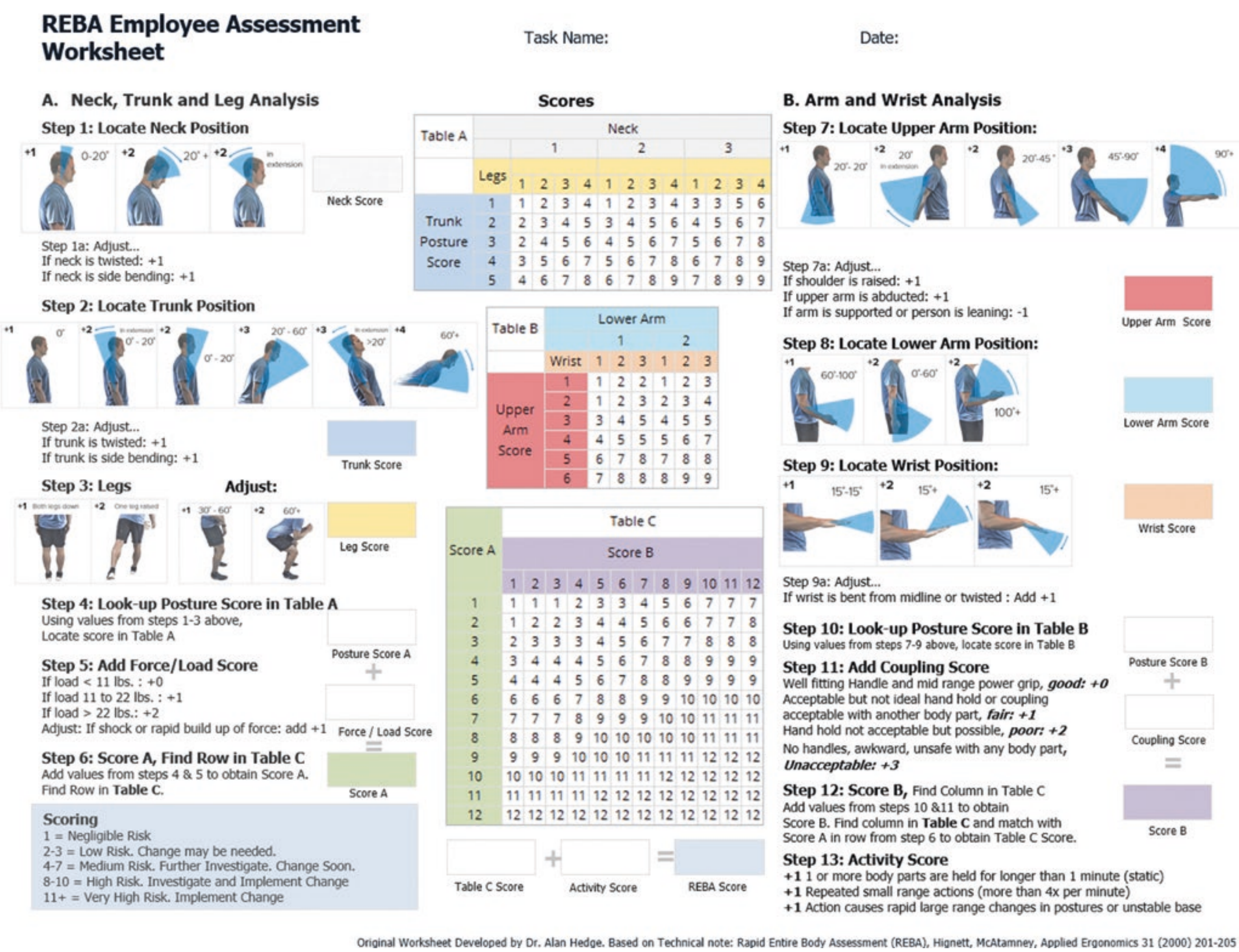

REBA Employee Assessment Worksheet

Task Name:

Date:

A. Neck, Trunk and Leg Analysis

Step 1: Locate Neck Position

+1 0-20° | +2 20°+ | +2 in extension

Neck Score

Step 1a: Adjust...
If neck is twisted: +1
If neck is side bending: +1

Step 2: Locate Trunk Position

+1 0° | +2 0°-20° in extension | +2 0°-20° | +3 20°-60° | +3 >20° in extension | +4 60°+

Step 2a: Adjust...
If trunk is twisted: +1
If trunk is side bending: +1

Trunk Score

Step 3: Legs

+1 Both legs down | +2 One leg raised

Adjust:

+1 30°-60° | +2 60°+

Leg Score

Step 4: Look-up Posture Score in Table A
Using values from steps 1-3 above,
Locate score in Table A

Posture Score A

+

Step 5: Add Force/Load Score
If load < 11 lbs. : +0
If load 11 to 22 lbs. : +1
If load > 22 lbs.: +2
Adjust: If shock or rapid build up of force: add +1

Force / Load Score

=

Step 6: Score A, Find Row in Table C
Add values from steps 4 & 5 to obtain Score A.
Find Row in **Table C.**

Score A

Scoring
1 = Negligible Risk
2-3 = Low Risk. Change may be needed.
4-7 = Medium Risk. Further Investigate. Change Soon.
8-10 = High Risk. Investigate and Implement Change
11+ = Very High Risk. Implement Change

Scores

Table A		Neck											
		1				2				3			
	Legs	1	2	3	4	1	2	3	4	1	2	3	4
Trunk Posture Score	1	1	2	3	4	1	2	3	4	3	3	5	6
	2	2	3	4	5	3	4	5	6	4	5	6	7
	3	2	4	5	6	4	5	6	7	5	6	7	8
	4	3	5	6	7	5	6	7	8	6	7	8	9
	5	4	6	7	8	6	7	8	9	7	8	9	9

Table B		Lower Arm					
		1			2		
	Wrist	1	2	3	1	2	3
Upper Arm Score	1	1	2	2	1	2	3
	2	1	2	3	2	3	4
	3	3	4	5	4	5	5
	4	4	5	5	5	6	7
	5	6	7	8	7	8	8
	6	7	8	8	8	9	9

Score A	Table C											
	Score B											
	1	2	3	4	5	6	7	8	9	10	11	12
1	1	1	1	2	3	3	4	5	6	7	7	7
2	1	2	2	3	4	4	5	6	6	7	7	8
3	2	3	3	3	4	5	6	7	7	8	8	8
4	3	4	4	4	5	6	7	8	8	9	9	9
5	4	4	4	5	6	7	8	8	9	9	9	9
6	6	6	6	7	8	8	9	9	10	10	10	10
7	7	7	7	8	9	9	9	10	10	11	11	11
8	8	8	8	9	10	10	10	10	10	11	11	11
9	9	9	9	10	10	10	11	11	11	12	12	12
10	10	10	10	11	11	11	11	12	12	12	12	12
11	11	11	11	11	12	12	12	12	12	12	12	12
12	12	12	12	12	12	12	12	12	12	12	12	12

Table C Score + Activity Score = REBA Score

B. Arm and Wrist Analysis

Step 7: Locate Upper Arm Position:

+1 20°-20° | +2 20° in extension | +2 20°-45° | +3 45°-90° | +4 90°+

Step 7a: Adjust...
If shoulder is raised: +1
If upper arm is abducted: +1
If arm is supported or person is leaning: -1

Upper Arm Score

Step 8: Locate Lower Arm Position:

+1 60°-100° | +2 0°-60° | +2 100°+

Lower Arm Score

Step 9: Locate Wrist Position:

+1 15°-15° | +2 15°+ | +2 15°+

Wrist Score

Step 9a: Adjust...
If wrist is bent from midline or twisted : Add +1

Step 10: Look-up Posture Score in Table B
Using values from steps 7-9 above, locate score in Table B

Posture Score B

+

Step 11: Add Coupling Score
Well fitting Handle and mid range power grip, ***good: +0***
Acceptable but not ideal hand hold or coupling
acceptable with another body part, ***fair: +1***
Hand hold not acceptable but possible, ***poor: +2***
No handles, awkward, unsafe with any body part,
Unacceptable: +3

Coupling Score

=

Step 12: Score B, Find Column in Table C
Add values from steps 10 &11 to obtain
Score B. Find column in **Table C** and match with
Score A in row from step 6 to obtain Table C Score.

Score B

Step 13: Activity Score
+1 1 or more body parts are held for longer than 1 minute (static)
+1 Repeated small range actions (more than 4x per minute)
+1 Action causes rapid large range changes in postures or unstable base

Original Worksheet Developed by Dr. Alan Hedge. Based on Technical note: Rapid Entire Body Assessment (REBA), Hignett, McAtamney, Applied Ergonomics 31 (2000) 201-205

Fig. 1 REBA Employee Assessment Worksheet [10]

3 Results

Forty-one operations were conducted in the study by a single experienced neurosurgeon (N.G.)—16 cranial and 25 spinal. The cranial operations were in the field of neuro-oncology—glial tumors, meningiomas, brain metastases, one pituitary adenoma and one hemangioblastoma. The spinal operations were more and comprised a much greater variety—from minimally invasive procedures such as microdiscectomy, spinal decompressions, trauma cases and spondylolisthesis to complex intramedullary tumors. Stratifying the operations by their complexity was outside the scope of this study. Spinal operations were conducted with a very typical position of the operator while using either the RDM or the OPMI; therefore, this led to similar REBA scores but with substantial improvement of the ergonomics while using the exoscope. In cranial operations, the results were much more diverse. Greater improvement in ergonomics while using the exoscope was noted during challenging cranial approaches where the operator needed to "look around corners," for instance, parasagittal craniotomies.

4 Discussion

The operative microscope is essential for achieving high standards in the everyday neurosurgical practice. A new class of equipment for intraoperative visualization and magnification, the Robotic Digital Microscope as an example of the exoscopes, has emerged as a substitute to the well-established neurosurgical operative microscope [6]. In some surgical fields, there have been attempts to replace the OPMI with 3D digital microscopes or exoscopes [11, 12]. 3D exoscopes and their advantages have already been reported, mainly in spinal surgery in small case series [13, 14].

The RDM was first shown to be comparable to the conventional OPMI in cadaver and animal studies [2, 3, 15]. When discussing image quality, exoscopes are equivalent to

Fig. 2 Intraoperative photograph of the setup during a cranial operation. The Robotic Digital Microscope (marked with blue arrow) is positioned to the right of the patient, next to the right hand of the neurosurgeon and next to the operating nurse. In this setup the main screen (yellow arrow) of the RDM is used by the assistant and the additional wider screen (green arrow), placed at the foot of the operating table, is used by the neurosurgeon. Notice the straight comfortable position of both neurosurgeons and the unobstructed line of view between them and the screens of the RDM [26]

Fig. 3 Intraoperative photograph during a spinal operation. There are a lot of supplementary devices during spinal operations; thus, their correct arrangement is very important for their easy and ergonomical use. The RDM is marked with blue arrow, which is placed behind the neurosurgeon. The long arm with mobile joints of the RDM make it possible in this position to not obstruct the line of view of the neurosurgeon to the wide screen (green arrow). The screen of the RDM (yellow arrow) is used by the assistant. The workstation with screens of the C-arm of the X-ray machine is marked with a gray arrow. The C-arm is removed after obtaining an intraoperative 3D image of the zone of interest and transferring the images to the neuronavigation. The camera of the neuronavigation (white arrow) is placed at the foot of the operating table and the workstation of the neuronavigation is placed next to the wide screen of the RDM in order to be in the most convenient position for the neurosurgeon. Notice again the *comfortable position* of the two neurosurgeons [26]

OPMI, and when combined with a 4K high-definition screen, exoscopes are even better [4, 16–18]. The magnification and brightness of exoscopes is superior and especially convenient for working in deep locations [1, 2, 17–19]. The wide screen is visible to everyone in the operating theater and enables good coordination between the operating surgeons, the assisting nursing staff and the anesthesiologists [2, 14]. Furthermore, the RDM is suitable for educational purposes [2, 20]. The "lock-on target" function is one of the most frequently used features of the RDM, with which the neurosurgeon moves around the zone of interest, always in focus, maneuvering with just the foot pedal. Thus, the operator is able to "look around corners" without leaving their comfortable posture, with a straight back and no neck flexion (Fig. 2) [2, 16, 17]. This greatly reduces the operator's effort and backpain even in prolonged and complicated cranial cases. The constant wearing of 3D glasses is pointed out as a possible drawback [14], but in our study, such observation was not confirmed.

However, the major asset of the RDM is probably the ability to enhance the ergonomics in the everyday neurosurgical practice [2, 5].

Continuous neck flexion is one of the reasons for the increased neck pain in surgeons (59%) compared to the general population (20%) [21]. It is reported that 73% of 417 neurosurgeons have complained of WMSDs [8]. Ergonomics is an emerging concept in the neurosurgical operating theatre that really needs improvement in the future. In a study by Auerbach et al., 4.6% of the surgeons were operated on for a cervical disk disease, while cervical radiculopathy in the general population is quite rarer—0.35% [21]. The use of RDM generates no neck or back strain, typical for the use of OPMI, which suggests a significant reduction in the WMSD that are becoming widespread in the neurosurgical community (Figs. 2 and 3).

The REBA score was introduced in 2000 to assess ergonomics in health care and other industries [10]. Since then, this score has been widely used for assessing ergonomics in the field of surgery [10, 22–25]. The REBA score is a standardized tool that was designed to quantitatively evaluate the postural strain and discomfort [25]. This score takes into consideration the whole body divided into segments and the type of activity conducted with each segment—static, dynamic and rapidly changing [25].

In our study with 41 patients, we found a considerable improvement in ergonomics while using an exoscope in daily neurosurgical practice. During spinal operations with an exoscope, the mean REBA score was 3, which is considered as a low risk for WMSD. In similar spinal operations conducted with OPMI, the REBA score was 4, which is considered a medium risk for WMSD and a change in the workflow is warranted. Even though the results look similar in spinal operations, the neck analysis during the calculating of the REBA score is stunning. The neck score is three times lower while using the exoscope, which shows a favourable effect on the ergonomics. This is substantial as the continuous neck flexion is the cause of premature degeneration in this spinal segment in the neurosurgical community. For challenging cranial approaches, the REBA score is 2.6 times lower for the exoscope cases (Fig. 4). The continuous neck flexion of the neurosurgeon during spinal operations could lead to WMSD (Fig. 5).

Exoscopes could be the solution to the ergonomics problem in the neurosurgical operating theatre. However, some comparative studies point out the use of exoscopes has a learning curve that is still unknown [2]. In our previous study, by using the NASA-TLX, we were able to evaluate the subjective workload of the transition from OPMI to RDM of an experienced neurosurgeon and outline the learning curve [26]. In total, 20 operations are needed with the RDM to ensure fluent workflow of an experienced neurosurgeon, and faster transition is observed in spinal cases [26].

Fig. 4 Intraoperative photograph while using OPMI in challenging cranial operations. Note the uncomfortable posture of the operator

Fig. 5 Intraoperative photograph during a spinal operation with OPMI. Note the continuous neck flexion of the operator and lateral flexion in the lumbar spine. This position is a prerequisite for WMSD in the future. This uncomfortable posture could be avoided by using an RDM

5 Conclusion

Exoscopes, including the RDM, are an emerging alternative to the conventional operative microscopes. The ergonomics during neurosurgical operations could be substantially improved with the implementation of the exoscope. For challenging cranial approaches, where the operator must frequently "look around corners" the exoscope has a major advantage compared with the OPMI—the REBA score is 2.6 times lower while using an exoscope. For spinal operations the neck score as part of the REBA score is three times lower for the exoscope, which leads to low risk for WMSD. The RDM could reduce the WMSD that are becoming widespread in the neurosurgical community.

References

1. Fiani B, Jarrah R, Griepp DW, Adukuzhiyil J. The role of 3D exoscope systems in neurosurgery: an optical innovation. Cureus. 2021;13(6):e15878. https://doi.org/10.7759/cureus.15878.
2. Hafez A, Haeren RHL, Dillmann J, Laakso A, Niemelä M, Lehecka M. Comparison of operating microscope and exoscope in a highly challenging experimental setting. World Neurosurg. 2021;147:e468–75. https://doi.org/10.1016/j.wneu.2020.12.093.
3. Herlan S, Marquardt JS, Hirt B, Tatagiba M, Ebner FH. 3D exoscope system in neurosurgery-comparison of a standard operating microscope with a new 3D exoscope in the cadaver lab. Oper Neurosurg. 2019;17(5):518–24. https://doi.org/10.1093/ons/opz081.
4. Langer DJ, White TG, Schulder M, Boockvar JA, Labib M, Lawton MT. Advances in intraoperative optics: a brief review of current exoscope platforms. Open Neurosurg. 2020;19(1):84–93. https://doi.org/10.1093/ons/opz276.
5. Maurer S, Prinz V, Qasem LE, et al. Evaluation of a novel three-dimensional robotic digital microscope (Aeos) in neurosurgery. Cancers. 2021;13(17):4273. https://doi.org/10.3390/cancers13174273.
6. Nishiyama K. From exoscope into the next generation. J Kor Neurosurg Soc. 2017;60(3):289–93. https://doi.org/10.3340/jkns.2017.0202.003.
7. Lavé A, Gondar R, Demetriades AK, Meling TR. Ergonomics and musculoskeletal disorders in neurosurgery: a systematic review. Acta Neurochir. 2020;162(9):2213–20. https://doi.org/10.1007/s00701-020-04494-4.
8. Gadjradj PS, Ogenio K, Voigt I, Harhangi BS. Ergonomics and related physical symptoms among neurosurgeons. World Neurosurg. 2020;134:e432–41. https://doi.org/10.1016/j.wneu.2019.10.093.
9. Bridger R. Introduction to ergonomics. 3rd ed. London: Taylor & Francis; 2009.
10. Hignett S, McAtamney L. Rapid entire body assessment (REBA). Appl Ergon. 2000;31(2):201–5. https://doi.org/10.1016/s0003-6870(99)00039-3.
11. Crosetti E, Arrigoni G, Manca A, Caracciolo A, Bertotto I, Succo G. 3D exoscopic surgery (3Des) for transoral oropharyngectomy. Front Oncol. 2020;10:16. https://doi.org/10.3389/fonc.2020.00016.
12. Piatkowski AA, Keuter X, Schols RM, van der Hulst R. Potential of performing a microvascular free flap reconstruction using solely a 3D exoscope instead of a conventional microscope. J Plast Reconstr Aesthet Surg. 2018;71(11):1664–78. https://doi.org/10.1016/j.bjps.2018.07.032.
13. Beez T, Munoz-Bendix C, Beseoglu K, Steiger HJ, Ahmadi SA. First clinical applications of a high-definition three-dimensional exoscope in pediatric neurosurgery. Cureus. 2018;10(1):e2108. https://doi.org/10.7759/cureus.2108.
14. Siller S, Zoellner C, Fuetsch M, Trabold R, Tonn JC, Zausinger S. A high-definition 3D exoscope as an alternative to the operating microscope in spinal microsurgery. J Neurosurg Spine. 2020;33:705–14. https://doi.org/10.3171/2020.4.SPINE20374.
15. Mamelak AN, Danielpour M, Black KL, Hagike M, Berci G. A high-definition exoscope system for neurosurgery and other microsurgical disciplines: preliminary report. Surg Innov. 2008;15(1):38–46. https://doi.org/10.1177/1553350608315954.
16. Ricciardi L, Chaichana KL, Cardia A, Stifano V, Rossini Z, Olivi A, Sturiale CL. The exoscope in neurosurgery: an innovative "point of view". A systematic review of the technical, surgical and educational aspects. World Neurosurg. 2019;124:136. https://doi.org/10.1016/j.wneu.2018.12.202.
17. Visocchi M, Mattogno PP, Ciappetta P, Barbagallo G, Signorelli F. Combined transoral exoscope and OArm-assisted approach for craniovertebral junction surgery: light and shadows in single-center experience with improving technologies. J Craniovertebr Junct Spine. 2020;11(4):293–9. https://doi.org/10.4103/jcvjs.JCVJS_176_20.
18. Visocchi M, Mattogno PP, Signorelli F. Exoscope and OArm: what we can learn in craniovertebral junction surgery. J Neurosurg Sci. 2020;65:616. https://doi.org/10.23736/S0390-5616.20.05221-2.
19. Krishnan KG, Schöller K, Uhl E. Application of a compact high-definition exoscope for illumination and magnification in high-precision surgical procedures. World Neurosurg. 2017;97:652–60. https://doi.org/10.1016/j.wneu.2016.09.037.
20. Ricciardi L, Mattogno PP, Olivi A, Sturiale CL. Exoscope era: next technical and educational step in microneurosurgery. World Neurosurg. 2019;128:371–3. https://doi.org/10.1016/j.wneu.2019.05.162.
21. Auerbach JD, Weidner ZD, Milby AH, Diab M, Lonner BS. Musculoskeletal disorders among spine surgeons: results of a survey of the Scoliosis Research Society membership. Spine. 2011;36(26):E1715–21. https://doi.org/10.1097/BRS.0b013e31821cd140.
22. Lim AK, Ryu J, Yoon HM, Yang HC, Kim SK. Ergonomic effects of medical augmented reality glasses in video-assisted surgery. Surg Endosc. 2022;36(2):988–98. https://doi.org/10.1007/s00464-021-08363-8.
23. Abdollahi T, Pedram Razi S, Pahlevan D, Yekaninejad MS, Amaniyan S, Leibold Sieloff C, Vaismoradi M. Effect of an ergonomics educational program on musculoskeletal disorders in nursing staff working in the operating room: a quasi-randomized controlled clinical trial. Int J Environ Res Public Health. 2020;17(19):7333. https://doi.org/10.3390/ijerph17197333.
24. Dwyer A, Huckleby J, Kabbani M, Delano A, De Sutter M, Crawford D. Ergonomic assessment of robotic general surgeons: a pilot study. J Robot Surg. 2020;14(3):387–92. https://doi.org/10.1007/s11701-019-00996-1.
25. Aaron KA, Vaughan J, Gupta R, Ali NE, Beth AH, Moore JM, Ma Y, Ahmad I, Jackler RK, Vaisbuch Y. The risk of ergonomic injury across surgical specialties. PLoS One. 2021;16(2):e0244868. https://doi.org/10.1371/journal.pone.0244868.
26. Gabrovsky N, Petrov M, Ilkov P, Iordanova I, Velinov N. Subjective workload measurement of the transition from a conventional operative microscope to a Robotic Digital Microscope. A pilot study. Brain Spine. 2022;2:100928. https://doi.org/10.1016/j.bas.2022.100928.

Post-mortem Imaging of Brain/Spine Injuries: The Importance of a Comprehensive Forensic Approach

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1 Introduction

Forensic analysis has shifted from the traditional (purely) autoptic approach to a comprehensive investigation performed by cross-functional teams [1]. Two of the biggest limitations of traditional autopsy are that (1) elements of medico-legal interest sometimes can be found in anatomical districts that are not usually dissected (e.g., the back) and (2) dissection ruins the anatomical identity of structures and, in general, makes it difficult to reconstruct a 3D image of the anomaly (e.g., the extension and the thickness of an intracranic hemorrhage, the description of bone fractures). Post-mortem imaging, especially virtual autopsy, can be extremely useful to overcome these limitations [2]. In particular, computed tomography (CT) imaging with its 3D volume rendering (VR) and MPR reconstructions allow flagging anomalies before the autopsy (thus orienting and guiding the dissection) and also to avoid the autopsy itself, in cases where—for instance—the families are against the autopsy for religious beliefs. Moreover, when opening the intracranic cavity can be hazardous at the autopsy (e.g., in cases of meningitis) and the institution has no autopsy rooms with proper level of safety, virtopsy can help to overcome this issue. In general, opting for a comprehensive forensic approach based on the combination of autopsy, virtual autopsy, and laboratory testing is often the best decision because when combining radiological, macroscopic, and microscopic findings, a certain cause of death can often be found.

In this scoping review, we briefly describe the main applications of the two most common post-mortem radiological techniques (computed tomography (CT) and magnetic resonance imaging (MRI)) to the forensic investigation of brain and spinal injuries.

2 Medical Malpractice

When medical malpractice is suspected, clinical autopsies are a powerful tool for the hospital to promptly detect medical errors (and thus compensate the patient without expensive lawsuits) and to improve its services. In these cases, causal inference can often only be reliably made by combining known medical history, clinical information, autopsy findings, and both ante- and post-mortem radiological images [3–6]. However, both clinical autopsies and post-mortem imaging represent a cost for the hospital. Wagensveld et al. reported that minimally invasive autopsies (MRI, CT, and CT-guided biopsies) had a mean cost of €1296 including brain biopsies and €1087 without brain biopsies, while the mean cost of a traditional autopsy was €991 including brain autopsy and €740 without brain autopsy [7]. Moreover, they found that the cause of the death was found by 67.7% of post-mortem CTs and by 85.4% of post-mortem MRIs. Virtopsy in not able to always find the cause of the death because some features, such as thromboembolism, remain difficult to investigate both by traditional autopsy and by imaging [8].

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3 Brain and Spinal Injuries at Post-mortem Computed Tomography

Traumatology is probably the most known field of application for virtopsy. In particular, when a traumatic cranial and/or spinal injury can be suspected, post-mortem CT and complete autopsy are considered the gold standard. For instance, in cases of brain trauma, the most common finding (subarachnoid hemorrhage) can be clearly identified, described, and quantified at the post-mortem CT, helping the pathologist to evaluate whether it could have been the cause of the death [9]. This kind of causal inference can be crucial, for example, when surgical evacuation has not been performed and thus malpractice of the neurosurgeon is suspected.

Regarding homicidal/suicidal scenarios and mass disasters, post-mortem CT is particularly valuable, since it can reliably flag both bone injuries (e.g., in cases of hanging or bone fractures caused by gunshots) and hyperdense objects (e.g., bullets, metallic fragments) (Figs. 1, 2, 3, and 4) [2, 10]. Moreover, in cases of penetrating brain injury, the trajectory can be inferred examining the stray given by the bullet fragments and the radiological appearance of skull holes (the entrance wound has an inward conical shape, while the exit wound has an outward conical shape) [1].

Post-mortem CT findings, especially if they concern the brain or the spine, must always be interpreted by expert forensic radiologists, since abnormal feature may be due to "common" post-mortem phenomena. For instance, Persson et al. reported that atlanto-axial rotatory subluxations often found at post-mortem CT are rarely due to ante-mortem traumas, mostly being caused by the post-mortem head rotation [11]. Another example is given by the normal post-mortem reduction in brain parenchymal density, that can be associated with a pseudosubarachnoid hemorrhage appearance (that can be easily misdiagnosed by a radiologist who does not know the typical post-mortem changes) [12].

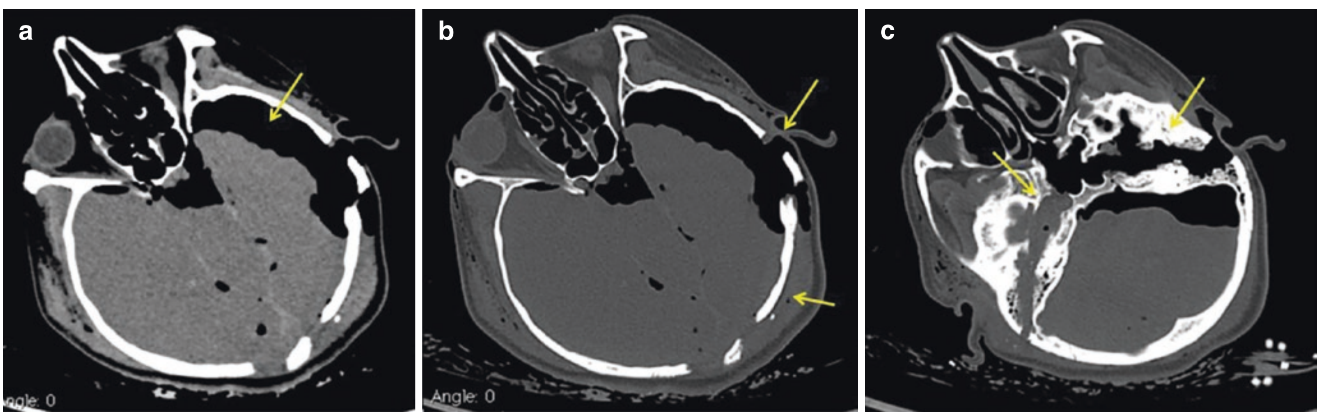

Fig. 1 Brain post-mortem CT scans: brain window (**a**), bone window (**b**, **c**). Pneumocephalus associated with subarachnoid hemorrhage (**a**), depressed fractures of occipital bone (**b**), frontal sinus (**a**), ethmoidal sinuses (**b**), base of skull through the middle cranial fossa involving both the petrous parts of the temporal bone with complete detachment of the posterior cranial fossa (**c**)

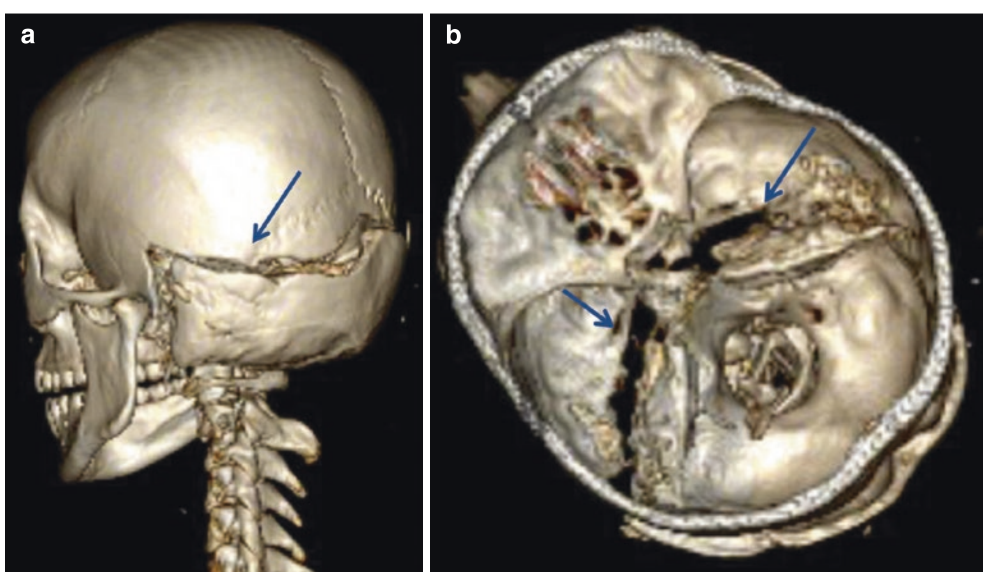

Fig. 2 Post-mortem CT scans obtained using 3D volume rendering technique: a fracture of the squamous part of the occipital bone (**a**) and of the cranial base (**b**) can be seen

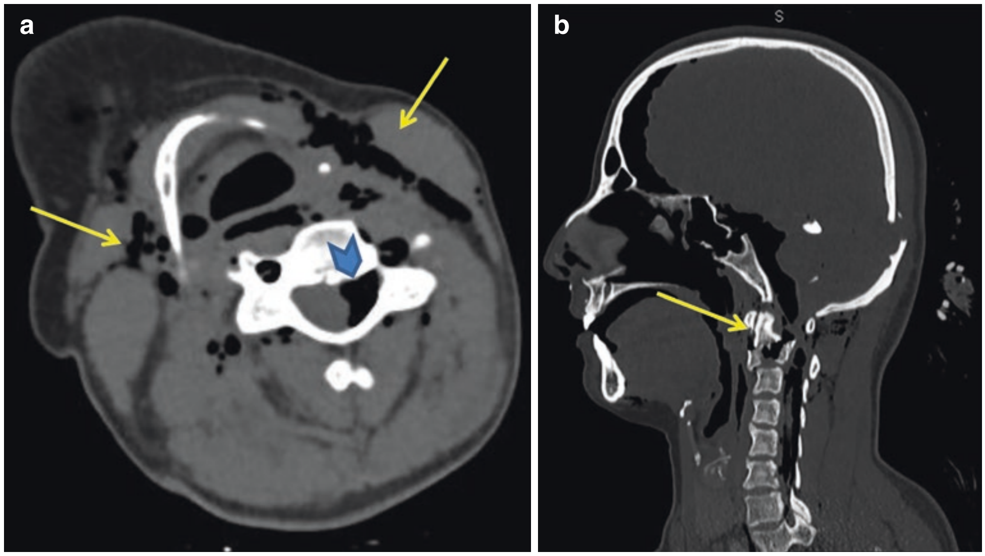

Fig. 3 Post-mortem CT scans of the neck. Emphysematous bubbles can be seen inside the soft tissue (yellow arrows) and the spinal canal (blue arrow) (**a**). In (**b**) a fracture of the epistrophus with anterior dislocation of bone fragments can be observed

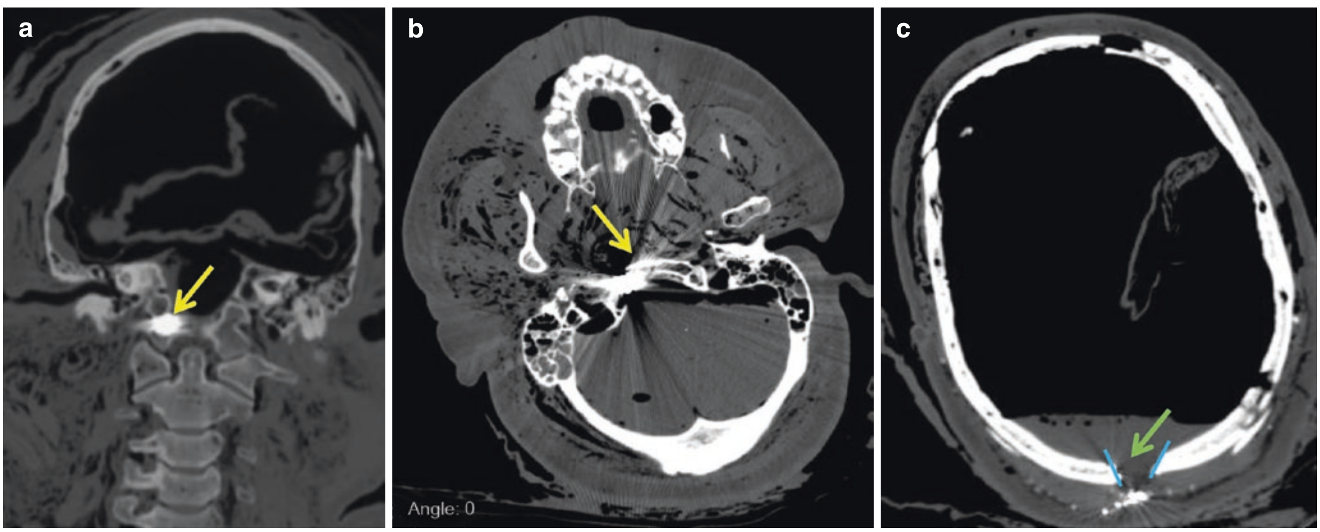

Fig. 4 Post-mortem CT scans obtained using multi-planar reformation in a case of head gunshot. A bullet fragment can be seen inside the clivus (**a**, **b**). In (**c**) a hole with an inward conical shape and surrounded by many small hyperdense fragments (bone? metal objects?)

4 Brain and Spinal Injuries at Post-mortem Magnetic Resonance Imaging

Growing evidence is emerging on the accuracy and reliability of MRI [13]. Similar to post-mortem CT, post-mortem MRI also has applications for neurosurgical traumatology: for instance, in cases of spinal trauma, it is able to show soft-tissue and ligament injuries that are very frequent accident injuries and cannot be investigated by CT [14]. Post-mortem MRI is particular important in cases of pediatric age. Indeed, especially in young cases, the diagnosis of spinal cord injuries (especially of the cervical spine) can often be missed before death because they are often not detectable by X-rays or CT (that are usually performed when a traumatized patient arrives at the emergency room) [15]. In these cases, performing MRI after death could reveal spinal injuries. Even in cases of fetal death (e.g., due to perinatal hypoxic-ischemic brain injury) post-mortem MRI can be indicated: Thayyil et al. compared traditional autopsy and "minimally invasive autopsy" (external examination of the cadaver, post-mortem MRI, metabolic/genetic testing and, for the fetuses, examination of placenta) in a study population of cadavers younger than 16 years, finding a high degree of concordance (especially in fetuses) [13]. In particular, they reported that minimally invasive autopsy succeeded in finding the cause of the death in more than the 89% of the cases.

Post-mortem MRI can also be used in cases of gunshot injuries: it can help to explore cavitation injuries (and to assess their extent) and flag microinjuries (e.g., microbleedings) caused by the temporary cavitations, because of the high spatial resolution of this technique [11]. However, optimal reliability and diagnostic accuracy of MRI are achieved in cases of small-caliber guns and/or gunshots from significant distances, since less severe bone and soft tissue damages occur under these circumstances [16].

This technique can also be applied to the specimens collected during the autopsy: for instance, postmortem microscopic resolution MRI of spinal cord fixed samples can be performed to detect a spinal cord lesion and for automated volumetric gray matter segmentation/quantitative spinal cord morphometry (e.g., quantification of the gray matter fraction) [17].

Finally, Coolen et al. evaluated the use of post-mortem MRI to investigate the heads 19 cases who died with COVID-19 (without known brain injuries), finding parenchymal anomalies (subcortical microbleeds and macrobleeds, corticosubcortical edematous changes evocative of posterior reversible encephalopathy syndrome, and nonspecific deep white matter changes), asymmetric olfactory bulbs (without downstream olfactory tract abnormalities), and no brainstem anomalies [18]. They also described these postmortem changes: "(1) the necessary adaptation of the FLAIR TI to obtain adequate water suppression, (2) increased T1WI signal intensity of the deep nuclei, (3) T2WI fat suppression, (4) DWI rim-like increased signal intensity, and (5) decreased parenchymal ADC values."

5 Training

Some authors advocated the use of virtopsy to achieve a better understanding of the surgical anatomy [19, 20]. For instance, Signorelli et al. underlined that dissection laboratory experience can be extremely helpful for the neurosurgeons to enhance their technical and non-technical (e.g., communication, leadership) skills, especially when innovative and/or complex approaches must be validated, and that in these cases, post-mortem CT scans are essential to guide the operator [10, 21, 22]. A better understanding of the surgical anatomy can also help to design new surgical approaches: Bodmer et al. evaluated the post-mortem CT scans of 192 cadavers to develop a sacral endoscopic approach, assessing anatomical variables such as the narrowest point of the sacral canal and the lateral and anteroposterior diameters [20].

6 Conclusions

Although CT represents the traditional approach to post-mortem imaging, MRI is proving to be a valuable tool to investigate brain and spinal injuries and lesions. These post-mortem radiological techniques can also be used to guide the surgeons in simulated surgical procedures on corpses in the context of training programs, thus helping operators to improve technical and non-technical skills and to reduce the risk of avoidable errors.

References

1. Oliva A, Grassi S, Grassi VM, Pinchi V, Floris R, Manenti G, Colosimo C, Filograna L, Pascali VL. Postmortem CT and autopsy findings in nine victims of terrorist attack. Int J Legal Med. 2021;135:605. https://doi.org/10.1007/s00414-020-02492-w.
2. Thali MJ, Jackowski C, Oesterhelweg L, Ross SG, Dirnhofer R. VIRTOPSY – The Swiss virtual autopsy approach. Legal Med. 2007;9:100. https://doi.org/10.1016/j.legalmed.2006.11.011.
3. Araki A, Ishikawa N, Takami S, Ishikawa N, Amano C, Takeshita H, Maruyama R. Interpretation of postmortem head computed tomography for non-traumatic in-hospital deaths by non-radiologists: a preliminary study. Springerplus. 2016;5:978. https://doi.org/10.1186/s40064-016-2653-z.
4. Filograna L, Manenti G, Arena V, Dell'Aquila M, Pascali VL, Natale L, Colosimo C, Grassi S, Floris R, Oliva A. Claimed medical malpractice in fatal SARS-CoV-2 infections: the importance of combining ante- and post-mortem radiological data and autopsy findings for correct forensic analysis. Forens Imaging. 2021;25:200454. https://doi.org/10.1016/j.fri.2021.200454.
5. Mizuno J, Nakagawa H, Chang H-S, Hashizume Y. Postmortem study of the spinal cord showing snake-eyes appearance due to damage by ossification of the posterior longitudinal ligament and kyphotic deformity. Spinal Cord. 2005;43:503. https://doi.org/10.1038/sj.sc.3101727.
6. Someya Y, Koda M, Hashimoto M, Okawa A, Masaki Y, Yamazaki M. Postmortem findings in a woman with history of laminoplasty for severe cervical spondylotic myelopathy. J Spin Cord Med. 2011;34:523. https://doi.org/10.1179/107902611X13069205199503.
7. Wagensveld IM, Hunink MGM, Wielopolski PA, van Kemenade FJ, Krestin GP, Blokker BM, Oosterhuis JW, Weustink AC. Hospital implementation of minimally invasive autopsy: a prospective cohort study of clinical performance and costs. PLoS One. 2019;14:e0219291. https://doi.org/10.1371/journal.pone.0219291.
8. Heinemann A, Vogel H, Heller M, Tzikas A, Püschel K. Investigation of medical intervention with fatal outcome: the impact of post-mortem CT and CT angiography. Radiol Med. 2015;120:835. https://doi.org/10.1007/s11547-015-0574-5.
9. Bertozzi G, Maglietta F, Sessa F, Scoto E, Cipolloni L, di Mizio G, Salerno M, Pomara C. Traumatic brain injury: a forensic approach: a literature review. Curr Neuropharmacol. 2020;18:538. https://doi.org/10.2174/1570159X17666191101123145.
10. Signorelli F, Stumpo V, Della Pepa GM, la Rocca G, Oliva A, Olivi A, Visocchi M. Step-up establishment of neurosurgical laboratory

starting with limited resources—tips and tricks. World Neurosurg. 2019;126:83. https://doi.org/10.1016/j.wneu.2019.02.034.
11. Persson A, Falk J, Berge J, Jackowski C. Atlanto-axial rotatory subluxations in postmortem CT: radiologists be aware of a common pitfall. Forensic Sci Int. 2013;225:9. https://doi.org/10.1016/j.forsciint.2013.01.001.
12. Sutherland T, O'Donnell C. The artefacts of death: CT post-mortem findings. J Med Imaging Radiat Oncol. 2018;62:203. https://doi.org/10.1111/1754-9485.12691.
13. Thayyil S, Sebire NJ, Chitty LS, Wade A, Chong W, Olsen O, Gunny RS, Offiah AC, Owens CM, Saunders DE, et al. Post-mortem MRI versus conventional autopsy in fetuses and children: a prospective validation study. Lancet. 2013;382:223. https://doi.org/10.1016/S0140-6736(13)60134-8.
14. Stäbler A, Eck J, Penning R, Milz SP, Bartl R, Resnick D, Reiser M. Cervical spine: postmortem assessment of accident injuries—comparison of radiographic, MR imaging, anatomic, and pathologic findings. Radiology. 2001;221:340. https://doi.org/10.1148/radiol.2212010336.
15. Atesok K, Tanaka N, O'Brien A, Robinson Y, Pang D, Deinlein D, Manoharan SR, Pittman J, Theiss S. Posttraumatic spinal cord injury without radiographic abnormality. Adv Orthop. 2018;2018:7060654. https://doi.org/10.1155/2018/7060654.
16. Gascho D, Deininger-Czermak E, Zoelch N, Tappero C, Sommer S, Hinterholzer N, Thali MJ. Noninvasive 7 tesla MRI of fatal craniocerebral gunshots – a glance into the future of radiologic wound ballistics. Forens Sci Med Pathol. 2020;16:595. https://doi.org/10.1007/s12024-020-00300-w.
17. Calabrese E, Adil SM, Cofer G, Perone CS, Cohen-Adad J, Lad SP, Johnson GA. Postmortem diffusion MRI of the entire human spinal cord at microscopic resolution. NeuroImage Clin. 2018;18:963. https://doi.org/10.1016/j.nicl.2018.03.029.
18. Coolen T, Lolli V, Sadeghi N, Rovai A, Trotta N, Taccone FS, Creteur J, Henrard S, Goffard J-C, Dewitte O, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. Neurology. 2020;95:e2016. https://doi.org/10.1212/WNL.0000000000010116.
19. Alkemade A, Groot JM, Forstmann BU. Do we need a human post mortem whole-brain anatomical ground truth in in vivo magnetic resonance imaging? Front Neuroanat. 2018;12:110. https://doi.org/10.3389/fnana.2018.00110.
20. Bodmer A, Ross S, Raabe A, Beck J, Ulrich C, Schucht P. Virtual autopsy to assess sacral anatomy: conditions for a minimal invasive approach to the spinal canal through the Hiatus Sacralis. Surg Neurol Int. 2017;8:290. https://doi.org/10.4103/sni.sni_313_17.
21. Signorelli F, Stumpo V, Oliva A, Pascali VL, Olivi A, Visocchi M. Mastering craniovertebral junction surgical approaches: the dissection laboratory experience at the Catholic University of Rome. Acta Neurochir Suppl. 2019;125:13.
22. Visocchi M, Barbagallo G, Pascali VL, Mattogno P, Signorelli F, Iacopino G, Germano' A, la Rocca G. Craniovertebral junction transanasal and transoral approaches: reconstruct the surgical pathways with soft or hard tissue endocopic lines? This Is the Question. Acta Neurochir Suppl. 2017;124:117.

Technologies in Anaesthesia for the Paediatric Patient

F. Tosi, R. Garra, R. Festa, and Massimiliano Visocchi

1 Physiological Changes in the Prone Position

1.1 Cardiovascular

Decreased Cardiac Index

When a patient is put into the prone position, an almost universal finding is a decrease in cardiac index (CI). In 16 patients [1] with cardiopulmonary disease, the most remarkable finding during surgery in the prone position was an average decrease of 24% in CI, which reflected a decrease in stroke volume with little change in heart rate.

Mean arterial pressure (MAP) was maintained by increased systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) also increased in most patients.

No changes were noted in mean right atrial or pulmonary artery pressures (PAP). Interestingly, these cardiac function alterations were only noted because cardiac output was measured. Normally, central venous and intra-arterial pressure measurements would not have identified this. The decrease in CI during prone position has also been confirmed elsewhere [2]. On the other hand, one study that analysed transoesophageal echocardiography in patients undergoing lumbar laminectomy [3] showed that although central venous pressure (CVP) increased slightly when patients were moved from supine to prone, CI did not change.

Nevertheless, it appears that the specific prone position used may influence these findings. A study performed in 21 patients undergoing lumbar surgery with direct PAP or IVC pressure monitoring [4] demonstrated that the flat prone position did not interfere with circulatory function but positioning with a convex saddle frame caused a decrease in CI and stroke volume index without significant increase in IVC pressure. It suggests that heart position at a hydrostatic level above the head and limbs may result in reduced venous return and consequently a reduced CI. A study [5] of four different surgical prone positions in 20 healthy non-anaesthetized volunteers (pillows under the thorax and pelvis with a free abdomen, position on an evacuatable mattress, position on a modified Relton–Hall frame or the knee–chest position) found no substantial changes in heart rate or MAP in any of the different positions, but CI decreased by 20% on the knee–chest position and by 17% on the modified Relton–Hall position. In the prone jack-knife position [2], head-down tilt caused CI to return to supine values and this was attributed to decompression of the IVC allowing an increased venous return to the heart.

It has been suggested that the decrease in CI may be due to elevated intra-thoracic pressures causing reduced arterial filling which leads to sympathetic activity increase via the baroceptor reflex. Consistent with this theory is the work which demonstrated that in prone patients decreased stroke volume is accompanied by an increased sympathetic activity (increased heart rate, total peripheral vascular resistance and plasma noradrenaline).

Recent studies suggest that the anaesthetic technique could affect haemodynamic variables in the prone position. One study [6] showed that when comparing total intra venous anaesthesia (TIVA) with inhalation anaesthesia by measuring MAP and heart rate in patients undergoing spinal surgery, a greater decrease in arterial pressure in the TIVA group was observed.

Another study [7] compared inhalation with intra venous maintenance anaesthesia by using non-invasive cardiac output measures in supine patients which were then pronated on a Montreal mattress. The authors found a decrease in CI and increase in SVR when the patients where pronated. The changes were greater during TIVA (decrease in CI of 25.9%) compared with inhalation anaesthesia (12.9%). Notwithstanding, such results may be explained by the change in propofol pharmacokinetics during prone position.

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Measured propofol concentrations have been observed to increase during target-controlled infusions when patients are transferred from supine position to prone, probably as a result of the decrease in cardiac output [8].

Inferior Vena Cava Obstruction

Obstruction of the IVC is likely to play a role in reducing cardiac output in at least some patients positioned prone. It is also clear that such obstruction contributes to increased blood loss during spinal surgery. Venous drainage obstruction forces blood to return to the heart by an alternative route (usually the vertebral column venous plexus of Batson). Given that these veins are thin-walled and contain little or no muscle tissue with few valves, any increase in pressure is transmitted and causes distension. This probably causes increased blood loss which adds to the difficulty in the surgical field, especially during lumbar spinal surgery.

The IVC obstruction issue is well recognized and various methods have been attempted to reduce blood loss such as the use of local anaesthetic infiltration, spinal and epidural anaesthesia and deliberate hypotension. In one study, IVC pressure was measured in six patients by comparing positions with and without a compressed abdomen. In all patients [9] abdominal compression resulted in a large increase in venous pressure by reaching more than 30 cm H_2O in a particular patient. The position that appeared to cause the least compression (changes of up to 4 cm H_2O) involved placing a large block under the chest and small sandbags under each anterior superior iliac crest. It was also noted that hypercarbia and any increase in pressure during expiration caused an increase in venous pressure.

When comparing IVC pressures in patients in the flat prone position, it was found that pressures were 1.5 times greater with respect to patients on the Relton–Hall frame, demonstrating the benefit of a support system that allows a free abdomen. This study also showed that induced hypotension had no significant effect on IVC pressure.

In summary, turning a patient into the prone position has significant effects on cardiovascular physiology, the most consistent of which being the reduction in CI. This has been variably attributed to a reduced venous return, to direct effects on arterial filling and reduced left ventricular compliance secondary to increased thoracic pressure. Other haemodynamic measures vary in a less predictable manner, although at least some patients demonstrate an increased sympathetic response to the change in position and the different anaesthetic techniques may influence the degree to which such changes occur. IVC obstruction is a well-recognized complication of prone positioning, and it is exacerbated by any degree of abdominal compression leading to decreased cardiac output, increased bleeding, venous stasis and consequent thrombotic complications. Careful positioning is therefore essential to minimize these risks.

1.2 Respiratory

Changes in Respiratory Physiology

The respiratory system is affected by an even more pronounced and clinically significant change in the prone position. Overall, functional residual capacity (FRC) decreases in comparison to the erect position. On the other hand, when compared to the supine position, FRC is seen to increase in the prone patient. Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) change minimally. In addition, pulmonary blood flow changes in the prone position.

It is common knowledge that pulmonary blood flow is gravity dependent. In the prone position, perfusion of the dependent lung would be increased compared to the nondependent lung. However, recent work has found that blood flow is distributed more uniformly throughout the lung in the prone position with respect to the supine position. As with pulmonary perfusion, lung ventilation is probably less dependent on gravitational forces than was once thought.

Recent work emphasizes that the architecture of the airway has a greater impact than gravity on the distribution of ventilation. This leads to improved matching of ventilation and perfusion, allowing for better oxygenation when properly placed in the prone position.

If not positioned correctly, excess abdominal compression could cause cephalad displacement of the diaphragm and encroach the lung. This may result in a decrease in FRC and lung compliance potentiating V/Q mismatch.

Lung Volumes

The most consistent finding is a relative increase in functional residual capacity (FRC) when a patient is moved from a supine to a prone position; forced vital capacity and forced expiratory volume in 1 s (FEV1) change very little [10].

Coonan and Hope [11] discussed, in detail, the cardiorespiratory effects of different body positions. The FRC of a patient going from upright and conscious to supine, anaesthetized and paralysed may decrease up to 44%, but considerably less (12%) when going from upright to prone. These findings were confirmed in a clinical context involving patients undergoing intervertebral disc surgery [12].

Measurements of FRC and arterial oxygen tension (PaO_2) were taken in supine patients and after 20 min in prone position. A significant increase was found in the FRC and PaO_2 [1.9 (SD 0.6) vs. 2.9 (0.7) L and 160 (37) vs. 199 [13] mmHg] when changing from supine to prone. The delivered tidal volumes and inspiratory flow rates were unchanged by the position as were the static compliances of the respiratory system (chest wall and lung). Although the resistance of the respiratory system was found to increase by 20% primarily as a result of changes in the viscoelastic properties of the chest wall, this did not seem to be of any clinical significance. Airway resistance was not altered by the change in position. The authors attributed the increase in FRC to the reduction of cephalad pressure on the diaphragm and the reopening of atelectatic segments.

The same study was repeated in obese patients (BMI >30 kg/m^2) [13] using a similar methodology and positioning, whereby the authors observed an increase in lung volumes, lung compliance and oxygenation when patients were turned to the prone position, although, in obese subjects, the average FRC when supine was significantly lower than in the non-obese group [1.9 (0.6) L compared with 0.894 (0.327) L].

In summary, there are clear differences in respiratory physiology between supine and prone positions, including an increase in FRC and the distribution changes of both ventilation and perfusion throughout the lungs. It is thought that this leads to an improved ventilation/perfusion matching, which results in a better oxygenation in the surgical patient.

1.3 Complications Associated with the Prone Position

Injury to the Central Nervous System

Injury to the central nervous system represents a rare but potentially catastrophic complication of the prone position. These injuries can be classified according to the underlying mechanism—arterial occlusion, venous occlusion, air entrainment, cervical spine injury or the repercussion of undiagnosed space-occupying lesions.

Injury to the Peripheral Nervous System

Peripheral nerve injury may occur in patients under anaesthesia in any position and is thought to be the result of nerve ischaemia from undue stretching or direct pressure. In this context, prone positioning might lead to a different pattern or frequency of nerve injury when compared with supine positioning.

1.4 Pressure Injuries

A wide variety of injuries can occur in the prone position as a result of the pressure applied to dependent parts of the body. These injuries can be thought of as being the result of either direct pressure or indirect pressure (when injury occurs as a result of pressure on or occlusion of the vascular supply).

Direct Pressure Injuries

Pressure Necrosis of the Skin

Direct pressure is a common cause of anaesthesia-related injury that can occur in the prone position. Most authors advise to closely pay attention to the positioning of the face, ears, breasts, genitalia and other dependent areas to prevent pressure sores or skin necrosis. However, there are few reports on the subject, and such complications are usually mentioned as part of case series of other complications. The skin areas mainly affected include the malar regions, iliac crests, chin, eyelids, nose and tongue [14–16].

Contact Dermatitis

A patient developed contact dermatitis of the face [17] with periorbital and lip swelling after undergoing surgery with the head placed in a specific device (PronePositioner). A case of contact dermatitis in response to a Bispectral Indexw monitor placed on the forehead was thought to have been exacerbated by the prone position as a continuous pressure potentiated contact with the electrode conductive gel [18].

Tracheal Compression

There have been four reported cases of tracheal compression occurring during surgery in the prone position [19–22]. In all patients, this was associated with thoracic scoliosis and the proposed mechanism involved a reduced anterior–posterior diameter of the chest, which resulted in the compression of the trachea between the spine and the sternum. Tracheal compression appears to be a problem only in patients with underlying anatomical abnormalities and has not yet been reported in those with normal habitus.

Salivary Gland Swelling

Bilateral painful swelling of the submandibular glands after surgery in the prone position with lateral rotation of the head has also been reported. Although the aetiology is not clear, the authors concluded that it probably resulted from salivary ducts stretching, leading to stasis and acute swelling.

Shoulder Dislocation

The distribution of pressure in the prone position can also lead to anterior dislocation of the shoulder.

Indirect Pressure Injuries

Macroglossia and Oropharyngeal Swelling

Macroglossia is a well-documented complication of surgery in the sitting position and is thought to result from excessive flexion of the head and neck causing obstruction to venous drainage. Swelling of the tongue and oropharynx can constitute a real emergency for the patient undergoing surgery in the prone position.

Visceral Ischaemia

Avoiding compression on the abdominal organs is as important as avoiding abdominal compression to facilitate the surgical field. Hepatic ischaemia with progressive metabolic acidosis and elevated liver enzymes has been described after prolonged surgery in the prone position [23, 24] with subsequent resolution, and a case of hepatic infarction after 10 h of surgery in the prone position has also been reported.

Peripheral Vessel Occlusion

The prone position can cause compression and occlusion of several peripheral vessels.

Ophthalmic Injury

Postoperative visual loss (POVL) after non-ocular surgery in any position is relatively rare. There are a few mechanisms by which prone positioning may lead to ophthalmic injury. The most obvious is the result of direct external pressure by a headrest or other support on the orbital contents which causes an increased intraocular pressure leading to retinal ischaemia and visual loss. This has been named 'Hollenhorst Syndrome' and is usually linked with findings related to central retinal artery occlusion. Ironically, such injury has recently been described as a result of using a device designed to protect the eyes [25]. Specific devices designed to support the head during the prone position are fashioned to leave an open space for the eyes by distributing the weight of the head between the bony structures. Mirror systems placed on the operating table can be helpful with eye checks.

POVL can occur in the absence of external impingement on the eyeball, for example, when the head has been pinned and no headrest or other support has been placed near the eyes. This situation tends to be associated with findings of ischaemic optic neuropathy on examination [26] and may also be bilateral (over 40% of patients in one review) [27]. The final common pathway in ischaemic optic neuropathy is the inadequate oxygenation of the optic nerve causing ischaemic damage and failure of impulse transmission. Some individuals may be more susceptible to this as a result of anatomical variation in the arterial supply or abnormal vessel autoregulation [28]. In any patient, however, oxygenation of the optic nerve depends on adequate perfusion of its neurones. Perfusion pressure to the optic nerve can be defined as the difference between MAP and intraocular pressure or venous pressure, whichever is greater. Consequently, an increase in intraocular or venous pressure or a decrease in arterial pressure result in greater likelihood of developing optic nerve ischaemia.

2 … and The Most Correct Anaesthetic Approach?

2.1 Pre-assessment

Firstly, discuss with the surgeon the required position and the predicted duration of the procedure. Then fully pre-assess the patient, including physical examination and informed consent for anaesthesia. Evaluate the airway carefully—cervical spine surgery is an indication for prone positioning and limited head and neck movements are common in these patients, complicating airway management. Focus on peripheral neuropathy risk factors (diabetes, alcohol consumption, B_{12} deficiency) and document pre-existing nerve injuries and neuropathies. Check for signs of vertebrobasilar insufficiency. Consider the need for invasive monitoring and appropriate consent. Perform pre-operative investigations as needed.

2.2 Pre-induction

Standard monitoring should be set up when the patient is in the supine position and an appropriate venous access should be established. The anterior cubital fossae should be avoided given that flexion of the arms will occlude this route when the patient is positioned prone for surgery. Place ECG electrodes on the patient's back where they will not interfere with surgery. Ensure that there is an adequate number of staff present to turn the patient after induction; they should be instructed on the technique using an awake volunteer for practice. The correct operating table should be in place and induction should take place on a separate moveable bed.

2.3 Induction

Induce anaesthesia appropriately and then secure the airway. A reinforced endotracheal tube (ETT) is often used. A laryngeal mask has been used in the prone position, but it is intuitively safer to fully secure the airway as intra-operative access is difficult. Secure the tube, preferably with tape and not a tube tie. The main reason for this is that when the patient is positioned prone the tie may become tighter and occlude venous drainage from the head and neck resulting in morbidity as discussed earlier.

Protect the eyes carefully. Initially, by covering with tape and then by placing protective extra padding over them and securing that in place with additional tape. Hard goggles have been designed to help protect the eyes in the prone position—if used, ensure that they are correctly placed, making sure there is no pressure on the ocular globes. Consider temperature monitoring—if continuous nasopharyngeal monitoring is needed, then insert the tube prior to taping the ETT as access to the nose and mouth may be difficult. Place arterial and central lines if required, but keep in mind that CVP interpretation may be difficult in the prone position. A urinary catheter is recommended in major procedures to aid in the assessment of circulation and fluid balance.

2.4 Positioning

As soon as the airway and all lines are secure, tell the theatre team members that you are ready for the prone position. Place the stretcher with the patient next to the operating table. Take control of the head and airway—as with all positioning, it is safest to disconnect the patient from the breathing circuit at this point. At least five other staff members (one of whom should be the surgeon) are required to safely turn the patient—two on each side and one controlling the legs and feet. The patient should be turned prone slowly and gently onto the operating table, while the anaesthetist coordinates the procedure. Care should be taken to avoid misplacement of intravenous lines and cannulas. Once positioning is complete, head and neck should be placed carefully preferably in a neutral position, on a soft head ring avoiding ocular pressure. Then perform a rapid but thorough assessment of the airway, breathing and circulation. It is not uncommon that the endotracheal tube gets misplaced into the right main bronchus as a result of increased neck flexion.

Arm positioning depends on surgery indication. In the Montreal mattress prone position, arms should be placed alongside the head on additional arm support. When moving the arms, do so one at a time and not simultaneously, such that greater ROM is allowed at the shoulder joint level (as per butterfly versus freestyle swimming strokes). To avoid brachial plexus stretching, ensure that the axillae are not under tension.

Perform a full head-to-toe assessment of the patient to verify that every potential pressure point is protected by padded material. When dealing with a Montreal mattress, assure that the abdomen is correctly placed. Next, perform a secondary assessment of airway, breathing and circulation prior to the commencement of surgery.

2.5 Intra-Operative Management

The same principles of intra-operative management of any anaesthetic technique also apply to prone positioning. The main difference lies in the fact that if a problem that requires returning to the supine position arises, there may be some delay before this can be done safely. As with all anaesthetic procedures, extremely careful preparation and a double-check prior to surgery initiation is crucial to prevent problems or potential adverse events related to position.

2.6 Emergence from Anaesthesia

Maintain adequate anaesthesia until the patient is repositioned in the supine position on the stretcher, given that it is harder to safely reposition a coughing or non-compliant patient. Anaesthetic emergence follows the same principles as any other anaesthetic process including post-operative examination.

References

1. Backofen JESJ. Hemodynamic changes with prone positioning during general anethesia. Anesth Analg. 1985;64:194.
2. Hatada T, Kusunoki M, Sakiyama T, et al. Hemodynamics in the prone jackknife position during surgery. Am J Surg. 1991;162:55–8.
3. Toyota S, Amaki Y. Hemodynamic evaluation of the prone position by transesophageal echocardiography. J Clin Anesth. 1998;10:32–5.
4. Yokoyama M, Ueda W, Hirakawa M, Yamamoto H. Hemodynamic effect of the prone position during anesthesia. Acta Anaesthesiol Scand. 1991;35:741–4.
5. Wadsworth R, Anderton JM, Vohra A. The effect of four different surgical prone positions on cardiovascular parameters in healthy volunteers. Anaesthesia. 1996;51:819–22.
6. Ozkose Z, Ercan B, Unal Y, et al. Inhalation versus total intravenous anesthesia for lumbar disc herniation: comparison of hemodynamic effects, recovery characteristics, and cost. J Neurosurg Anesthesiol. 2001;13:296–302.
7. Sudheer PS, Logan SW, Ateleanu B, Hall JE. Haemodynamic effects of the prone position: a comparison of propofol total intravenous and inhalation anaesthesia. Anaesthesia. 2006;61:138–41.
8. Takizawa D, Hiraoka H, Nakamura K, Yamamoto K, Horiuchi R. Influence of the prone position on propofol pharmacokinetics. Anaesthesia. 2004;59:1250–1.
9. Lee TC, Yang LC, Chen HJ. Effect of patient position and hypo- tensive anesthesia on inferior vena caval pressure. Spine. 1998;23:941–7; discussion 7–8.
10. Lumb AB, Nunn JF. Respiratory function and ribcage contribution to ventilation in body positions commonly used during anesthesia. Anesth Analg. 1991;73:422–6.
11. Coonan TJ, Hope CE. Cardio-respiratory effects of change of body position. Can Anaesth Soc. 1983;30:424–37.
12. Pelosi P, Croci M, Calappi E, et al. The prone positioning during general anesthesia minimally affects respiratory mechanics while improving functional residual capacity and increasing oxygen tension. Anesth Analg. 1995;80:955–60.
13. Pelosi P, Croci M, Calappi E, et al. Prone positioning improves pulmonary function in obese patients during general anesthesia. Anesth Analg. 1996;83:578–83.
14. Anderton JM. The prone position for the surgical patient: a historical review of the principles and hazards. Br J Anaesth. 1991;67:452–63.
15. Drummond JC. Macroglossia, Dejavu [comment]. Anesth Analg. 1999;89:534–5.
16. Smith RH. One solution to the problem of the prone position for surgical procedures. Anesth Analg. 1974;53:221–4.
17. Jericho BG, Skaria GP. Contact dermatitis after the use of the PronePositioner. Anesth Analg. 2003;97:1706–8.
18. Pousman RM, Eilers WA III, Johns B, Jung H. Irritant contact dermatitis after use of Bispectral Index sensor in prone position. Anesth Analg. 2002;95:1337–8.
19. Bagshaw ON, Jardine A. Cardiopulmonary complications during anaesthesia and surgery for severe thoracic lordoscoliosis. Anaesthesia. 1995;50:890–2.
20. Kai Y, Yamaoka A, Irita K, Zaitsu A, Takahashi S. Transient tracheal obstruction during surgical correction of scoliosis in a 105 patient with Marfan's syndrome. Masui. 1995;44:868–73.

21. Mesrobian RB, Epps JL. Midtracheal obstruction after Harrington rod placement in a patient with Marfan's syndrome. Anesth Analg. 1986;65:411–3.
22. Rittoo DB, Morris P. Tracheal occlusion in the prone position in an intubated patient with Duchenne muscular dystrophy. Anaesthesia. 1995;50:719–21.
23. Yuen VMY, Chow BFM, Irwin MG. Severe hypotension and hepatic dysfunction in a patient undergoing scoliosis surgery in the prone position. Anaesth Intensive Care. 2005;33:393–9.
24. Ziser A, Friedhoff RJ, Rose SH. Prone position: visceral hypoperfusion and rhabdomyolysis. Anesth Analg. 1996;82:412–5.
25. Roth S, Tung A, Ksiazek S. Visual loss in a prone-positioned spine surgery patient with the head on a foam headrest and goggles covering the eyes: an old complication with a new mechanism. Anesth Analg. 2007;104:1185–7.
26. Lee L, Roth MD, Posner KL, et al. The American Society of Anesthesiologists Postoperative visual loss registry: analysis of 93 spine surgery cases with postoperative visual loss. Anesthesiology. 2006;105:652–9.
27. Ho VTG, Newman NJ, Song S, Ksiazek S, Roth S. Ischemic optic neuropathy following spine surgery. J Neurosurg Anesthesiol. 2005;17:38–44.
28. Roth S, Barach P. Postoperative visual loss: still no answers—yet [comment]. Anesthesiology. 2001;95:575–7.

Further Reading

Kwee MM, et al. The prone position during surgery and its complications: a systematic review and evidence-based guidelines. Int Surg. 2015;100(2):292–303.

Edgcombe H, et al. Anaesthesia in the prone position. Br J Anaesth. 2008;100:165–83.

The Funnel: From the Skull Base to the Sacrum. New Trends and Technologies in Anaesthesia for the Adult Patient

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Countless advances in paediatric neurosurgery have significantly improved the outcome of infants and children suffering from central nervous system (CNS) lesions.

The physiological and developmental differences that characterize paediatric patients present a huge challenge to both neurosurgeons and anaesthetists. In paediatric surgery, the prone position is used for spine surgery, encephalocele repair and suboccipital craniotomies.

The enormous existing differences between adults and children require a great deal of attention to be paid to the paediatric neurosurgical patient. It is not uncommon to find that children with signs and symptoms of intracranial hypertension often have advanced disease. From a physiological point of view there are many considerations to underline.

Cerebral blood flow is closely related to metabolic demand, and both increase soon after birth in a proportional manner. The self-regulating blood pressure in a new-born normally ranges from 20 to 60 and changes are to be considered according to the age [1]. Such range is consistent with the relatively low brain metabolic requirements and low blood pressure that characterize the perinatal period.

Another important difference found in paediatric patients when compared to adults is defined by a higher percentage of cardiac output being directed to the brain, given that, in the infant and child, the head occupies the largest body surface area, and thus needs more blood flow. As a result, the child is at greater risk for significant haemodynamic instability during neurosurgical procedures.

More importantly, the cerebral blood flow autoregulation curve is characterized by extreme variations at its lower and upper limits. Given the narrow range at either end of the auto-regulation curve, marked hypotension and/or hypertension places the infant at risk for cerebral ischaemia or intraventricular haemorrhage, respectively [2].

1 Anesthesiological Management

The management of children affected by neurosurgical pathologies is multidisciplinary and should be set on several fronts.

The main challenges involve:

- The potential need for massive blood components transfusions: this is of particular importance, especially in children undergoing surgery in the first months of life [3, 4]. In these patients, the nadir of physiological anaemia often coincides with surgery, thus leading to a greater number of intraoperative transfusions.
- Prolonged anaesthesia in paediatric age that may be often complicated by various forms of syndrome-related problems.

It is therefore a task of the anaesthesiology team to manage the ventilation, anticoagulation and transfusion support of these patients during and after surgery. All this must be done taking into consideration the pathophysiological and clinical conditions. In addition, airway management must be as accurate as possible [5–7] given the dysmorphic features that are often encountered.

The problems to managed may be divided schematically into three large groups:

1. preoperative
2. intraoperative:
   (a) induction and maintenance of anaesthesia;
   (b) blood loss control and transfusion support;
   (c) prone position
3. postoperative.

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2 Preoperative Issues

Several studies have revealed that infants and children are at higher risk of morbidity and mortality than any other age group [8].

Respiratory and cardiac events account for most of these complications.

However, one of the major pitfalls in the management of infants and children undergoing neurosurgery relates to the presence of coexisting pathologies. Very often, the neurosurgical pathology accounts for only one of the many pathologies that the paediatric patient is affected by. The management of the paediatric neurosurgical patient, especially when considering the prone position, requires a thorough and careful evaluation of the airways, which are commonly altered in syndromic patients [9].

It must be recalled that some paediatric patients are affected by syndromes involving the craniofacial massif.

In many craniofacial syndromes, the difficulty in managing the airways may be present from the very beginning during mask ventilation after anaesthesia induction has begun. Besides taking into consideration potential infectious problems, the significant incidence of OSAS must also be accounted for in airway management of these patients. The obstruction can be at various levels and often creates a marked anatomical distortion of the nasopharyngeal district; in most cases, this distortion is clinically significant and often causes obstructive apnoea. Every so often, patients requiring CPAP are scheduled for tracheostomy to stabilize the respiratory tract to ensure a more regular intra and post-operative course, especially in long duration and prone interventions.

It is not uncommon that cardiac morbidity related to congenital heart disease arises during the first year of life [10]. Congenital heart disease, often not evident soon after birth, commonly emerge during surgery when haemodynamic changes caused by aesthetic agents, mechanical ventilation and blood loss unmask these heart defects. Echocardiography can be helpful in evaluating heart function and motion and a paediatric cardiologist should always evaluate patients with suspected problems to help optimize heart function prior to surgery.

Risk factors that indicate a potential or probable need of blood transfusion should also be considered and evaluated prior to surgery.

It is necessary to consider:

- Type of surgery (craniofacial surgery, correction of scoliosis and cardiac surgery are associated with increased blood loss);
- Pre-existing comorbidities (heart or lung conditions, diabetes, kidney problems, etc.);
- Preoperative haemoglobin/haematocrit value adjusted for age and weight;
- Presence or absence of clinical signs of anaemia or hypovolemia;
- Preoperative treatment with anticoagulants.

Besides the importance of a multidisciplinary approach when dealing with clinical problems in these patients, it is fundamental to assess risk factors that can be modified before surgery such as the interruption of anticoagulant therapy and the weight of the small patient. The procrastination of the intervention, when possible, aims to reach an optimal weight, thus reducing the risk of periprocedural issues related to transfusion requirements. It is also necessary to establish preoperative fasting [11, 12], to calculate and set the intraoperative fluid therapy [13, 14] according to the clinical condition of the patient and type of surgery. This is done to prevent an excessive administration of perioperative fluids from causing acidosis, coagulation alterations, peripheral tissues oedema and, rarely, pulmonary oedema. At the same time, optimal fluid management is mandatory so that eventual blood loss can be managed appropriately.

Conversely, excessive fluid restriction can lead to hypovolemia with hypoperfusion, tissue hypoxia and oxygen deficit. It is important to remark that paediatric patients are easily susceptible to dehydration, so that overall fluid restriction should be less stringent than in the adult patient. Severe dehydration is most frequently due to vomiting, diarrhoea and fever. In this context, careful clinical evaluation of the Refill Time must be carried out, as well as of the sensory and mental status, fontanelle appearance (whether sunken or not) and other signs and symptoms of impaired hydration. It will therefore be necessary to correct the dehydration state in the preoperative period through the administration of crystalloids boluses (SER, electrolytic replenishment solution) during the first hour of surgery.

Fluid balance optimization therefore represents a fundamental determinant for better outcome of the young patient.

3 Intraoperative Issues

3.1 Induction and Maintenance of Anaesthesia

In children with upper airway obstruction and no tracheostomy, anaesthesia induction may represent a considerable trigger for OSAS development; it is therefore necessary to assess and plan with extreme attention for airway management in these patients, so that arising problems can be anticipated and appropriately handled.

In addition to upper airway obstruction that may occur during the anaesthesia induction, it is crucial to consider the effect on the cardiovascular system and central nervous system exerted by a chronic obstruction of the upper airways. The recurrent respiratory obstruction that develops during sleep leads to a reduction in cerebral perfusion pressure (CPP), which may cause long-term negative effects on the patient's neuro-cognitive development. Regarding anaesthesiologic management in the intraoperative setting, a balanced general anaesthesia should be preferred that includes muscle relaxants, narcotics and inhalational agents [15, 16]. The depth of anaesthesia aims to maintain haemodynamic balance so that blood pressure and heart rate are kept within 20% from baseline. Anaesthetic techniques that avoid increases in intracranial pressure are preferred in patients who may have reduced intracranial compliance [17–19].

Fluid intake in the perioperative period must be modulated according to both basal demand of the small patient (maintenance) and pre-existing deficit (fasting and dehydration), as well as considering intraoperative losses (blood and third space).

One of the main intraoperative challenges for paediatric anaesthetists is massive blood loss occurring during neurosurgery so that transfusion is needed in the majority of cases [20, 21]. Blood volume percentage is representatively greater in children compared to adults, given the younger age and the weight. This is due both to the greater cranial surface that syndromic children may have compared to non-syndromic peers and to the greater blood supply at the cranial level that is typical of children. Prolonged interventions (duration greater than 5 h) are more frequently associated with a greater blood volume loss (BVL). It is also known that hypothermia contributes to the development of coagulopathy [22], and therefore an increase in BVL.

There may be specific surgical phases characterized by sudden and significant blood loss; knowledge of such phases allows the anaesthetist to correctly predict and prepare for the correct management of bleeding [23–25].

In addition to the specific surgical phases associated with acute blood loss, it must not be forgotten that the risk of bleeding is present during the entire surgical procedure, and it also persists during the postoperative period [26].

So-called blood saving techniques have been developed that consist in procedures aimed at reducing blood loss with consequent minimization of the need for blood or coagulation factors transfusion following multimodal and multidisciplinary approaches, given the various requirements, including medico-legal, economic, practical, ethical and religious [27]. Such techniques can be performed with relative ease both in adults and older children, while it is certainly more difficult in infants and new-borns, whereby significant limitation is represented by the reduced oxygen transport capacity that can derive from the aforementioned approaches.

The concept of 'transfusion trigger', introduced by Adams and Lundy in 1940, identifies a haematocrit of 30% and a haemoglobin value of 10 g/dL as the minimum acceptable concentration.

To date, transfusion triggers vary according to centres and circumstances [28].

It is not easy to quantify the blood loss in a child during surgery, especially if it is a major surgery. Moreover, the haematocrit does not always represent a clear image of the intraoperative volume state and it should be added that blood management programs (PBM, patient blood management) still have limited application in the paediatric field [29].

If neurosurgery is known for one feature, it is its long duration. This feature requires careful preservation of bony prominences such as the elbow condyles, the sacrum, the ankles and the iliac crests. It is also necessary to ensure that the limbs are in a neutral position to avoid stretching or compressing the peripheral nerves. Eyes should be lubricated with wetting agents or antibiotic ointments and be carefully taped or padded to prevent injury to the cornea. Urinary catheters are advisable for long surgical procedures to prevent bladder distension and to aid in fluid management [30].

As with most other paediatric surgical procedures, patient position—especially the prone position—presents some challenges for neurosurgery. Although patients, given their small size, frequently disappear under the drapes and surgical equipment (Fig. 1), the anaesthetist must make every effort to ensure an unobstructed view of the patient and guarantee access to every part of them, especially the venous line and to the airways.

Many neurosurgical procedures are performed in the prone position and assessing the endotracheal tube in such position becomes very difficult. There are numerous occasions in which the tube may be accidentally displaced in this position. Such event is an emergency situation and requires immediate intervention, which includes changing the position having sometimes to remove the pin attachment that

Fig. 1 Paediatric surgical procedure

secures the head, turning the patient and reintubating as soon as possible. This could be a life-threatening event and has been the focus of quality improvement programs related to airway management in recent years. Accidental tube displacement can be a potentially disastrous event and may be due to factors such as the reduced adhesion of the patch as a result of contact with the disinfectant or salivary secretions, the weight of the breathing circuit that 'pulls' the endotracheal tube, the natural gravity force in the prone position, a poor positioning of the head and face during the execution of the position, inadequate measures of the chosen endotracheal tube. These factors not only lead to airway loss, but also to other associated morbidities such as tissue trauma to the face and airways, bronchospasm, aspiration pneumonia and arrhythmias. This can be seen in any surgical procedure performed in the prone position and in any patient but it becomes much more importance when dealing with paediatric patients as a lower safety margin is given by the shorter tube length and circumference, both in orotracheal or nasotracheal intubation. In paediatric patients, improved tube safety is essential and therefore proper ETT fixation is a must for the safe conduct of the paediatric neurosurgical procedure in the prone position. In addition, flexion of the neck in such position may misplace the endotracheal tube causing intubation of a main bronchus and consequent impaired ventilation.

Posterior fossa explorations are frequently performed with the baby prone (Fig. 2). When that is the case, the prone position requires extreme flexion of the neck so that the suboccipital skull is exposed, which often leads to kinking of the endotracheal tube. The use of armoured endotracheal tubes minimizes this problem.

When establishing the prone position, it is important to ensure that the patient's weight does not rest entirely on the abdomen, being instead supported by padding under the pelvis and chest. Excessive abdominal pressure prevents lung ventilation and leads to inferior vena cava compression and distension of the epidural venous plexus, both of which increase surgical blood loss during spinal surgery. Extreme neck flexion can impair venous or lymphatic drainage from the tongue and cause postoperative macroglossia. Excessive head flexion or extension may cause brain stem compression in patients with Arnold–Chiari malformation.

Fig. 2 Prone position

4 Postoperative Issues

Prevention and early diagnosis of postoperative issues is made possible only and exclusively by careful observation in an intensive care unit with serial neurological examinations and invasive haemodynamic monitoring.

Respiratory syndromes are the main complication after posterior fossa craniotomies [31]. Airway oedema may require endotracheal intubation for a long time after surgery. Respiratory centres ischemia or oedema in the brain stem can interfere with the regular and spontaneous resumption of respiratory activity, thus leading to postoperative apnoea. Children with Chiari malformations may be more prone to respiratory depression [32].

References

1. Pryds O. Control of cerebral circulation in the high-risk neonate. Ann Neurol. 1991;30:321–9.
2. Soriano SG, Eldredge EA, Rockoff MA. Pediatric neuroanesthesia. Anesthesiol Clin N Am. 2002;20:389–404.
3. Goobie S, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. Pediatr Anesth. 2014;24:678–89.
4. Orliaguet GA, Bruyere M, Meyer PG, et al. Comparison of Perioperative blood salvage and postoperative reinfusion of drained blood during surgical correction of craniosynostosis in infants. Paediatr Anaesth. 2003;13:797–804.
5. Steinbok P, Heran N, Hickdonmez T, et al. Minimizing blood transfusions in the surgical correction of coronal and metopic craniosynostosis. Childs Nerv Syst. 2004;20:445–52.
6. Morray JP, Geiduschek JM, Ramamoorthy C, et al. Anesthesia-related cardiac arrest in children: initial findings of the Pediatric Perioperative Cardiac Arrest (POCA) Registry. Anesthesiology. 2000;93:6–14.
7. Nargozian CD. The difficult airway in the pediatric patient with craniofacial anomaly. Anesthesiol Clin North Am. 1999;16:839–52.
8. Cohen MM, Cameron CB, Duncan PG. Pediatric anesthesia morbidity and mortality in the perioperative period. Anesth Analg. 1990;70:160–7.
9. Thomas K, Hughes C, Johnson D, Das S. Anesthesia for surgery related to craniosynostosis: a review. Part 1. Paediatr Anaesth. 2012;22(11):1033–41.
10. Boneva RS, Botto LD, Moore CA, Yang Q, Correa A, Erickson JD. Mortality associated with congenital heart defects in the United States: trends and racial disparities, 1979–1997. Circulation. 2001;103:2376–81.
11. Wood KB, Simons M, Evasiuk A, Mazurak V, Dicken B, Ridley D, Larsen B. Surgical fasting guidelines in children: are we putting them into practice? J Pediatr Surg. 2016;51:1298.

12. Singer M. Management of fluid balance: a European perspective. Curr Opin Anaesthesiol. 2012;25(1):96–101.
13. Pearse RM, Ackland GL. Perioperative fluid therapy. BMJ. 2012;26:344.
14. Thacker JK, Moundord WK, Ernst FR, Krukas MR, Mythen MG. Perioperative fluid utilization variability and association with outcomes: considerations for enhanced recovery efforts in sample US surgical populations. Ann Surg. 2016;263(3):502–10.
15. Wedgwood JJ. Peri-operative haemoglobin: an overview of current opinion regarding the acceptable level of haemoglobin in the perioperative period. Eur J Anesthesiol. 1996;13:316.
16. Roberton NR. Use of albumin in neonatal resuscitation. Eur J Pediatr. 1997;156:428–31.
17. Greenough A. Use and misuse of albumin infusions in neonatal care. Eur J Pediatr. 1998;157:699–702.
18. Emery E, Greenough A, Gamsu H. Randomised controlled trial of colloid infusions in hypotensive preterm infants. Arch Dis Child. 1992;67:1185–90.
19. Ferguson DJM, Barker J, Jackson IT. Anaesthesia for craniofacial osteotomies. Ann Plast Surg. 1983;10:333.
20. Howe PW, Cooper MG. Blood loss and replacement for paediatric cranioplasty in Australia - a prospective national audit. Anaesth Intensive Care. 2012;40:107–13.
21. Park C, Wormald J, Miranda BH, Ong J, Hare A, Eccles S. Perioperative blood loss and transfusion in craniosynostosis surgery. J Craniofac Surg. 2018;29:112–5.
22. Williams GD, Ellenbogen RG, Gruss JS. Abnormal coagulation during pediatric craniofacial surgery. Plast Reconstr Surg. 2001;35:5–12.
23. American Society of Anesthesiologists. More on the changing indications for transfusion of blood components during anesthesia. Anesthesiology. 1996;84:498.
24. American Society of Anesthesiologists. Practice guidelines for blood component therapy. A report by the American society of Anesthesiologists Task Force on blood component therapy. Anesthesiology. 1996;84:732.
25. Velardi F, Di Chirico A, Di Rocco C, Fundarò C, Serafini R, Piastra M, Viola L, Pietrini D, Pusateri A, Stoppa F. No allogenic blood transfusion: protocol for the surgical correction of craniosynostoses. Childs Nerv Syst. 1998;14:722.
26. Faberowski LW, Black S, Mickle JP. Blood loss and transfusion practice in the perioperative management of craniosynostosis repair. J Neurosurg Anesthesiol. 1999;11:167–72.
27. Goobie SM, Faraoni D, Zurakowski D, DiNardo JA. Association of preoperative anemia with postoperative mortality in neonates. JAMA Pediatr. 2016;170:855–62.
28. Goobie SM, DiNardo JA, Faraoni D. Relationship between transfusion volume and outcomes in children undergoing noncardiac surgery. Transfusion. 2016;56:2487–94.
29. Goobie SM, Haas T. Perioperative bleeding management in pediatric patients. Curr Opin Anaesthesiol. 2016;29:352–8.
30. Krane EJ, Domino KB. Anesthesia for infants and children. In: Anesthesia for pediatric neurosurgery. 7th ed. Philadelphia, PA: Mosby Elsevier; 2006.
31. Meridy HW, Creighton RE, Humphreys RB. Complications during neurosurgical procedures in the prone position. Can J Anaesth. 1974;21:445–52.
32. Waters KA, Forbes P, Morielli A, et al. Sleep-disordered breathing in children with myelomeningocele. J Pediatr. 1998;132:672–81.

Methods and Principles of the Intraoperative Neurophysiologic Monitoring in Neurosurgery

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1 Introduction

Intraoperative neurophysiologic monitoring (IONM) is an innovation introduced in neurosurgery in the past decades. The study of the techniques and the technology evolution of recording have permitted the application of intraoperative neurophysiology to many surgical fields such as cranial and spinal neuro-oncology, functional and vascular, as well. The aim of IONM is to support and guide the neurosurgeon to obtain the best surgical result possible, preventing the occurrence of neurological deficits.

IONM is founded on two main techniques: monitoring and mapping. Monitoring means acquiring signals continuously or at close intervals to study the variations throughout the surgery. The mapping technique is based on the electrophysiological possibility to stimulate a specific area of the nervous system to identify eloquent or critical structures, to preserve the anatomical area, and to guide the surgeon. The stimulation during mapping gives real-time information, and the constant and productive collaboration between the surgeon and the neurophysiologist appears crucial to avoid irreversible consequences [1, 2].

2 Somatosensory Evoked Potentials (SSEP)

The somatosensory evoked potentials assess the integrity of the sensory pathways. SSEP monitors the dorsal column–medial lemniscus pathway. During spine and cerebral surgery, this technology is run by administering an electric stimulus on a peripheral sensory nerve and recording the electric potential generated by the primary sensory cortex [3]. Most of the time, the median nerve and the ulnar nerve (at the wrist) are used to study SEPs in the upper limbs (Fig. 1). In the lower extremities, the tibial nerve at the external malleolus is used. Intraoperative neurophysiological monitoring (IONM) with somatosensory evoked potentials (SSEP) is widely used for real-time assessment of spinal cord function. Multiple clinical studies have demonstrated that significant changes in SSEP waveforms indicate an increased risk of postoperative neurologic deficit. Although

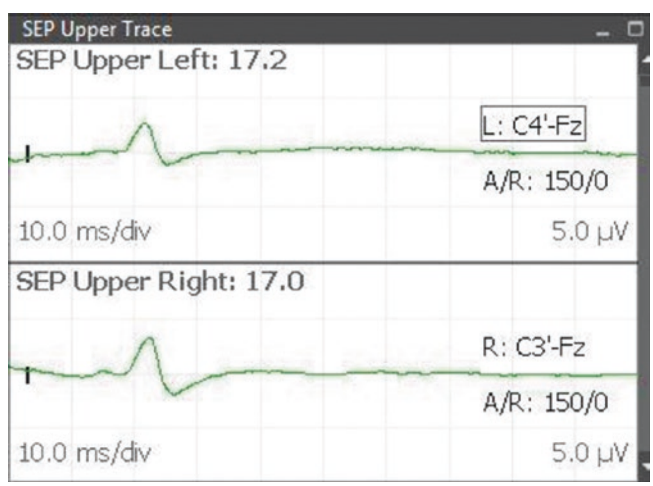

Fig. 1 Somatosensory evoked potential recorded bilaterally from the upper limbs

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similar studies have reported a high rate of false negative, both in spinal and cranial surgery [4, 5].

Various types of SSEP changes, including reversible change, irreversible change, and loss of response, could be detected during intraoperative monitoring, and it is important to underline the diagnostic value of each to perform the best surgical strategy. Several factors could affect the transmission of these signals such as temperature, nerve compression, systemic and neural perfusion, anesthetic type and dose, etc. In particular, as the primary effect of anesthetic agents is on synaptic transmission, the greater the number of synapses between the stimulus and recording sites, the greater the effect of the anesthetic agent.

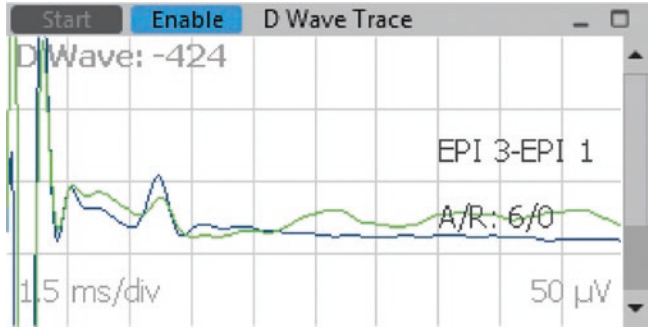

Fig. 2 D-wave variation. Blue trace: basal acquisition, green trace: intraoperative acquisition. The green trace shows 35% amplitude decrease

3 Motor Evoked Potentials (MEPs)

MEPs provide information on the integrity of the motor pathway. MEPs monitor the efferent motor pathways from the motor cortex to the muscle through corticospinal (or corticobulbar) tracts [6]. To evoke the MEP, transcranial electrical stimulation activates the axons of the large Betz cells located in the motor cortex measured through the neurogenic potential generated at the distal end of the spinal cord or peripheral nerve [4]. The locations for measuring myogenic potential could be: abductor pollicis brevis, dorsal interosseous muscle, and forearm flexors in the upper extremities and abductor hallucis, quadricepitis, or tibialis anterior muscles in the lower extremities [7]. During open cranial procedures, MEPs may also be produced by directly stimulating the cortex and/or subcortical white matter (direct cortical stimulation). Trans cranial MEP stimulation requires stimulus intensities from 100 to 400 V or 40–200 mA and a pulse width of between 50 and 500 ms.

MEPs provide information on the anatomical-functional integrity of the anterior medullary cords and subcortical bundles. The interpretation does not have well-defined guidelines [8, 9]: some authors give as an alarm criterion a reduction in amplitude of 50%, others instead only the complete disappearance of the potentials. Some factors could affect the predictive values of intraoperative MEP changes. MEPs from the muscles controlled by a large number of corticospinal fibers, for example, have high specificity, whereas MEPs measured from those controlled by a small number of corticospinal fibers have high sensitivity [10, 11].

The response of motor cortex stimulation can also be recorded as "waves" along the spinal cord. These responses consist of two waves: a direct wave (D-wave) that is the action potential generated in the corticospinal axons followed by indirect waves (I-waves), which are action potentials resulting from cortical activation of internuncial neurons.

The recording is performed using a sterile electrode, placed epidural, caudally to the surgical site before beginning the cord manipulation. The D-wave is a negative wave, with variable latency depending on the studied level of the cord. Both MEPs and D-wave are used to monitor the integrity of the corticospinal tract, but they have different features and provide different information. The D-wave involves no synapses such that anesthetics, at normal concentrations, have very little effect. Single stimulation pulses can be used to generate D-waves essentially eliminating movements and minimizing anesthetic constraints. In general, this technique is only used when the spinal cord is exposed (e.g., intramedullary surgery).

Regarding D wave interpretation, amplitude decreases of less than 50% suggest absence or transitory motor deficit. Decreases of more than 50% indicate the onset of slower recovery or definitive deficits [3, 12].

MEPs and D-wave are therefore essential and complementary for a complete monitoring of motor function (Figs. 2 and 3).

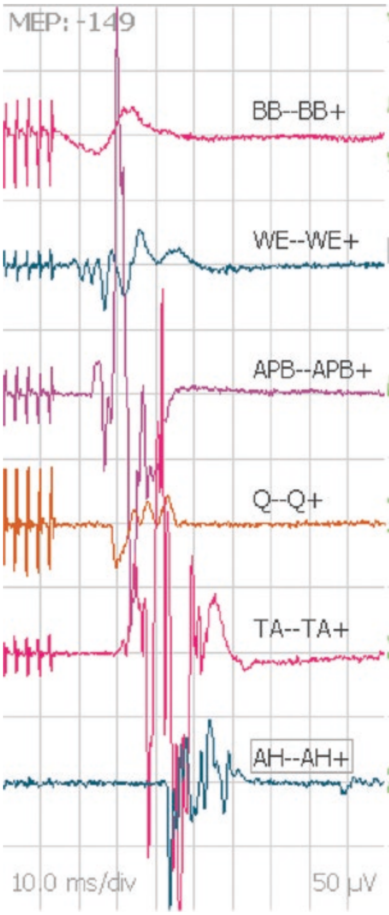

Fig. 3 Motor evoked potentials

4 Cortico Bulbar MEPs (CBMEPs)

CBMEPs are the application of the MEPs technique to the study of the cortico-bulbar tract. Appropriate changes in the position of the stimulation dipole and in the stimulation techniques allow monitoring the integrity of the motor cranial nerves: the stimulation dipole is C3-Cz for the muscles of the right side and C4-Cz for those of the left side (according with the international 10–20 system). Once the activation threshold has been identified, it is necessary to administer a single pulse, at the same current intensity and pulse width as the train of stimuli. This precaution is necessary to avoid direct peripheral activation of the cranial nerves [13].

The most studied muscles are masseter (V cranial nerve), orbicularis of the eye and orbicularis of the mouth (VII cranial nerve), vocal cords (X cranial nerve), trapezius (XI cranial nerve), and tongue (XII cranial nerve) (Fig. 4).

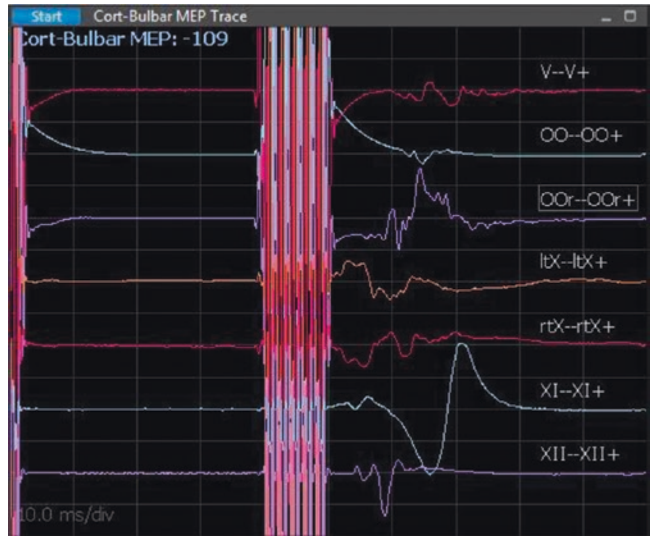

Fig. 4 Cortico-bulbar motor evoked potentials

5 Intraoperative EMG

Free-running EMG is the standard technique to monitor peripheral nerves, roots, or cranial motor nerves during surgery. Intraoperative EMG signals are activated during cranial motor nerves damaging or after an irritative stimulus. The duration, morphology, and persistence of EMG reflects the severity of neural injury. As described in some studies, the longer EMG train persists, the more likely neural deficits follow after surgery. However, EMG signals could persist even after ischemic or transection injury [14].

6 Auditory Evoked Potentials (BAEP)

Monitoring or mapping of cranial nerves (CNs) or nuclei is an integral part of infratentorial brain tumor surgery. BAEP is performed by delivering acoustic stimuli of a clicking sound, which includes a wide range of frequencies, through earplugs and recording potentials from electrodes at the mastoid process or earlobes, referred to as a cephalic electrode placed in Cz [12]. Auditory evoked potentials study the integrity of the auditory pathway and the functions of the brain stem.

The recorded wave is polyphasic with different components, numbered from I to VII. The most commonly studied in IOM are the I, III, and V waves, which represent cochlear potential (latency about 1.5 ms), cochlear nuclei (about 4 ms), and lateral lemniscus (6 ms), respectively. Monitoring BAEP change are mainly focused on the "amplitude reduction" of waves as well as the interwave latencies [15].

7 Visual Evoked Potentials (VEPs)

VEPs are potential that provide information on the integrity of the visual pathway. The stimulus is a luminous flash of variable color (red, blue, or white), administered by means of LED diodes mounted on specific glasses. To verify the productive efficacy of the stimulus, the electroretinogram (ERG), a polyphasic wave that is recorded by placing a recording electrode at the external canthus and a reference electrode at nasion level, is recorded.

The cortical potential is recorded from three different leads O1-Fz, O2–Fz, and Oz-Fz (electrodes positioned according to the international system 10–20) with O1, O2, and Oz active electrodes and Fz reference.

The studied response is found to be around 100 ms (P100), all amplitude variations greater than 50% are considered significant [6, 16].

8 Mapping Techniques for Cranial Nerves and Nerve Roots

Nerve mapping consists of recording muscle activations given by direct nerve stimulation. This technique makes use of a stimulation probe available to the neurosurgeon that allows administering current directly to the nervous tissue (nerves, roots, etc.). In addition, each muscles response certifies the integrity of the pathway from the stimulation site to the effector muscle. By properly choosing the muscles to observe, any motor nerve tract can be studied.

For example, for the ponto-cerebellar angle, the muscles studied (homolaterally to the surgical site) are masseter (V cn) orbicularis oculi and orbicularis oris (VII cn), vocal muscles (X cn), trapezius (XI cn), and tongue (XII cn) (Fig. 5).

For the pathologies involving cauda equina or cono medullaris, the muscles studied are (bilaterally) vastus lateral (L4), anterior tibial and abductor of the big toe (L5), sural triceps (S1), and external anal sphincter (S2–S5).

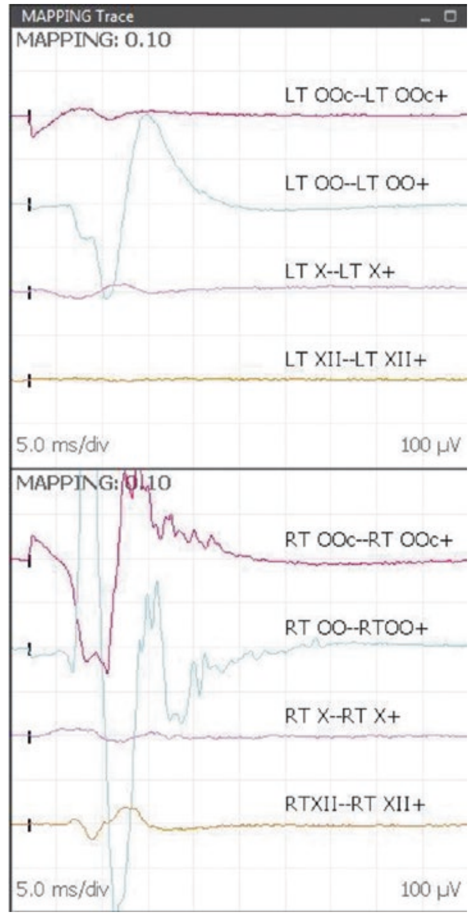

Fig. 5 Mapping of the floor of IV ventricle. Activation of right VII nerve

9 Conclusion

The development of methods for intraoperatively identifying (mapping) and continuously testing the functional integrity of the nervous structure (monitoring) has become fundamental during brain and spine surgery.

Intraoperative neurophysiological monitoring (IONM) is considered the standard of care during many procedures, including spinal, intracranial, and vascular surgeries, where there is a risk of neurological damage. Close communication and collaboration between the surgical team, neurophysiologist, and anesthesiologist is mandatory to obtain high-quality neuromonitoring, thus preventing neurologic injuries, and gaining the best surgical "safe" result. Multidisciplinary teams can improve the efficacy and the safety of the procedures, decreasing the risk of misinterpretation of the neurophysiological changes.

References

1. Pastor J, Vega-Zelaya L, Pulido P, Garnés-Camarena O, Abreu A, Sola RG. Role of intraoperative neurophysiological monitoring during fluorescence-guided resection surgery. Acta Neurochir. 2013;155(12):2201–13.
2. Skinner SA, Cohen BA, Morledge DE, McAuliffe JJ, Hastings JD, Yingling CD, McCaffrey M. Practice guidelines for the supervising professional: intraoperative neurophysiological monitoring. J Clin Monit Comput. 2014;28(2):103–11.
3. Deletis V, Sala F. Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: a review focus on the corticospinal tracts. Clin Neurophysiol. 2008;119(2):248–64.
4. Buhl LK, Bastos AB, Pollard RJ, Arle JE, Thomas GP, Song Y, Boone MD. Neurophysiologic intraoperative monitoring for spine surgery: a practical guide from past to present. J Intensive Care Med. 2021;36(11):1237–49.
5. Reddy RP, Chang R, Rosario BP, Sudadi S, Anetakis KM, Balzer JR, Crammond DJ, Shaw JD, Thirumala PD. What is the predictive value of intraoperative somatosensory evoked potential monitoring for postoperative neurological deficit in cervical spine surgery?-a meta-analysis. Spine J. 2021;21(4):555–70.
6. Legatt AD, Emerson RG, Epstein CM, MacDonald DB, Deletis V, Bravo RJ, López JR. ACNS guideline: transcranial electrical stimulation motor evoked potential monitoring. J Clin Neurophysiol. 2016;33(1):42–50.
7. Park JH, Hyun SJ. Intraoperative neurophysiological monitoring in spinal surgery. World J Clin Case. 2015;3(9):765–73.
8. Calancie B. Intraoperative neuromonitoring and alarm criteria for judging MEP responses to transcranial electric stimulation: the threshold-level method. J Clin Neurophysiol. 2017;34(1):12–21.
9. Szelényi A, Hattingen E, Weidauer S, Seifert V, Ziemann U. Intraoperative motor evoked potential alteration in intracranial tumor surgery and its relation to signal alteration in postoperative magnetic resonance imaging. Neurosurgery. 2010;67(2):302–13.
10. Kim SM, Yang H, Park SB, Han SG, Park KW, Yoon SH, et al. Pattern-specific changes and discordant prognostic values of individual leg-muscle motor evoked potentials during spinal surgery. Clin Neurophysiol. 2012;123:1465–70.
11. Langeloo DD, Journée HL, de Kleuver M, Grotenhuis JA. Criteria for transcranial electrical motor evoked potential monitoring during spinal deformity surgery: a review and discussion of the literature. Clin Neurophysiol. 2007;37(6):431–9.
12. Kim K, Cho C, Bang MS, Shin HI, Phi JH, Kim SK. Intraoperative neurophysiological monitoring: a review of techniques used for brain tumor surgery in children. J Kor Neurosurg Soc. 2018;61(3):363–75.
13. Deletis V, Fernández-Conejero I. Intraoperative monitoring and mapping of the functional integrity of the brainstem. J Clin Neurol. 2016;12(3):262–73.
14. Guérit JM. Neuromonitoring in the operating room: why, when, and how to monitor? Electroencephalogr Clin Neurophysiol. 1998;106(1):1–21.
15. Matthies C, Samii M. Management of vestibular schwannomas (acoustic neuromas): the value of neurophysiology for intraoperative monitoring of auditory function in 200 cases. Neurosurgery. 1997;40(3):459–68.
16. York D. Visual evoked potentials during surgery. Handb Clin Neurophysiol. 2008;8:172–7.

Part I

Brain and Skull Base

Diffusion Tensor Imaging Technique Delineating the Prognosis for Cerebellar Mutism in Posterior Fossa Tumors: A New Tool

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Abbreviations

CMS Cerebellar mutism syndrome
DTC Dentato-thalamo-cortical tract
DTI Diffusion tensor imaging
FA Fractional anisotropy
SCP Superior cerebellar peduncle

1 Introduction

Cerebellar mutism is a morbid complication of posterior fossa surgery in children. It was described by Rebate et al. in 1985 [1, 2] and was named variedly like cerebellar mutism, ataxic mutism, cerebellar mutism syndrome, syndrome of mutism, subsequent dysarthria, and posterior fossa syndrome. In 1995, the board of the Posterior Fossa Society presented an international consensus on cerebellar mutism syndrome (CMS) [3, 4]. CMS is characterized by delayed onset mutism/reduced speech and emotional lability after cerebellar or fourth ventricular tumor surgery, along with some others features [5].

Studies reported the incidence between 11% and 29% [6]. CMS mostly occurs after surgery but may follow trauma, vascular incidents, and infections [7–9]. CMS develops within 1–6 days and may last for a few days to months. Recovery is spontaneous, most often with some deficits but occasionally complete [10, 11]. The delayed onset and spontaneous reversal suggests a secondary process such as dynamic perfusional or neurotransmitter disturbances, edema, or axonal injury [3, 12].

Patho-physiological causes for CMS have been proposed, including surgical disruption of vermis, superior cerebellar peduncle (SCP), and/or dentate thalamo cortical tracts (DTC) running in the superior cerebellar peduncle. In the past decade, diffusion tensor imaging (DTI) techniques have enormously helped in this search (Fig. 1) [2, 13].

Our study is unique in the way we compared preoperative DTI images to the post-operative images and analyzed the fractional anisotropy changes in DTC tract, thus advocating, prognosticating and revealing the main pathophysiological cause for CMS.

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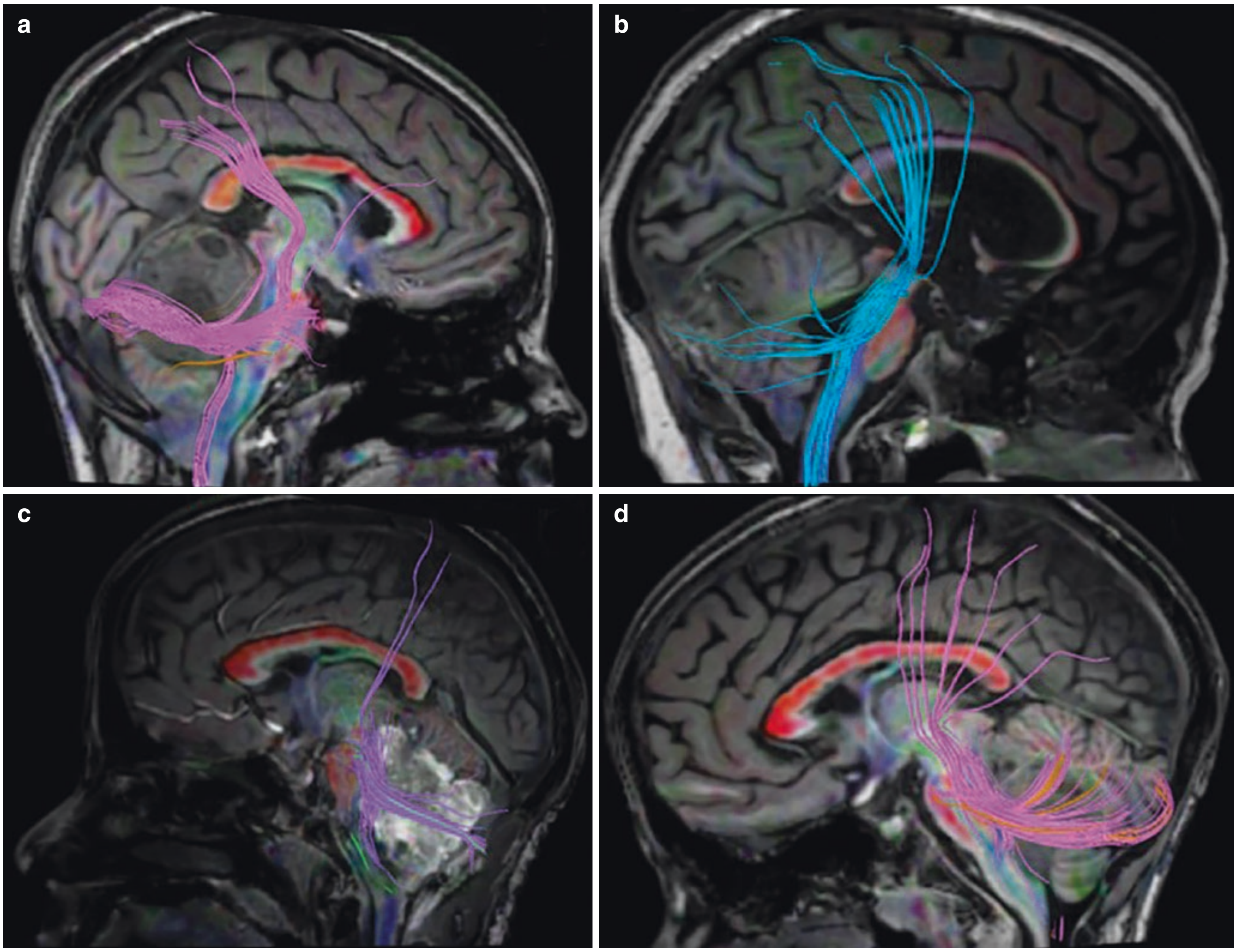

Fig. 1 MRI showing diffusion tensor imaging: (**a**, **c**) are preoperatively scans, (**b**) postoperative scan revealing destruction of DTC and patient developed CMS, (**d**) postoperative scan in which DTC fibers got better with non-occurrence of CMS

2 Materials and Methods

We had ethical committee approval for our prospective study and included 38 consecutive patients who underwent surgery for midline posterior fossa tumors in our institution between January 2019 and May 2021, with an age range of 4–49 years. Proper written consent was taken from all patients or their legal guardians and patients with relapsed tumors, former chemotherapy or radiotherapy, and mental retardation or neurobehavioral psychological problems were all excluded. Detailed clinical examination and DTI was performed preoperatively and postoperatively (within 48 h) for each patient. Speech behavior was followed for a week after surgery in all patients. All underwent midline suboccipital craniectomy, and we assessed the patient throughout their clinical course from tumor diagnosis, through development of CMS, and to the language resolution. Analysis of preoperative DTI scans was done to explore any clinical or radiographic findings that could help identify any risk factor for developing mutism. Post op. scans were assessed for changes in fractional anisotropy of white matter tracts and correlation with mutism so as to determine the causative disrupted fiber tract.

The collected data were transformed into variables, coded, and entered in Microsoft Excel. Data were analyzed and statistically evaluated using SPSS-PC-25 version. Quantitative data were tested using the Mann–Whitney "U" test, while for preoperative and postoperative comparison the Wilcoxon sign rank test was used. Qualitative data expressed in percentage were tested by chi square test or Fisher's exact test. Spearman correlation coefficient was used and p value less than 0.05 was considered statistically significant.

The magnetic resonance (MR) examinations were performed on a 3 T MR system (Philips 3 T Ingenia; Philips medical system). DTI was performed using a single-shot spin-echo echo-planar imaging pulse sequence. Images were analyzed using DTI Studio, obtaining the main eigenvector, and fractional anisotropy (FA) maps with color coding were made to define the regions of interest (ROIs) within the superior cerebellar peduncle (SCP; dentato-thalamo-cortical efferent cerebellar tract) and the middle cerebellar peduncle (MCP; cerebro-ponto-cerebellar afferent tract), and cerebellar white matter (CWM). We used anatomical landmarks to identify the SCP that formed the wall of the fourth ventricle and was noted to be medial and superior to the MCP, which was visualized as a large white fiber tract linking the pons and the cerebellar hemisphere. Manual ROIs within the right and left SCPs, MCPs, and right and left CWM MCPs, and the average FA within the ROI for each white matter tract were recorded.

3 Results

A total of 38 patients were included in our study, who were divided into two groups. Group A included patients who did not develop CMS, and group B had patients who developed CMS. Only five of all 38 developed mutism, four (80%) of which were male. No significant difference was seen in gender in both the groups (p value: 1.0). CMS developed at a mean-age of 9.4 years in group B, unlike the mean-age of 22.72 years in group A (p value: 0.02). Brainstem compression and the location of tumor also did not correlate with CMS (p value >0.15). Maximum and minimum tumor sizes in group A were 58 mm and 14 mm, respectively, and 64 and 40 mm in group B. The average tumor size of 5 cm is strongly correlated with the development of CMS (p value 0.02). All patients with CMS had midline tumors (p value 0.15).

In group A, 11 patients were operated via the telovelar approach, five via transvermian, and the remaining patients via the transcerebellar approach, whereas in in group B all underwent the transvermian approach. Incision in the superior part of vermis (p value <0.001) and resection of tumor involving SCP (p value <0.001) was a significant risk factor for development of CMS, whereas complete total resection was done in nine patients of group A and three patients of group B (p value <0.06) (Table 1).

Residual lesions were found in the cerebellar hemisphere, fourth ventricle floor, vermis, fourth ventricle wall, and SCP in decreasing order but did not signify CMS (Table 1). Histology included medulloblastoma and pilocytic astrocytoma in most cases, but group B patients had medulloblastoma only.

We noted and compared the fractional anisotropy values (FA values) in left and right SCP, MCP, and left and right CBW in all patients preoperatively and postoperatively (Table 2).

A statistically significant difference was noted between postoperative and preoperative FA values of the

Table 1 Intraoperative features noted for Group A non-CMS patients, Group B CMS patients

	Group A (n = 33)	Group B (n = 5)	Total (n = 38)	
Parameters	Non-CMS	CMS		p value
Part of vermis resected				
Inferior	1 (3.0%)	0	1 (2.6%)	1.0
Middle	6 (18.2%)	2 (40.0%)	8 (21.1%)	0.27
Superior	0	5 (100.0%)	5 (13.2%)	<0.001
Estimated tumor resection at surgery				
Complete	17 (51.5%)	5 (100.0%)	22 (57.9%)	0.06
Incomplete	16 (48.5%)	0	16 (42.1%)	
Superior cerebellar peduncle involvement				
No	32 (97.0%)	0	32 (84.2%)	<0.001
Yes	1 (3.0%)	5 (100.0%)	6 (15.8%)	
Extent of resection				
Complete	9 (27.3%)	3 (60.0%)	12 (31.6%)	0.30
Near total	10 (30.3%)	2 (40.0%)	12 (31.6%)	0.64
Partial	10 (30.3%)	0	10 (26.3%)	0.29
Subtotal	4 (12.1%)	0	4 (10.5%)	1.0
Residual lesion				
Fourth ventricle floor	7 (21.2%)	0	7 (18.4%)	0.56
Fourth ventricle lateral wall	1 (3.0%)	0	1 (2.6%)	1.0
Vermis	4 (12.1%)	0	4 (10.5%)	1.0
Superior cerebellar peduncles	1 (3.0%)	0	1 (2.6%)	1.0
Cerebellar hemisphere	10 (30.3%)	0	10 (26.3%)	0.29

Table 2 DTI parameters fractional anisotropy (FA) values for right and left superior cerebellar peduncle (SCP), middle cerebellar peduncle (MCP), and right and left cerebellar white matter tract (CBW) pre-operatively and post-operatively

Parameters	Group A (n = 33) Non-CMS	Group B (n = 5) CMS	p value group
Left SCP			
Preop	0.445 ± 0.066	0.480 ± 0.063	0.34
Postop	0.445 ± 0.064	0.398 ± 0.062	0.15
p value b/w preop and postop	0.76	0.04	
Right SCP			
Preop	0.434 ± 0.054	0.475 ± 0.061	0.15
Postop	0.434 ± 0.054	0.407 ± 0.050	0.17
p value b/w preop and postop	0.29	0.04	
MCP			
Preop	0.484 ± 0.061	0.459 ± 0.030	0.25
Postop	0.483 ± 0.060	0.457 ± 0.031	0.29
p value b/w preop and postop	0.22	0.58	
Left CBW			
Preop	0.450 ± 0.067	0.427 ± 0.048	0.33
Postop	0.448 ± 0.060	0.424 ± 0.049	0.32
p value b/w preop and postop	0.12	0.49	
Right CBW			
Preop	0.454 ± 0.077	0.412 ± 0.095	0.36
Postop	0.454 ± 0.076	0.409 ± 0.102	0.34
p value b/w preop and postop	0.69	0.50	

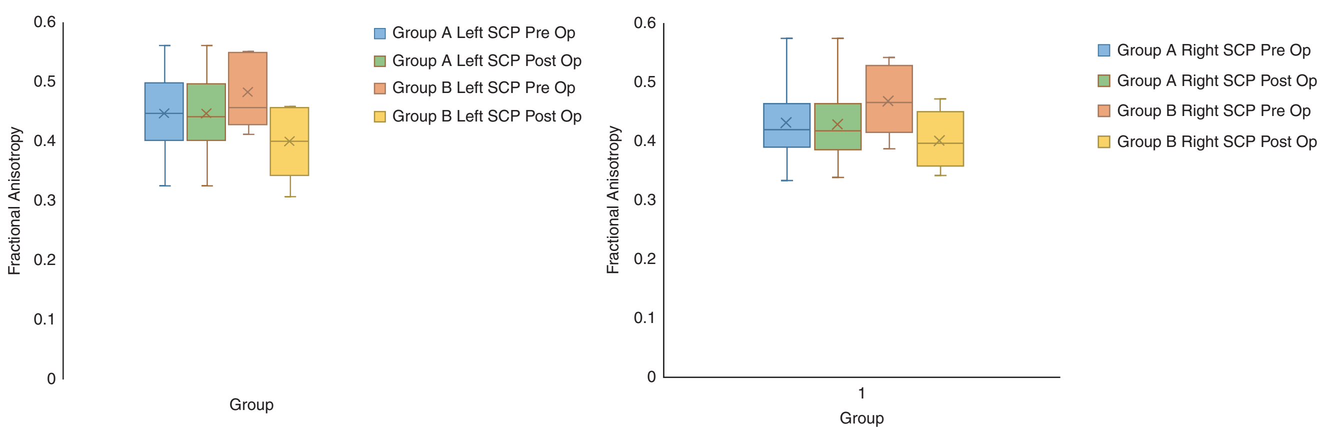

Fig. 2 Boxplot showing comparison of preoperative and postoperative fractional anisotropy (FA) values between both groups A-Non CMS & B -CMS post surgery in right and left superior cerebellar peduncle (SCP)

SCP (p value <0.01). For the entire group B cohort, a statistically significant decrease in SCP FA value was noted postoperatively. Mean FA of MCP and CBW preoperatively and postoperatively was not found to be significantly associated with development of CMS (Table 2). The boxplot graphs (Fig. 2) reveal the conclusion that only SCP correlated with the mutism occurrence and not the CBW or MCP (Fig. 3).

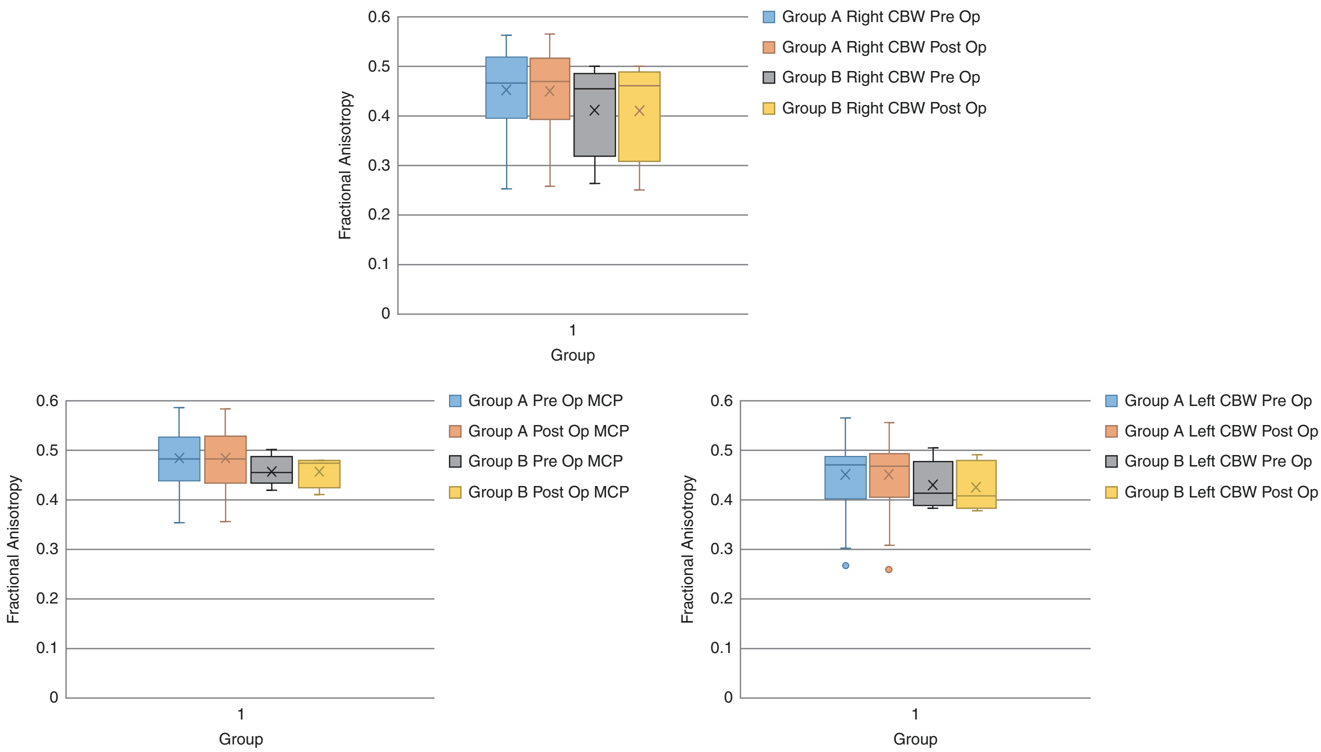

Fig. 3 Boxplot showing comparison of preoperative and postoperative fractional anisotropy (FA) values between both groups A-Non CMS & B-CMS post surgery in right and left cerebellar white matter (CBW) and middle cerebellar peduncle (MCP)

4 Discussion

The pathophysiological cause of post-surgical CMS has been evolving for the past few years, with a proposal of vermis by Daiely et al. in 1995, and the dentato-thalamo-cortical pathway within superior cerebellar peduncle by Morris et al. in 2009 [13–15].

We had 13% incidence of CMS, which is quite lower than the reported incidence in the other studies. Of the patients with CMS, 80% were male in our study which was also observed by Catsman-Berrevoets et al., though no sex predilection was shown in the study by McEvoy et al. [6, 16, 17].

Age correlation with the presence of CMS was not seen like in the studies by Iidan et al. and Marie et al. [18, 19].

In our study only midline tumors developed CMS, similar to the Kotil et al. study reporting a 6–7 times greater risk [20]. Tumors of size >5 cm, predilects mutism, similar to that reported by Gora et al., although Sean et al. found no size affiliation [17, 21]. Mussi and Rhoton proposed the telovelar approach rather than the transvermian approach, our results also advocates the same as all CMS patients underwent surgery via the transvermian approach [22].

CMS only appeared in medulloblastomas cases unlike other studies, which may be due to aggressive surgery in medulloblastomas leading to tract injury [21].

DTI helps to study the anatomic substrates by quantitative measurement of anisotropy with a map of fractional anisotropy (FA) for these tracts within the cerebellar peduncles with different colors using tractography algorithms with 3D visualization based on eigenvectors and eigen values [23].

Law et al. found that the right cerebello thalamus cerebral pathway was significantly compromised, whereas Ojemann et al., McEvoy, and Morris et al. suggested disruption of SCP to be the causative factor. It is indeed the DTC tract within the SCP that gets disrupted [13, 17, 24, 25].

The majority of cerebellar projections (75%) to the primary motor cortex (M1) come from the dentate nucleus [26, 27]. These dentate fibers pass through the ipsilateral superior cerebellar peduncle, tegmental decussation, and synapse with the contralateral ventrolateral thalamic nucleus, from where the second order axons arise to terminate in the primary motor cortex as well as secondary and tertiary association areas within the frontal and parietal lobes. Thus, cerebellum influences planned motor activity as well as cognition and behavior. The dentate nucleus has evolved in humans, especially in its ventral part, thus controlling the non-motor functions unlike monkeys [28].

In our prospective study, we noticed marked changes in the FA values, preoperatively and postoperatively, of the DTC tract within SCP in CMS patients. In Fig. 1a, b, DTI

Table 3 Comparison of the change between the pre-operative and post-operative FA values in both groups, separately for superior cerebellar peduncle (SCP), middle cerebellar peduncle (MCP), and cerebellar white matter tract (CBW)

	Group A (*n* = 33)	Group B (*n* = 5)	
Change in FA value b/w preop and postop	Non-CMS	CMS	*p* value
Left SCP	0.016 ± 0.012	0.082 ± 0.038	<0.01
Right SCP	0.018 ± 0.010	0.068 ± 0.042	<0.01
MCP	0.012 ± 0.007	0.002 ± 0.014	0.10
Left CBW	0.016 ± 0.014	0.002 ± 0.007	<0.01
Right CBW	0.012 ± 0.012	0.002 ± 0.008	0.10

preoperative and postoperative is shown, which reveals destruction of the DTC tract and development of CMS, and in Fig. 1c, d, the DTC fibers got better postoperatively and patients had no occurrence of CMS. No such alterations were seen in the white matter of MCP or CBW. Similar results were obtained by Kusano et al. and Morris et al., who were the first to use DTI in their study, and also by a recent study from Berlin as well [23, 29, 30]. We analyzed the FA value changes of all three tracts right and left CBW, MCP, and right and left SCP; plotting in the boxplot graph revealed only the SCP changes significantly correlated with the mutism occurrence (Fig. 2). The graph shows the comparison between preoperative and postoperative FA values in all tracts and makes the SCP the primary substrate.

Our study shows that the FA values diminution of SCP, actually of the DTC tract, is the sole cause for mutism; therefore, any attempt to prevent injury to the DTC tract or anatomically the SCP during surgery can be helpful in preventing the morbid mutism in a large number of pediatric patients with posterior fossa tumors.

With this thought in mind, we searched the literature to know how to identify DTC tract intraoperatively like the facial nerve. Neurophysiological monitoring of the cerebellum and posterior fossa connection is not frequent and is mostly limited to the cranial nerve nuclei and brainstem.

Iwata and Ugawa in extraoperative settings demonstrated EMG changes following transcranial magnetic stimulation of motor cortex M1, when modulation by cerebellar stimulation was applied in time difference, decrement when applied at 5–8 milliseconds (ms) and facilitation when done within 3 ms. This normal physiology was not seen in patients with lesions affecting the cerebellar hemisphere, dentate nucleus, superior cerebellar peduncle, and motor thalamus, while it was maintained in patients with lesions affecting the middle cerebellar peduncle or pontine nucleus. Thus, confirming the cerebellar modulation of motor activity via the DTC pathway [31].

Thus, if cerebello-M1 modulation is used intraoperatively as a monitoring technique, it can reflect injury to the DTC pathway, ultimately helping in functional outcome of children. Though it appears difficult,

Giampiccolo et al. recently published a study on the feasibility of cerebello-cortical stimulation for intraoperative neurophysiological monitoring of cerebellar mutism and found positive results [32].

Therefore, DTC neuromonitoring can be the future trend in pediatric posterior fossa surgeries.

Since we propose DTC within the SCP as the primary structure responsible for the development of CMS, surgical strategies should be used and developed for intraoperative DTC neuromonitoring, to protect it and thereby prevent CMS (Table 3).

5 Conclusion

CMS is a frequent complication of posterior fossa surgery and the DTC tract is strongly proposed as the pathophysiological substrate. Injury to the DTC tract should be prevented with the help of DTI FA maps and exploring the newer avenues in intraoperative neuro-monitoring, to prevent morbid CMS.

References

1. Rekate HL, Grubb RL, Aram DM, Hahn JF, Ratcheson RA. Muteness of cerebellar origin. Arch Neurol. 1985;42:697–8.
2. Pollack IF, Polinko P, Albright AL, Towbin R, Fitz C. Mutism and pseudobulbar symptoms after resection of posterior fossa tumors in children: incidence and pathophysiology. Neurosurgery. 1995;37:885–93.
3. Gudrunardottir T, Sehested A, Juhler M, Schmiegelow K. Cerebellar mutism: review of the literature. Childs Nerv Syst. 2011;27:355–63.
4. Gudrunardottir T, De Smet H, Bartha-Doring L, Van Dun K, Verhoeven J, Paquier P, et al. Posterior fossa syndrome and cerebellar mutism. In: Mariën P, Monti M, editors. The linguistic cerebellum. 1st ed. Oxford: Academic Press, Elsevier; 2015. p. 257–81.
5. Gudrunardottir T, Morgan AT, Lux AL, Walker DA, Walsh KS, Wells EM, et al. Consensus paper on post-operative pediatric cerebellar mutism syndrome: the Iceland Delphi results. Childs Nerv Syst. 2016;32:1195–203.
6. Robertson PL, Muraszko KM, Holmes EJ, Sposto R, Packer RJ, Gajjar A, Dias MS, Allen JC. Incidence and severity of postoperative cerebellar mutism syndrome in children with medulloblastoma: a prospective study by the Children's Oncology Group. J Neurosurg. 2006;105:444–51.
7. Erşahin Y, Mutluer S, Saydam S, Barçin E. Cerebellar mutism: report of two unusual cases and review of the literature. Clin Neurol Neurosurg. 1997;99:130–4.

8. Shiihara T, Watanabe M, Honma A, Kato M, Morita Y, Ichiyama T, Maruyama K. Rotavirus associated acute encephalitis/encephalopathy and concurrent cerebellitis: report of two cases. Brain and Development. 2007;29:670–3.
9. Miyakita Y, Taguchi Y, Sakakibara Y, Matsuzawa M, Kitagawa H. Transient mutism resolving into cerebellar speech after brain stem infarction following a traumatic injury of the vertebral artery in a child. Acta Neurochir. 1999;141:209–13.
10. Gelabert-González M, Fernández-Villa J. Mutism after posterior fossa surgery. Review of the literature. Clin Neurol Neurosurg. 2001;103:111–4.
11. Turgut M. Transient "cerebellar" mutism. Childs Nerv Syst. 1998;14:161–6.
12. McMillan HJ, Keene DL, Matzinger MA, Vassilyadi M, Nzau M, Ventureyra EC. Brainstem compression: a predictor of postoperative cerebellar mutism. Childs Nerv Syst. 2009;25:677–81.
13. Morris EB, Phillips NS, Laningham FH, Patay Z, Gajjar A, Wallace D, Boop F, Sanford R, Ness KK, Ogg RJ. Proximal dentato thalamo cortical tract involvement in posterior fossa syndrome. Brain. 2009;132:3087–95.
14. Dailey AT, McKhann GM II, Berger MS. The pathophysiology of oral pharyngeal apraxia and mutism following posterior fossa tumor resection in children. J Neurosurg. 1995;83:467–75.
15. Puget S, Boddaert N, Viguier D, Kieffer V, Bulteau C, Garnett M, Callu D, Sainte-Rose C, Kalifa C, Dellatolas G, Grill J. Injuries to inferior vermis and dentate nuclei predict poor neurological and neuropsychological outcome in children with malignant posterior fossa tumors. Cancer. 2009;115:1338–47.
16. Catsman-Berrevoets CE, Van Breemen M, van Veelen ML, Appel IM, Lequin MH. Supratentorial arterial ischemic stroke following cerebellar tumor resection in two children. Pediatr Neurosurg. 2005;41:206–11.
17. McEvoy SD, Lee A, Poliakov A, Friedman S, Shaw D, Browd SR, Ellenbogen RG, Ojemann JG, MacDonald CL. Longitudinal cerebellar diffusion tensor imaging changes in posterior fossa syndrome. NeuroImage Clin. 2016;12:582–90.
18. Ildan F, Tuna M, Erman T, Gocer AI, Zeren M, Cetinalp E. The evaluation and comparison of cerebellar mutism in children and adults after posterior fossa surgery: report of two adult cases and review of the literature. Acta Neurochir. 2002;144:463–73.
19. Mariën P, De Smet HJ, Wijgerde E, Verhoeven J, Crols R, De Deyn PP. Posterior fossa syndrome in adults: a new case and comprehensive survey of the literature. Cortex. 2013;49:284–300.
20. Kotil K, Eras M, Akçetin M, Bilge T. Cerebellar mutism following posterior fossa tumor resection in children. Turk Neurosurg. 2008;18:89–94.
21. Gora NK, Gupta A, Sinha VD. Cerebellar mutism syndrome following midline posterior fossa tumor resection in children: an institutional experience. J Pediatr Neurosci. 2017;12:313–9.
22. Mussi ACM, Rhoton AL Jr. Telovelar approach to the fourth ventricle: microsurgical anatomy. J Neurosurg. 2000;92(5):812–23.
23. Mori S, van Zijl PC. Fiber tracking: principles and strategies—a technical review. NMR Biomed. 2002;15:468–80.
24. Law N, Greenberg M, Bouffet E, Taylor MD, Laughlin S, Strother D, et al. Clinical and neuroanatomical predictors of cerebellar mutism syndrome. Neuro-Oncology. 2012;14:1294–303.
25. Ojemann JG, Partridge SC, Poliakov AV, Niazi TN, Shaw DW, Ishak GE, Lee A, Browd SR, Geyer JR, Ellenbogen RG. Diffusion tensor imaging of the superior cerebellar peduncle identifies patients with posterior fossa syndrome. Childs Nerv Syst. 2013;29:2071–7.
26. Hoover JE, Strick PL. The organization of cerebellar and basal ganglia outputs to primary motor cortex as revealed by retrograde transneuronal transport of herpes simplex virus type 1. J Neurosci. 1999;19(4):1446–63.
27. Dum RP, Strick PL. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. J Neurophysiol. 2003;89(1):634–9. https://doi.org/10.1152/jn.00626.2002.
28. Matano S. Brief communication: proportions of the ventral half of the cerebellar dentate nucleus in humans and great apes. Am J Phys Anthropol. 2001;114(2):163–5. https://doi.org/10.1002/1096-8644(200102)114:23.0.CO;2-F.
29. Soelva V, Hernáiz Driever P, Abbushi A, Rueckriegel S, Bruhn H, Eisner W, et al. Fronto-cerebellar fiber tractography in pediatric patients following posterior fossa tumor surgery. Childs Nerv Syst. 2013;29:597–607.
30. Kusano Y, Tanaka Y, Takasuna H, Wada N, Tada T, Kakizawa Y, et al. Transient cerebellar mutism caused by bilateral damage to the dentate nuclei after the second posterior fossa surgery. Case report. J Neurosurg. 2006;104:329–31.
31. Iwata NK, Ugawa Y. The effects of cerebellar stimulation on the motor cortical excitability in neurological disorders: a review. Cerebellum. 2005;4(4):2018–23. https://doi.org/10.1080/14734220500277007.
32. Giampiccolo D, Basaldella F, Badari A, Squintani GM, Cattaneo L, Sala F. Feasibility of cerebello-cortical stimulation for intraoperative neurophysiological monitoring of cerebellar mutism. Childs Nerv Syst. 2021;37(5):1505–14. https://doi.org/10.1007/s00381-021-05126-7.

Image-Guided Surgery in Complex Skull Base and Facial Fractures: Initial Experience on the Role of Intra-Operative Computer Tomography

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1 Introduction

Cranio-facial fractures (CFF) are often a challenge because of the complexity of the anatomy region and the great number of vital structures that are located and protected by the cranio-facial bones. Anterior skull base fractures, especially, involves the intracranial compartment with the possibility of a cerebrospinal fluid (CSF) leak and the orbit with its contents. Indeed, repair of complex CFF involves more than simply "putting the pieces together." The goals of surgery include to repair or prevent CSF leaks, prevent enophthalmos/hypoglobus, diplopia, reduction of visual acuity, nerves sensory loss, restoration of occlusion, mastication and reconstruction of an esthetic and symmetric facial skeleton [1, 2]. The complex anatomy of the region and their pathological modifications makes this surgery a real challenge for surgeons and the reported rate of revision is approximately 15% [3]. In recent years, we have tested the efficacy of the intraoperative use of portable CT scans (iCT) (portable 8-slices small-bore CT scanner -CereTom®; NeuroLogica, Danvers, MA, USA, and a portable full-body 32-slice CT scanner -BodyTom® Elite, NeuroLogica, Danvers, MA, USA) for gliomas surgery [4–8]. The aim of this paper is to retrospectively evaluate our experience of iCT in CFF surgery to establish if this tool can improve the safety of this complex surgery.

2 Materials and Methods

A retrospective case control study on using intraoperative CT for a multidisciplinary approach (i.e., cranio-maxillofacial and neurosurgical) to cranio-facial complex fractures has been performed. Data has been prospectively collected and different variables have been analyzed. The preoperative diagnosis, fracture patterns, number of scans/patient, and any changes in surgical procedure based on the information obtained from the CT scan and operative report were recorded and collected.

For this study, consecutive patients suffering from facial fractures were selected and no distinction of age, sex, or ethnicity was made: a total number of 12 patients, 10 males and 2 females was included in this study.

In all cases, fractures were caused by high-energy trauma, with a constant involvement of skull-base and facial bones. Eight patients needed the ICU before and after surgery because of serious general conditions related to the trauma. Cases with brain swelling or intracranial hemorrhages requiring emergency surgical treatment were excluded.

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Indeed, all the cases included in the present study underwent elective surgery, after stabilizing general conditions.

The study population was divided into two groups "case" and "control."

The case group (total six patients) included all those who underwent intraoperative CT, while the control group (total six patients) included all the patients treated without intraoperative CT.

Data were collected from January 2018 to June 2021. Two neuronavigation systems were used for intraoperative neuronavigation (StealthStation S7 and Stealth station S8 Medtronic, Minneapolis, MN, USA). For the acquisition of intraoperative images, the following devices were used: a small-bore 8-slice portable CT scanner and 32-slice portable CT scanner with 85 cm gantry (Bodytom; Samsung-Neurologica, Danvers, MA, USA), respectively. Patients in the case group were operated on using radiolucent skull clamp and pre-operative and intra-operative scans were acquired. An intra-operative CT scan was used to check, according to surgeons' point of view, the accuracy of reconstruction and to visualize complications early. All surgeries were performed by a multidisciplinary team, including neurosurgeons and maxillofacial surgeons. Post-operative CT scans were collected for the objective analysis of the accuracy (Figs. 1, 2 and 3).

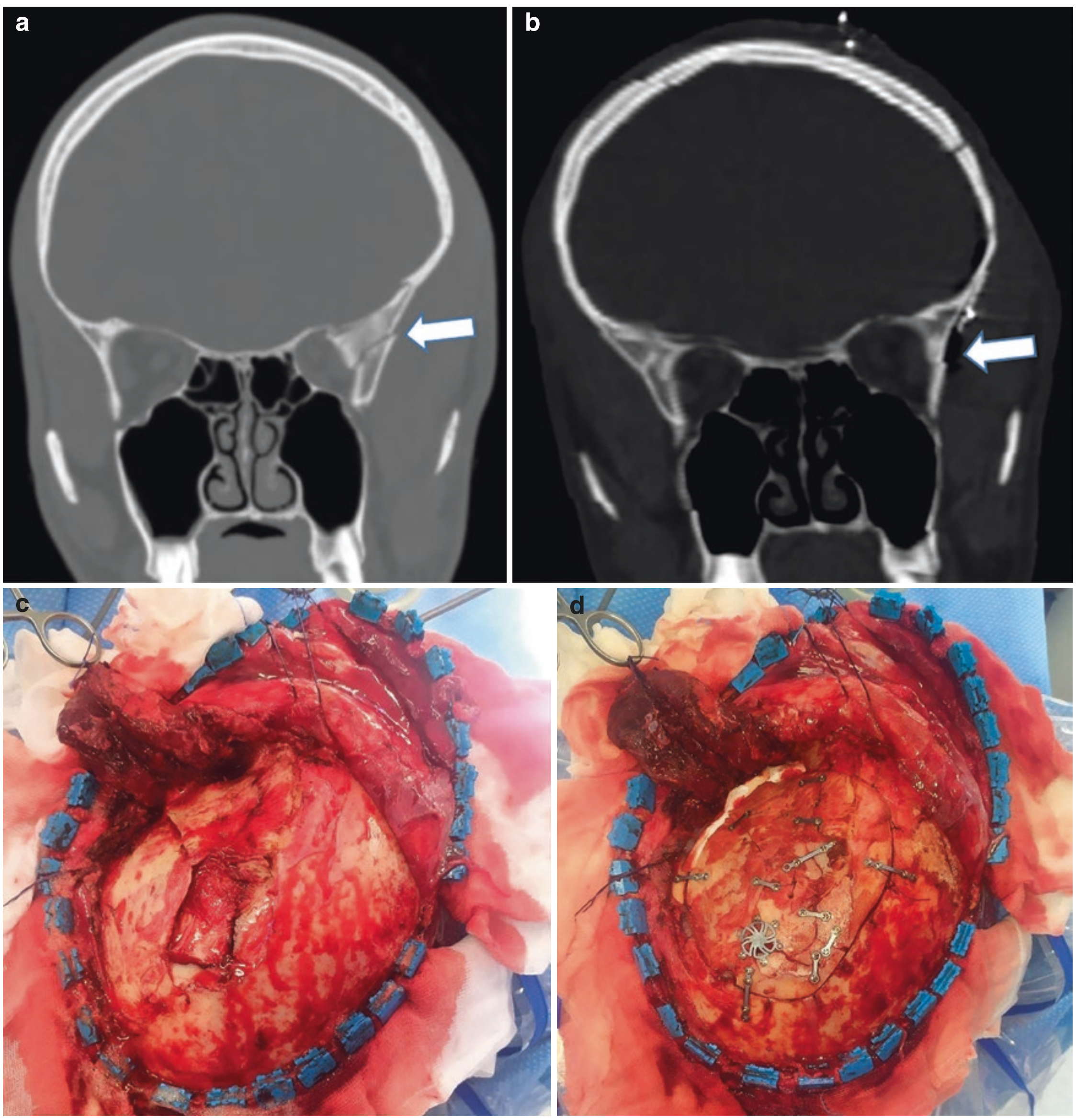

Fig. 1 Image A shows a coronal section of a CT scan with the evidence of a depressed fracture of left fronto-temporo-parietal bones involving the sphenoid wing. White arrow indicates the orbital fracture with compression of the orbital content. Image B shows the intraoperative orbital decompression. In C and D, the intraoperative view before and after treatment

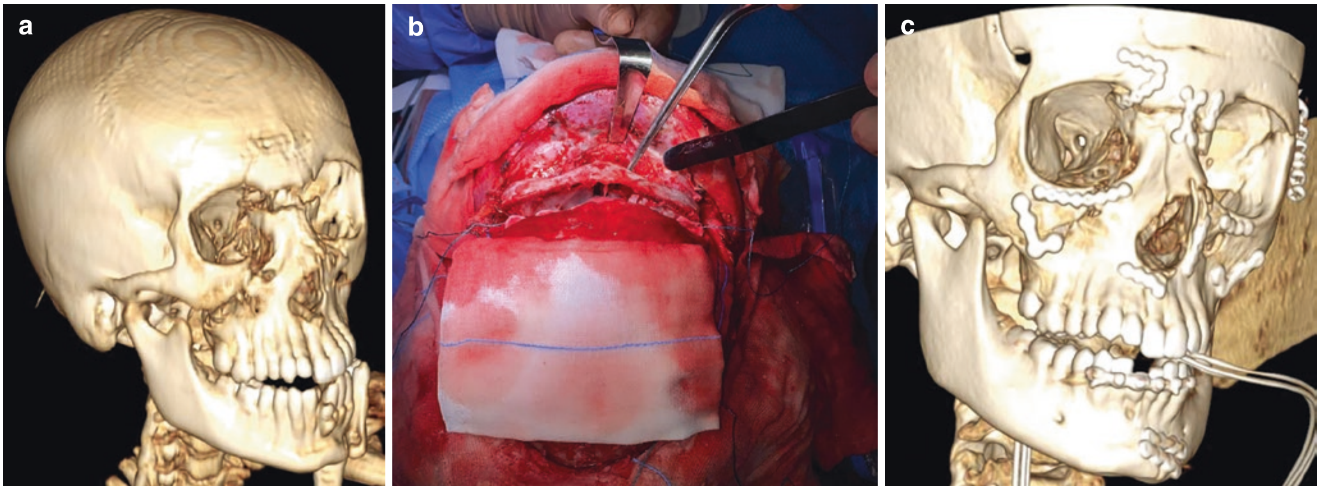

Fig. 2 Image A shows a 3D reconstruction of a complex trauma with craniofacial disconnection, in B we can see an intraoperative view of a surgical approach. In image C the radiological post-operative results

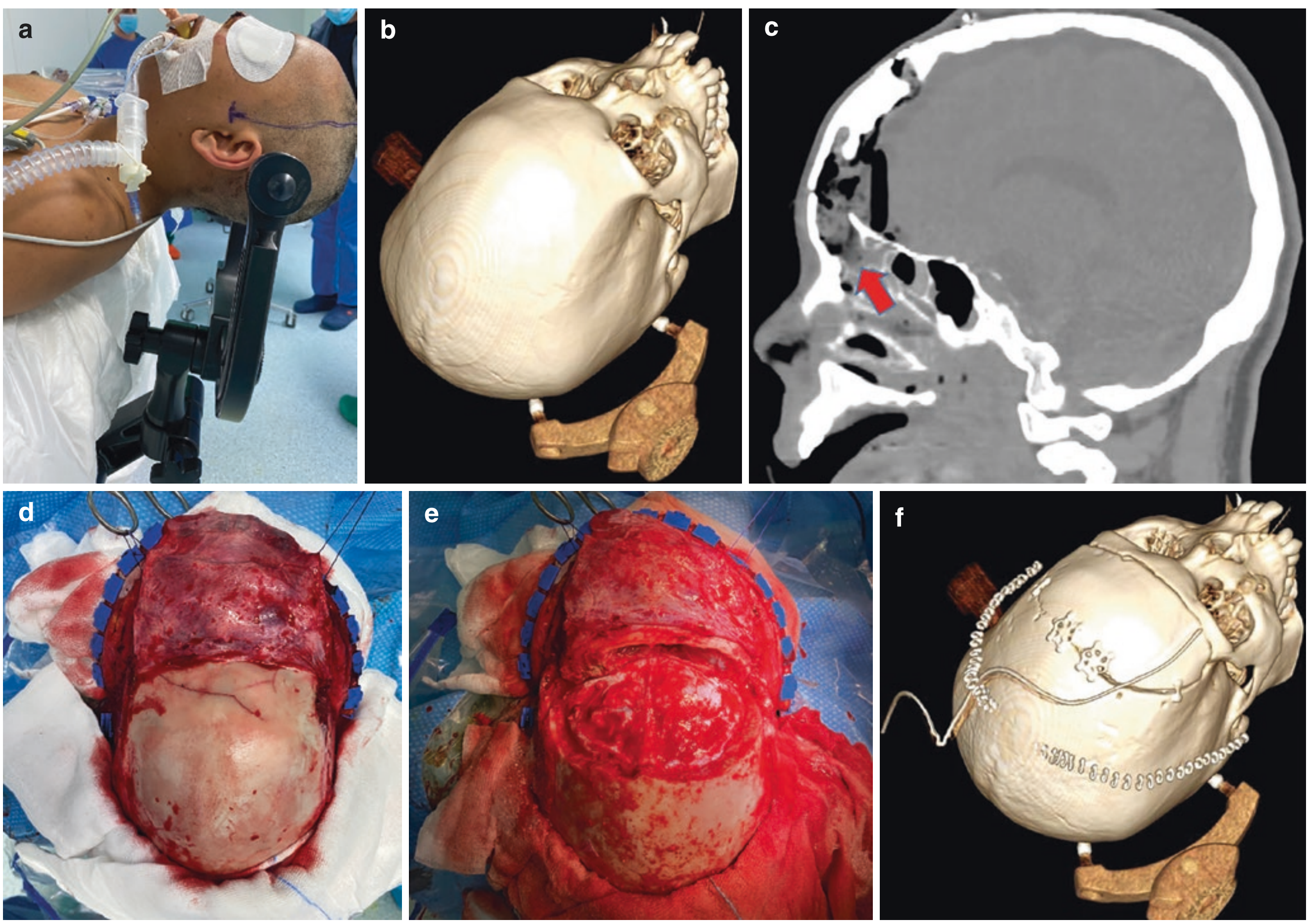

Fig. 3 Image A shows a patient positioned with radiolucent Mayfield clamp; in B we can see the intraopreoperative CT scan. D and E show the bi-coronal approach step by step, while in C we can see the intraoperative CT scan with the evidence of fat plug in the correct position (red arrow). F depicts the post-operative result

DICOM data of each CT scan were imported in Mimics Research 19.0 software (Materialize NV, Leuven, Belgium), a range of grayscale values of each radiographic volume—thresholding—was set and a three-dimensional (3D) reconstructions of the patient's bone tissue was performed.

The 3D image was obtained then imported on 3-Matic research design software 11.0 (Materialize NV, Leuven, Belgium) to generate the "mirror" of the skull in respect to the sagittal plane. To obtain reproducible and objective data, the same anthropometric parameters as the distance intercanthal side, distance intercanthal medial, glabella, zygion, gonion, and floor sagittal were set. A colorimetric map scale analysis was performed to evaluate the differences in millimeters for each point of the patient's bone tissue with respect to the evaluated mirror (Fig. 4). A comparative analysis of the accuracy of reconstruction based on intra- or postoperative TC was made and the average distances between the reconstructed fracture and the normal anatomy were recorded and compared in the case and control groups. Changes of the surgical strategy and complications have also been recorded. The statistical analysis was carried out using SPSS (v.20.0, SPSS Inc., U.S.A).

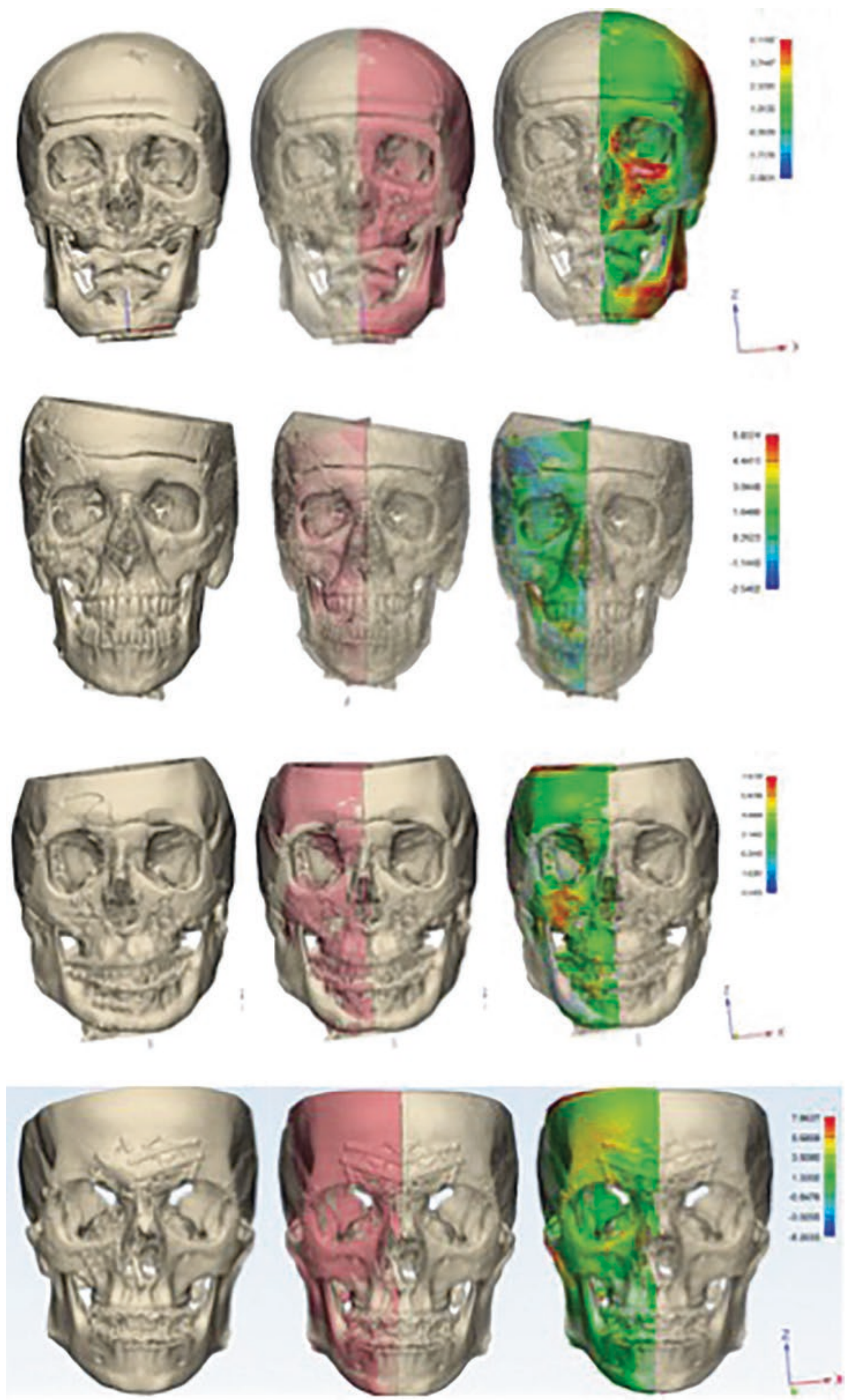

Fig. 4 The application of the mirroring method to measure the accuracy of fracture reconstruction is demonstrated in this picture

3 Results

The analysis of accuracy of reconstruction, performed by the mirroring method described above, demonstrated an average value of distances constantly lower in the case group compared with the control group (Table 1). All differences measured on different spatial plans were statistically significant. These data are related to the higher accuracy of reconstruction in cases performed with i-CT. Changes of surgical strategy (i.e., replacement of micro-plates, re-orientations of bony fragments) were realized in 4 out of 6 cases in the i-CT group. The incidence of re-operation rate was the same in two groups: in one case of i-CT group and in one case of control group further surgery was required because of recurrent CSF leakage. One patient in the case group and one patient in the control group died because of deterioration of general conditions (not related with cranio-facial surgery). Data were tested for normality through the Shapiro–Wilk test and were normally distributed in all cases (SPSS). Thus, parametric statistical analysis was applied: average and analysis of variance (ANOVA) were performed (Fig. 5).

Table 1 Accuracy analysis using the mirroring method: the results of accuracy according to different spatial plans are summarized

Reference plan	Case group Average distance in mm	Standard deviation	Control group Average distance in mm	Standard deviation
Transverse plane	4,9984	0,6832	5,3569	0,6219
Sagittal plane	1,5396	0,49164	1,6227	0,9685
Frontal plane	-3,5917	1,149	-3,2472	1,2299

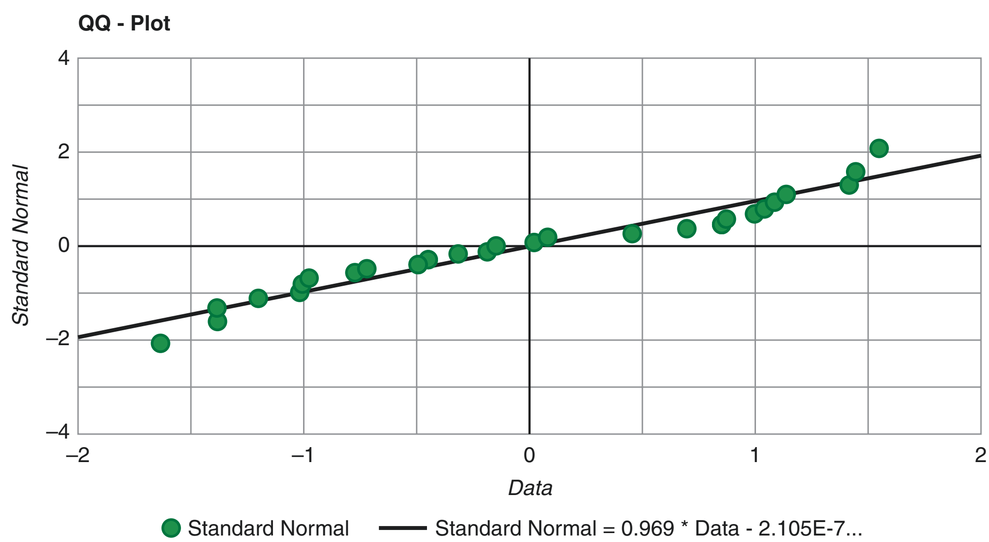

Fig. 5 Results of statistical analysis are summarized in this figure

4 Discussion

Surgery of craniofacial fractures represent a challenge both for neurosurgeons and maxillo-facial surgeons. Combined, a multidisciplinary approach is related to the best clinical result, as it allows, through a unique surgical procedure, skull base, meningeal, and facial reconstruction and management of concomitant brain lesion. The basic goal of craniofacial fractures surgery is to achieve the best clinical and radiological result in a single-stage effective surgery, reducing the impact of complications. In this scenario, the assistance of technologies and tools such as neuronavigation or intraoperative imaging devices may play an important role in increasing the safety and effectiveness of surgery. The use of neuronavigation is the standard of care in different neurosurgical procedures, and its use is also extending to maxillofacial surgery. Some authors report their experience using neuronavigation in the surgical management of facial surgery, with promising results. They highlighted the importance of neuronavigation to increase the precision of fractures' reduction [9–11]. However, the role of intraoperative devices such as intraoperative CT-scan in facial surgery has not been well described, as the availability of CT scanners is limited to a few selected centers. Conversely, the role of i-CT in neurosurgery is well defined and the importance of this tool in brain tumor surgery has been reported by several papers [4–8].

In this preliminary case control study, we investigated the role of i-CT in complex cranio-facial multidisciplinary surgery. The accuracy of reconstruction was measured with a computerized mirroring method, based on a three-dimensional reconstructed CT scan. The method proposed to objectively evaluate the accuracy is widely used in maxillofacial surgery, particularly for pre-operative planning. In our study, we used the same method to measure the impact of i-CT in accuracy of reconstruction of complex cranio-facial surgery. In our vision, i-CT may drastically change the approach to this challenging pathology adding more information compared with neuronavigation. Indeed, the availability of multiplanar or 3D images of reconstruction before closure is definitely associated with a better outcome. Moreover, the correction of skull base fractures can be effectively and safely made, as i-CT allows intraoperative correction of unsatisfactorily reduced fractures, particularly in those cases where a direct visual control of correction is not feasible (i.e., orbital, sphenoidal fractures).

Another interesting finding of our study is related to the lack of differences in complication rate comparing the two groups. Despite a statistically significant positive impact of i-CT in accuracy of reconstruction, we did not find any difference in complication and re-operation rate. In all cases requiring revision surgery in both groups, persistent CSF leakage was observed.

This study has some limitations. Data are preliminary and, albeit prospectively collected, they have been retrospectively analyzed. We did not perform randomization to include patients, and enrollment in the case or control group was made only according to the availability of the intraoperative CT scanner. Moreover, the sample is very small and statistical analysis is not conclusive. However, the importance of this study is related to the demonstration of the feasibility and effectiveness of intraoperative CT scans in patients with complex cranio-facial fractures. Preliminary data documented a potential superiority of i-CT guided surgery in comparison to traditional surgery in terms of accuracy and safety.

5 Conclusion

This study analyzes preliminary results of the application of i-CT in multidisciplinary surgery of cranio-facial fractures. Further studies and larger clinical series should be performed to address the role of intraoperative imaging guidance in skull base and maxillofacial surgery.

References

1. Cuddy K, Khatib B, Bell RB, Cheng A, Patel A, Amundson M, et al. Use of intraoperative computed tomography in Craniomaxillofacial trauma surgery. J Oral Maxillofac Surg. 2018;76:1016–25. https://doi.org/10.1016/j.joms.2017.12.004.
2. Morrison CS, Taylor HO, Collins S, Oyelese A, Sullivan SR. Use of intraoperative computed tomography in complex craniofacial trauma: an example of on-table change in management. Craniomaxillofac Trauma Reconstr. 2014;7:298–301. https://doi.org/10.1055/s-0034-1378179.
3. Shyu VB, Chen H-H, Chen C-H, Chen C-T. Clinical outcome following intraoperative computed tomography-assisted secondary orbital reconstruction. J Plast Reconstr Aesthet Surg. 2021;74:341–9. https://doi.org/10.1016/j.bjps.2020.08.049.
4. Barbagallo GMV, Morrone A, Certo F. Intraoperative computed tomography and awake craniotomy: a useful and safe combination in brain surgery. World Neurosurg. 2018;119:e159–66. https://doi.org/10.1016/j.wneu.2018.07.078.
5. Barbagallo GMV, Palmucci S, Visocchi M, Paratore S, Attinà G, Sortino G, et al. Portable intraoperative computed tomography scan in image-guided surgery for brain high-grade gliomas: analysis of technical feasibility and impact on extent of tumor resection. Oper Neurosurg (Hagerstown). 2016;12:19–30. https://doi.org/10.1227/NEU.0000000000001112.
6. Barbagallo G, Maione M, Peschillo S, Signorelli F, Visocchi M, Sortino G, et al. Intraoperative computed tomography, navigated ultrasound, 5-amino-levulinic acid fluorescence and neuromonitoring in brain tumor surgery: overtreatment or useful tool combination? J Neurosurg Sci. 2019; https://doi.org/10.23736/S0390-5616.19.04735-0.

7. Barbagallo GMV, Altieri R, Garozzo M, Maione M, Di Gregorio S, Visocchi M, et al. High grade glioma treatment in elderly people: is it different than in younger patients? Analysis of surgical management guided by an intraoperative multimodal approach and its impact on clinical outcome. Front Oncol. 2020;10:631255. https://doi.org/10.3389/fonc.2020.631255.
8. Barbagallo GMV, Certo F, Di Gregorio S, Maione M, Garozzo M, Peschillo S, et al. Recurrent high-grade glioma surgery: a multimodal intraoperative protocol to safely increase extent of tumor resection and analysis of its impact on patient outcome. Neurosurg Focus. 2021;50:E20. https://doi.org/10.3171/2020.10.FOCUS20744.
9. Dai JH, Xu DD, Yang CY, Li ZB, Li Z. Treatment of sagittal fracture of the zygomatic arch root assisted by surgical navigation technology. J Craniofac Surg. 2018;29(4):1031–3. https://doi.org/10.1097/SCS.0000000000004276; PMID: 29381608.
10. Baek MK, Jung JH, Kim ST, Oh NR, Bang YJ, Kang IG. Is surgical navigation useful for treating zygomatic arch fractures? J Craniofac Surg. 2017;28(5):e417–9. https://doi.org/10.1097/SCS.0000000000003645; PMID: 28538075.
11. Catanzaro S, Copelli C, Manfuso A, Tewfik K, Pederneschi N, Cassano L, Cocchi R. Intraoperative navigation in complex head and neck resections: indications and limits. Int J Comput Assist Radiol Surg. 2017;12(5):881–7. https://doi.org/10.1007/s11548-016-1486-0; Epub 2016 Sep 22. PMID: 27659282.

Pediatric Meningiomas: Current Insights on Pathogenesis and Management

Luis Azmitia, Gerardo Taylor, Luca Massimi, and Massimiliano Visocchi

1 Introduction

Differently from adults, where meningiomas account for 13.4–27.3% of primary intracranial tumors, pediatric meningiomas (PMs) represent only 0.4–4% of all intracranial tumors in children [1]. The mean age at diagnosis is approximately 13 years [2]. Furthermore, in the series also considering young adults, the age at diagnosis ranges between 6.5 and 38.5 years, while a male predominance is reported with a male/female ratio usually being 1.5/1 [3, 4]. The presence of tumoral cysts, the predominant involvement of the supratentorial space (Fig. 1), the relatively common intraventricular location, the possibly missing dural attachment, the clinical onset with raised intracranial pressure, and the good prognosis in case of radical excision are the main characteristics of PMs [2].

However, the two most important distinctive aspects of PMs compared with adult forms, are: (1) the significant association with neurofibromatosis (namely, NF-2), which can account for 20% of cases (even 40% in some series), and with previous brain irradiation (possibly because of the vulnerability of partially immature arachnoid cells) [3, 4]. The association with syndromes and the immature arachnoid would also explain the relatively high number of histological subtypes [5]; and (2) the trend to develop high-grade variants (WHO grade II and III, Table 1), with subsequent impact on the clinical course and the prognosis [6].

These peculiarities withstand the interest that PMs raise in the clinical practice, even though they are rare tumors, and there is a need to increase the current knowledge on their pathogenesis and management. The following paragraphs summarize the most recent advances on the topic.

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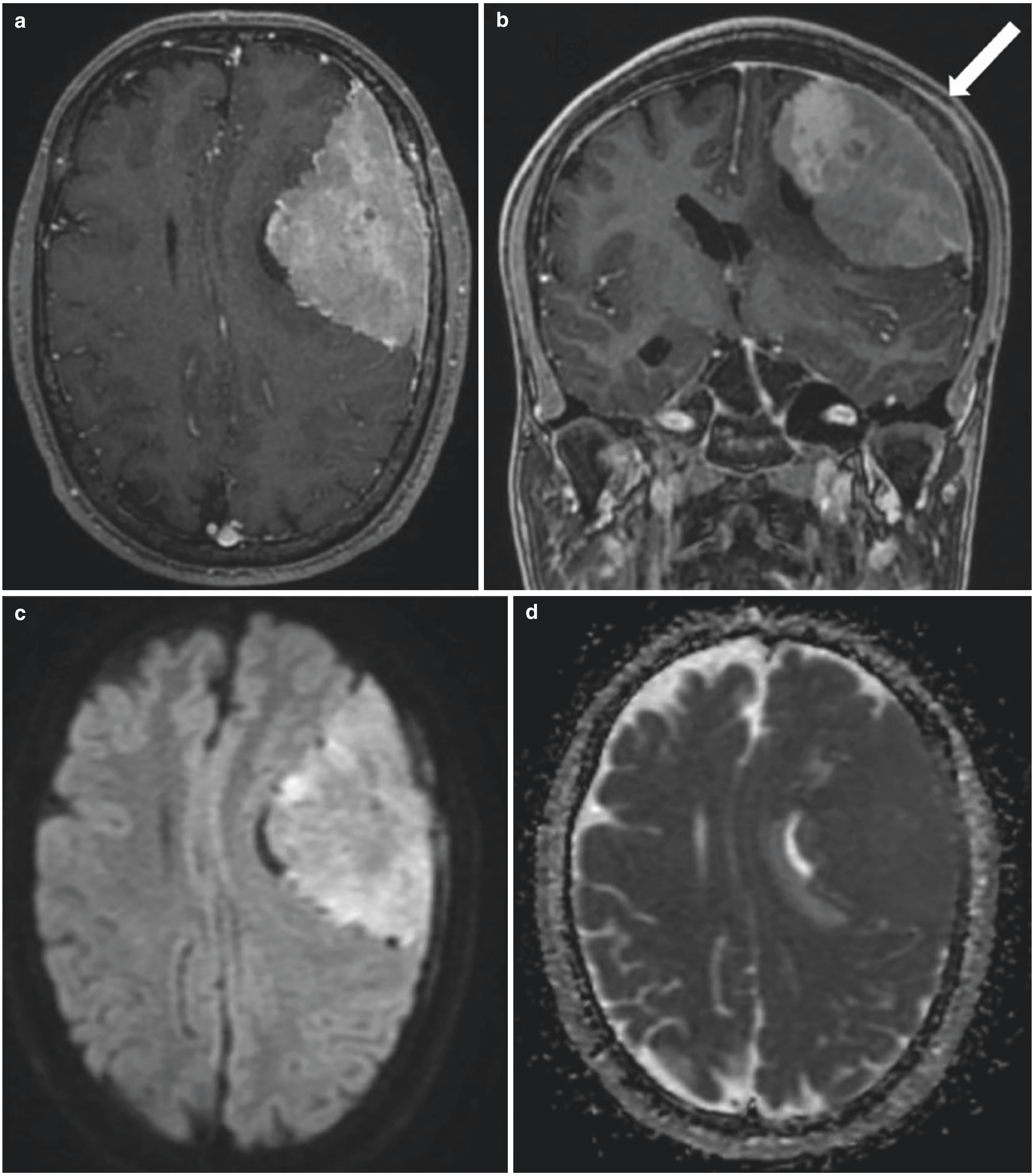

Fig. 1 MRI of a 14-year-old boy evidencing the presence of a pediatric meningioma. After administration of gadolinium (**a**, **b**) a non homogeneous enhancement is appreciated, with partial involvement of the overlying skull (arrow). The DWI sequences (**c**, **d**) suggest an increased cellularity of the tumour

Table 1 World Health Organization Classification Meningioma Classifications. (Adapted from Louis et al. 2016)

WHO I (Meningioma)	WHO II (Atypical)	WHO III (Malignant or anaplastic)
Menngiothelial	Chordoid	Papillary
Fibrous (fibroblastic)	Clear Cell	Rhabdoid
Transitional (mixed)	Atypical	Anaplastic
Psammomatous		
Angiomatous		
Microcystic		
Secretory		
Lymphoplasmacyte-rich		
Metaplastic		

2 Pathogenesis: Embryology, Location, and Molecular Aspects

The tumorigenesis of PMs is believed to have its origin in the interaction between a niche of stem cells and the immature arachnoid. Therefore, the embryology of the meninges is crucial to understand this process. As summarized by Boetto et al. [5], during days 22–24 of the embryogenesis, the neural crest surrounds the neural axis and, immediately after, a group of mesenchymal cells covers the neural tube by migrating from the midbrain (days 24–28). The meningeal coverings would be the result of the interaction between the mesoderm and neural crest, although this process has not been validated in humans yet. During days 33–41, the resulting mesenchymal cells spreading toward the midbrain, the forebrain, and the spinal cord originate the primary meninx. Afterwards, the primary meninx differentiates into the endomeninx (inner layer) and ectomeninx (outer layer), namely during days 34–48. The endomeninx will form the pia mater and the primitive subarachnoid space (days 45–55), while the ectomeninx will form the dural sinuses, the vertebrae and the skull (around day 55). At the end of this process, the arachnoid consists of fibroblasts, connective tissue and fluid, the arachnoid villi projecting into the dural sinuses and the major cortical veins. The pia matter separates the subarachnoidal space from the subpial and cortical perivascular spaces. Cells contained in this subarachnoidal space, namely the arachnoid cap cells and, more recently, the prostaglandin D2 synthase (PGDS)-positive meningeal precursor cells, are proposed as the best candidates to explain the origin of the meningioma cells [5]. The intense immunoreactivity to PGDS showed by meningioma cells supports the potential role of PGDS in the tumorigenesis [7].

As a result of the embryological process, some anatomical and pathological correlations can be found [5]. Accordingly, meningothelial meningiomas are more likely to involve the skull base, while fibroblastic meningiomas the convexity; WHO II and III meningiomas are mainly located at the convexity/parasagittal space, while WHO I meningiomas at the skull base. According to the old anatomical classification by Merten et al., most PMs were supratentorial (66% out of a total of 32 patients) and distributed as follows: 8 intraventricular, 7 sphenoidal, 7 at falx and parasagittal, 7 at the convexity, and 3 para-sellar [8]. Currently, an anatomical classification based on the location alone is no longer followed while the correlation between the pathology and the location plays an important role, especially as far as the neurosurgical indication is concerned, as demonstrated by the rich number of subtypes (15 variants) in the WHO classification (see Table 1) [9]. The predilection of PMs for high WHO grades (up to 60% are WHO II and 13% are WHO III) and the infrequent involvement of infratentorial location (except for NF-2) are an example of the results of the relationship between pathology and location [3, 10]. One of the most recently published series, investigating the characteristics of PMs in the Mexican population, confirmed the previous observations about the predilection for the male sex (M/F 1.3) and the supratentorial location (75%) [11]. In this series (42 children), seizures, paresis, and visual defects were detected other than raised ICP. The transitional meningioma was the most common histotype.

However, the most relevant information on the PMs behavior currently comes from the genetic analysis. Youngblood and colleagues investigated the genomic profiles of more than 3000 meningiomas, demonstrating a map of specific genomic subgroups (namely HH, KLF4, NF2, PI3K POLR2, SMARCB1, TRAF7, and MU) and their origin in the skull [12]. Even though this study was performed in adults, patients under 25 years clearly showed a higher association with NF-2 and MU (and a few cases with TRAF7 pathway alone), differently from other subgroups. Thus, in this study, NF-2 correlated with a high incidence in men and a predilection for the middle cranial fossa, the falx cerebry, and the tentorium cerebelli. Instead, crista galli, middle skull base, and sella turcica were the preferential locations of MU and TRAF7 pathways [12]. Furthermore, with specific regard to PMs, in their study on 50 children, Toland et al. confirmed the loss-of-function mutations in NF2 and the chromosome 22 losses as common findings, while the pathogenic variants of other genes (SMARCB1, FUBP1, BRAF, TERT promoter, CHEK2, SMAD, and GATA3) were rarely encountered [13]. Similarly, the H3K27 hypomethylation (biomarker in adult meningiomas) was not found in children. The authors also established a threshold of 6 mitoses per 10 high powered fields to predict the risk of recurrence. The rarity of these types of mutation patterns in children has been confirmed by the series described by Libert and Prayson, where only one out of 45 patients with clear cells meningioma (commonly found in the posterior cranial fossa and correlating with the SMARCE1 mutations) was a pediatric case (4-year-old boy with NF-1 and SMARCE1 mutation harboring a cavernous sinus PM invading the posterior fossa) [14]. The detailed genomic analysis of 37 affected children provided by Kirches et al. confirms and adds some important data: (1) the aggressive behavior presented by the majority of PMs (70% of the series were WHO grade II or III meningiomas); (2) the frequent occurrence of some cytogenetic aberrations, such as the loss of chromosome 22 (62% of cases), chromosome 1 (24%), chromosome 18 (19%), and chromosome 14 (14%)—these aberrations being more expressed by NF-2 patients; (3) the possible separation of PMs into three groups according to the DNA methylation profiles: group 1, composed of clear cell and papillary meningiomas; group 2A, mainly composed of atypical meningiomas; and group 2B, showing rare high-grade subtypes (such as rhabdoid or chordoid meningioma). NF2 PMs belong exclusively to groups 1 and 2A. These features were demonstrated to be specific to PMs if compared with adult meningiomas (105 cases) [15].

Another relevant field concerning the pathogenesis and the current investigations on PMs is the differentiation between radio-induced (RI) and non-radio-induced (NRI) tumors. In a recent series including 35 PMs (24 cases were NRI and 11 RI tumors) [16], the authors found some differences that deserve mention: (1) the mean age at diagnosis was lower in NRI (10.7 ± 5.7 years) than in RI (17.3 ± 3.5 years), as a result of the time elapsed from the irradiation and the secondary tumor appearance; (2) 8/24 children with NRI tumors (33%) experienced tumor recurrence or progression (clear cell meningioma in three cases, grade I and grade I meningioma with atypical features in two cases each, atypical meningioma in one cases) while no recurrences or progressions were detected among RI tumors; (3) According to the univariate analysis, age at diagnosis ≤10 years, clear cell meningioma, and NRI etiology were predictors of tumor recurrence/progression, with a significant correlation with increased MIB-1 staining index (SI). On multivariate analysis, the younger age at diagnosis and the higher MIB-1 SI resulted as independent risk factors for recurrence. Although an elevated MIB-1 SI statistically correlated with atypia, atypia did not affect the tumor recurrence/progression. An interesting study carried out on a Netherlands population (6015 cancer surviving children <18 years, 1551 of them with irradiation) revealed the occurrence of 93 RI PMs, 95.7% of them having received previous irradiation [17]. The median age at diagnosis was 31.8 years, ranging from 13.2 to 50.5 years. Most of the patients presented with symptoms (90.3%) and a significant proportion of them (one third) showed synchronous meningiomas. All patients received a treatment (surgery with/without radiotherapy). It is worth noting that, differently from the previous study, at late follow-up, 40.9% of survivors developed new meningiomas and 23.7% had a recurrence.

3 Management: Diagnosis and Treatment

Brain CT scan maintains a role in PMs diagnosis where a quick diagnosis is needed, e.g., in case of children with signs or symptoms of raised ICP or abrupt onset with seizures. Moreover, an angio-CT scan (sometimes more useful than angio-MRI) can be used for the surgical planning of PMs with encasement of major vessels [18]. Anyway, when a PM is suspected, the diagnosis has to be confirmed by MRI which can properly show the often atypical appearance of PMs. These radiological peculiarities include [3, 19]: (1) the presence of cystic components in up to 24% of cases (only 2–7% in adults), probably resulting from hemorrhage, necrosis, or glial response and (2) frequent location in the intraventricular space and absence of dural adhesion in 13 to 30% of cases (both uncommon in adults). The occurrence of the so-called MWODA (meningioma without dural attachment) is explained by the possible origin of PMs by the arachnoid cap cells of the perivascular spaces. Moreover, the radiological sign of a dural tail found in some cases could actually be the result of a neoplastic dural infiltration or reactive vessels draining toward the adjacent dura rather than a real dural tail while vasogenic edema with adjacent cerebral gliosis is observed in 25.5% to 55.9% of the cases. The latter finding suggests an "aggressive" radiological appearance that can be ruled out by using multiparametric MRI. However, the experience with spectroscopy MRI is limited and the results are not always conclusive [20, 21]. Also, Diffusion (DWI) and Perfusion (PWI) MRI, which seemed to be more promising than spectroscopy, failed to provide a reliable tumor staging [22, 23]. Recently, the rich vascularization of meningiomas has been easily demonstrated by IntraVoxel Incoherent Motion (IVIM) and Dynamic Susceptibility Contrast MRI, whose parameters can be proposed for the tumor staging [23]. IVIM MRI, in particular, has been proved to be successful in discriminating between grade I and grade II meningiomas and even among different tumor subtypes (e.g., secretory, angiomatous, fibrous meningiomas) [22].

In the largest meta-analysis available on PMs, (677 cases), published on 2011, 518, and 547 children, were eligible to investigate the relapse free survival (RFS) and the overall survival (OS), respectively [24]. NF-2 significantly affected the outcome, since NF-2 patients showed both worse RFS and 10-year OS compared with non-NF-2 patients. Similar results were found matching the tumoral grade with RFS: WHO III PMs presented a shorter RFS than grade I and II. Moreover, the multivariable analysis clearly showed better RFS and OS in case of tumor gross total resection (GTR) compared with subtotal resection. Radiotherapy did not affected RFS nor

OS. The mortality rate at 5–7-year follow-up was 12.7%, which is similar to the rate reported by a coeval study (16.1% after 4.8-year follow-up) [25]. The authors concluded that the initial surgical resection is the strongest independent prognostic factor in PMs; therefore, an aggressive surgical management should be considered at the beginning of the treatment as well as a second look surgery should be performed in case of subtotal removal (if safely feasible). On these grounds, GTR remains the goal standard treatment of PMs, whenever possible. To favor this goal, some quite widely diffused tools, such as neuronavigation, intraoperative ultrasounds and Doppler, and preoperative embolization of the feeding vessels can be successfully used [3, 26]. In adults 5-ALA has shown a capacity to maximize the radicality of surgery (particulary when infiltrating the skull base) but in PMs, there is no specific experience yet. Additionally, 5-ALA seems to be safe and effective in driving the surgical resection but without significantly increasing the rate of GTR of pediatric brain tumors [27, 28]. In spite of the often large size of PMs (diameter > 5 cm in 70% of cases in some series), a GTR is obtained in 70–87% of cases, with a late OS ranging around 85% [29, 30]. It is worth noting that GTR should not be achieved at any cost because an aggressive surgical behavior can significantly increase the postoperative morbidity and worsen the patients' quality of life.

Radiotherapy (RT) is recommended in children with incomplete tumor resection as long as the age is appropriate, when an aggressive grade is confirmed, and when the residual tumor cannot be managed surgically [4, 31]. Indeed, RT (usually gamma-knife or cyberknife) is the most important resource in case of recurrent PMs [19]. However, the role of RT in PMs remains under debate. Actually, some series, where even a 43% rate of recurrence has been reported in grade I PMs (not significantly different from that observed in the WHO II and III of the same series) would support the use of RT [30]. On the other hand, the experience of some authors, who observed that 4 out of 7 patients undergoing gamma-knife for incomplete tumor resection developed a recurrence of their PM, would discourage its use [31]. Therefore, each case should be discussed by a dedicated multidisciplinary tumor board taking into consideration the risks related to the tumor recurrence and those arising from the effects of RT on immature brains [32]. On the other hand, based on the promising results obtained in adults [33], Rombi et al. recently treated two children with unresectable PMs by proton-therapy [34]. The authors were able to control the disease progression (follow-up 39 and 33 months, respectively) with acceptable toxicity (brain edema and small cavernoma in the first case, no side effect in the second patient).

An aid for the management of PMs could come from chemotherapy (CT), even if no specific chemotherapeutic schemes have been proposed so far. Zwerdling and Dothage treated three patients, respectively, with intrathecal methotrexate (survival 16 months); vincristine, fosfamide, Adriamycin, and cyclophosphamide (survival 4 months); and hydroxyurea plus a phase II agent (survival "still alive" at the time of publication) [33]. A sporadic experience with bevacizumab and irinotecan followed by avastatin has also been reported: Großbach et al. reported a 1-year-old patient with a subtotal resection of a suprasellar atypical meningioma followed by adjuvant radiation plus bevacizumab and irinotecan in an attempt to avoid radiation in a very young child/brain. Nevertheless, this patient underwent RT following a second subtotal resection after recurrence of the tumor at the age of 6 years [4]. In all the aforementioned cases, CT was following surgery and/or used in combination with RT. As far as NF-2-related PMs are concerned, the role of everolimus (the orally administered mTORC1 inhibitor used to improve the auditory functions in patients with bilateral vestibular schwannomas) is still debated. This drug is also used with the goal to slow tumor progression in NF2 children with vestibular schwannoma or meningiomas. However, a recent presurgical (phase 0) clinical trial demonstrated an incomplete inhibition of mTORC1 by everolimus, thus explaining the limited antitumor effect of this drug reported in the clinical experience [35].

4 Conclusions

PMs are rare tumors actively investigated because of the partially unclear pathogenesis and the hard management in the case of unresectable tumors. In spite of the embryological observations suggesting the role of embryological remnants of immature arachnoid for the tumorigenesis and the tumor location, the results of the molecular investigations are not as rich as in the adult counterpart. NF-2 and RT remain the main "etiological" factors together with some chromosomal aberrations. The recent advances in MRI development seem to be promising to differentiate between grade I and high-grade PMs (which are significantly more frequent than in adults). The prognosis of PMs mainly depends on the initial surgical resection (namely GTR), since RT, which is the main treatment option in case of tumor recurrence or progression, did not demonstrate to increase the RFS and OS, while CT still misses effective protocols.

Conflicts of Interest No conflicts of interest.

References

1. Liu H, Luo W, Li J, Yang J, Xu Y. Pediatric infratentorial meningiomas: a series of 19 cases and review of the literature. Childs Nerv Syst. 2017;33(5):777–86.
2. Jain S, Muzumdar D, Shah A, Goel A. A treatise on pediatric meningiomas: single-center retrospective cohort experience and review of literature. J Pediatr Neurosci. 2020;15(3):238–44.

3. He W, Liu Z, Teng H, Tang L, Jie D, Duan Z, et al. Pediatric meningiomas: 10-year experience with 39 patients. J Neuro-Oncol. 2020;149(3):543–53.
4. Grossbach AJ, Mahaney KB, Menezes AH. Pediatric meningiomas: 65-year experience at a single institution. J Neurosurg Pediatr. 2017;20(1):42–50.
5. Boetto J, Peyre M, Kalamarides M. Meningiomas from a developmental perspective: exploring the crossroads between meningeal embryology and tumorigenesis. Acta Neurochir (Wien). 2021;163(1):57–66.
6. Chan RC, Thompson GB. Intracranial meningiomas in childhood. Surg Neurol. 1984;21(4):319–22.
7. Kawashima M, Suzuki SO, Yamashima T, Fukui M, Iwaki T. Prostaglandin D synthase (β-trace) in meningeal Hemangiopericytoma. Mod Pathol. 2001;14(3):197–201.
8. Merten DF, Gooding CA, Newton TH, Malamud N. Meningiomas of childhood and adolescence. J Pediatr. 1974;84(5):696–700.
9. Louis DN, Perry A, Reifenberger G, Von DA, Figarella-Branger D, Cavenee WK. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol. 2016;131(6):803–20.
10. Azmitia LM. Meningeomas en Pacientes Pediátricos. (Meningiomas in Paediatric patients). In: Neuro-Oncología Pediátrica Temas Selectos. 1st ed. Espana: Editorial Academica Espanola; 2021. p. 388.
11. Santana-González A, Pérez-Ramírez M, Ramírez-Reyes G, Sánchez-Rodríguez G, Ferman-Cano F, López-Aguilar E. Management experience of pediatric meningioma in a Mexican reference center. Ann Diagn Pathol. 2021;55:151811.
12. Youngblood MW, Duran D, Montejo JD, Li C, Omay SB, Özduman K. Correlations between genomic subgroup and clinical features in a cohort of more than 3000 meningiomas. J Neurosurg. 2019;133(5):1345–54.
13. Toland A, McNulty SN, Pekmezci M, Evenson M, Huntoon K, Pierson CR. Pediatric meningioma: a clinicopathologic and molecular study with potential grading implications. Brain Pathol. 2020;30(6):1134–43.
14. Libert DM, Prayson RA. Pediatric clear cell meningioma involving the middle cranial fossa in the context of NF2 and SMARCE1 mutations. Ann Diagn Pathol. 2020;46:151516.
15. Kirches E, Sahm F, Korshunov A, Bluecher C, Waldt N, Kropf S. Molecular profiling of pediatric meningiomas shows tumor characteristics distinct from adult meningiomas. Acta Neuropathol. 2021;142(5):873–86.
16. Fouda MA, Day EL, Zurakowski D, Scott RM, Smith ER, Marcus KJ. Predictors of progression in radiation-induced versus nonradiation-induced pediatric meningiomas: a large single-institution surgical experience. J Neurosurg Pediatr. 2021;11:1–7.
17. Verbruggen LC, Kok JL, Teepen JC, Janssens GO, de Boer CM, Stalpers LJA. Clinical characteristics of subsequent histologically confirmed meningiomas in long-term childhood cancer survivors: a Dutch LATER study. Eur J Cancer. 2021;150:240–9.
18. Guo H, Liang H, Wang J, Wen S, Wang Y, Wang Y. Giant intraparenchymal meningioma in a female child: case report and literature review. Cancer Manag Res. 2021;13:1989–97.
19. Hong S, Usami K, Hirokawa D, Ogiwara H. Pediatric meningiomas: a report of 5 cases and review of literature. Childs Nerv Syst. 2019;35(11):2219–25.
20. Vescovi MC, Bagatto D, Capo G, Maieron M, Marin D, Pegolo E, u. a. A multimodal approach to the treatment of Intraparenchymal meningioma in a 7-year-old boy: a case report. Pediatr Neurosurg. 2018;53(3):175–81.
21. Liang W, Li M. Rare parenchyma meningioma in an adolescent female with cheek tingling. Medicine (Baltimore). 2016;95(15):e3408.
22. Yiping L, Kawai S, Jianbo W, Li L, Daoying G, Bo Y. Evaluation parameters between intra-voxel incoherent motion and diffusion-weighted imaging in grading and differentiating histological subtypes of meningioma: a prospective pilot study. J Neurol Sci. 2017;372:60–9.
23. Zampini MA, Buizza G, Paganelli C, Fontana G, D'Ippolito E, Valvo F. Perfusion and diffusion in meningioma tumors: a preliminary multiparametric analysis with dynamic susceptibility contrast and IntraVoxel incoherent motion MRI. Magn Reson Imaging. 2020;67:69–78.
24. Kotecha RS, Pascoe EM, Rushing EJ, Rorke-Adams LB, Zwerdling T, Gao X. Meningiomas in children and adolescents: a meta-analysis of individual patient data. Lancet Oncol. 2011;12(13):1229–39.
25. Thuijs NB, Uitdehaag BMJ, Van Ouwerkerk WJR, van der Valk P, Vandertop WP, Peerdeman SM. Pediatric meningiomas in the Netherlands 1974-2010: a descriptive epidemiological case study. Childs Nerv Syst. 2012;28(7):1009–15.
26. Stanuszek A, Piątek P, Kwiatkowski S, Adamek D. Multiple faces of children and juvenile meningiomas: a report of single-center experience and review of literature. Clin Neurol Neurosurg. 2014;118:69–75.
27. Labuschagne J. 5-aminolevulinic acid-guided surgery for focal pediatric brainstem gliomas: a preliminary study. Surg Neurol Int. 2020;11:334.
28. Labuschagne JJ. The use of 5-aminolevulinic acid to assist gross total resection of paediatric posterior fossa tumours. Pediatr Neurosurg. 2020;55(5):268–79.
29. Amirjamshidi A, Mehrazin M, Abbassioun K. Meningiomas of the central nervous system occurring below the age of 17: report of 24 cases not associated with neurofibromatosis and review of literature. Childs Nerv Syst. 2000;16(7):406–16.
30. Isikay I, Hanalioglu S, Narin F, Basar I, Bilginer B. Long-term outcomes of pediatric meningioma surgery: single center experience with 23 patients. Turk Neurosurg. 2020;30(1):124–33.
31. He W, Liu Z, Teng H, Tang L, Jie D, Duan Z. Pediatric meningiomas: 10-year experience with 39 patients. J Neurooncol. 2020;149(3):543–53.
32. Bhakta N, Liu Q, Ness KK, Baassiri M, Eissa H, Yeo F. The cumulative burden of surviving childhood cancer: an initial report from the St Jude lifetime cohort study (SJLIFE). Lancet. 2017;390(10112):2569–82.
33. Hanft S, Canoll P, Bruce JN. A review of malignant meningiomas: diagnosis, characteristics, and treatment. J Neuro-Oncol. 2010;99(3):433–43.
34. Rombi B, Ruggi A, Sardi I, Zucchelli M, Scagnet M, Toni F. Proton therapy: a therapeutic opportunity for aggressive pediatric meningioma. Pediatr Blood Cancer. 2021;68(5):e28919.
35. Karajannis MA, Mauguen A, Maloku E, Xu Q, Dunbar EM, Plotkin SR. Phase 0 clinical trial of Everolimus in patients with vestibular schwannoma or meningioma. Mol Cancer Ther. 2021;20(9):1584–91.

Tuberculum Sellae Meningioma: Report of Two Cases and Literature Review of Limits of the Transcranial and Endonasal Endoscopic Approaches

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1 Introduction

Tuberculum sellae (TS) meningioma is one of the most frequent meningiomas of the anterior skull base (21%), arising from the dura of the tuberculum sellae, chiasmatic sulcus, limbus sphenoidale, and diaphragma sellae [1].

According to their location, the early optic canal involvement (reported in 10% to 90% of TS meningiomas) and the resulting compression and elevation of the optic nerves and chiasm, visual deficits are generally the main symptoms [2, 3]. In addition, they may extend anteriorly to the planum sphenoidale or posteriorly to the diaphragma and infundibulum, with tumor filling the pituitary fossa, thus determining more complex clinical pictures [2].

Herein we review the literature concerning the preferred surgical approaches to TS meningiomas; additionally, we describe two explicative cases, operated on by our group using different approaches, with the aim to critically revise surgical indications and contraindications.

Case 1 (Fig. 1) A 45-year-old patient with a 2-year history of headache, visus decline in the right eye, and bitemporal hemianopsia. An MRI showed a sellar/suprasellar lesion, approximately 18×17×19 mm, with enhancement and dural implant at the level of tuberculum sellae, determining compression of the homolateral optic nerve. An Angio-CT scan highlighted its relationships with the carotid artery laterally and the A1-Acoa complex above, excluding a stenosis hyperostosis of the optic foramen. In October 2021, the patient underwent a right frontal-temporal craniotomy, a resection of the tuberculum sellae lesion with decompression of the right optic nerve. Histopathology revealed WHO grade I meningioma. The post-operative course was uneventful with reported improvement of the campimetric vision in the right eye. A post-operative MRI revealed a macroscopically complete lesion removal.

Case 2 (Fig. 2) A 68-year-old hypertensive patient with a history of clipping of ruptured middle cerebral artery aneurysm in 1978 and in 2015 and evidence, since 2019, of a sellar lesion, initially suspected to be pituitary macroadenoma. Then, serial MRI showed a progressive volumetric increase of the lesion, with concomitant slight reduction of the right temporal visual field. Laboratory exams showed increased prolactin values (88 ng/dL) and a mild hypothyroidism. In October 2021, the patient underwent surgery via the trans-sphenoidal endonasal approach. Histological examination revealed: WHO grade I meningioma. In the postoperative period, the patient experienced an improvement of visual symptoms.

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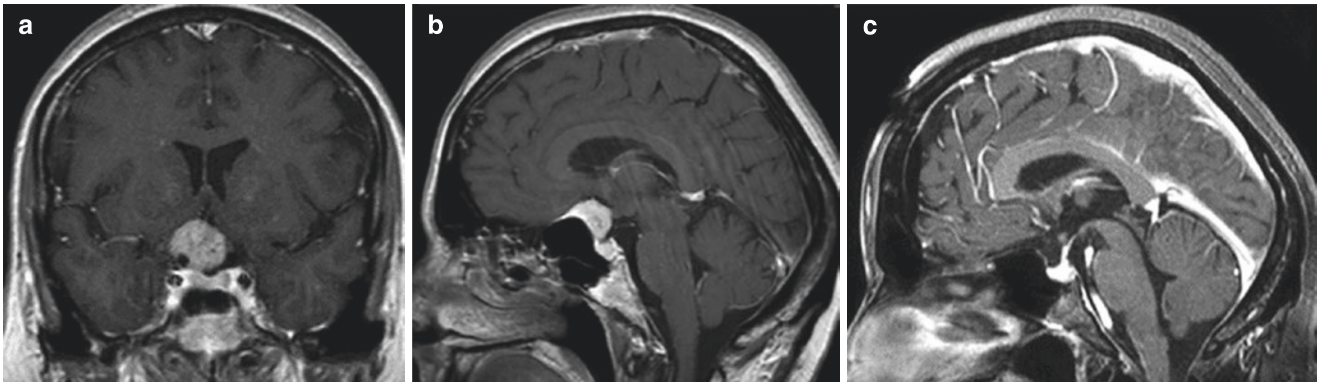

Fig. 1 Coronal (**a**) and sagittal (**b**) preoperative MRI scan with contrast enhancement showing a tuberculum sellae meningioma. (**b**) Post operative sagittal MRI scan confirming gross total resection of the tumor

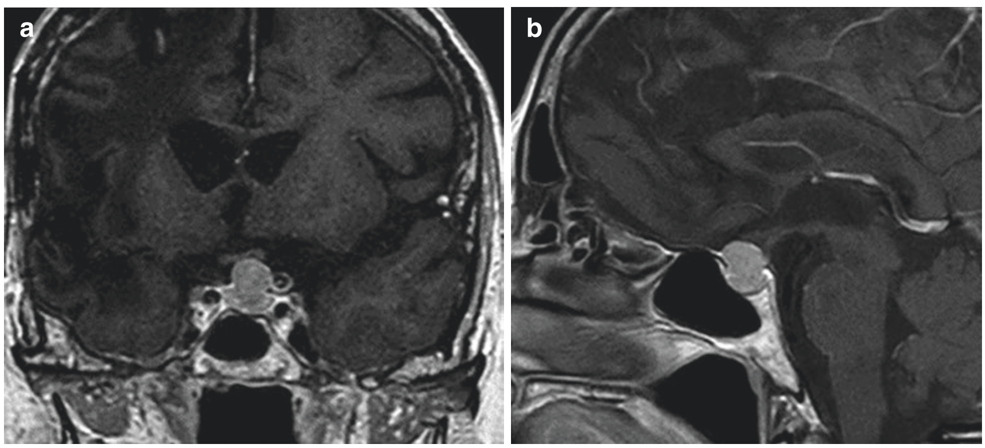

Fig. 2 Coronal (**a**) and sagittal (**b**) MRI scan with contrast enhancement showing a tuberculum sellae meningioma

2 Surgical Technique

2.1 Frontal-Temporal Approach

The patient is positioned supine with the head rotated 15° away from the side of the larger tumor extension. In patients with strictly midline tumors, the approach is from the non-dominant side [4]. A curvilinear skin incision is performed starting anterior to the tragus at the root of the zygomatic arch and ending at the hairline in the midline and a frontal-temporal craniotomy is performed. The craniotomy at the frontal base is extended close to the frontal sinus to enhance the anterior view of the chiasm and the opposite optic nerve. The greater sphenoid wing and the orbital roof are drilled to flatten the line of work and improve the visual path to the tuberculum area. The dura is opened and reflected anteriorly, the basal cisterns are opened, the optic nerve is identified in the cisternal segment. Tumor debulking starts with devascularization of the dural base, in the midline at the tuberculum sellae with low-intensity bipolar cautery; thereafter, it is removed under the chiasmatic cistern in a contralateral to ipsilateral direction to respect the optic nerves and carotid arteries, if they were covered by tumor. After that, the tumor is dissected from the pituitary stalk and from the interpeduncular cistern. A bony decompression of the optic canal and the optic nerve is performed using a small diamond drill with abundant irrigation to prevent heating of the optic nerve. Finally, the tumor is removed from the optic canal. The dura is closed in a watertight method and the bone flap replaced.

2.2 The Endoscopic Endonasal Approach

The transsphenoidal approach represents the most direct and least traumatic surgical technique for the treatment of sellar lesions. The surgical technique has extensively been described elsewhere. The position of the carotids is localized by direct visualization or using a micro-Doppler probe. After bony opening, the dura above and below the diaphragm is coagulated and opened. After tumor volume reduction, the tumor capsule is dissected sharply away from arachnoid attachments.

3 Discussion

The tuberculum sellae is a slight bony elevation separating the anterior roof of the pituitary fossa from the prechiasmal sulcus.

TS meningiomas originating in the tuberculum sellae and diaphragma sellae region overall account for 5–12% of all intracranial meningiomas. There is a difference between tuberculum sella and diaphragma sella meningiomas. In the tuberculum tumors, there is usually a good plain of arachnoid membrane between the tumor and the pituitary stalk. By contrast, in diaphragma sellae meningioma, the arachnoid membrane is usually missing, and therefore the risk of injuring the stalk is greater [5].

They commonly present with visual deterioration: gradual vision loss in one eye, followed by gradual visual disturbance in the contralateral eye. Another characteristic presentation is the chiasmal syndrome, described by Cushing and Eisenhardt in 1929, that includes a primary optic atrophy with asymmetric bitemporal field defects in adult patients showing a normal sella on a plain skull radiograph [6]. Other possible symptoms include headache, anosmia, seizures, and, rarely, pituitary dysfunction.

The anatomical boundaries of these tumors are laterally the internal carotid and the posterior communicating arteries, the optic nerves and their arachnoid pouch anteriorly, the Liliequist arachnoid membrane and the pituitary stalk posteriorly and the chiasm, the lamina terminalis and the A1 segments superiorly [3, 4].

Surgical options include craniotomy approaches (extended bifrontal, tailored bifrontal, interhemispheric, orbitozygomatic, pterional, and subfrontal eyebrow approaches) [6, 7], or the endonasal endoscopic transsphenoidal approach. The choice of the proper approach remains a matter of debate [2, 4, 8, 9] depending on location, size and lateral tumor extension, or cranial or caudal invasiveness.

McDermott and colleagues proposed a grading scale that considers tumor size, relationship with the optic nerves and with the adjacent arteries [6, 10].

Typically, these tumors are located medially to the optic nerves, and therefore are approached by the subfrontal approach, which allows good access to both ipsilateral and contralateral optic nerves [11, 12]. The internal carotid artery and the anterior cerebral artery on both sides can also be controlled, especially when these structures are adherent or encased by the tumor [2]. In addition, this approach provides bilateral exposure and thus removal of the roof of the optic canal. The opening and decompression of the optic canal permit more extensive and safe manipulation of the nerve and the removal of the tumor below the nerve and within the optic canal [2]. TS meningiomas extending anteriorly and pushing the optic nerves laterally should be considered for a modified frontal approach [12].

The orbitozygomatic approach has traditionally been used and provides similar advantages to the bifrontal approach, allowing less exposure [11].

The supraorbital subfrontal eyebrow approach is another option, especially when combined with angled endoscopic assistance [7].

Several authors have reported good surgical outcomes using the pterional approach for these tumors [5, 13–15], especially those determining upward dislocation of the optic structures and without anterior extension [12].

Compared to the subfrontal approach, the pterional one proved to also lessen the risk of excessive brain retraction, postoperative subdural hygromas, and injury of the olfactory nerves [16] (see Table 1).

Over the past decade, many authors have reported surgical experiences with anterior skull base meningiomas operated on via the endoscopic endonasal approach (EEA), elucidating its feasibility and safety in selected cases [17–23].

The endoscopic endonasal approach (EEA) presents several advantages (see Table 2). First, a completely extracranial route is utilized, which avoids any brain retraction or manipulation of the optic chasm and nerves or arteries [1, 17–24]. Moreover, it allows an early devascularization, giving an arachnoid cleavage plane to remove the tumor, and therefore, it reduces the risk of damage by perforating vessels and optochiasmatic feeder [1, 17–24]. Therefore, the early decompression of the optic apparatus may avoid any direct injury and thus could yield a better functional outcome [1, 24]. On the other hand, limits of this approach are the relevant risk of CSF leaks, the intracranial extension of the lesions beyond

Table 1 Comparison between the two most used transcranial approaches (bifrontal and pterional approach)

	Bifrontal approach	Pterional approach
Advantages and indications	Meningiomas extending anterior the optic nerves pushed laterally rostral tumors Very large tuberculum sellae tumors extending to the frontal base	Meningiomas extending lateral optic structures upward Lower risk of CSF leak or infection from frontal sinus transgression Minimizing injury to the olfactory nerves Less brain exposure Dorsal tumors
Disadvantages	The occurrence of CSF leakage or infection from frontal sinus transgression Injury of the olfactory nerves Brain retraction Increased incidence of postoperative subdural hygromas	Meningiomas not extend anteriorly

Table 2 Comparison between transcranial and transsphenoidal approach

	Transcranial (pterional/bifrontal) approach	Endnasal endoscopic approach
Advantages	Relative/low risk of CSF leak Good visualization of optic nerveGood access to optic canalsStandard microsurgical dissection technique Control of adherent or encased vessels	Faster recoveryEarly devascularization of tumorNo brain retractionMinimal manipulation of optic apparatus Reduce the risk of indirect injury to the optic structures Midline noncalcified tumors
Disadvantages	Breach of frontal sinus if largeBrain retractionDifficult to remove tumor if it extends anterior to planum	Risk of CSF leakPotential loss of olfactionDifficult to remove tumor in optic canal when superolateral to optic nerve Difficult to dissect adherent/encased small vessels at posterior margin Non-pneumatized sphenoidal sinus

the lateral limits of the approach, above the roof of the orbit or with encasement of the carotid artery and its major branches. Therefore, this approach should be reserved to strictly midline tumors, with little eccentric lateral growth, those in patients with a large sphenoid sinus, and tumors situated entirely inferior and medial to the optic nerves, with no encasement of major vessels [1, 24–26].

4 Conclusion

Despite the refinements of surgical techniques over the past decades, dealing with TS meningioma remains a complex surgical challenge, especially the choice of the proper approach. The relationship of the tumor with the optic nerves, optic canal, and anterior cerebral artery complex are important issues that have to be considered. Both transcranial and endonasal approaches, in experienced hands, can allow complete resection of the lesion.

References

1. Zoli M, Guaraldi F, Pasquini E, Frank G, Mazzatenta D. The endoscopic endonasal management of anterior skull base meningiomas. J Neurol Surg B Skull Base. 2018;79(S04):S300–10.
2. Margalit N, Kesler A, Ezer H, Freedman S, Ram Z. Tuberculum and diaphragma sella meningioma—surgical technique and visual outcome in a series of 20 cases operated over a 2.5-year period. Acta Neurochir. 2007;149(12):1199–204.
3. Li-Huaa C, Linga C, Li-Xub L. Microsurgical management of tuberculum sellae meningiomas by the frontolateral approach: surgical technique and visual outcome. Clin Neurol Neurosurg. 2011;113(1):39–47.
4. George IJ, Vallo B. Tuberculum sellae meningiomas: microsurgical anatomy and surgical technique. Neurosurgery. 2002;51:1432–40.
5. Dolenc V. Microsurgical anatomy and surgery of the central skull base. Vienna: Springer Verlag (Wien); 2003.
6. Safaee MM, McDermott MW, Benet A, Theodosopoulos PV. Tailored extended bifrontal craniotomy for anterior skull base tumors: anatomic description of a modified surgical technique and case series. Oper Neurosurg (Hagerstown). 2017;14(4):386–94.
7. Wilk A, Zieliński G, Witek P, Koziarski A. Outcome assessment after surgical treatment of tuberculum sellae meningiomas—a preliminary report. Turk Neurosurg. 2016;26:824–32.
8. Al-Mefty O, Holoubi A, Rifai A, Fox JL. Microsurgical removal of suprasellar meningiomas. Neurosurgery. 1985;16:364–72.
9. Kinjo T, Al-Mefty O, Ciric I. Diaphragma sellae meningiomas. Neurosurgery. 1995;36:1082–92.
10. Magill ST, McDermott MW. Tuberculum Sellae Meningiomas, handbook of clinical neurology, vol. 170. Amsterdam: Elsevier; 2020. p. 13–23.
11. Magill ST, Morshed RA, Lucas C-HG, Aghi MK, Theodosopoulos PV, Berger MS, de Divitiis O, Solari D, Cappabianca P, Cavallo LM, McDermott MW. Tuberculum sellae meningiomas: grading scale to assess surgical outcomes using the transcranial versus transsphenoidal approach. Neurosurg Focus. 2018;44(4):E9.
12. Schmidek and sweet: operative neurosurgical techniques. Surgical management of midline anterior skull base meningiomas: 417–428.
13. Fahlbusch R, Schott W. Pterional surgery of meningiomas of the tuberculum sellae and planum sphenoidale: surgical results with special consideration of ophthalmological and endocrinological outcomes. J Neurosurg. 2002;96:235–43.
14. Grisoli F, Diaz-Vasquez P, Riss M, Vincentelli F, Leclercq TA, Hassoun J, Salamon G. Microsurgical management of tuberculum sellae meningiomas. Results in 28 consecutive cases. Surg Neurol. 1986;26:37–44.
15. Pamir MN, Ozduman K, Belirgen M, Kilic T, Ozek MM. Outcome determinants of pterional surgery for tuberculum sellae meningiomas. Acta Neurochir. 2005;147:1121–30.
16. Nakamura M, Roser F, Struck M, Vorkapic P, Samii M. Tuberculum sellae meningiomas: clinical outcome considering different surgical approaches. Neurosurgery. 2006;59:1019–29.
17. Elshazly K, Kshettry VR, Farrell CJ, Nyquist G, Rosen M, Evans JJ. Clinical outcome after endoscopic endonasal resection of tuberculum Sella meningiomas. Oper Neurosurg (Hagerstown). 2018;14(05):494–502.
18. Song SW, Kim YH, Kim JW, et al. Outcomes after transcranial and endoscopic endonasal approach for tuberculum meningiomas-a retrospective comparison. World Neurosurg. 2018;109:e434–45.
19. Koutourousiou M, Fernandez-Miranda JC, Stefko ST, Wang EW, Snyderman CH, Gardner PA. Endoscopic endonasal surgery for suprasellar meningiomas: experience with 75 patients. J Neurosurg. 2014;120(06):1326–39.
20. Koutourousiou M, Fernandez-Miranda JC, Wang EW, Snyderman CH, Gardner PA. Endoscopic endonasal surgery for olfactory groove meningiomas: outcomes and limitations in 50 patients. Neurosurg Focus. 2014;37(04):E8.
21. Van Gompel JJ, Frank G, Pasquini E, Zoli M, Hoover J, Lanzino G. Expanded endonasal endoscopic resection of anterior fossa

meningiomas: report of 13 cases and meta-analysis of the literature. Neurosurg Focus. 2011;30(05):E15.

22. Khan OH, Krischek B, Holliman D, et al. Pure endoscopic expanded endonasal approach for olfactory groove and tuberculum sellae meningiomas. J Clin Neurosci. 2014;21(06):927–33.
23. Mascarella MA, Tewfik MA, Aldosari M, Sirhan D, Zeitouni A, Di Maio S. A simple scoring system to predict the resectability of skull base meningiomas via an endoscopic endonasal approach. World Neurosurg. 2016;91:582–591.e1.
24. Abbassy M, Woodard TD, Sindwani R, Recinos PF. An overview of anterior skull base meningiomas and the endoscopic endonasal approach. Otolaryngol Clin N Am. 2016;49(01):141–52.
25. Goel A, Muzumdar D, Desai KI. Tuberculum sellae meningioma: a report on management on the basis of a surgical experience with 70 patients. Neurosurgery. 2002;51:1358–63; discussion 1363–1354.
26. Margalit NS, Lesser JB, Moche J, Sen C. Meningiomas involving the optic nerve: technical aspects and outcomes for a series of 50 patients. Neurosurgery. 2003;53:523–32; discussion 532–523.

VHL: Trends and Insight into a Multi-Modality, Interdisciplinary Approach for Management of Central Nervous System Hemangioblastoma

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1 Introduction

Von Hippel-Lindau (VHL) disease is a rare autosomal dominant genetic condition associated with tumours arising in multiple organs. It is caused by a germline mutation affecting the *VHL* gene located on chromosome 3 [1]. VHL is a classical tumour suppressor gene with loss of the wild type allele leading to tumorigenesis [2]. VHL has been clinically classified into two categories, based on the presence (type 2 disease) or absence (type 1 disease) of phaeochromocytomas, with further subdivision of type 2 disease based on the presence (2B) or absence (2A and 2C) of renal cancer. This clinical variation results from a close genotype–phenotype relationship in which type 1 disease arises from deletions and truncating mutations, whilst missense mutations are responsible for type 2 disease [3–5].

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1.1 Haemangioblastomas

Of patients with VHL, 60–90% will develop multiple haemangioblastomas in their lifetime [6, 7]. Haemangioblastomas can be sporadic, but 20–30% of all haemangioblastomas are in association with VHL [8]. These lesions are benign (WHO grade 1) and cause symptoms from mass effect of the tumour itself or the associated cyst, but can also spontaneously haemorrhage into these lesions [9]. They are highly vascular tumours, and although they can occur anywhere in the CNS, they have a predilection for the posterior fossa (predominantly in the cerebellum) and spinal cord. In a large series published by Glasker et al. 63% of haemangioblastomas were localised in the cerebellum. The majority of these were in the cerebellar hemispheres, 5% were in the brainstem and 32% were in the spinal canal [10]. They represent 3% of all CNS tumours [10–12].

Some studies suggest that it is not the capillaries but the stromal cells that are neoplastic, and the capillary growth is secondary to VEGF expression [13]. The underlying pathological process in the formation of these haemangioblastomas is thought to be explained by the 'two hit hypothesis' which describes the requirement for biallelic inactivation of the tumour suppressor gene in the affected cells [1]. This is also the case for all VHL-associated pathologies.

1.2 Other Manifestations

VHL has many manifestations outside of the central nervous system. These include renal cell carcinomas, renal cysts, phaeochromocytomas, paragangliomas, pancreatic cysts and neuroendocrine tumours [1]. Blindness and deterioration in vision can also result from retinal haemangioblastomas, and this remains a major complication of VHL [7]. Endolymphatic sac tumours are papillary epithelial neoplasms highly associated with VHL. The endolymphatic duct in the posterior petrous bone is affected by tumours and patients experience

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progressive ipsilateral deafness, tinnitus, vertigo and vestibular dysfunction [14]. In addition, arterial hypertension resulting from phaeochromocytoma development has also been identified as a cause of retinal damage in these patients [15, 16]. The cardiovascular effects of phaeochromocytomas are particularly relevant peri-operatively when adequate and staged adrenoreceptor blockade is necessary to minimise the risk of life-threatening catecholaminergic crisis [17]. This multisystem nature of the disease therefore requires an interdisciplinary team to best manage these patients at every stage, including timing and prioritisation of surgery and peri-operative care and safety.

2 Methods

In this narrative review, we provide an update on the management and emerging therapies in this challenging group of patients, with particular attention to the focussed treatment and considerations in haemangioblastomas of the posterior fossa and spinal cord.

We present the experience of two VHL referral centres and draw on the expertise of the authors in managing these patients in a multidisciplinary team setting, to advance our understanding of an interdisciplinary approach. Emphasis is focused on combining different modalities and on individually tailored decision making with a holistic approach rather than isolated systems. In addition to the experience of the authors, we describe exemplary cases to demonstrate some of the challenges and highlight multimodality management. We review the available literature on VHL-related posterior fossa and spinal haemangioblastomas, by searching through PubMed, Google Scholar and EBSCO.

3 Results and Discussion

3.1 Molecular Genetics and Pathophysiology

Hypoxia-inducible factors (HIFs) are heterodimeric oxygen-sensitive basic helix-loop-helix transcription factors that play central roles in cellular adaptation to low oxygen environments. The Von Hippel-Lindau tumour suppressor protein (pVHL) is the substrate recognition component of an E3 ubiquitin ligase and functions as a prime regulator of HIF activity by targeting the hydroxylated HIF-α subunit for ubiquitylation and rapid proteosomal degradation under normoxic conditions [18]. Cells with dysfunctional pVHL cannot degrade HIF1α, which therefore accumulates in the cell nucleus, where it acts as a master transcription factor for a myriad of genes involved in the response to hypoxia, including vascular endothelial growth factor (VEGF) [19, 20]. Therefore: VEGF is one of the genes upregulated by HIF-1 and is the primary cytokine related to angiogenesis [21]. Herein lies the predisposition of VHL patients to angiogenic tumours of the eye and CNS.

With regard to the influence of VHL mutations and tumour behaviour, the literature is somewhat confusing. Some data on clear cell renal cancer suggest that, with the loss of pVHL expression, there is worse cancer survival [22]. Other data have suggested that VHL mutation and hypermethylation is associated with poor prognosis [23, 24]. Patard et al. describe that high levels of carbonic anhydrase 1X staining (a target of HIF transcriptional activator) predicts functional VHL loss, indicating VHL events that impart a significant failure of HIF suppression. Targeted therapy against HIF1α has the potential for treating the tumours associated with Von Hippel-Lindau disease. mTOr inhibitors (e.g. everolimus) have been used with efficacy in renal carcinoma in those with VHL, and those without, suggesting a common pathway. HIF-1α acted as a downstream molecule of mTOR and regulated glucagon-like peptide-1 (GLP-1) receptor-induced metabolism reprogramming via the PI3K/mTOR pathway [25, 26]. In a pancreatic cancer hypoxic microenvironment, HIF-1α mediated tumorigenic crosstalk between tumour parenchyma and stroma—and influenced the epithelial/mesenchyme transition (EMT)—so it is important in the metastatic potential for cancers [27]. The potential for histone de-acetylase inhibitors is discussed below.

3.2 Natural History

Natural history studies in VHL have shown that haemangioblastomas have a characteristically saltatory growth pattern. Their growth is interrupted by long quiescent periods, and new haemangioblastomas can arise over this time period [28–30]. This is well demonstrated by Ammerman et al. who studied CNS hemangioblastoma progression in VHL patients they serially imaged and clinically evaluated for at least 10 years [28]. In 94% of haemangioblastomas that were followed up, there were periods of rapid growth followed by periods of quiescence and 97% demonstrated radiological progression. Almost half (45%) of haemangioblastomas requiring surgery were not apparent on initial imaging. Artificial intelligence and machine learning algorithms may in the future prove useful in radiological prediction models.

It is not clear what factors drive these periods of rapid growth in haemangioblastomas. There is some evidence of association between pregnancy and enlargement of the cystic component, which can have a significant effect on both the mother and developing foetus [31].

3.3 Multi-Disciplinary Approach and Decision Making

Patients with VHL are affected by a multi-system disorder and are likely to require input from a range of specialties including, but not limited to, ophthalmology, nephrology, urology, endocrinology, neurosurgery, audiology, otolaryngology, oncology, clinical genetics and neuro and visceral radiology at various points in their lives. Cohesive and collaborative working between these specialties is required to provide integrated patient-centred care [12] and is deemed essential in the care of patients with VHL by the international VHL Alliance. Multi-disciplinary teamworking allows treatment prioritisation in patients with multiple synchronous lesions, which can be obscured without appropriate, and often wide ranging, inter-speciality dialogue. For example, in the multimodal management of CNS haemangioblastomas treatment, decision-making will primarily involve neurosurgery, neuroradiology and radiation oncology. However, the other members of the MDT are likely to also contribute to peri-operative management—for example, endocrinology in pre-operative adrenoreceptor blockade in a patient with a co-existing phaeochromocytoma and nephrology in a patient with end stage renal disease requiring dialysis.

The onset of VHL-associated morbidity may be seen as early as childhood and continues throughout adult life and has the potential to have significant effects on educational, occupational and reproductive decisions. This can be further complicated by the inherited nature of the condition and the prior experiences of affected family members. This is particularly relevant when discussing asymptomatic screening detected lesions. Lifelong follow-up is mandatory and the streamlining of imaging and clinic appointments is highly desirable to minimise impacts on daily life. In our experience, the role of a clinical nurse specialist to co-ordinate appointments and therapies and provide a point of communication with the patient and their families is fundamental to this.

3.4 Treatment Modalities

Surgery

Haemangioblastomas can be cured surgically with a complete resection. It therefore stands to reason that, if indicated, this is the treatment of choice. Surgery can be performed with minimal morbidity in the majority of cases [6, 29, 32]. Indications are symptomatic tumours or enlarging lesions on surveillance. There is some debate as to whether radiological progression in the absence of any symptoms should be an indication for surgical intervention. The main argument for operating prophylactically is that developing pre-operative symptoms are usually not reversible and in experienced hands, the morbidity of this procedure is low [9, 33]. In cases of impending CSF flow obstruction, then surgery should be performed in a timely fashion. For haemangioblastomas in the brainstem, the risk of causing morbidity is slightly higher than in the cerebellum. As such it is recommended that these lesions are operated on only when they become symptomatic or if any further growth increases the risk of surgery [32]. Rather predictably, if there is a residuum then the risk of recurrence is significantly higher [29, 34]. Surgery can be particularly challenging for larger lesions. Figure 1 demonstrates a surgically treated lesion from our practice.

The use of indocyanine green (ICG) video angiography has also been described to assist with the resection of haemangioblastomas. ICG helps localise the lesions intra-operatively and are associated with a superior complete resection rate, although this has not been trialed [35–37]. Adjuncts such as CO_2 lasers have also been suggested, but these are not considered the standard [9, 38]. Neuromonitoring in spinal haemangioblastomas is well supported in the literature. Westphal et al. have recently published their experience of 500 intramedullary spinal cases over 35 years describing their refinement strategies, including neuromonitoring. Whilst this includes other pathologies, the principles and added safety of neuromonitoring remains applicable to haemangioblastoma surgery.

Embolisation

Some authors have suggested pre-operative embolisation as an adjunct to minimise bleeding [39–41]. The counter argument to this is that it is often not necessary provided the tumour is not entered and the interface between tumour and brain is dissected carefully, avoiding excessive retraction and using low power bipolar diathermy [9]. Both in our experience and reflected in the published literature, embolisation can be used as an adjunct to surgical management to minimise bleeding from the nodule in highly selected cases. As demonstrated in Fig. 3, some haemangioblastomas can be extensive with a rich blood supply. Pre-operative embolisation is not without risk. Ene et al. report their experience from two high volume centres, and in those patients who underwent pre-operative embolisation, there was a 25% risk of neurological deficit, and in 15% these were permanent [42]. There are no reports in our literature review that have looked at embolisation alone as a treatment choice for these patients.

Stereotactic Radiosurgery

Stereotactic radiosurgery (SRS) has become more commonly employed in the management of haemangioblastomas, as an emerging treatment option. Historically, fractionated radiotherapy was used for inoperable, recurrent or residual tumours. Stereotactic radiosurgery has obvious

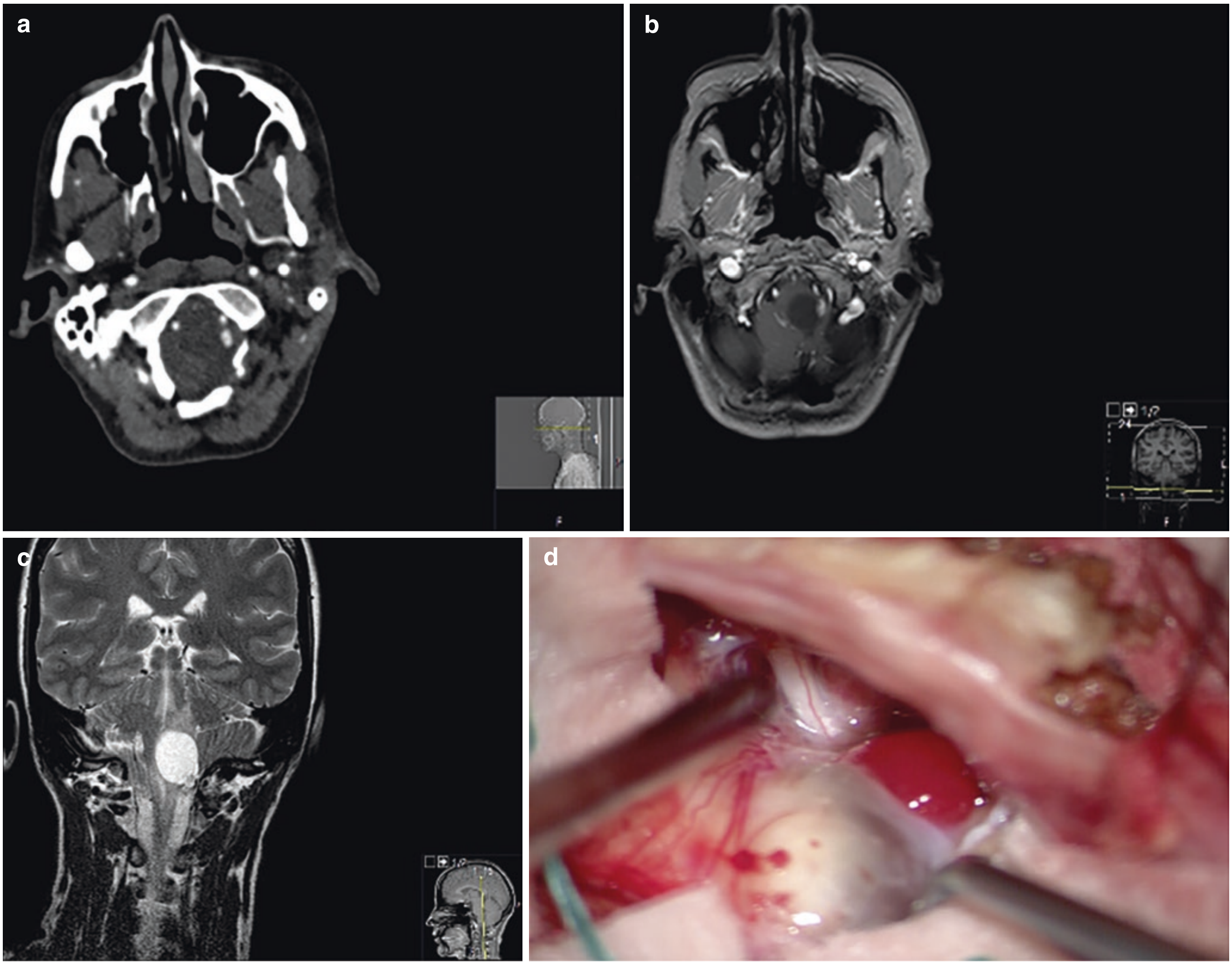

Fig. 1 Pre-operative CT angiogram (**a**) and MRI (**b**: axial T1 gadolinium; **c**: coronal T2) with intraoperative views (**d**) of haemangioblastoma in close proximity to accessory nerve and vertebral artery

advantages over surgery, it is less invasive and has a lower rate of morbidity. Large single radiation fractions are best for all SRS treated vascular tumours. SRS is also better suited to smaller or surgically inaccessible lesions [43]. Gamma Knife (GK) has been used as an alternative to surgery for small tumours or inoperable sites [44]. Evidence suggests that GK is effective at reducing the solid component of the tumour but does not reduce the size of the cyst, for which surgery may still be required [45].

In 1997, we published our early experience using radiosurgery for the treatment of brain haemangioblastoma [46]. We reported the 40 month follow up of six SRS treated lesions in five patients. Four lesions demonstrated a complete response and the fifth lesion demonstrated stability. We described a sixth lesion which abutted the optic apparatus and pituitary, which we treated with conventionally fractionated radiotherapy; this demonstrated a partial response. We discussed our experience with anecdotal Von Hippel-Lindau cases where the cerebellum was heavily involved with multiple haemangioblastomas. In this situation, we recommended conventionally fractionated radiotherapy (50–55 Gy) to the posterior fossa (with brainstem not exceeding radiation tolerance) and later for SRS, for any lesions which had not durably responded to the radiotherapy. We have expanded our experience since that time and now face the challenges of more difficult cases, of which the intramedullary spinal lesions are the most complex. Figure 2 demonstrates a case from our experience of a spinal hemangioblastoma treated with cyber knife.

Over the past few years, there have been a number of reviews looking at cyber knife for spinal haemangioblastomas. Pan et al. recently published a 10-year experience in which image guided cyber knife for spinal haemangioblastoma is safe and effective, particularly in patients with

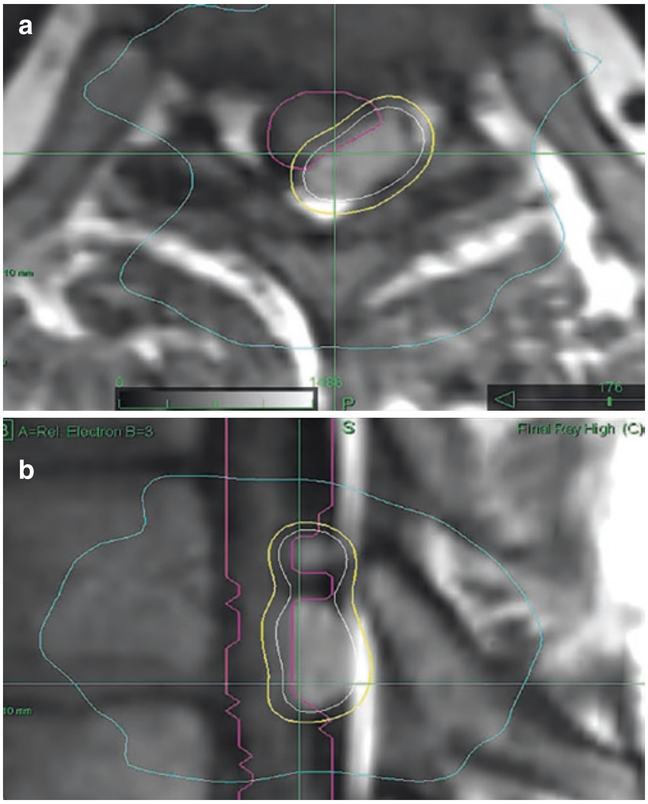

Fig. 2 Isodosimetric plan for two adjacent spinal haemangioblastomas in the lower thoracic cord, treated by single dose SRS (Cyberknife). Top (**a**) axial view and (**b**) lower panel: sagittal view. The spinal cord (plus 1 mm planning margin) is outlined in magenta and the targets' marginal 10 and 9 Gy isodoses are in white and yellow—with the lesion circumscribed within these isodoses. The maximum dose to each lesion was 12 GY

VHL. Control rates at 5 years were 92%, with an improvement of symptoms in 77% [43]. Interesting is the success of SRS in the treatment of spinal haemangioblastomas, notwithstanding the need to frequently compromise on full SRS dose (given the proximity/abutment of the spinal cord to the tumour). Indeed, frequently the spinal cord partly surrounds the target—and the dose prescription is compromised to ensure the radiation tolerance of the cord is not exceeded.

Multimodal Treatment

Such cases of combined SRS and surgery are not reported in the literature, with the exception of one recent case report [47]. Rates of control with SRS have been reported as 80–90% with haemangioblastomas. More centres are therefore utilising this to treat asymptomatic tumours in VHL with an aim to reduce the need for future surgery [48]; however, other authors feel that SRS should not be used prophylactically to treat asymptomatic tumours [29]. A 90% progression free survival has been demonstrated with SRS in both sporadic and VHL-associated haemangioblastomas [29]. This however, appears to infer a diminishing benefit from the point of treatment, with control rates reducing to 70%, 61% and 51% at 8, 10 and 15 years, respectively [29]. Other centres have reported higher control rates of 80% at 10 years [48]. In complex cases, we have utilised multimodal management. We present a case (Fig. 3) of a large haemangioblastoma that was treated with combined embolisation, surgery and SRS to residual tumour. Combining modalities is emerging and is, to the best of our knowledge, underreported. The flexibility of options and individualisation makes this concept attractive in selected cases, but further studies are needed.

Medical Treatments

The molecular mechanism driving tumorigenesis in VHL-related lesions has been well elucidated [1] and provides promising therapeutic avenues with the potential to treat all VHL-deficient tumours in an individual regardless of tumour type or location.

Inhibition of HIF-2α, which is upregulated by pVHL loss, results in downregulation of HIF target gene expression and suppression of angiogenic sprouting in a zebrafish model of VHL [30]. Belzutifan, a HIF-2α inhibitor, has very recently been approved by the US Food and Drug Administration for the treatment of cancers (including haemangioblastomas) in adult patients with VHL disease based on results from an ongoing phase II trial (NCT03401788). Inhibition of histone deacetylases (HDACs) induces degradation of HIF-1α, [49] stabilises pVHL and attenuates growth of VHL-deficient tumours in mice [32]. Results of a phase I trial of the HDAC inhibitor vorinostat in VHL-associated haemangioblastomas are eagerly awaited (NCT02108002). Targeting the HIF-responsive VEGF pathway is another attractive therapeutic goal in VHL and trials are currently evaluating the role of the antiangogenic tyrosine kinase inhibitors PTK787/ZK22258 (NCT0052013) and pazopanib (NCT01436227) in haemangioblastomas in VHL.

Surveillance

For tumours that are asymptomatic, the consensus supported by most authors is for surveillance scans. The modality of choice is gadolinium enhanced MRI. There is no available guidance on what the time interval should be, and indeed there appears to be variation between different centres on scanning intervals. As previously mentioned, the natural history of haemangioblastomas is that they go through quiescent periods and growth periods, and this can and will vary from case to case. It is therefore important to try and tailor surveillance where possible to the individual case. This is dictated by previous growth patterns as well as treatment priorities with regard to other systemic problems. The multidisciplinary team is therefore key in deciding such management decisions. A point of contact for patients will also be able to tailor long-term surveillance to the patients'

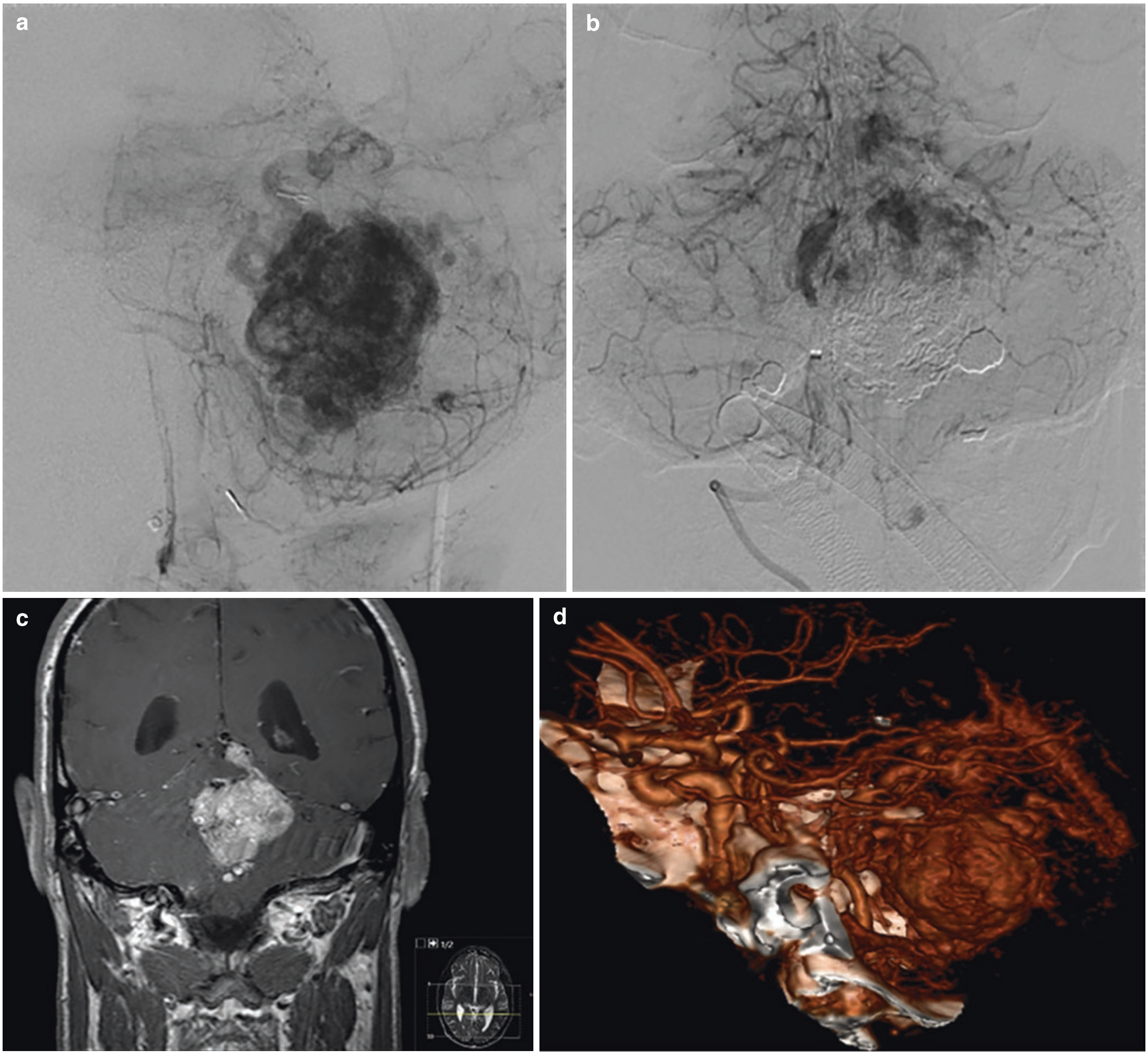

Fig. 3 A large, complex haemangioblastoma. (**a** and **b**) Angiogram shows partial embolisation; (**c**) Coronal T1 with gadolinium; (**d**) pre-operative 3D reconstruction with CTA. Patient was treated with a combination of modalities: partial embolisation, followed by surgery and SRS

personal circumstances as well. Artificial intelligence is increasingly used to provide predictive models and automation of decision making.

4 Conclusion

The management of haemangioblastomas has classically been surgical resection or surveillance. In association with VHL, the age of onset is early and so any treatment offered must be durable. In addition to this, treatment options must consider the rest of the features of VHL and so must the timing. If a lesion is not causing symptoms, we need to consider the best time to intervene in an unpredictable natural history. Technologies are improving to increase the safety of surgical resection and in attempting to predict from prior imaging when a lesion is likely to start growing again. In addition to this, multimodal treatments are being utilised in the management of these patients. Radiosurgery is becoming increasingly important in therapy. Furthermore, medical interventions targeting the angiogenesis pathways may provide systemic options allowing the treatment of multiple VHL-associated lesion types. These decisions and treatments should be considered in an interdisciplinary fashion with the patients' condition and treatments options at the centre of this. Treatment in every aspect is becoming more personalised.

References

1. Schunemann V, Huntoon K, Lonser RR. Personalized medicine for nervous system manifestations of von Hippel-Lindau disease. Front Surg. 2016;3:39.
2. Seizinger BR, Rouleau GA, Ozelius LJ, Lane AH, et al. Von Hippel-Lindau disease maps to the region of chromosome 3 associated with renal cell carcinoma. Nature. 1988;332(6161):268–9.
3. Clifford SC, Cockman ME, Smallwood AC, Mole DR, et al. Contrasting effects on HIF-1alpha regulation by disease-causing pVHL mutations correlate with patterns of tumourigenesis in von Hippel-Lindau disease. Hum Mol Genet. 2001;10(10):1029–38.
4. Hoffman MA, Ohh M, Yang H, Klco JM, et al. von Hippel-Lindau protein mutants linked to type 2C VHL disease preserve the ability to downregulate HIF. Hum Mol Genet. 2001;10(10):1019–27.
5. Zbar B, Kishida T, Chen F, Schmidt L, et al. Germline mutations in the Von Hippel-Lindau disease (VHL) gene in families from North America, Europe, and Japan. Hum Mutat. 1996;8(4):348–57.
6. Lonser RR, Butman JA, Huntoon K, Asthagiri AR, et al. Prospective natural history study of central nervous system hemangioblastomas in von Hippel-Lindau disease. J Neurosurg. 2014;120(5):1055–62.
7. Maher ER, Yates JR, Harries R, Benjamin C, et al. Clinical features and natural history of von Hippel-Lindau disease. Q J Med. 1990;77(283):1151–63.
8. Neumann HP, Eggert HR, Weigel K, Friedburg H, et al. Hemangioblastomas of the central nervous system. A 10-year study with special reference to von Hippel-Lindau syndrome. J Neurosurg. 1989;70(1):24–30.
9. GLASKER, S. Central nervous system manifestations in VHL: genetics, pathology and clinical phenotypic features. Familial Cancer. 2005;4(1):37–42.
10. Gläsker S, Bender BU, Apel TW, Natt E, et al. The impact of molecular genetic analysis of the VHL gene in patients with haemangioblastomas of the central nervous system. J Neurol Neurosurg Psychiatry. 1999;67(6):758–62.
11. Ho VB, Smirniotopoulos JG, Murphy FM, Rushing EJ. Radiologic-pathologic correlation: hemangioblastoma. AJNR Am J Neuroradiol. 1992;13(5):1343–52.
12. Neumann HP, Eggert HR, Scheremet R, Schumacher M, et al. Central nervous system lesions in von Hippel-Lindau syndrome. J Neurol Neurosurg Psychiatry. 1992;55(10):898–901.
13. Migliorini D, Haller S, Merkler D, Pugliesi-Rinaldi A, et al. Recurrent multiple CNS hemangioblastomas with VHL disease treated with pazopanib: a case report and literature review. CNS Oncol. 2015;4(6):387–92.
14. Thompson LD. Endolymphatic sac tumor. Ear Nose Throat J. 2013;92(4–5):184–8.
15. Ba-Abbad RA, Nowilaty SR. Bilateral optic disc swelling as the presenting sign of pheochromocytoma in a child. Medscape J Med. 2008;10(7):176.
16. Shah V, Zlotcavitch L, Herro AM, Dubovy SR, et al. Bilateral papillopathy as a presenting sign of pheochromocytoma associated with von Hippel-Lindau disease. Clin Ophthalmol. 2014;8:623–8.
17. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(6):1915–42.
18. Maxwell PH, Wiesener MS, Chang GW, Clifford SC, et al. The tumour suppressor protein VHL targets hypoxia-inducible factors for oxygen-dependent proteolysis. Nature. 1999;399(6733):271–5.
19. Elvidge GP, Glenny L, Appelhoff RJ, Ratcliffe PJ, et al. Concordant regulation of gene expression by hypoxia and 2-oxoglutarate-dependent dioxygenase inhibition: the role of HIF-1alpha, HIF-2alpha, and other pathways. J Biol Chem. 2006;281(22):15215–26.
20. Schödel J, Oikonomopoulos S, Ragoussis J, PUGH CW, et al. High-resolution genome-wide mapping of HIF-binding sites by ChIP-seq. Blood. 2011;117(23):e207–17.
21. Levy AP, Levy NS, Goldberg MA. Hypoxia-inducible protein binding to vascular endothelial growth factor mRNA and its modulation by the von Hippel-Lindau protein. J Biol Chem. 1996;271(41):25492–7.
22. Schraml P, Struckmann K, Hatz F, Sonnet S, et al. VHL mutations and their correlation with tumour cell proliferation, microvessel density, and patient prognosis in clear cell renal cell carcinoma. J Pathol. 2002;196(2):186–93.
23. Brauch H, Weirich G, Brieger J, Glavac D, et al. VHL alterations in human clear cell renal cell carcinoma: association with advanced tumor stage and a novel hot spot mutation. Cancer Res. 2000;60(7):1942–8.
24. Patard JJ, Fergelot P, Karakiewicz PI, Klatte T, et al. Low CAIX expression and absence of VHL gene mutation are associated with tumor aggressiveness and poor survival of clear cell renal cell carcinoma. Int J Cancer. 2008;123(2):395–400.
25. Carlessi R, Chen Y, Rowlands J, Cruzat VF, et al. GLP-1 receptor signalling promotes β-cell glucose metabolism via mTOR-dependent HIF-1α activation. Sci Rep. 2017;7(1):2661.
26. Van de Velde S, Hogan MF, Montminy M. mTOR links incretin signaling to HIF induction in pancreatic beta cells. Proc Natl Acad Sci U S A. 2011;108(41):16876–82.
27. Jin X, Dai L, Ma Y, Wang J, et al. Implications of HIF-1α in the tumorigenesis and progression of pancreatic cancer. Cancer Cell Int. 2020;20:273.
28. Ammerman JM, Lonser RR, Dambrosia J, Butman JA, et al. Long-term natural history of hemangioblastomas in patients with von Hippel-Lindau disease: implications for treatment. J Neurosurg. 2006;105(2):248–55.
29. Asthagiri AR, Mehta GU, Zach L, Li X, et al. Prospective evaluation of radiosurgery for hemangioblastomas in von Hippel-Lindau disease. Neuro-Oncology. 2010;12(1):80–6.
30. Wanebo JE, Lonser RR, Glenn GM, Oldfield EH. The natural history of hemangioblastomas of the central nervous system in patients with von Hippel-Lindau disease. J Neurosurg. 2003;98(1):82–94.
31. Resche F, Moisan JP, Mantoura J, de Kersaint-Gilly A, et al. Haemangioblastoma, haemangioblastomatosis, and von Hippel-Lindau disease. Adv Tech Stand Neurosurg. 1993;20:197–304.
32. Weil RJ, Lonser RR, Devroom HL, Wanebo JE, et al. Surgical management of brainstem hemangioblastomas in patients with von Hippel-Lindau disease. J Neurosurg. 2003;98(1):95–105.
33. Van Velthoven V, Reinacher PC, Klisch J, Neumann HP, et al. Treatment of intramedullary hemangioblastomas, with special attention to von Hippel-Lindau disease. Neurosurgery. 2003;53(6):1306–13; discussion 1313-1304
34. Smalley SR, Schomberg PJ, Earle JD, Laws ER, et al. Radiotherapeutic considerations in the treatment of hemangioblastomas of the central nervous system. Int J Radiat Oncol Biol Phys. 1990;18(5):1165–71.
35. Hojo M, Arakawa Y, Funaki T, Yoshida K, et al. Usefulness of tumor blood flow imaging by intraoperative indocyanine green

videoangiography in hemangioblastoma surgery. World Neurosurg. 2014;82(3–4):e495–501.
36. Molina CA, Pennington Z, Ahmed AK, Westbroek E, et al. Use of intraoperative indocyanine green angiography for feeder vessel ligation and en bloc resection of intramedullary hemangioblastoma. Oper Neurosurg (Hagerstown). 2019;17(6):573–9.
37. Tamura Y, Hirota Y, Miyata S, Yamada Y, et al. The use of intraoperative near-infrared indocyanine green videoangiography in the microscopic resection of hemangioblastomas. Acta Neurochir. 2012;154(8):1407–12; discussion 1412.
38. Herrmann HD, Neuss M, Winkler D. Intramedullary spinal cord tumors resected with CO_2 laser microsurgical technique: recent experience in fifteen patients. Neurosurgery. 1988;22(3):518–22.
39. Eskridge JM, Mcauliffe W, Harris B, Kim DK, et al. Preoperative endovascular embolization of craniospinal hemangioblastomas. AJNR Am J Neuroradiol. 1996;17(3):525–31.
40. Tampieri D, Leblanc R, Terbrugge K. Preoperative embolization of brain and spinal hemangioblastomas. Neurosurgery. 1993;33(3):502–5; discussion 505.
41. Vázquez-Añón V, Botella C, Beltrán A, Solera M, et al. Preoperative embolization of solid cervicomedullary junction hemangioblastomas: report of two cases. Neuroradiology. 1997;39(2):86–9.
42. Ene CI, Xu D, Morton RP, Emerson S, et al. Safety and efficacy of preoperative embolization of intracranial hemangioblastomas. Oper Neurosurg (Hagerstown). 2016;12(2):135–40.
43. Pan J, Ho AL, D'Astous M, Sussman ES, et al. Image-guided stereotactic radiosurgery for treatment of spinal hemangioblastoma. Neurosurg Focus. 2017;42(1):E12.
44. Niemelä M, Lim YJ, Söderman M, Jääskeläinen J, et al. Gamma knife radiosurgery in 11 hemangioblastomas. J Neurosurg. 1996;85(4):591–6.
45. Richard S, Campello C, Taillandier L, Parker F, et al. Haemangioblastoma of the central nervous system in von Hippel-Lindau disease. French VHL study group. J Intern Med. 1998;243(6):547–53.
46. Chakraborti PR, Chakrabarti KB, Doughty D, Plowman PN. Stereotactic multiple are radiotherapy. IV--Haemangioblastoma. Br J Neurosurg. 1997;11(2):110–5.
47. Bartoš R, Lodin J, Marek T, Sameš M, et al. Combined treatment of a medulla oblongata hemangioblastoma via permanent cysto-cisternal drainage and (postponed) gamma knife radiosurgery: a case report and review of the literature. Int J Neurosci. 2020;132:1–5.
48. Hanakita S, Koga T, Shin M, Takayanagi S, et al. The long-term outcomes of radiosurgery for intracranial hemangioblastomas. Neuro-Oncology. 2014;16(3):429–33.

Kong X, Lin Z, Liang D, Fath D, et al. Histone deacetylase inhibitors induce VHL and ubiquitin-independent proteasomal degradation of hypoxia-inducible factor 1alpha. Mol Cell Biol. 2006;26(6):2019–28.

Further Reading

Ben-Skowronek I, Kozaczuk S. Von Hippel-Lindau syndrome. Horm Res Paediatr. 2015;84(3):145–52.

Sung DI, Chang CH, Harisiadis L. Cerebellar hemangioblastomas. Cancer. 1982;49(3):553–5.

Petroclival Clinoidal Folds and Relationships with Arachnoidal Membranes and Neural Structures of Anterior and Middle Incisural Spaces: Old Neuroanatomical Terms for a New Neurosurgical Speech in Cadaver Labs with Limited Resources Era. Part I: Osteology and Structural Anatomy of Dura Mater

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1 Introduction

Neurosurgical diseases have a devastating impact on society. It is estimated that approximately 14 million essential neurosurgical cases develop worldwide annually, of which more than 80% arise in low- and middle-income countries. Neurosurgical cadaveric dissection remains largely unexploited as a learning tool for the training of surgeons in developing countries, often because of the assumed high costs [1]. The anterior and middle incisural spaces are brain regions of remarkable anatomic and neurosurgical interest due to complex relationships between bony, dural, arachnoidal, and neurovascular structures [2–14].

These areas are located at the junction between the sphenoid and the basal portion of the temporal bone (petrous bone, petrous apex, upper petro-clival region) and the free edge of the tentorium encircles them. The insertion of the tentorium itself to the petrous apex and the anterior and posterior clinoid processes give rise to three distinct dural folds or ligaments: the anterior petro-clinoid ligament, the posterior petro-clinoid ligament, and the inter-clinoid ligament. These dural folds participate to the dorsal lateral part of the roof of the cavernous sinus named "the oculomotor triangle" [2–5].

The primary purpose of this study is to describe the anatomy of this region with particular emphasis on the relationships between the anterior margin of the free edge of the tentorium and the sphenoid and petrous bone portions, as mentioned above. Moreover, we would like to examine the relationships between these compartments and the arachnoid membranes of the basal cisterns belonging to the anterior and middle incisural spaces.

We performed anatomical dissections mostly on fresh (less than 48 h post-mortem), non-formalin-fixed or injected specimens, to prevent arachnoid membranes changes and artifacts due to formalin-fixation process [13, 15, 16].

Under the patronage of Neurorehabilitation and Reconstructive Committee WFNS.

In memory of Professor Pasquale Ciappetta. Uncomparable neurosurgeon, patience master, and unforgettable friend.

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Nonetheless, formalin-fixed, or injected samples were used occasionally in this study for describing specific anatomical details apart from arachnoid-related structures. In addition, some of the photographs presented in this study were obtained "in vivo" during neurosurgical procedures involving this particular region.

This study highlights the need for a detailed anatomical comprehension of this region when performing neurosurgical practice with particular regard to the surgical treatment of pathologies involving the anterior and middle skull base.

The study has been subdivided into two parts to respect editorial guidelines.

The first part involves osteology and the structural organization of the dura mater of the region of interest.

2 Materials and Methods

In our laboratory, we normally use two kinds of anatomic preparations:

- Fresh cadavers of individuals who died between 24 and 48 h previously in nontraumatic circumstances when a diagnostic examination is expected and the head/neck represents an area of interest.
- Fresh-frozen specimens, purchased from private companies. To reduce costs, we perform all phases of specimen preparation, thawing, irrigation, fixation, perfusion, and storage according to a protocol developed in our Research Center.

In this study, we used eight fresh, non-formalin-fixed non-silicon-injected and five formalin-fixed silicon-injected adult cadaver heads.

The cranial vault was removed circumferentially to expose the entire skull base. The brains were left in place to allow better visualization and understanding of the relationships between the arachnoid membranes located in the central skull base, the sellar region, and anterior and lateral incisural spaces.

The study was focused on the description of the relationships between bony (anterior clinoid process, posterior clinoid process, optic canal, optic strut, superior orbital fissure) dural (anterior and posterior petroclinoid ligament, interclinoid ligament, proximal and distal dural ring, carotid-oculomotor membrane, falciform ligament, diaphragma sellae, carotid collar), arachnoid (basal arachnoid membrane, medial carotid membrane, Liliequist's membrane, perimesencephalic cisterns of the anterior and middle incisural space), and neurovascular structures (optic nerve, oculomotor nerves, internal carotid artery and its main branches).

For the description of osteology and structural anatomy of the dura mater of this region, we used frozen formalin-fixed human specimens.

A CANON 1Ds MarkIII camera was used to take high-definition photographs, using a MacroLens 100 mm or MP-E 65 1-5X to obtain a reproduction ratio of 1:1 or more (2:1–3:1). The operating microscope (Carl Zeiss Corp., Oberkochen, Germany) was used to perform dissections and examinations.

3 Results

3.1 Anterior and Posterior Clinoid Process

The anterior clinoid process is the bony prominence located at the medial limit of the lesser sphenoid wing. It represents the bony component of both the superior orbital fissure and anterior portion of the roof of the cavernous sinus (Figs. 1 and 2).

Three main sites of attachment characterize the connection of the anterior clinoid to the skull: the lesser sphenoid wing laterally, the roof of the optic canal and the planum sphenoidale medially and the optic strut inferior-medially. The optic strut extends from the inferior-medial margin of the anterior clinoid process to the body of the sphenoid bone, separating the superior orbital fissure from the optic canal and representing the lateral portion of the floor of the optic canal (Fig. 2).

The posterior clinoid processes represent the postero-lateral appendix of the dorsum sellae (Fig. 1). Both these structures are the site of attachment of dural folds derived from duplication of the anterior margin of the free edge of the tentorium at the petrous apex.

3.2 Structural Anatomy of Dura Mater in the Middle Cranial Fossa

The anterior clinoid process together with its dural attachments represents the anterior portion of the roof of the cavernous sinus. A thick layer of dura mater superiorly covers the clinoid process, also called the "meningeal layer" or "dura propria." This layer is continuous anterior-laterally with the falciform ligaments that represent the posterior-lateral portion of the roof of the optic canal. Medially, the dura propria continues as diaphragma sellae extending until the clivus, while posterior-medially it constitutes the distal dural ring, embracing the internal carotid artery (ICA) and representing the superior limit of the clinoid segment of the ICA itself (Fig. 3).

Upon intradural removal of the anterior clinoid process performed by cutting its three points of attachment to the skull base (lesser sphenoid wing, orbital roof and planum sphenoidale, optic strut), it is possible to reveal a deeper

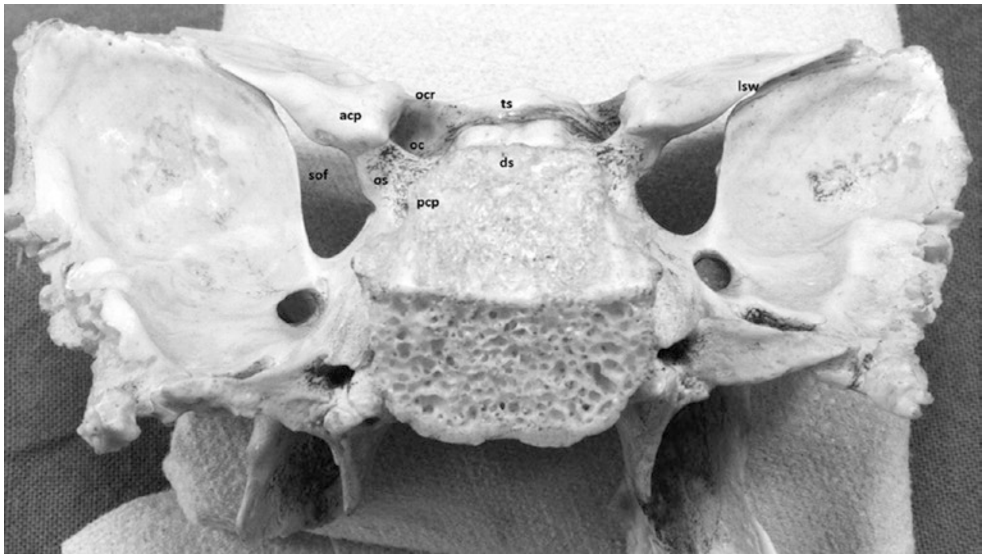

Fig. 1 Sphenoid bone, posterosuperior view. The anterior clinoid process (acp) is the bony prominence localized at the medial limit of the lesser sphenoid wing (lsw). It represents the bony component of both the superior orbital fissure (sof) and anterior portion of the roof of the cavernous sinus. The connection of the anterior clinoid to the skull is characterized by three main sites of attachment: the lesser sphenoid wing laterally, the roof of the optic canal (ocr) and the planum sphenoidale medially, and the optic strut (os) inferior-medially

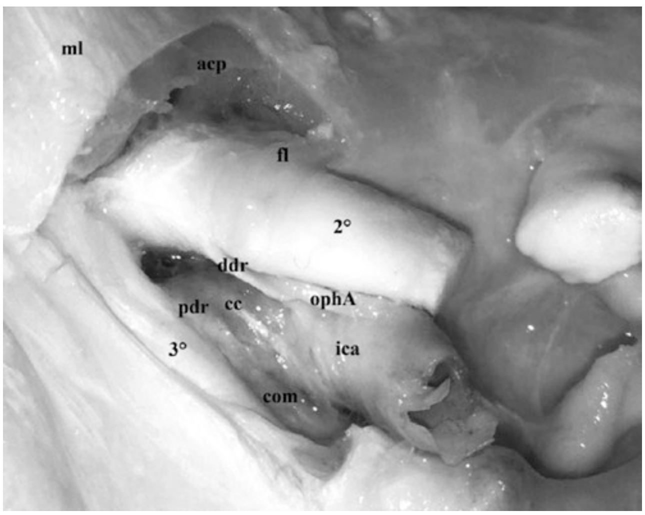

Fig. 3 Formalin-fixed, injected specimens, posterosuperior view, left side. The left anterior clinoid process (acp) has been removed through an intradural clinoidectomy, and the periosteal layer of dura mater localized below the clinoid has been exposed. The triangular area constituted by dura mater between the optic nerve and the oculomotor nerve is called the "carotid triangle" and represents the deepest layer of the anterior half of the roof of the cavernous sinus (the first two layers are the meningeal dura and the bony component of the anterior clinoid process). The denomination of the dura in this region is variable and depends on the localization of the membrane itself. Between the oculomotor nerve and the ICA (ica) it forms the carotid-oculomotor membrane (com) separating the oculomotor nerve from the ICA. At the exit point of the ICA from the cavernous sinus at the anterior portion of the carotid triangle, the carotid-oculomotor membrane surrounds the ICA constituting the proximal dural ring (pdr), which represents the inferior limit of the clinoid segment. The same layer of dura mater accompanies the clinoid portion of the ICA as the carotid collar (cc). fl, falciform ligament; 2°, optic nerve; 3°, oculomotor nerve

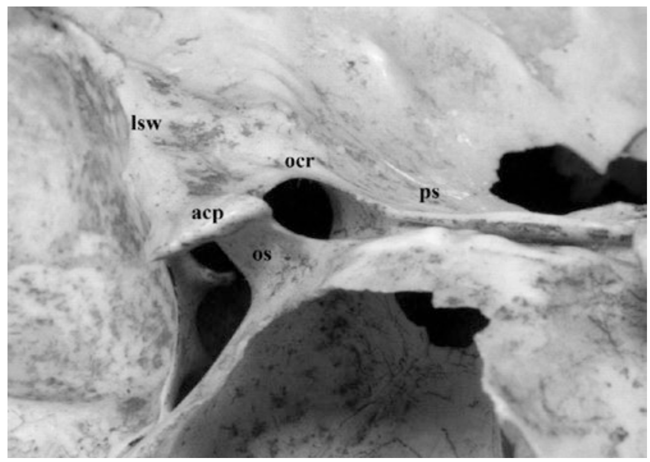

Fig. 2 Anterior clinoid process, magnified view. Attachment points of the anterior clinoid to the skull can be clearly identified: lesser sphenoid wing laterally (lsw), optic canal roof (ocr), and planum sphenoidale (ps) anteromedially, optic strut (os) inferior-medially. The optic strut is also the main constituent of the floor of the optic canal

layer dura mater (also known as "periosteal layer" or "reticular layer") that cover the inferior surface of the anterior clinoid.

The dural layer between the optic nerve and the third cranial nerve constitutes the so-called carotid triangle, which represent the deepest layer of the anterior half of the cavernous sinus roof (Fig. 3). It forms the carotid-oculomotor membrane separating the oculomotor nerve from the ICA.

When the ICA exits the cavernous sinus at the anterior portion of the carotid triangle, it is encircled by the carotid-oculomotor membrane constituting the proximal dural ring, which represents the inferior limit of the clinoid segment of the ICA itself. The same layer of dura mater accompanies the clinoid portion of the ICA forming the so-called carotid collar (Fig. 3). On the medial side, the dural collar is easily accessible from a dural pouch named as "carotid cave" by Kobayashi [9].

Posteriorly, the reticular layer of the carotid-oculomotor membrane and the meningeal layer of the distal dural ring merge to constitute a single layer of dura, which covers the triangular space between the petrous apex and the anterior and posterior clinoid processes.

4 Discussion

The anterior and middle incisural spaces are regions of remarkable anatomical and surgical interest [2–14]. Rhoton introduced the term "incisural space," and it is used to describe areas of the central nervous system located between the free edge of the tentorium and the upper brainstem [2]. The anterior incisural space is positioned anteriorly to the brainstem while the middle incisural space is lateral [2].

These regions are characterized by complex relationships between bony structures of the skull base, dura mater, arachnoid membranes, cisternal spaces, cranial nerves, and vascular structures [2–9].

Despite the well-known advantages of the fresh non-formalin-fixed dissection procedures [13, 15, 16], we preferred to use formalin-fixed silicon-injected specimens for the description of the osteology and structural anatomy of this region.

Using this technique, we have defined the structural anatomy of the dura mater surrounding the anterior clinoid process and covering the middle cranial fossa well.

As mentioned above, in this region, the dura mater is composed of two layers; a thick layer, also known as the meningeal layer, and a thin one, also known as the periosteal layer. The thick dural layer covers the superior surface of the anterior clinoid and connects with the dura of the falciform ligament and the diaphragma sellae. Moreover, on the medial side, the dura propria encircles the ICA constituting the distal dural ring, which represents the superior limit of the clinoid segment of the ICA itself [2–5, 10] (Fig. 3).

Intradural removal of the anterior clinoid process exposes a further triangular-shaped space called "carotid triangle" made by a second thinner layer of dura known as "periosteal" or "reticular" dura [2–5, 11]. This layer constitutes the so-called carotid-oculomotor membrane, which surrounds the internal carotid artery giving place to the proximal dural ring and the carotid collar [2–5]. The first represents the origin of the clinoid segment of the ICA; the carotid collar adheres to the ICA itself in its clinoid portion, forming a pouch on the medial side also known as "carotid cave" where intracranial aneurysms commonly develop [2–5, 10] (Fig. 3).

An accurate knowledge of the anatomy of this region is pivotal from a neurosurgical point of view since several pathologies, both neoplastic and vascular, involve it.

More extensive considerations regarding surgical applications of the anatomy of this region will be made in the next part of this study.

5 Conclusions

In the first part of this study, we performed an accurate study of the osteology and structural anatomy of the dura mater of the sphenoid bone, middle cranial fossa with particular interest paid to the anterior clinoid process. Accurate knowledge of this region is pivotal from a neurosurgical point of view since this area is the location of several pathologies of neurosurgical interest. Moreover, the anatomy of these structures is preparatory for the description of the subsequent part of this paper.

References

1. Signorelli F, Stumpo V, Della Pepa GM, La Rocca G, Oliva A, Olivi A, Visocchi M. Step-up Establishement of neurosurgical laboratory starting with limited resources—tips and tricks. World Neurosurg. 2019;pii:S1878-8750(19)30445. https://doi.org/10.1016/j.wneu.2019.02.034.
2. Rhoton AL Jr. Tentorial incisura. Neurosurgery. 2000;47(3 Suppl):S131–53.
3. Rhoton AL Jr. The cavernous sinus, the cavernous venous plexus, and the carotid collar. Neurosurgery. 2002;51(4 Suppl):S375–410; Review. PubMed PMID: 12234454.
4. Umansky F, Valarezo A, Elidan J. The superior wall of the cavernous sinus: a microanatomical study. J Neurosurg. 1994;81(6):914–20.
5. Yasuda A, Campero A, Martins C, Rhoton AL Jr, de Oliveira E, Ribas GC. Microsurgical anatomy and approaches to the cavernous sinus. Neurosurgery. 2008;62(6 Suppl 3):1240–63. https://doi.org/10.1227/01.neu.0000333790.90972.59.
6. Inoue K, Seker A, Osawa S, Alencastro LF, Matsushima T, Rhoton AL Jr. Microsurgical and endoscopic anatomy of the supratentorial arachnoidal membranes and cisterns. Neurosurgery. 2009;65(4):644–64. https://doi.org/10.1227/01.NEU.0000351774.81674.32; discussion 665. PubMed PMID: 19834369.
7. Martins C, Yasuda A, Campero A, Rhoton AL Jr. Microsurgical anatomy of the oculomotor cistern. Neurosurgery. 2006;58(4 Suppl 2):ONS-220-7; discussion ONS-227-8. PubMed PMID: 16582644.
8. Joo W, Yoshioka F, Funaki T, Rhoton AL Jr. Microsurgical anatomy of the abducens nerve. Clin Anat. 2012;25(8):1030–42. https://doi.org/10.1002/ca.22047; Epub 2012 Feb 14. PubMed PMID: 22334502.
9. Joo W, Rhoton AL Jr. Microsurgical anatomy of the trochlear nerve. Clin Anat. 2015;28(7):857–64. https://doi.org/10.1002/ca.22602; Epub 2015 Aug 28. Review. PubMed PMID: 26223856.
10. Kobayashi S, Kyoshima K, Gibo H, Hegde SA, Takemae T, Sugita K. Carotid cave aneurysms of the internal carotid artery. J Neurosurg. 1989;70(2):216–21.
11. Seoane E, Tedeschi H, de Oliveira E, Wen HT, Rhoton AL Jr. The pretemporal transcavernous approach to the interpeduncular and prepontine cisterns: microsurgical anatomy and technique application. Neurosurgery. 2000;46(4):891–8; discussion 898-9. PubMed PMID: 10764262.

12. McLaughlin N, Ma Q, Emerson J, Malkasian DR, Martin NA. The extended subtemporaltranstentorial approach: the impact of trochlear nerve dissection and tentorialincision. J Clin Neurosci. 2013;20(8):1139–43. https://doi.org/10.1016/j.jocn.2012.11.006; Epub 2013 Jun 3. PubMed PMID: 23743353.
13. Ciappetta P, Pescatori L. Anatomic dissection of arachnoid membranes encircling the pituitary stalk on fresh, non-formalin-fixed specimens: Anatomoradiologic correlations and clinical applications in Craniopharyngioma surgery. World Neurosurg. 2017;108:479–90. https://doi.org/10.1016/j.wneu.2017.07.138; Epub 2017 Jul 31.
14. Pescatori L, Niutta M, Tropeano MP, Santoro G, Santoro A. Fourth cranial nerve: surgical anatomy in the subtemporaltranstentorial approach and in the pretemporal combined inter-intradural approach through then fronto-temporo-orbito-zygomaticcraniotomy. A cadaveric study. Neurosurg Rev. 2017;40(1):143–53. https://doi.org/10.1007/s10143-016-0777-9; Epub 2016 Aug 22.
15. Saboori P, Sadegh A. Histology and morphology of the brain sub-arachnoid trabeculae. Anat Res Int. 2015;2015:2015279814.
16. Benet A, Rincon-Torroella J, Lawton MT, González Sánchez JJ. Novel embalming solution for neurosurgicalsimulation in cadavers. J Neurosurg. 2014;120:1229–37.

Petroclival Clinoidal Folds and Relationships with Arachnoidal Membranes of Anterior and Middle Incisural Spaces: Old Neuroanatomical Terms for a New Neurosurgical Speech in Cadaver Labs with Limited Resources Era. Part II: Free Edge of the Tentorium, Petroclinoid Folds, and Incisural Spaces

Pescatori Lorenzo, Tropeano Maria Pia, Lorenzo Gitto, Massimiliano Visocchi, Francesco Signorelli, and Ciappetta Pasqualino

1 Introduction

In the first part of this article, we explained why cadaver lab dissection plays a pivotal role in Neurosurgery.

The constant increase of neurosurgical pathologies in low and middle income countries represents a huge challenge for the neurosurgical community, especially the necessity to prepare a new generation of effective and autonomous neurosurgeons [1]. In this scenario we tried to demonstrate how, even in low resource setting, it is possible to perform clear and educational anatomic dissection [1, 2]. The choice of a very complex anatomic region such as the petroclinoid area as well as the incisural spaces reflects our willingness to demonstrate the effectiveness of our dissection techniques [3–15].

After describing the osteology of the petroclival region and the structural anatomy of the dura mater in the middle cranial fossa, we are going to examine the relationships between the petroclinoid dural folds, the anterior and middle incisural spaces, and the neurovascular structures of this region.

To avoid the formalin fixation process artifacts on arachnoid membranes and neurovascular structures, this part of the study was entirely performed on fresh non-formalin-fixed human specimens [14, 16, 17].

2 Materials and Methods

Thirteen anatomical specimens, including five injected specimens, were dissected in this study.

In the first part of the study, osteology of the petroclival region and structural anatomy of the dura mater in the middle cranial fossa were described on five formalin-fixed, silicon-injected cadaveric heads.

The description of the tentorial incisura, petroclinoid folds, and incisural spaces is the result of dissections mostly performed on fresh (less than 48 h post-mortem), non-formalin-fixed nor injected specimens. As mentioned above,

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In memory of Professor Pasquale Ciappetta. Uncomparable neurosurgeon, patience master, and unforgettable friend.

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this dissection technique prevents arachnoid membranes changes and artifacts due to the formalin fixation process [14, 16, 17]. The cadaver work is the result of the cooperation between three national university laboratories in Italy.

The cranial vault was removed circumferentially to expose the entire skull base. The brain was left in place to allow better visualization and understanding of the relationships between the arachnoid membranes located in the central skull base, the sellar region, and anterior and lateral incisural spaces.

This part of the study focused on the description of the relationships between the tentorial incisura, petroclinoid ligaments, and anterior and middle incisural spaces.

A CANON 1Ds MarkIII camera was used to take high-definition photographs, using a MacroLens 100 mm or MP-E 65 1-5X to obtain a reproduction ratio of 1:1 or more (2:13:1). The operating microscope (Carl Zeiss Corp., Oberkochen, Germany) was used to perform dissections and examinations.

3 Results

3.1 Free Edge of the Tentorium and Petroclinoid Folds

The term "free edge of the tentorium" indicates the margin of the tentorium, which is not attached to the skull and delimits the incisural space on the medial side.

Anteriorly, it is fixed to the petrous apex and splits into two distinct components also known as dural folds or ligaments (Fig. 1a).

The first component is the anterior petro-clinoid ligament, which connects to the anterior clinoid process; the second component is made by the posterior petro-clinoid ligaments, which join to the posterior clinoid. Moreover, between the anterior and posterior clinoid processes, the dura of the skull base depicts a distinguishable dural fold called the interclinoid ligament (Fig. 1a).

These dural folds delimit a triangular space, pierced by the oculomotor nerve, which is commonly called the "oculomotor triangle" (Fig. 1a). It represents the posterior part of the roof of the cavernous sinus through which the oculomotor and trochlear nerves enter the cavernous sinus. The oculomotor nerve penetrates the dura in the central region of the oculomotor triangle, and the trochlear nerve enters the dura at its posterolateral edge (Fig. 1a–c).

The Gruber ligament or petro-sphenoid ligament (PSL) passes between the folds of the posterior petro-clinoid ligament from the petrous apex to the lateral border of the dorsum sellae, just below the posterior clinoid process (Fig. 1c).

As mentioned above, the free edge of tentorium represents the lateral boundary of the tentorial incisura.

As a consequence, the tentorial incisura may be defined as the anatomical region located between the free edge of the tentorium and the upper brainstem (Figs. 1c, 2). It represents the only existing communication between the supratentorial and infratentorial space.

3.2 Incisural Spaces

Three different portions of the incisural space are identified: anterior, middle, and posterior incisural spaces. The anterior incisural space is located anteriorly to the brainstem; the middle incisural space is placed laterally to it; the posterior incisural space is positioned posteriorly (Figs. 1c, 2). The mesencephalon, the pons and the superior surface of the cerebellar hemispheres occupy the incisural space.

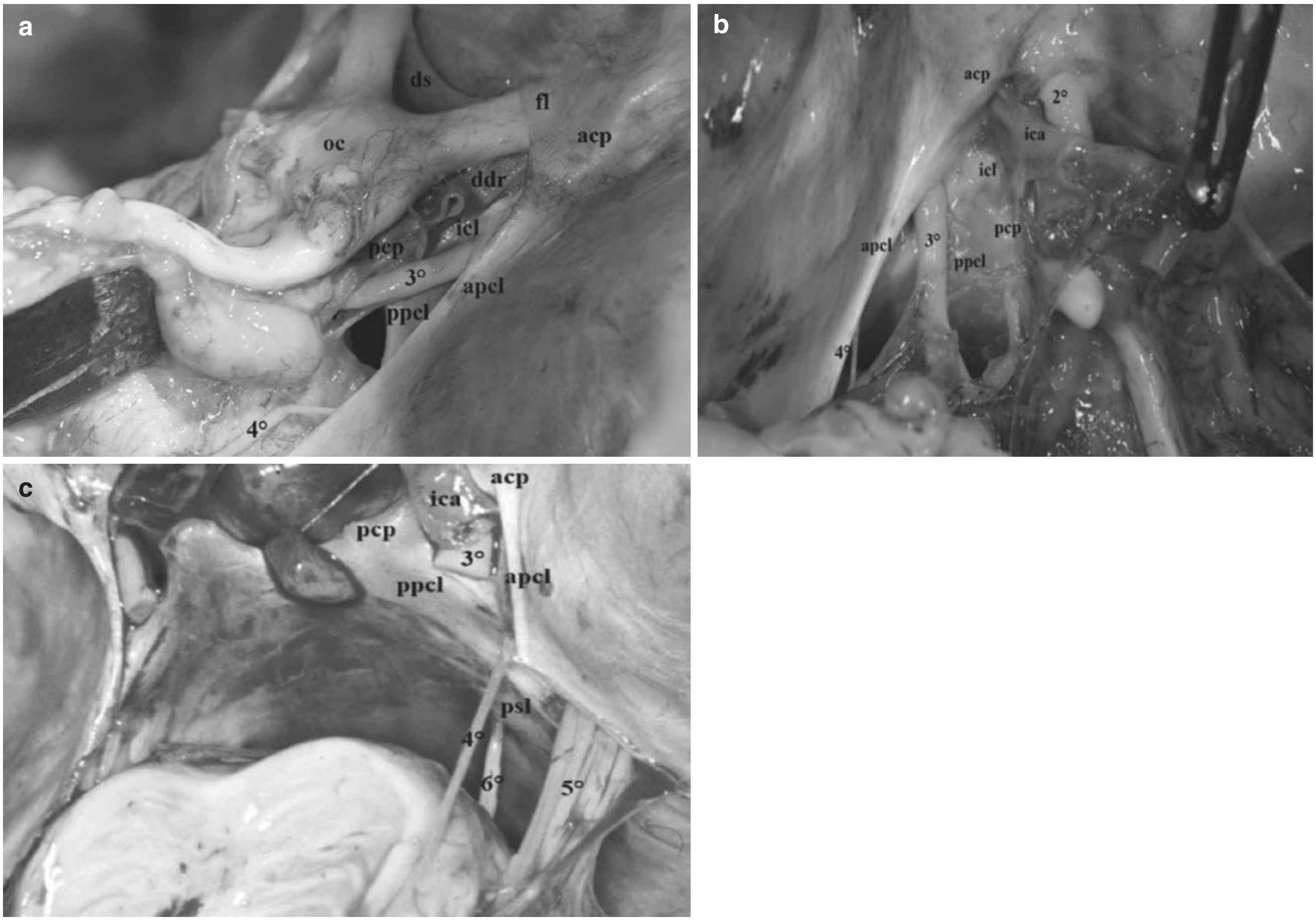

Fig. 1 These pictures show the relationships between dural folds, bony structures, and cranial nerves. (**a**) Fresh, non-formalin-fixed specimen, anatomic dissection, right side. The dura propria cover the superior surface of the anterior clinoid process (acp). Anterolaterally this dural layer is continuous with the falciform ligaments (fl) which represents the postero-lateral portion of the roof of the optic canal. Medially, together with the basal arachnoid membrane, the dura propria continues as diaphragma sellae (ds) extending until the clivus. Here, it constitutes posterior-medially the distal dural ring (ddr) embracing the internal carotid artery (ICA) and representing the superior limit of the clinoid segment of the ICA itself. In this dissection, the dural folds constituting the oculomotor triangle are evident: anterior petroclinoid ligament (apcl), posterior petroclinoid ligament (ppcl), interclinoid ligament (icl). The oculomotor nerve (3°) penetrating in the central part of the oculomotor triangle can be clearly observed. Posteriorly, the trochlear nerve (4°) pierces the tentorium. (**b**) Fresh, non-formalin-fixed specimen, anatomic dissection, left side. In this dissection, the dural folds forming the oculomotor triangle can be observed. The first two components are the anterior and posterior petroclinoid ligaments (apcl, ppcl) coursing between the petrous apex and the anterior and posterior clinoid process, respectively (acp, pcp). The third component is the interclinoid ligament (icl) localized between the anterior and posterior clinoids. The cisternal portion and the petroclinoid portion of the oculomotor nerve can be seen (see text for details). The oculomotor nerve (3°) penetrates the dura in the central part of the oculomotor, whereas the trochlear nerve (4°) enters the dura at the posterolateral edge of this triangle. (**c**) Fresh non-formalin-fixed specimens, anatomic dissection. The arachnoid trabeculae of the mesencephalic portion of the Lilequist's membrane were removed, and the oculomotor nerves (3°) were dissected to show the space between the upper-middle clivus and the brainstem within the posterior half of the anterior incisural space. On the right side, below the cisternal portion of the fourth (4°) and the fifth (5°) cranial nerves the sixth cranial nerve (6°) exits the brainstem at the pontomedullary sulcus and ascends within the prepontine cistern to pierce the dura of the clivus and eventually enters within the Dorello's canal. The roof of the channel is constituted by the petrous sphenoid ligament (aka Gruber's ligament, psl) running between the petrous apex and the dorsum sellae just below the posterior clinoid process (pcp). Further, structures observable in this dissection are the anterior clinoid process (acp), the anterior petroclinoid ligament (apcl), and the ICA (ica)

Fig. 2 Fresh non-formalin-fixed specimen anatomic dissection, superior view of the skull base. The cerebral hemispheres were removed, and the tentorium (t) was transected in a mediolateral direction from the tentorial edge to show the anterior and middle incisural spaces and their content. The anterior incisural space is the part of incisural space localized ventral to the brain stem. Postero-inferiorly, it spreads between the brainstem and the clivus; anteriorly, it encircles the optic chiasm. Above the optic chiasm, it reaches the subcallosal area. Below the chiasm and the third ventricular floor, it extends backward until it enters the interpeduncular fossa and cistern. The middle incisual space is lateral to the brain stem. m, mesencephalon, p, pons; ba, basilar artery; ce, cerebellar hemisphere; 5°, trigeminal nerve; 6°, abducens nerve; 3°, oculomotor nerve; 2°, optic nerve; oc, optic chiasm

4 Discussion

The second part of our study focused on the description of the tentorial incisural, petroclinoid ligaments, and incisural spaces.

As explained in part I of this study, the term "incisural space" was introduced by Rothon to describe the area of the central nervous system located between the free edge of the tentorium and the upper brainstem [3].

Depending on the location with respect to the brainstem, the incisural spaces have been divided into anterior (in front of the brainstem), middle (lateral to the brainstem), and posterior (behind the brainstem) [3].

Previous studies focused their attention on this topic, but they were performed on formalin-fixed cadaver specimens [3–10].

In the presented study, we had the chance to dissect fresh specimens, enabling us to avoid the changes and artifacts due to the formalin fixation process. Indeed, it has been reported that formalin leads to arachnoid membranes morphological changes, affecting the accuracy of the dissections and adding bias to anatomical descriptions [16, 17].

Dissecting fresh specimens gave us the possibility to better understand and describe the anatomical relationships between the dural folds and the arachnoid membranes in this region.

The performed dissections mainly focused on evaluating the region of the skull base known as the "oculomotor triangle," characterized by dural folds running between the petrous apex and the anterior and posterior clinoid processes [3–6].

In our study, the three main components of this triangle were clearly identifiable in all the performed dissections. The anterior and posterior petro-clinoid ligaments, running between the petrous apex and the anterior and posterior petro-clinoid process, respectively, derive from a duplication of the free edge of the tentorium at the petrous apex. The third component of the triangle includes the interclinoid ligament formed by a thickening of the dura propria extended between the anterior and posterior clinoid processes (Fig. 1a–c).

The petroclinoid portion of the oculomotor nerve penetrates the triangle in its central part passing through an elliptical opening known as the oculomotor porus [5, 8] (Fig. 1a, b).

The superior dissection experience provided by fresh cadavers in our study, above all regarding cisternal anatomy, demonstrates the feasibility of establishing a neurosurgical cadaver dissection laboratory for training and research purposes even in the presence of limited resources, in a context in which sophisticated embalming techniques are not exploited.

5 Conclusions

In the second part of this study, a detailed description of the anatomy of the tentorial incisura, petroclinoid folds, and incisural spaces was given. The possibility to perform dissections on fresh specimens augmented the accuracy of the description given eliminating the formalin fixation process artifacts. Moreover, using this technique reduces the specimen preparation costs, making the dissection feasible even in the presence of limited resources.

References

1. Signorelli F, Stumpo V, Della Pepa GM, La Rocca G, Oliva A, Olivi A, Visocchi M. Step-up establishement of neurosurgical laboratory starting with limited resources—tips and tricks. World Neurosurg. 2019;pii:S1878-8750(19)30445. https://doi.org/10.1016/j.wneu.2019.02.034.
2. Signorelli F. The craniovertebral junction and laboratory experience: the Italian paradox. Acta Neurochir Suppl. 2019;125:11–2. https://doi.org/10.1007/978-3-319-62515-7_2.
3. Rhoton AL Jr. Tentorial incisura. Neurosurgery. 2000;47(3 Suppl):S131–53.
4. Rhoton AL Jr. The cavernous sinus, the cavernous venous plexus, and the carotid collar. Neurosurgery. 2002;51(4 Suppl):S375–410; Review.
5. Umansky F, Valarezo A, Elidan J. The superior wall of the cavernous sinus: a microanatomical study. J Neurosurg. 1994;81(6):914–20.
6. Yasuda A, Campero A, Martins C, Rhoton AL Jr, de Oliveira E, Ribas GC. Microsurgical anatomy and approaches to the cavernous sinus. Neurosurgery. 2008;62(6 Suppl 3):1240–63.
7. Inoue K, Seker A, Osawa S, Alencastro LF, Matsushima T, Rhoton AL Jr. Microsurgical and endoscopic anatomy of the supratentorial arachnoidal membranes and cisterns. Neurosurgery. 2009;65(4):644–64; discussion 665.
8. Martins C, Yasuda A, Campero A, Rhoton AL Jr. Microsurgical anatomy of the oculomotor cistern. Neurosurgery. 2006;58(4 Suppl 2):ONS-220-7; discussion ONS-227-8.
9. Joo W, Yoshioka F, Funaki T, Rhoton AL Jr. Microsurgical anatomy of the abducens nerve. Clin Anat. 2012;25(8):1030–42.
10. Joo W, Rhoton AL Jr. Microsurgical anatomy of the trochlear nerve. Clin Anat. 2015;28(7):857–64.
11. Kobayashi S, Kyoshima K, Gibo H, Hegde SA, Takemae T, Sugita K. Carotid cave aneurysms of the internal carotid artery. J Neurosurg. 1989;70(2):216–21.
12. Seoane E, Tedeschi H, de Oliveira E, Wen HT, Rhoton AL Jr. The pretemporal transcavernous approach to the interpeduncular and prepontine cisterns: microsurgical anatomy and technique application. Neurosurgery. 2000;46(4):891–8; discussion 898-9.
13. McLaughlin N, Ma Q, Emerson J, Malkasian DR, Martin NA. The extended subtemporal transtentorial approach: the impact of trochlear nerve dissection and tentorial incision. J Clin Neurosci. 2013;20(8):1139–43.
14. Ciappetta P, Pescatori L. Anatomic dissection of arachnoid membranes encircling the pituitary stalk on fresh, non-formalin-fixed specimens: Anatomoradiologic correlations and clinical applications in Craniopharyngioma surgery. World Neurosurg. 2017;108:479–90.
15. Pescatori L, Niutta M, Tropeano MP, Santoro G, Santoro A. Fourth cranial nerve: surgical anatomy in the subtemporal transtentorial approach and in the pretemporal combined inter-intradural approach through then fronto-temporo-orbito-zygomatic craniotomy. A cadaveric study. Neurosurg Rev. 2017 Jan;40(1):143–53.
16. Saboori P, Sadegh A. Histology and morphology of the brain subarachnoid trabeculae. Anat Res Int. 2015;2015:2015279814.
17. Benet A, Rincon-Torroella J, Lawton MT, González Sánchez JJ. Novel embalming solution for neurosurgical simulation in cadavers. J Neurosurg. 2014;120:1229–37.

Petroclival Clinoidal Folds and Relationships with Arachnoidal Membranes of Medial Incisural Space: Old Neuroanatomical Terms for a New Neurosurgical Speech in Cadaver Labs with Limited Resources Era. Part III: Arachnoid Membranes, Cranial Nerves, and Surgical Implications

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1 Introduction

In the first two parts of our study, in a "low resource laboratory", we described [1, 2] the anatomy of the anterior and middle incisural spaces by describing the regional osteology, the structural anatomy of the dura mater of the middle cranial fossa, as well as the tentorial incisura and petroclinoid folds [3–14].

In the third part, we complete our study of the arachnoid membranes and cranial nerves of the anterior and middle incisural spaces. In the description of these structures, the usefulness of the dissection on fresh, non-formalin-fixed human specimens is clearly demonstrated.

Moreover, we identified and described surgical implications of these anatomical topics in different types of neurosurgical procedures dealing with this anatomic area.

Even though current literature contains plenty of anatomical studies detailing even the most hidden and tangled meander of human skull base and superb dissection images and drawings are currently available, few studies demonstrated how, even in low-resource setting and without elaborate specimens preparation, good-quality dissection exploring very complex and deep skull base structures are feasible [1, 2].

2 Materials and Methods

The description of the structures in this part of the study was obtained by performing anatomical dissections only on fresh (less than 48 h post-mortem), non-formalin-fixed or injected specimens, to prevent arachnoid membranes changes and artifacts due to the formalin fixation process [14–16].

After removing the cranial vault circumferentially, leaving the brain in place, we examined the anatomy of arachnoid membranes and cranial nerves of the anterior and middle incisural spaces.

In addition, some of the photographs presented in this study were obtained "in vivo" during neurosurgical procedures involving this particular region.

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A CANON 1Ds MarkIII camera was used to take high-definition photographs, using a MacroLens 100 mm or MP-E 65 1-5X to obtain a reproduction ratio of 1:1 or more (2:1–3:1). The operating microscope (Carl Zeiss Corp., Oberkochen, Germany) was used to perform dissections and examinations.

3 Results

3.1 The Liliequist's Membrane (Figs. 1a–d, 2)

The Liliequist's membrane originates from the outer arachnoid membrane located in correspondence to the posterior clinoid processes and the dorsum sellae. As it spreads caudally and superiorly between the oculomotor nerves, it splits into two distinct membranes: the diencephalic and mesencephalic sheets. The diencephalic sheet extends upward and backward, connecting to the posterior portion of the mamillary bodies and separating the chiasmatic and the interpeduncular cistern. The lateral margin of both the mesencephalic and diencephalic sheets continues into the arachnoid membrane, surrounding the oculomotor nerves. In all the performed dissections, trabeculae originating from the superior surface of the Liliequist's membrane co-joined to the inferolateral surface of the optic chiasm and the posterior and postero-lateral surface of the pituitary stalk overlapped the basal arachnoid membrane.

3.2 Pituitary Stalk and Pituitary Stalk Cisternal Space (Figs. 1a–d, 2)

The pituitary stalk is a neural peduncle connecting the hypophysis to the floor of the third ventricle. It crosses the anterior incisural space entering the opening of the diaphragma sellae. The pituitary stalk is contained almost entirely within the chiasmatic cistern. A brief portion of the distal third of the pituitary stalk adjacent to the diaphragma sellae is extra-arachnoidal. In all the performed dissections, it was possible to identify the arachnoid components encircling the neural tissue of the stalk. The basal arachnoid membrane covers the stalk circumferentially and reflecting upward over its surface at the penetrating site on the diaphragma sellae.

The anterolateral surface and the posterolateral surface are also entirely and constantly encircled by trabeculae originating from the medial carotid membrane and the Liliequist's membrane, respectively. These three distinct components create a "funnel-shaped" arachnoid collar around the pituitary stalk, thus delimiting a cisternal space separated from, but at the same time contained within, the chiasmatic cistern.

3.3 Cranial Nerves (See Figs. 1, 2, 3 Part II)

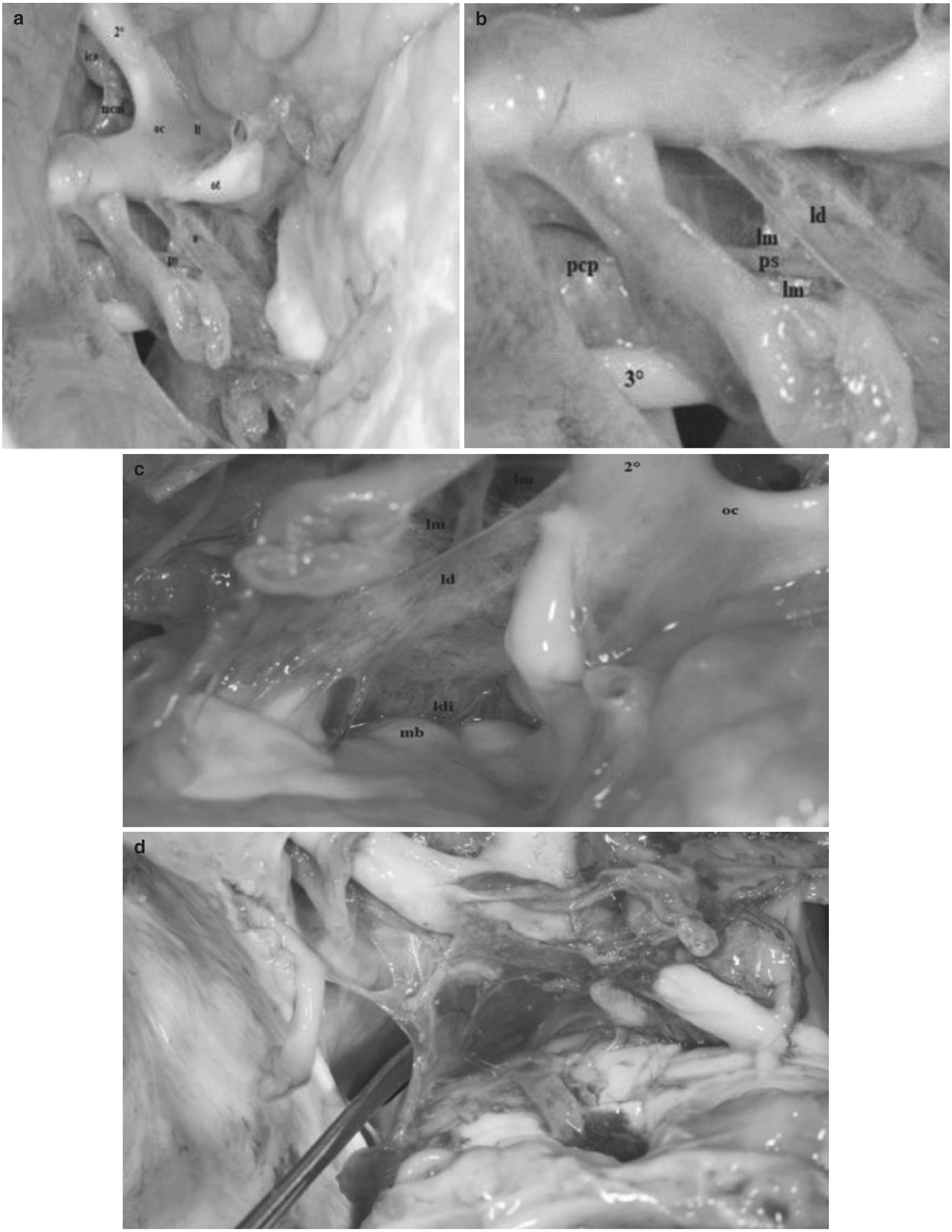
Cranial nerves related to the anterior and middle incisural space are the optic nerves, oculomotor nerve, trochlear nerve, trigeminal nerve, and abducens nerve.

The oculomotor nerve may be subdivided into four distinct segments: cisternal, petroclinoid, trigonal, and cavernous.

The fourth cranial nerve may be divided into three distinct segments: cisternal, tentorial, and cavernous.

The trigeminal nerve originates on the anterolateral margin of the pons, and runs through the pre-pontine cistern toward the petrous apex where it lies on the trigeminal impression. Here, the dural duplication of the tentorial edge's anterior margin depicts a cavity called trigeminal porus. The trigeminal nerve, surrounded by its cistern, passes the porus entering Meckel's cave, located in the space between the periosteal and meningeal layers of the middle fossa. The

Fig. 1 a Fresh, non-formalin-fixed specimen anatomic dissection simulating a left frontotemporal trans-Sylvian approach. Some of the arachnoid membranes of the anterior space were exposed. The medial carotid membrane (mcm) origin from the inferior-medial side of the supraclinoid ICA (ica) and attaches on the inferolateral surface of the optic chiasm (oc) reflecting over the anterolateral surface of the pituitary stalk (ps). It separates the carotid from the chiasmatic cistern. Above the optic chiasm, the lamina terminalis (lt) is visible. Posteriorly and inferiorly, arachnoid trabeculae belonging to the basal arachnoid and the diencephalic portion of Liliequist's membrane are visible (**a**). *ot* optic tract. (**b**) Fresh, non-formalin-fixed specimen, anatomic dissection simulating a left frontotemporal trans-Sylvian approach, magnification. The components of Liliequist's membrane can be identified. The diencephalic portion (**d**) runs from the dorsum sellae to the mammillary bodies, whereas the mesencephalic portion (lm) extends from the dorsum sellae to the pontomesencephalic sulcus (3°, oculomotor nerve; pcp, posterior clinoid process; ps, pituitary stalk). (**c**) Fresh, non-formalin-fixed specimen, anatomic dissection, left side. The frontal lobe has been spatulated, and through a more frontal trajectory, the diencephalic portion of Liliequist's membrane (**d**) can be observed and followed until its attachment (ldi) to the mammillary bodies (mb). Below the diencephalic component, the mesencephalic portion (lm) separating the interpeduncular from the pre-pontine cistern is visible. (oc, optic chiasm; 2°, optic nerve). (**d**) Fresh non-formalin-fixed specimen, superolateral view, left side. The dissector has been placed below the mesencephalic portion of Liliequist's membrane to demonstrate how it separates the prepontine cistern from the interpeduncular one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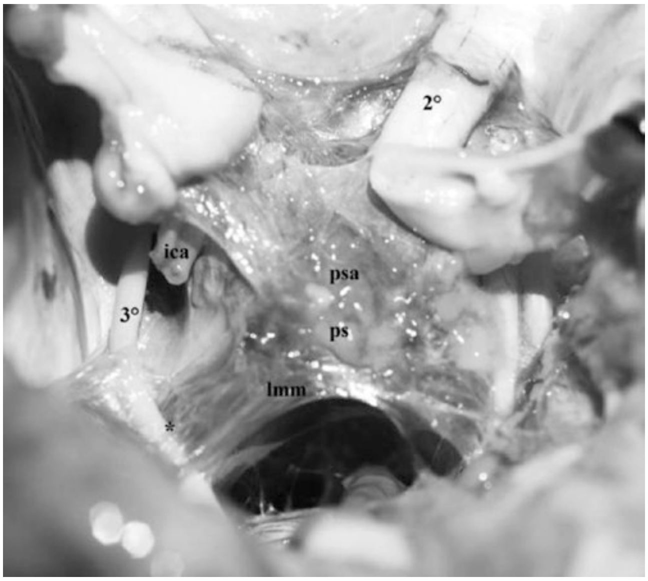
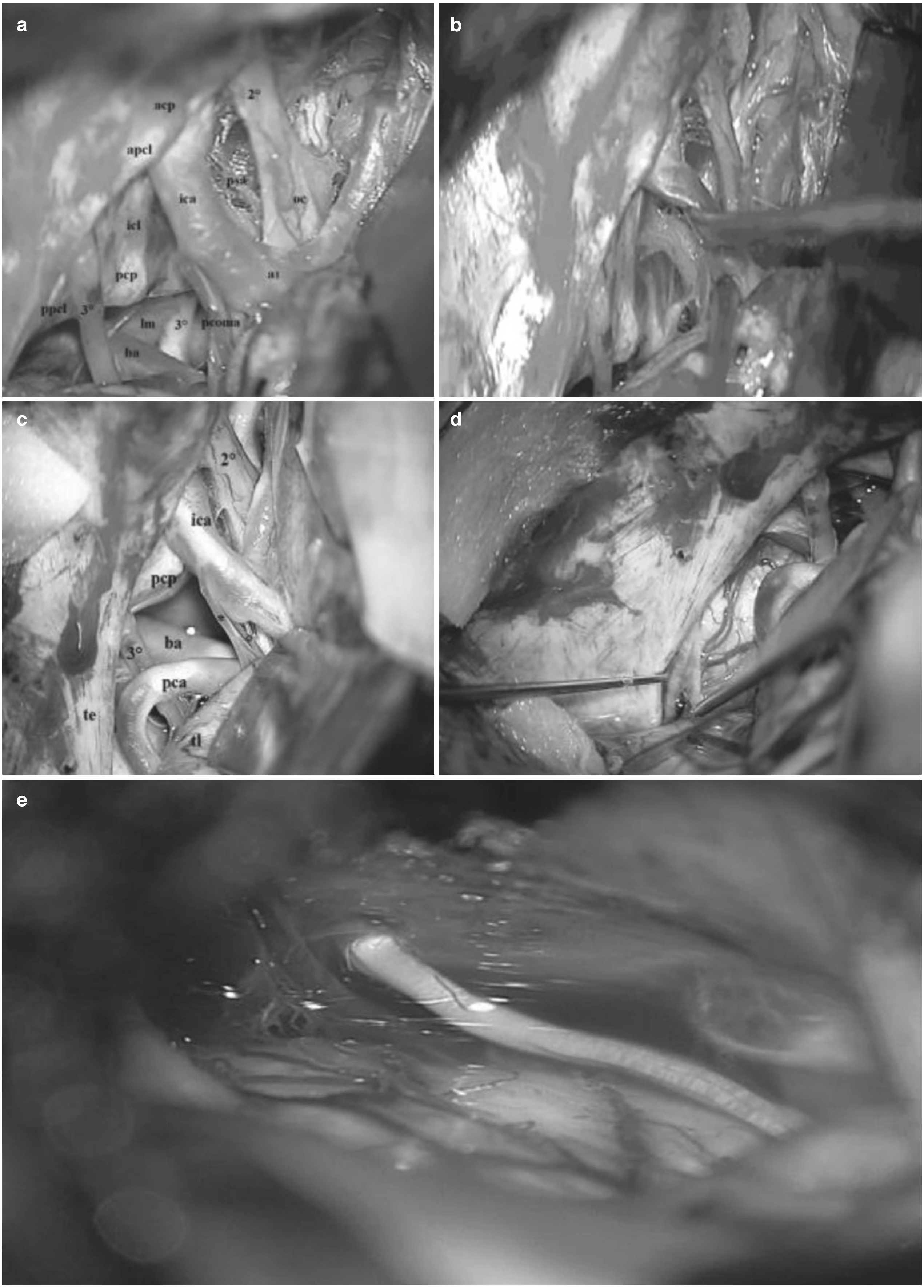


Fig. 2 Fresh, non-formalin-fixed specimen anatomic dissection, superior view. The frontal and temporal lobes were removed leaving the basal arachnoid membrane in place, and the optic chiasm was dissected. In this dissection, the anterior incisural space and the arachnoid membranes of the region can be visualized. The pituitary stalk (ps) is approximately localized in the central part of the anterior incisural space. Anteriorly, it is covered by arachnoid trabeculae (psa) originating from the medial carotid membrane and the basal arachnoid membrane of the frontal lobes. Posteriorly, the mesencephalic portion of Liliequist's membrane (lmm) runs from the dorsum sellae to the ponto-mesencephalic sulcus separating the pre-pontine incompletely from the interpeduncular cistern. Ventral trabeculae of Liliequist's membrane cover the posterior surface of the pituitary stalk completing, together with the arachnoid membrane as mentioned above, the funnel-shaped arachnoid collar delimiting the pituitary stalk cisternal space. Posterolaterally, note the accurate reflection of Liliequist's membrane over the oculomotor nerve (*)

cave hosts the Gasserian Ganglion, which is the origin of the three sensory roots of the fifth cranial nerve.

The abducens nerve ascends from the infra-tentorial part of the anterior incisural space. The nerve originates from the pontomedullary sulcus, and runs upward in the pre-pontine cistern, which represents the sole intracranial visible portion of this nerve. Then, it pierces the dura mater covering the clivus and passes below the petrosphenoid ligament to enter the cavernous sinus.

Fig. 3 Neurosurgical applications in skull base surgery. (**a**) Intraoperative photograph. A clinical case illustrating the pre-temporal view from the left side. A left temporal polectomy was performed for the removal of a glioblastoma cerebri. The anterior incisural space was exposed. The component of the oculomotor triangle can be clearly observed. *apcl* anterior petroclinoid ligament, *ppcl* posterior petroclinoid ligament, *icl* interclinoid ligament. In the central part of the triangle, the oculomotor nerve (3°) enters the oculomotor porus. The oculomotor nerve can be followed posteriorly in its cisternal within the interpeduncular cistern until it reaches its origin at the brainstem below the posterior cerebral artery. On the left side, the arachnoid membranes, including Liliequist's membrane, were dissected. Conversely, on the right side, the mesencephalic portion of Liliequist's membrane attaching on the contralateral third cranial nerve (3°) can be identified. Anteriorly, on the left side, between the ICA (ica) and the optic nerve (2°), trabeculae coming from the medial carotid membrane and reflecting over the pituitary stalk can be observed (psa). *a1* anterior cerebral artery, *oc* optic chiasm, *acha* anterior choroideal artery. (**b**) After the dissection of the arachnoid membranes of the anterior incisural space has been completed, the ICA can be easily mobilized. In this picture, the dissector has been used to show the pituitary stalk dislocating the ICA anteromedially. (**c**) Another clinical case illustrating the subtemporal view from the left side. The left temporal lobe (tl) has been lifted, and the middle incisural space can be exposed. A more lateral route increases the operative view of the interpeduncular cistern. The third cranial nerve (3°) can be followed until its origin below the posterior cerebral artery (pca). Medially, both the anterior-posterior communicating artery (*) and its perforators constituting the pre-mammillary artery (°) can be identified. (te, tentorial edge; ica, ICA; pcp, posterior clinoid process; 2°, optic nerve). (**d**) The tentorial edge (te) has been lifted up through the use of a microsurgical hook. Below the microsurgical hook, the fourth cranial nerve running within the ambient cistern can be observed. (**e**) Intraoperative photograph, another clinical case. A right temporal suboccipital approach has been performed, and the tentorium has been opened. The infratentorial compartment of the middle incisural space has been exposed and the sixth cranial nerve entering the Dorello's channel can be observed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4 Discussion

4.1 Anatomic Considerations

In the third part of the study of this complex and fascinating region of the skull base, we focused our attention on the description of the anatomy of the arachnoid membranes and cranial nerves of the middle and incisural spaces. In the previous studies, we demonstrated how, even in the presence of limited resources, a detailed and clear anatomic study can be performed [1, 2]. In this last part, beyond the anatomic description, we also discuss the neurosurgical applications of this study.

The peculiarity of our study is that it was mainly performed on fresh non-formalin-fixed specimens to avoid the changes and artifacts due to the formalin fixation process [15–17].

Dissecting fresh specimens gave us the possibility to better understand and describe the anatomical relationships between the dural folds and the arachnoid membranes in this region.

Just above the distal dural ring, it was possible to appreciate the arachnoid sheets of the medial arachnoid membrane. This membrane separated the chiasmatic cistern from the carotid one and contributed to the formation of the anterolateral portion of the funnel-shaped arachnoid collar delimiting the pituitary stalk cistern [7, 14] (Figs. 1a–d, 2).

Our dissection on fresh specimens was particularly useful to explore the dorsum sellae allowing to discern the anatomy of the Liliequist's membrane accurately, thus identifying both the mesencephalic and the diencephalic portions. To the best of our knowledge, no other studies were able to show both the components of the Liliequist's membrane.

In particular, our research highlights that the diencephalic portion of the Liliequist's membrane joins the mammillary bodies. We also observed that the cisternal portion of the oculomotor nerve represents the pillar attaching to the mesencephalic part of the membrane, thus separating the prepontine from the interpeduncular cistern incompletely [7, 14] (Figs. 1a–c, 2).

Furthermore, it was possible to identify the trabeculae from Liliequist's membrane running from the dorsum sellae toward the posterior surface of the pituitary stalk, completing the arachnoid collar, and encircling the same pituitary stalk and delimiting its cisternal space [14].

In our dissections, the following structures were clearly identified: the petroclinoid ligaments running below the posterior petroclinoid ligament and forming the roof of the Dorello's canal (through which the abducens nerve penetrates the cavernous sinus) (Fig. 3, part II); the fourth cranial nerve in its cisternal and tentorial segment (Figs. 1, 2 part II); the trigeminal root passing from the prepontine cistern to Meckel's cave through the trigeminal porus at the petrous apex [3, 4, 9, 10] (Figs. 1, 2, 3 part II).

The superior dissection experience provided by fresh cadavers in our study, above all regarding cisternal anatomy, demonstrates the feasibility of establishing a neurosurgical cadaver dissection laboratory for training and research purposes even in the presence of limited resources, in a context in which sophisticated embalming techniques are not exploited.

4.2 Surgical Considerations

This study highlights the need for a detailed anatomical comprehension of this region when performing neurosurgical practice with particular regard to the surgical treatment of pathologies involving the anterior and middle skull base.

Accurate knowledge of the anterior and middle incisural spaces with the related bony, dural, arachnoidal, and neurovascular structures is crucial in neurosurgical practice. In fact, vascular and neoplastic pathologies commonly involve these anatomical areas, making them frequently exposed during surgical procedures using pterional, pre-temporal, and sub-temporal approaches [7, 10–14, 17] (Fig. 3a–e). Although the above-mentioned anatomic structures contribute to maintaining the anatomical relationships between the neurovascular components of these regions, at the same time, their presence may impair the surgical exposure by occluding a complete view of the same neurovascular elements [3–10]. As a consequence, the partial or complete removal of these osteo-dural structures is required to expand the operative corridors, allowing a proper surgical procedure [6, 11–14, 17].

For example, intradural or extradural removal of the anterior clinoid process is commonly performed in neurosurgical practice [6, 12, 17]. This allows exposing the clinoidal segment of the ICA ensuring the "proximal control" in the management of paraclinoidal aneurysms arising within the carotid cave, as well as hypophyseal and carotid-ophthalmic aneurysms [6, 12, 17].

The removal of the anterior clinoid process allows unroofing the optic canal to remove tumors spreading within the canal, such as meningiomas and craniopharyngiomas [6, 12, 14, 17].

Regarding craniopharyngiomas, accurate knowledge of the arachnoid membranes around the pituitary stalk is crucial during surgical removal. A strong relationship exists between the tumor, the basal arachnoid membrane, and the trabecular components of the medial carotid and Liliequist's membrane attaching over the pituitary stalk. As a result, it may jeopardize the search on a plane of dissections between the tumor, the pituitary stalk, the optic-chiasm structures, and the arterial components of the region [14].

After a proper anterior clinoidectomy, more surgical space may be obtained by the incision of the dura mater of the distal dural ring and by opening of the carotid oculomotor membrane. It must be completed by a meticulous dissection of the arachnoid adhesions of the region [6].

These maneuvers are particularly relevant if a pre-temporal approach is requested, since they allow an extensive exposure of the oculomotor nerve from the trigonal to the cisternal portion, widely exposing the interpeduncular cistern [6, 12] (Fig. 3a, b).

For these reasons, a well performed pre-temporal approach accompanied by extensive mobilization of dural and arachnoid membranes should be reasonably considered as the main surgical option for the management of aneurysms placed at the high basilar bifurcation level, as well as other pathologies located in the upper and ventral brainstem [6, 12, 17].

Moreover, a posterior clinoidectomy with occlusion of the posterior communicating artery at the P1–P2 junction makes the pre-temporal approach a valid second option to the subtemporal route for aneurysms in low laying basilar bifurcation [6, 12, 17].

The subtemporal approach is mainly performed to expose the middle incisural space [13, 17] (Fig. 3c, d). Using this approach, the ambiens and the interpeduncular cisterns may be widely exposed [13, 17].

In neurosurgical practice, this approach is used primarily for the management of low lying basilar bifurcation aneurysms, meningiomas of the free margin of the tentorium, and other lesions involving the lateral portion of the mesencephalon and the upper lateral pons at the trigeminal root origin. Using this approach, the possibility to make an incision on the tentorial edge after visualization of the entrance of the fourth cranial nerve, together with the dissection of Liliequist's membrane, allows enlarging the surgical view exposing both the supratentorial and infratentorial portions of the upper brainstem [13, 17] (Fig. 3c–e).

5 Conclusions

1. A systematic approach based on the stepwise analysis of the dural, bony, and neurovascular structures, by dissections performed on fresh specimens, including arachnoid membranes and cisterns, provides neurosurgeons the necessary neuroanatomical understanding required to successfully manage the numerous pathologies involving the anterior and middle incisural spaces.
2. Detailed anatomical knowledge of these regions finds actual applications in neurosurgical practice since the anterior and middle incisural spaces are often surgically exposed to the high prevalence of neoplasms and vascular events. The high-definition pictures reported in this study could represent useful support to understand the anatomy of this complex region.
3. Finally, our study could provide guidance to neurosurgical centers in which resources are limited that are either planning to establish their own cadaver dissection laboratory or failed to do so because of the supposed high-costs.

References

1. Signorelli F, Stumpo V, Della Pepa GM, La Rocca G, Oliva A, Olivi A, Visocchi M. Step-up establishement of neurosurgical laboratory starting with limited resources—tips and tricks. World Neurosurg. 2019;pii:S1878-8750(19)30445. https://doi.org/10.1016/j.wneu.2019.02.034.
2. Signorelli F. The craniovertebral junction and laboratory experience: the Italian paradox. Acta Neurochir Suppl. 2019;125:11–2. https://doi.org/10.1007/978-3-319-62515-7_2.
3. Rhoton AL Jr. Tentorial incisura. Neurosurgery. 2000;47(3 Suppl):S131–53.
4. Rhoton AL Jr. The cavernous sinus, the cavernous venous plexus, and the carotid collar. Neurosurgery. 2002;51(4 Suppl):S375–410; Review.
5. Umansky F, Valarezo A, Elidan J. The superior wall of the cavernous sinus: a microanatomical study. J Neurosurg. 1994;81(6):914–20.
6. Yasuda A, Campero A, Martins C, Rhoton AL Jr, de Oliveira E, Ribas GC. Microsurgical anatomy and approaches to the cavernous sinus. Neurosurgery. 2008;62(6 Suppl 3):1240–63.
7. Inoue K, Seker A, Osawa S, Alencastro LF, Matsushima T, Rhoton AL Jr. Microsurgical and endoscopic anatomy of the supratentorial arachnoidal membranes and cisterns. Neurosurgery. 2009;65(4):644–64; discussion 665.
8. Martins C, Yasuda A, Campero A, Rhoton AL Jr. Microsurgical anatomy of the oculomotor cistern. Neurosurgery. 2006;58(4 Suppl 2):ONS-220-7; discussion ONS-227-8.
9. Joo W, Yoshioka F, Funaki T, Rhoton AL Jr. Microsurgical anatomy of the abducens nerve. Clin Anat. 2012;25(8):1030–42.
10. Joo W, Rhoton AL Jr. Microsurgical anatomy of the trochlear nerve. Clin Anat. 2015;28(7):857–64.
11. Kobayashi S, Kyoshima K, Gibo H, Hegde SA, Takemae T, Sugita K. Carotid cave aneurysms of the internal carotid artery. J Neurosurg. 1989;70(2):216–21.
12. Seoane E, Tedeschi H, de Oliveira E, Wen HT, Rhoton AL Jr. The pretemporal transcavernous approach to the interpeduncular and prepontine cisterns: microsurgical anatomy and technique application. Neurosurgery. 2000;46(4):891–8; discussion 898-9.
13. McLaughlin N, Ma Q, Emerson J, Malkasian DR, Martin NA. The extended subtemporal transtentorial approach: the impact of trochlear nerve dissection and tentorial incision. J Clin Neurosci. 2013;20(8):1139–43.
14. Ciappetta P, Pescatori L. Anatomic dissection of arachnoid membranes encircling the pituitary stalk on fresh, non-formalin-fixed specimens: anatomoradiologic correlations and clinical applications in Craniopharyngioma surgery. World Neurosurg. 2017;108:479–90.
15. Saboori P, Sadegh A. Histology and morphology of the brain subarachnoid trabeculae. Anat Res Int. 2015;2015:2015279814.
16. Benet A, Rincon-Torroella J, Lawton MT, González Sánchez JJ. Novel embalming solution for neurosurgical simulation in cadavers. J Neurosurg. 2014;120:1229–37.
17. Pescatori L, Niutta M, Tropeano MP, Santoro G, Santoro A. Fourth cranial nerve: surgical anatomy in the subtemporal transtentorial approach and in the pretemporal combined inter-intradural approach through then fronto-temporo-orbito-zygomatic craniotomy. A cadaveric study. Neurosurg Rev. 2017;40(1):143–53.

Avoiding the Blinded Funnel: A Combined Single Piece Fronto-Temporo-Orbito-Zygomatic Craniotomy Endoscopic-Assisted Approach with Multimodal Assistance for an Epidermoid Tumor of Meckel's Cave-Case Report

A. Curcio, F. F. Angileri, R. Zaccaria, and Antonino Francesco Germanò

1 Introduction

Intracranial epidermoid cysts are benign lesions that represent 0.2–1.8% of all intracranial lesions [1]. Tumors of Meckel's cave represent less than 0.5% of all intracranial tumors [2]. Epidemroid cysts of the Meckel's cave are very rare and mostly have been reported as single cases or very small series [3]. Surgical access to Meckel's cave is a challenge due to the confluence of critical neurovascular structures. Many corridors of access have been developed and proposed based on the specific location of the tumor and its extent of involvement in adjacent structures [4, 5]. We report a case of an epidermoid cyst involving the left Meckel's cave approached through a single piece fronto-temporo-orbito-zygomatic craniotomy with endoscopic assistance.

2 Material and Methods

A 51-year-old woman presented with numbness paresthesia and pain over the left side of the face, and tingling paresthesia over the left side of the superior lip. Neurological examination showed a left trigeminal nerve hypoesthesia with no motor branch damage and abnormal left corneal reflex. MR showed a 42 × 41 × 33 mm lesion indissociable from Meckel's cave and cavernous sinus, extending into the temporal pole, with a fair peripheral enhancement and fibrous intralesional shoots. The lesion exerted medial compression on the left carotid, and anterior invasion of pterygopalatine fossa. CT scan showed an inhomogeneous tumor with bone thinning of the greater sphenoid wing, carotid canal, and dorsum sellae; a digital subtraction angiography (DSA) was obtained to rule out vascular malformation and to better explore the vascular anatomy of the region. Under neurophysiologic monitoring, we performed a single piece fronto-temporo-orbito-zygomatic craniotomy. Lumbar cerebrospinal drainage was placed preoperatively. A piezoelectric scalpel was used to cut the zygomatic process of the temporal bone, near its root, and the frontal process of the zygomatic root. Craniotomy was completed cutting the lateral face of the zygomatic bone, between the two processes, and the sphenofrontal suture. The orbital part of the zygomatic bone was fractured and the bone flap was removed in one piece (Fig. 1). The temporal lobe was extradurally gently retracted exposing middle cranial fossa until the spinosum foramen and the middle meningeal artery. The dura mater was divided reaching the enlarged Meckel's cave with an interdural corridor. Neuronavigation was used to identify and confirm major anatomical landmarks. The tumor appeared as an encapsulated, pearly avascular lesion that seemed to originate from between the two dural layers with a macroscopical suspect of an epidermoid cyst. The lesion was removed piecemeal trough the small corridor using the endoscope to look around blind corners. To this purpose, 30 and 45° endoscopes have been employed both

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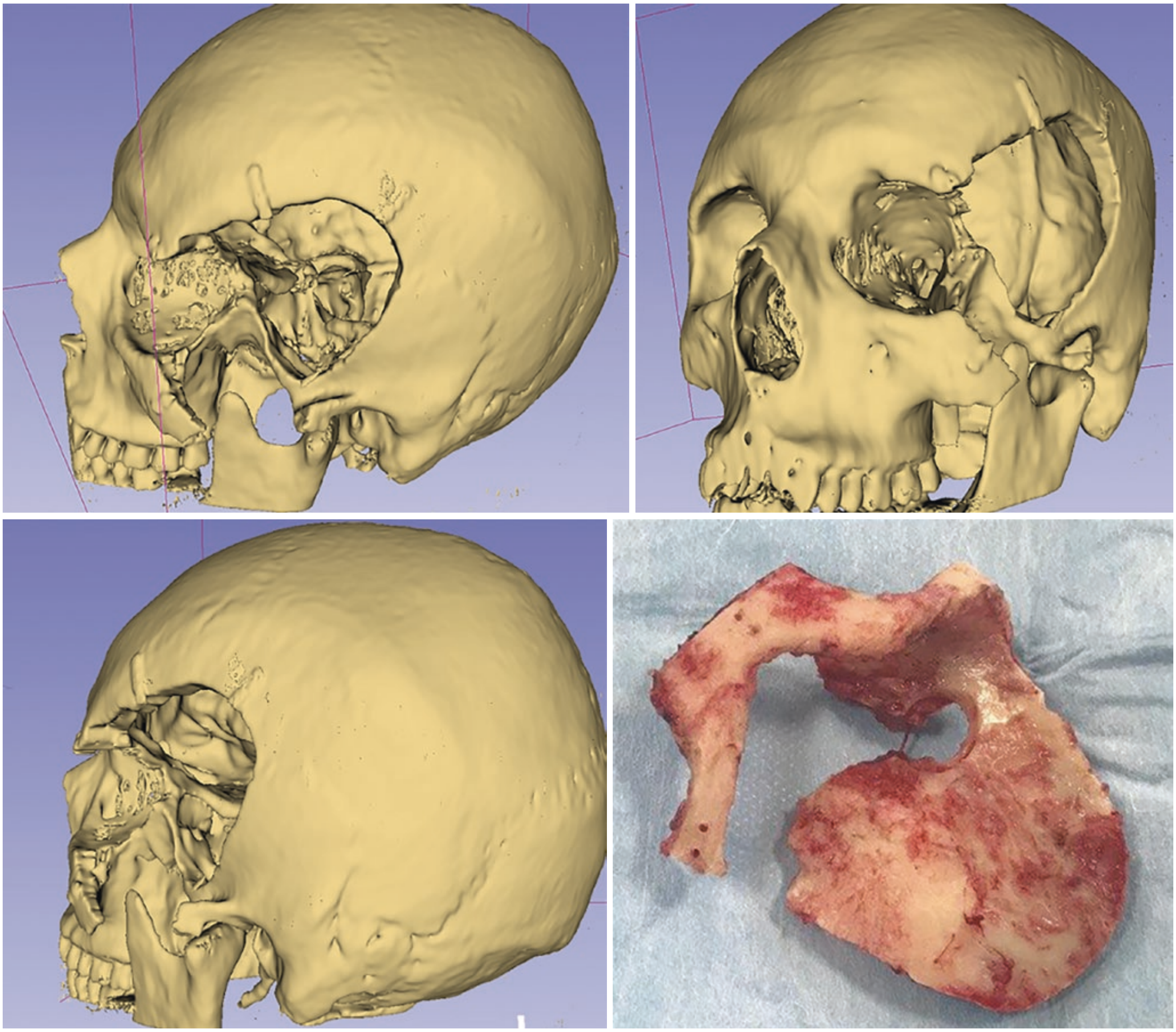

Fig. 1 3-D reconstruction of craniotomy. Lower right image shows the single piece FTOZ

as a visualization tool and to guide tumor removal. After generous decompression, the basal dura was incised to access the intradural portion of the cyst (Fig. 2). The gasserian ganglion and fifth cranial nerve branches were displaced medially and sharply dissected from the tumor capsule. A microdoppler probe was adopted to identify the carotid artery and its relationship with the tumor. Finally, the tumor was completely resected.

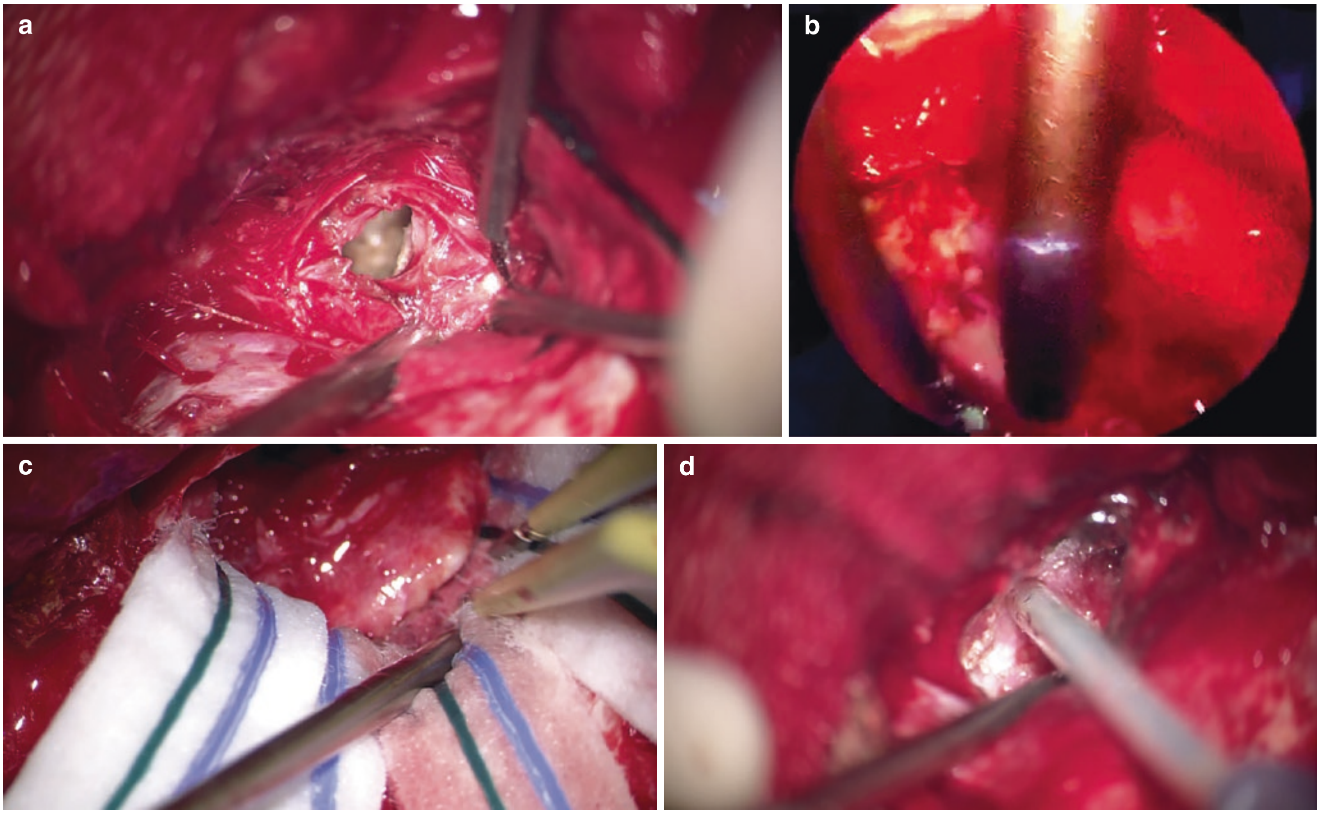

Fig. 2 (**a**) Extradural subtemporal approach to the tumor within Meckel's Cave. (**b**) Endoscopy-assisted resection of residual dermoid cyst, on the left part of the image. (**c**) Intradural approach with cottonoid protecting left temporal pole. (**d**) Doppler probe for carotid localization

3 Results

The post-operative course was uneventful and the patient was discharged in 5 days. Histological examination confirmed the epidermoid cyst. At 3 months follow-up, both facial pain and numbness resolved. MR scan demonstrated the complete removal (Fig. 3).

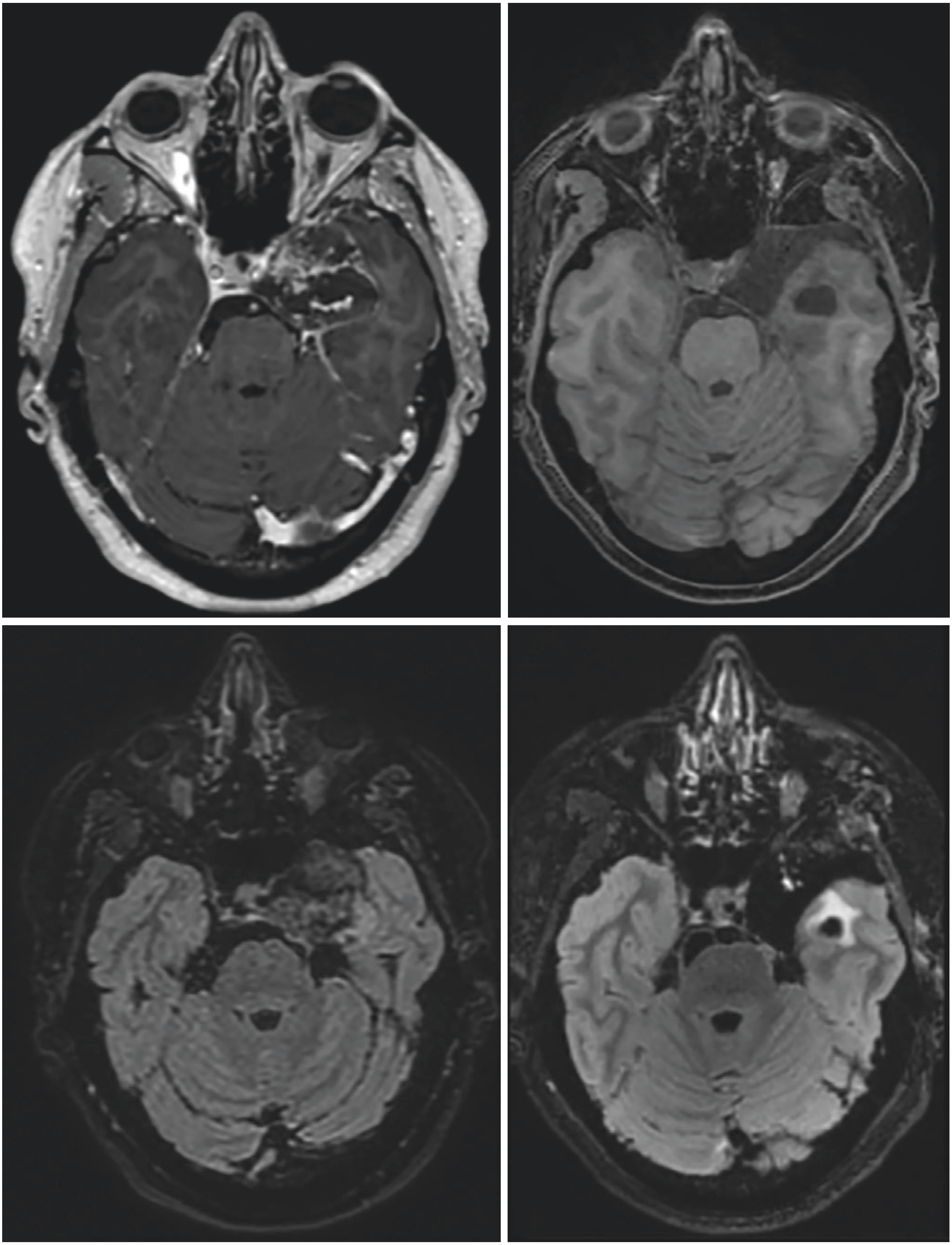

Fig. 3 Comparative MRI images of pre-operative lesion (left column) and post-operative images (right column). No residual tumor is apparent and complete left temporal lobe integrity is noticed

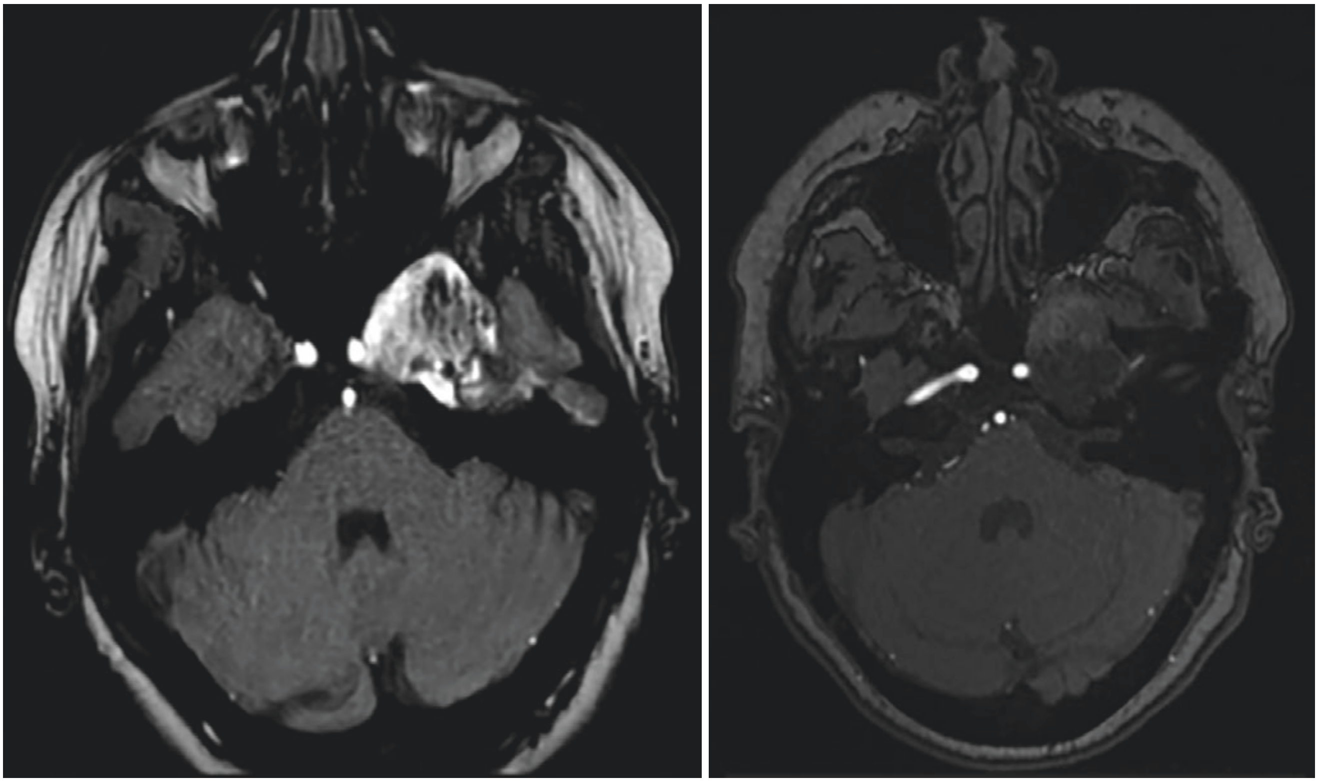

Fig. 3 (continued)

4 Discussion

The most common tumors in Meckel's cave are neurinomas and meningiomas [6, 7]. Epiermoid cysts in Meckel's cave are very rare and only case reports and a small series have been published [1–15]. We found only 18 cases described in the literature, and only 10 described the surgical approaches. The most common symptom for Meckel's cave lesion is facial hypesthesia (49%) and facial pain (10%) [9] due to a compression of the Vth cranial nerve branches: in our case all three branches were involved. The most common approach proposed to resect these lesions is a subtemporal intradural approach [3]. In two cases, an orbitozygomatic craniotomy was employed. In our case, we adopted the latter strategy with the aim of neuronavigation, neuromonitoring, microdoppler, and endoscopic assistance. To the best of our knowledge, this is the only case operated on with this multimodal intraoperative assistance. We adopted an interdural–intradural approach. The endoscopic tool, as described by Lan et al. [9], was essential in exploring and removing tumor in blind spots, thus minimizing the surgical corridor. The advantage was mostly appreciated because of the avascular characteristic of the epidermoid cyst. Moreover, using intraoperative microdoppler helped in identifying and preserving the integrity of the carotid artery in a converted anatomy due to extensive tumor growth. Finally, neurophysiologic monitoring prevented damage to the fifth cranial nerve. Our report underlines once more the employment of multimodal surgical assistance, such as neuromonitoring, endoscopic assistance, and intraoperative microdoppler as very useful tools in obtaining safe maximal resection even in large skull base tumors. However, these tools do not exclude the judicious and meticulous microsurgical technique and anatomic knowledge to manage these complex lesions: "A fool with a tool is still a fool" as mentioned by Grady Booch. In conclusion, Meckel's cave tumors are rare entities and epidermoid cysts are anecdotal with only a few cases reported in the literature. Their surgical removal is challenging due to the complex anatomy of the region. We successfully adopted a multimodal surgical technique using a one piece fronto-temporo-orbito-zygomatic craniotomy, an interdural–intradural approach. Endoscopic assistance, neuromonitoring and intraoperative Doppler appeared very useful in minimizing morbidity and obtaining complete resection.

Conflict of Interest The authors report no conflicts of interest with respect to the materials or methods used in this study or the results specified in this document.

References

1. Furtado SV, Hegde AS. Trigeminal neuralgia due to a small Meckel's cave epidermoid tumor: surgery using an extradural corridor. Skull Base. 2009;19(5):353–7.
2. Beck DW, Menezes AH. Lesions in Meckel's cave: variable presentation and pathology. J Neurosurg. 1987;67(5):684–9.
3. Chui M, Tucker W, Hudson A, Bayer N. High resolution CT of Meckel's cave. Neuroradiology. 1985;27(5):403–9.
4. Busch CM, Prickett JT, Stein R, Cuoco JA, Marvin EA, Witcher MR. Meckel cave epidermoid cyst presenting as multiple cranial nerve deficits due to indirect Tumoral compression of the cavernous sinus: a case report and literature review. World Neurosurg. 2019;121:88–94.
5. Miyasaka Y, Morii S, Tachibana S. A case of paratrigeminal epidermoid originated in the Meckel's cave (Japanese). Neurol Surg. 1976;4(5):483–8.
6. Arai A, Sasayama T, Koyama J, Fujita A, Hosoda K, Kohmura E. Epidermoid cyst in Meckel's cave with unusual computed tomography and magnetic resonance imaging findings. Neurol Med Chir (Tokyo). 2010;50(8):701–4.
7. Mehta DS, Malik GB, Dar J. Trigeminal neuralgia due to cholesteatoma of Meckel's cave. Case report. J Neurosurg. 1971;34(4):572–4.
8. Kapila A, Steinbaum S, Chakeres DW. Meckel's cave epidermoid with trigeminal neuralgia: Ct findings. J Comput Assist Tomogr. 1984;8(6):1172–4.
9. Lan Q, Tanudjaja J, Chen AL. Subtemporal keyhole approach to Meckel's cave epidermoid cyst: case report and review of literature. Indian J Neurosurg. 2014;03(1):50–3.
10. Miyazawa N, Yamazaki H, Wakao T, Nukui H. Epidermoid tumors of Meckel's cave: case report and review of the literature. Neurosurgery. 1989;25(6):951–5.
11. Nadkarni T, Dindorkar K, Muzumdar D, Goel A. Epidermoid tumor within Meckel's cave—case report. Neurol Med Chir (Tokyo). 2000;40(1):74–6.
12. Ohta H, Ottomo M, Nakamura T, Yokota A. A case of epidermoid tumor inside the Meckel's cave. Neurol Surg. 1997;25(10):943–7.
13. Podeur P, Okhremchuk I, Morvan JB, Vatin L, Rivière D, de Faria A, Joubert C, Dagain A. Multiple intracranial epidermoid cysts: case report. Rev Laryngol Otol Rhinol (Bord). 2015;136(4):159–62.
14. Sun DQ, Menezes AH, Howard MA, Gantz BJ, Hasan DM, Hansen MR. Surgical management of tumors involving Meckel's cave and cavernous sinus: role of an extended middle fossa and lateral sphenoidectomy approach. Otol Neurotol. 2018;39(1):82–91.
15. Yuh WTC, Wright DC, Barloon TJ, Schultz DH, Sato Y, Cervantes CA. MR imaging of primary tumors of trigeminal nerve and Meckel's cave. Am J Roentgenol. 1988;151(3):577–82.

Middle Meningeal Artery Embolization for the Management of Chronic Subdural Hematomas: A New-Old Treatment

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1 Middle Meningeal Artery Embolization for the Management of Chronic Subdural Hematomas: The Problem and How We Work

1.1 The Disease and the Management

The treatment and management of chronic subdural hematomas (cSDH) remain controversial. These chronic extra axial collections have conventionally been treated either conservatively (observation) or more aggressively with surgical evacuation [1]. cSDH treatment is burdened by elevated recurrence rates (ranging from 5% to 37%) that result in the need for repeated surgical interventions and hospital admissions with all the consequences [2–9]. Moreover, surgical evacuation may lead to inoculation of microorganisms into the subdural space, further developing into a subdural empyema [10]. To aggravate the situation, this pathology is typical of the older population, who often suffers from multiple comorbidities and who are also often under antiplatelet therapy [1]. It is estimated that by 2030, with the aging population and the prevalent use of anticoagulation and antiplatelet medications, there will be more than 60,000 new cases of SDH per year, making cSDH the most common neurosurgical diagnosis in adults at that time [11].

Middle meningeal artery (MMA) embolization has emerged as a safe and minimally invasive treatment for newly diagnosed or recurrent cSDH. The rationale is the elimination of neovascularization through embolization; in this way, the progression and recurrence of cSDH are arrested [12–15]. Early case reports and case series have shown encouraging results that include early brain re-expansion, decreased hematoma progression, and decreased hematoma recurrence [6, 16, 17]. MMA embolization has been reported to effectively and safely treat patients with cSDH either as stand-alone or adjunctive therapy [16, 18], with a low complication rate and with a significantly lower treatment failure rate than either surgical or medical therapy [19]. Moreover, there are also at least 11 ongoing randomized trials to evaluate this approach (NCT04270955, NCT04750200, NCT03307395, NCT04742920, NCT04816591, NCT04372147, NCT04511572, NCT04402632, NCT04410146, NCT04095819, NCT04272996).

1.2 Middle Meningeal Artery Embolization

The MMA provides the predominant blood supply to the fragile neo vessels that spontaneously rupture along the membrane of the cSDH, leading to volume expansion and recurrence [20]. Moreover, on histopathology studies, cSDH membranes reveal highly permeable endothelial gap junctions within microcapillaries that produce neovascular leakiness and fragility, which are further responsible for repeated cSDH rebleeding [21].

The aim of middle meningeal artery (MMA) embolization is to devascularize the subdural membranes to stop the continuous accumulation of blood products in favor of reabsorption. This technique has been employed as the sole therapy and as a preoperative or postoperative adjunct to surgical evac-

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uation with the intention of reducing postoperative recurrence [18]. Primary embolization may be preferred for those able to tolerate SDH for weeks to months given the natural history of spontaneous resolution. Patients with an urgent indication for surgical decompression can be considered for MMA postoperative embolization [22].

Srivastan et al. presented a meta-analysis of nine of the available MMA embolization case series and reported a markedly lower recurrence rate for cSDH after embolization compared with conventional management (2.1% vs. 27.7%, OR 0.087, 95% CI 0.026 to 0.292, $P < 0.001$) [23]. In a 60-patients case series, primary MMA embolization allowed

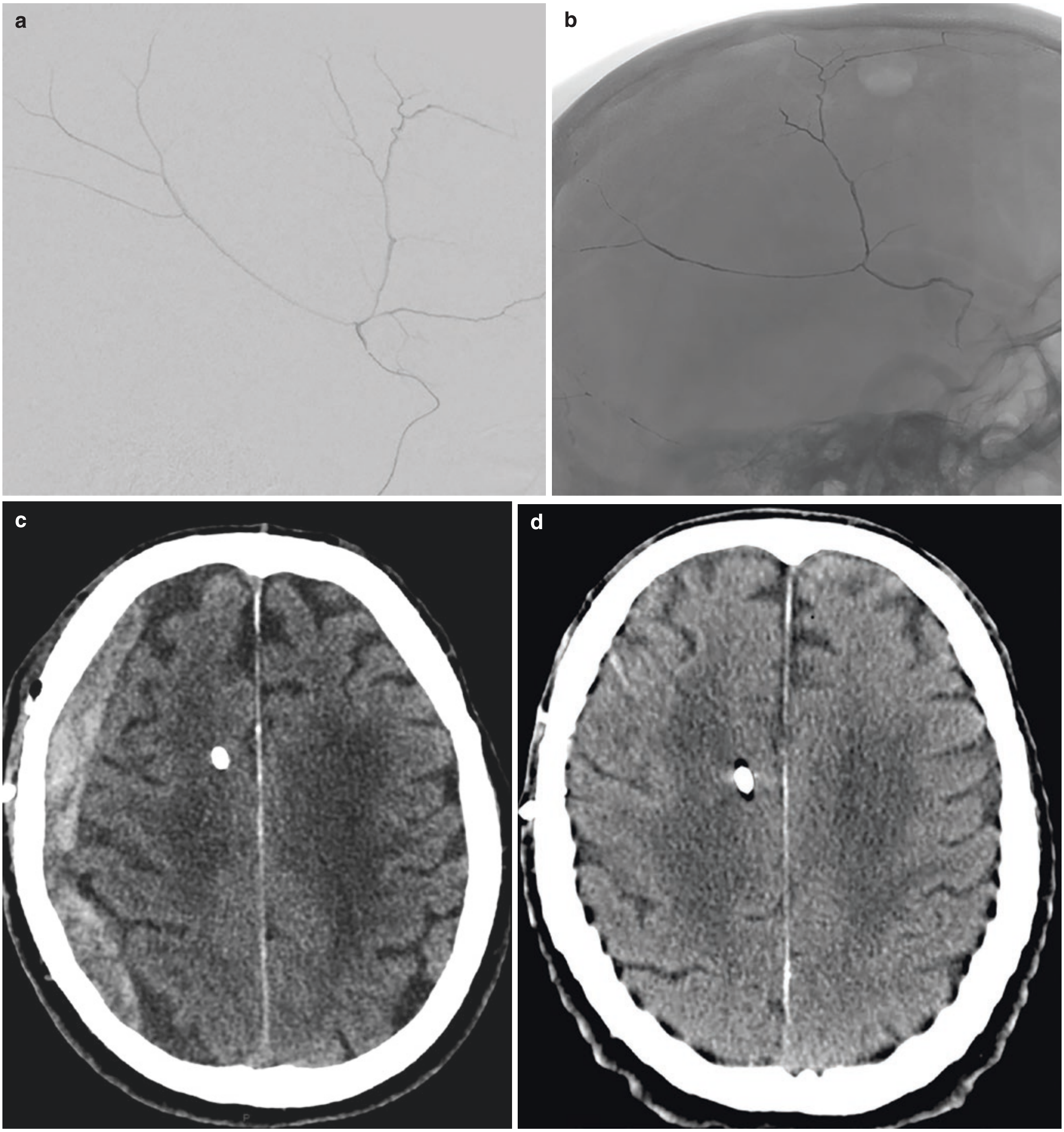

Fig. 1 (**a**) DSA (upper left) showing selective catheterization of right MMA. The MMA and its branches are patent, with distal arterial flow. (**b**) X-ray (upper right) showing the MMA branches completely filled with EVOH copolymer after embolization. (**c**) Axial (lower left) CT head scan showing the mixed density, right sided cSDH with moderate mass effect before embolization. (**d**) Follow-up (lower right) axial CT head scan obtained 4 weeks after left MMA embolization showing complete resolution of cSDH

avoiding surgery in 92% of cSDHs, with improvement in clinical symptoms and reduction in size of SDH on follow-up imaging studies [6] (Fig. 1).

Patient selection for MMA embolization is an important consideration. Some suggest that it should be based on the SDH size: 10 mm in greatest thickness, which is commonly used for triaging surgical candidates, is gaining acceptance as an appropriate threshold for MMA embolization selection [16]. Furthermore, certain patient populations, such as those with indications for anticoagulation, likely warrant consideration for MMA embolization [24]. Not least, MMA embolization could significantly reduce hospital costs associated with unexpected additional treatments [25].

Technical Note

MMA embolization is usually performed either with polyvinyl alcohol particles (PVA, 150–250 microns in diameter) or with liquid embolic agents (such as EVOH copolymers). PVA mainly penetrate as distally as flow allows. Elderly individuals with cSDH have often very small meningeal arteries; therefore, only a small volume of PVA can be injected and the degree of distal penetration could be limited. Moreover, PVA itself is not spontaneously radiopaque. Therefore, during the injection, the degree of distal penetration and the entity of the embolization are difficult to evaluate. In addition, reflux into potentially unsafe branches can be difficult to discern [18]. On the other hand, embolization with PVA can be done without the need for analgesia making the procedure faster and reducing anesthesiologic risks.

EVOH copolymers (mainly used for cerebro-medullary vascular malformations [26]) can be injected into the distal vasculature to achieve the filling of the subdural membranes, keeping prudent control of any reflux to other meningeal branches [18]; however, the injection is associated with intense pain requiring deeper sedation, with all the predictable consequences on duration and procedural risks.

1.3 Conclusion

MMA embolization for cSDH is safe and seems to be associated with a decreased rate of post-surgical recurrence and incomplete resolution compared with both surgical and conservative management. MMA embolization may be effective in both the primary treatment of mildly symptomatic cSDH and in case of recurrence.

Conflict of Interest All the authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

1. Schwarz J, Carnevale JA, Goldberg JL, Ramos AD, Link TW, Knopman J. Perioperative prophylactic middle meningeal artery embolization for chronic subdural hematoma: a series of 44 cases. J Neurosurg. 2021;135(6):1627–35.
2. Abboud T, Dührsen L, Gibbert C, Westphal M, Martens T. Influence of antithrombotic agents on recurrence rate and clinical outcome in patients operated for chronic subdural hematoma. Neurocirugia. 2018;29(2):86–92.
3. Almenawer SA, Farrokhyar F, Hong C, et al. Chronic subdural hematoma management: a systematic review and meta-analysis of 34829 patients. Ann Surg. 2014;259(3):449–57.
4. Gernsback J, Kolcun JPG, Jagid J. To drain or two drains: recurrences in chronic subdural hematomas. World Neurosurg. 2016;95:447–50.
5. Ivamoto HS, Lemos HP, Atallah AN. Surgical treatments for chronic subdural hematomas: a comprehensive systematic review. World Neurosurg. 2016;86:399–418.
6. Link TW, Boddu S, Paine SM, Kamel H, Knopman J. Middle meningeal artery embolization for chronic subdural hematoma: a series of 60 cases. Neurosurgery. 2019;85(6):801–7.
7. Liu W, Bakker NA, Groen RJM. Chronic subdural hematoma: a systematic review and meta-analysis of surgical procedures: a systematic review. J Neurosurg. 2014;121(3):665–73.
8. Scerrati A, Visani J, Ricciardi L, Dones F, Rustemi O, Cavallo MA, De Bonis P. To drill or not to drill, that is the question: nonsurgical treatment of chronic subdural hematoma in the elderly. A systematic review. Neurosurg Focus. 2020;49(4):E7.
9. Xu C, Chen S, Yuan L, Jing Y. Burr-hole irrigation with closed-system drainage for the treatment of chronic subdural hematoma: a meta-analysis. Neurol Med Chir (Tokyo). 2016;56(2):62–8.
10. Mattogno PP, La Rocca G, Signorelli F, Visocchi M. Intracranial subdural empyema: diagnosis and treatment update. J Neurosurg Sci. 2019;63(1):101–2.
11. Balser D, Farooq S, Mehmood T, Reyes M, Samadani U. Actual and projected incidence rates for chronic subdural hematomas in United States veterans administration and civilian populations. J Neurosurg. 2015;123(5):1209–15.
12. Hong H-J, Kim Y-J, Yi H-J, Ko Y, Oh S-J, Kim J-M. Role of angiogenic growth factors and inflammatory cytokine on recurrence of chronic subdural hematoma. Surg Neurol. 2009;71(2):161–5.
13. Jafari N, Gesner L, Koziol JM, Rotoli G, Hubschmann OR. The pathogenesis of chronic subdural hematomas: a study on the formation of chronic subdural hematomas and analysis of computed tomography findings. World Neurosurg. 2017;107:376–81.
14. Kitazono M, Yokota H, Satoh H, Onda H, Matsumoto G, Fuse A, Teramoto A. Measurement of inflammatory cytokines and thrombomodulin in chronic subdural hematoma. Neurol Med Chir (Tokyo). 2012;52(11):810–5.
15. Shono T, Inamura T, Morioka T, Matsumoto K, Suzuki SO, Ikezaki K, Iwaki T, Fukui M. Vascular endothelial growth factor in chronic subdural haematomas. J Clin Neurosci. 2001;8(5):411–5.
16. Ban SP, Hwang G, Byoun HS, Kim T, Lee SU, Bang JS, Han JH, Kim C-Y, Kwon O-K, Oh CW. Middle meningeal artery embolization for chronic subdural hematoma. Radiology. 2018;286(3):992–9.
17. Kim E. Embolization therapy for refractory hemorrhage in patients with chronic subdural hematomas. World Neurosurg. 2017;101:520–7.
18. Fiorella D, Arthur AS. Middle meningeal artery embolization for the management of chronic subdural hematoma. J Neurointerv Surg. 2019;11(9):912–5.
19. Catapano JS, Ducruet AF, Nguyen CL, et al. A propensity-adjusted comparison of middle meningeal artery embolization versus conventional therapy for chronic subdural hematomas. J Neurosurg. 2021;135(4):1208–13.

20. Foreman P, Goren O, Griessenauer CJ, Dalal SS, Weiner G, Schirmer CM. Middle meningeal artery embolization for chronic subdural hematomas: cautious optimism for a challenging pathology. World Neurosurg. 2019;126:528–9.
21. Tanaka T, Kaimori M. Histological study of vascular structure between the dura mater and the outer membrane in chronic subdural hematoma in an adult. No Shinkei Geka. 1999;27(5):431–6.
22. Fiorella D, Hirsch JA, Arthur AS. Embolization of the middle meningeal artery for the treatment of chronic subdural hematoma: considerations for pragmatic trial design. J Neurointerv Surg. 2021;13(4):295–7.
23. Srivatsan A, Mohanty A, Nascimento FA, Hafeez MU, Srinivasan VM, Thomas A, Chen SR, Johnson JN, Kan P. Middle meningeal artery embolization for chronic subdural hematoma: meta-analysis and systematic review. World Neurosurg. 2019;122:613–9.
24. Hirai S, Ono J, Odaki M, Serizawa T, Nagano O. Embolization of the middle meningeal artery for refractory chronic subdural haematoma: usefulness for patients under anticoagulant therapy. Interv Neuroradiol. 2004;10(2_suppl):101–4.
25. Joyce E, Bounajem MT, Scoville J, et al. Middle meningeal artery embolization treatment of nonacute subdural hematomas in the elderly: a multiinstitutional experience of 151 cases. Neurosurg Focus. 2020;49(4):E5.
26. Lozupone E, Bracco S, Trombatore P, Milonia L, D'Argento F, Alexandre A, Valente I, Semeraro V, Cioni S, Pedicelli A. Endovascular treatment of cerebral dural arteriovenous fistulas with SQUID 12. Interv Neuroradiol. 2020;26(5):651–7.

Supraorbital Keyhole Versus Pterional Approach: A Morphometric Anatomical Study

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1 Introduction

When approaching the base of the brain, the pterional (PT) craniotomy, as originally described by Yasargil and Fox in 1975, is still considered the standard approach for most lesions located in the anterior cranial fossa, sellar region, middle cranial fossa, and to reach the anterior aspect of the Willis' circle vessels [1, 2]. However, considerable literature describing the limitations of this approach exists [3, 4], and significant efforts have been made in the past to optimize the related surgical exposure [5–8]. A variety of orbital-cranial and orbital-zygomatic extensions have been developed over the past two decades, but some of these modifiers revealed a significant complexity, resulting in prolonged operative time, increased surgical morbidity, and even inferior cosmetic results [9].

The unprecedented technology advance of the past decade, especially with regard to computer-imaged three-dimensional rendering, endorsed a significant progress of pre-operative planning and simulation, allowing less invasive craniotomies, to the point of reassessing the "keyhole" concept as described by Perneczky and his group [10]. Recently, a systematic review of the literature addressing the minimally invasive alternative approaches to PT craniotomy has been published [11].

The aim of the present study was to compare the microsurgical anatomy exposed by the SO craniotomy, as originally described, with the standard PT approach and to evaluate its effectiveness with the development of current visualization technologies. The volumes of the surgical corridors and the respective areas of surgical exposure were quantfied and fundamental anatomical target points were used to define the relative morphometry. The influence of the head position was also studied to show the consequent surgical anatomy variation.

2 Material and Methods

Eight cadaveric heads injected with colored silicone were used for this study, according to protocols broadly described. In three specimens, a total of 5 mL of contrast agent (Gastroview, Mallinckrodt, St. Louis, MO) was added to the arterial and venous silicon mixture to enhance radiological vascular anatomy. In addition to the cadaveric heads, one dry skull was used to test the accuracy of the navigational measurements.

Magnetic resonance imaging (MRI) was performed in all specimens prior to dissection with axial, coronal, and sagittal T1- and T2-weighted acquisitions. Computer tomography (CT) were obtained prior and after dissection. Five small titanium skull screws were placed in all specimens prior to the scans for navigational purposes.

A cranial entry point (CEP) was chosen for each approach, representing the main axis of the surgical corridor. The "keyhole" burr hole, at the most proximal aspect of the temporal line, represented the CEP in the SO approach; the lateral aspect of the superior orbital fissure defined the CEP of the PT approach.

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2.1 Neurosurgical Laboratory and Equipment

All dissections were performed with a standard operating microscope (VM 900, Wedel Moeller, Wedel, Germany) connected to a navigational system (Brain Lab, Heimstetten, Germany) and a PC computer (Inspiron 8000, Dell computers, Austin, TX) for data analysis and picture transfer. "Auto-fusion" software provided from BrainLab was used to merge MRI with CT images, allowing simultaneous definition of brain tissue, neurovascular anatomy, and bony structures of the skull base. After pre-surgical calibration and navigation, standard BrainLab software was used to define volumetric measurements, as well as for calculating anatomical distances and angles. Standard microsurgical instruments were used for all microsurgical dissections.

2.2 Surgical Approaches and Techniques

All specimens were stabilized and carefully positioned using a Mayfield headrest (Mayfield, Ohio Medical Instrument Company, Cincinnati, OH). The SO and PT approaches were performed using 30° and 45° of head rotation and 10° of retro-flexion. A lateral eyebrow incision was made for the SO approach, whereas a standard frontotemporal incision was used for the PT approach.

2.3 Statistical Analysis

Statistical differences between craniotomy sizes and surgical corridors were tested using a two-tailed Student's *t*-test for unpaired samples. Comparison among the various distances measurements, areas of exposure, and angles were obtained using analysis of variances (ANOVA), followed by post-hoc procedures. Differences were regarded as statistically significant at $p < 0.05$.

3 Results

3.1 Craniotomy Sizes and Target Distances

Sixteen dissections were carried out and no significant differences between left and right sides were noticed. The averaged craniotomy size for the PT approach measured 1899.73 ± 646.51 mm^2 while the SO keyhole equaled 525.44 ± 102.30 mm^2 ($p < 0.005$).

The respective measurements of the 13 anatomical targets from the CEP are reported in Table 1. The surgical distances through the SO craniotomy were significantly longer when compared to the PT approach increasing from 20 to 38.2% (ipsilateral optic canal and ipsilateral anterior clinoid, respectively) ($p < 0.01$). For both approaches, the most remote target was represented by the contralateral ICA-A1 bifurcation at 67.42 ± 10.21 mm when approached via a PT craniotomy and at 82.05 ± 8.87 mm via the SO. The closest anatomical landmark was the ipsilateral anterior clinoid reachable at 37.82 ± 8.03 mm by the PT approach and at 52.28 ± 4.52 mm using the SO craniotomy.

Table 1 Distances (mm) of each of the thirteen anatomical targets measured from the Cranial Entry Point following Supraorbital (SO) and Pterional Craniotomy (PT). Each value represents the mean ± standard deviation of eight SO and eight PT approaches

	SO		PT	
	mm	sd	mm	sd
Anterior Clinoid Ipsilateral	52,8	4,52	37,97	7,19
Ant Clin Contralateral	64,41	7,06	53,68	4,47
Tub Sellae	69,78	7,36	53,65	6,93
Optic Can Ipsi	53,3	4,02	40,98	5,25
Optic Can Contra	67,79	7,01	56,5	7,36
Dural Ring/OA Contra	64,79	8,41	51,97	10,2
Chiasm Ant	67,48	7,22	52,93	7,06
Lam Term	71,41	7,03	58,17	6,73
Trifurc Ipsi	66,15	6,88	50,58	7,25
Acom	68,14	7,6	54,68	7,39
Post Clin Ipsi	67,65	6,8	53,23	7,53
Basilar tip	77,75	6,02	62,93	8,79
ICA/A1 Contra	82,05	8,87	67,42	10,21

3.2 Surgical Corridors and Areas of Exposure

The volume of the PT corridor resulted in 24.88 ± 6.24 cm^3 and the volume of the SO keyhole corridor was 22.19 ± 5.81 cm^3, showing no significant difference. The area of the surgical exposure and the profile of the surgical field differed, also according to the degree of the head rotation. In the PT approach with the head rotated 45°, the exposed area had a triangular shape and was calculated to be 113.66 ± 27.00 mm^2. When the head was rotated 30°, the area of the exposed zone decreased to 65.30 ± 17.23 mm^2 ($p = 0.01$).

The SO keyhole exposed rather a quadrangular area in both head positions. The area of this polygon was calculated to measure 100.12 ± 14.07 mm^2, at 30°. A rotation of 45° discovered a wider area, equaling 142.77 ± 27.68 mm^2 ($p = 0.005$) (Fig. 1a, b). Comparing the two approaches, there was no significant difference when the head was rotated by 45°. However, with 30° of rotation, the supraorbital approach exposed a better surgical view than the PT ($p < 0.01$).

The angle between the two optic nerves (OA) showed substantial variations in the two approaches, with further dif-

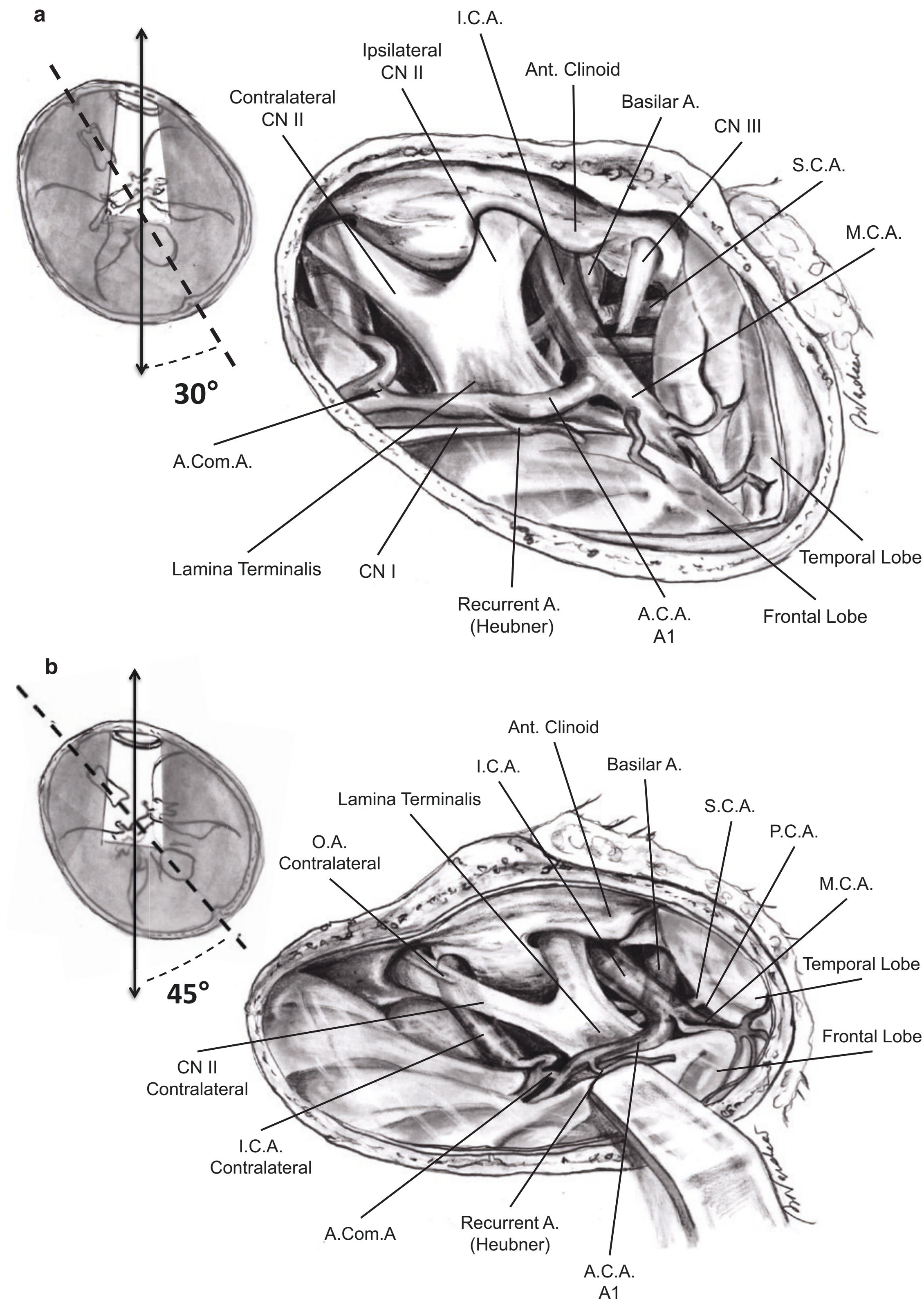

Fig. 1 (**a**, **b**) Illustration showing the SO keyhole exposition of a quadrangular area. The area of this polygon differs according to the degree of the head rotation. At 30°, it measured 100.12 ± 14.07 mm^2 (**a**). A rotation of 45° (**b**) discovers a wider area, equaling 142.77 ± 27.68 mm^2. CN I, olfactory nerve; CN II, optic nerve; CN III, oculomotor nerve; I.C.A., internal carotid artery; Ant. Clinoid, anterior clinoid process; Basilar A., basilar artery; S.C.A, superior cerebellar artery; M.C.A, middle cerebral artery; A.C.A A1, segment 1 of the anterior cerebral artery; Recurrent A., Heubner recurrent artery; A.Com.A, anterior communicating artery; P.C.A., posterior cerebral artery; O.A, ophtalmic artery. (Original drawings by B. Nardacci, M.D.)

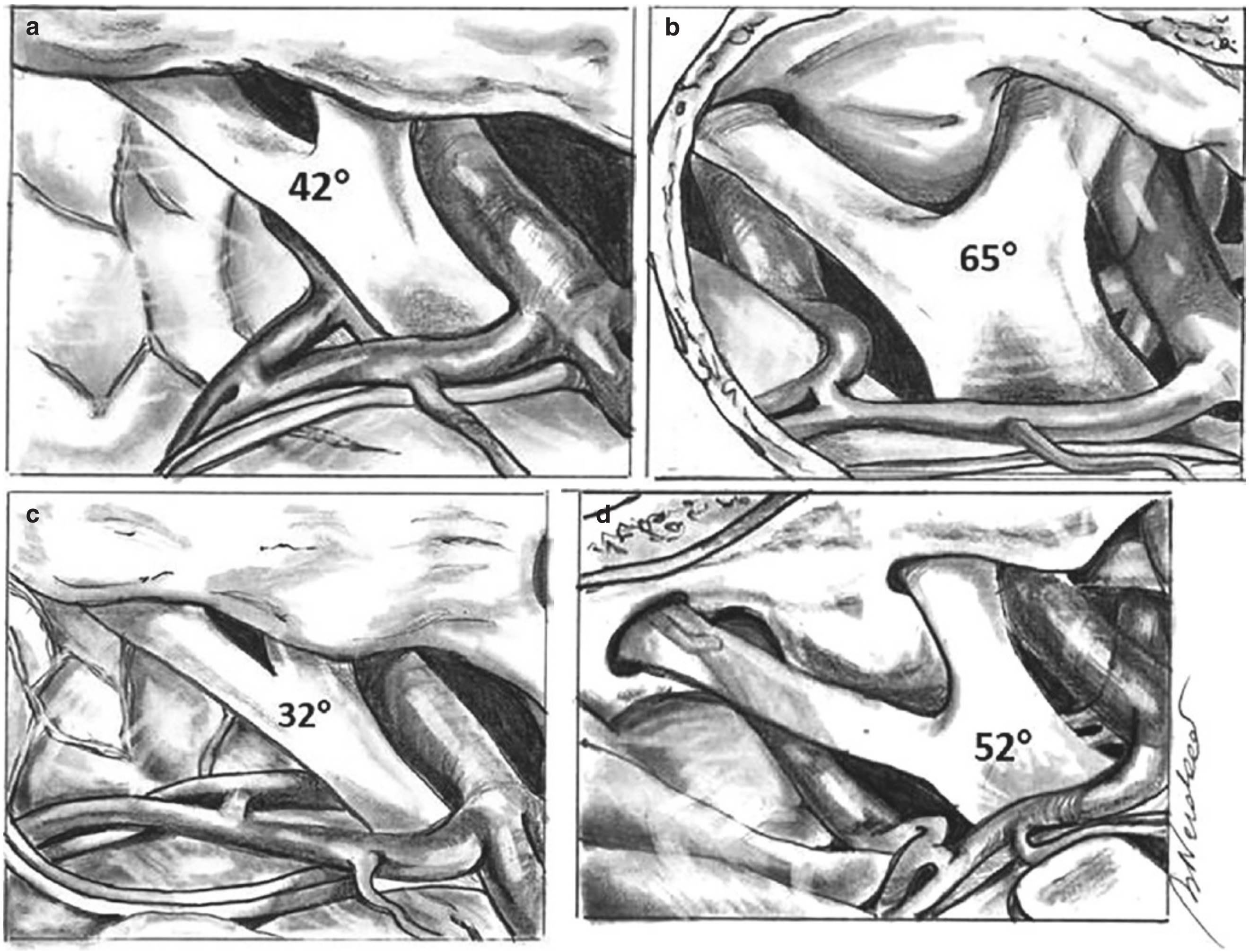

Fig. 2 (**a–d**) Illustration showing the variations of the angles between the optic nerves (OA) according to the chosen approach and to the degree of head rotation. With the head rotated by 30°, the OA angle measured 42° in the PT approach (**a**) and 65° in the SO (**b**). Further rotation to 45° narrowed the OA to 32° in the PT (**c**) and to 52° in the SO (**d**). (Original drawings by B. Nardacci, M.D.)

ferences related to the head position (Fig. 2a–d). With the head rotated by 30°, OA measured 42° in the PT approach and 65° in the SO ($p < 0.0001$). Further rotation to 45° narrowed the OA to 32° in the PT and to 52° in the SO ($p < 0.0001$). These differences were also significant within the same approach: 42° vs. 32° in the PT approach ($p = 0.01$), and 65° vs. 52° in the SO keyhole ($p < 0.001$), from 30° to 45°, respectively. The optic-carotid angle (OCA) did not show significant variations when comparing the two approaches with the same degree of head rotation.

4 Discussion

The current anatomical study was designed to compare the “standard” PT approach with the more recently proposed and well-accepted “supraorbital keyhole” in exposing the anterior skull base and the basal cisterns of the brain. Although the difference in the craniotomy size was striking, the volume of the surgical corridor to the “working area” was not different and complete access to all landmarks was possible from both approaches, confirming the “keyhole theory” that the intracranial optical field widens with increasing distances from the keyhole. However, comparison of the two approaches showed that the surgical area of exposure was different in sizes and morphology and strictly dependent on the degree of head rotation. The distances to the targets were significantly longer coming from the SO keyhole. An intuitive explanation is that this route approaches the brain through a more rostral, sub-frontal aspect, rather than lateral, accessing the parasellar region almost perpendicularly, with also significant differences of the angles from which each structure was observed and with visualization of the contralateral anatomy.

A precise quantification of the area of exposure obtained through the PT craniotomy is indeed a rather complicated matter since the actual "surgical window" is dependent on the entity of the frontal and temporal lobes retraction. Schwartz et al., using a frameless sterotactic device, reported that the area of exposure of a standard fronto-temporal approach was 2915 ± 585 mm^2, values very similar to the area of our PT craniotomy size [12].

In an attempt to define the actual size of the "working area under the microscope," we noticed that by increasing the head rotation from 30 to 45°, the PT exposed area increased significantly, as the medial edge of the surgical field changed from the lamina terminalis to the contralateral optic canal. Gonzales et al. calculated that the maximal exposure area of this triangle was approximately 100 mm^2, a value similar to our area with 45° of head rotation [13]. Interestingly, the only significant difference regarded the angle between the two optic nerves with no change of the optic-carotid angle. A direct surgical implication of this data is that in the PT approach, the head orientation becomes extremely important when approaching lesions located in the anterior skull base and cisterns. However, only minor changes were noticed in the optic carotid space, which remains quite a narrow field to expose the deeper structures such as the basilar tip.

The exposure of the anterior skull base obtained with the SO resulted rather satisfactory, showing the widest optic angle with an optimal sub-chiasmatic window. One disadvantage of the SO route is certainly represented by the longer distance and the narrow corridor of work; however, from this study, the use of standard micro-instruments revealed no limitation of the surgical view. Coming from a frontal-lateral trajectory, certainly the surgical corridor to the parasellar region was significantly longer; however, this difference decreased when approaching contralateral targets and retrosellar structures. Menovsky and colleagues, reported for the first time that the SO craniotomy can be safely used to approach lesions located in the interpeduncular fossa and that one of the fundamental advantages of this approach was the good view of the contralateral III nerve and the contralateral PCA and SCA [14].

5 Conclusions

Although the PT craniotomy represents one of the most versatile approaches in the field of neurosurgery, this anatomical study provided the morphometric evidence that the SO keyhole could represent an appropriate alternative and an interesting option to add to the neurosurgical armamentarium to approach certain lesions in the parasellar region. The comparison with the PT approach demonstrated that this keyhole, especially with 30° of head rotation, offers an adequate surgical exposure and optimal visualization of supra- and retrosellar structures.

References

1. Yasargil MG, Fox JL. The microsurgical approach to intracranial aneurysms. Surg Neurol. 1975;3(1):7–14; PMID: 1111150.
2. Yasargil MG, Antic J, Laciga R, Jain KK, Hodosh RM, Smith RD. Microsurgical pterional approach to aneurysms of the basilar bifurcation. Surg Neurol. 1976;6(2):83–91; PMID: 951657.
3. Schlitt M, Quindlen EA. Osteoplastic pterional craniotomy. South Med J. 1989;82(5):592–5. https://doi.org/10.1097/00007611-198905000-00012; PMID: 2717984.
4. de Andrade Júnior FC, de Andrade FC, de Araujo Filho CM, Carcagnolo FJ. Dysfunction of the temporalis muscle after pterional craniotomy for intracranial aneurysms. Comparative, prospective and randomized study of one flap versus two flaps dieresis. Arq Neuropsiquiatr. 1998;56(2):200–5. https://doi.org/10.1590/s0004-282x1998000200006; PMID: 9698728.
5. Brock M, Dietz H. The small frontolateral approach for the microsurgical treatment of intracranial aneurysms. Neurochirurgia (Stuttg). 1978;21(6):185–91. https://doi.org/10.1055/s-0028-1090343; PMID: 724020.
6. Chehrazi BB. A temporal transsylvian approach to anterior circulation aneurysms. Neurosurgery. 1992;30(6):957–61. https://doi.org/10.1227/00006123-199206000-00029; PMID: 1614606.
7. Harland SP, Hussein A, Gullan RW. Modification of the standard pterional approach for aneurysms of the anterior circle of Willis. Br J Neurosurg. 1996;10(2):149–53. https://doi.org/10.1080/02688699650040296; discussion 153. PMID: 8861305.
8. Yagmurlu K, Safavi-Abbasi S, Belykh E, Kalani MYS, Nakaji P, Rhoton AL Jr, Spetzler RF, Preul MC. Quantitative anatomical analysis and clinical experience with mini-pterional and mini-orbitozygomatic approaches for intracranial aneurysm surgery. J Neurosurg. 2017;127(3):646–59. https://doi.org/10.3171/2016.6.JNS16306; Epub 2016 Nov 18. PMID: 27858574.
9. Gonçalves DB, Dos Santos MIA, de Cristo Rojas Cabral L, Oliveira LM, da Silva Coutinho GC, Dutra BG, Martins RV, Reis F, Paiva WS, de RLO A. Esthetics outcomes in patients submitted to pterional craniotomy and its variants: a scoping review. Surg Neurol Int. 2021;12:461. https://doi.org/10.25259/SNI_485_2021; PMID: 34621576; PMCID: PMC8492413.
10. van Lindert E, Perneczky A, Fries G, Pierangeli E. The supraorbital keyhole approach to supratentorial aneurysms: concept and technique. Surg Neurol. 1998;49(5):481–9. https://doi.org/10.1016/s0090-3019(96)00539-3; discussion 489–90. PMID: 9586924.
11. Rychen J, Croci D, Roethlisberger M, Nossek E, Potts M, Radovanovic I, Riina H, Mariani L, Guzman R, Zumofen DW. Minimally invasive alternative approaches to Pterional craniotomy: a systematic review of the literature. World Neurosurg. 2018;113:163–79. https://doi.org/10.1016/j.wneu.2018.02.016; Epub 2018 Feb 13. PMID: 29452317.
12. Schwartz MS, Anderson GJ, Horgan MA, Kellogg JX, McMenomey SO, Delashaw JB Jr. Quantification of increased exposure resulting from orbital rim and orbitozygomatic osteotomy via the fronto-temporal transsylvian approach. J Neurosurg. 1999;91(6):1020–6. https://doi.org/10.3171/jns.1999.91.6.1020; PMID: 10584849.
13. Gonzalez LF, Crawford NR, Horgan MA, Deshmukh P, Zabramski JM, Spetzler RF. Working area and angle of attack in three cranial base approaches: pterional, orbitozygomatic, and maxillary extension of the orbitozygomatic approach. Neurosurgery. 2002;50(3):550–5; discussion 555–7. PMID: 11841723.
14. Menovsky T, Grotenhuis JA, de Vries J, Bartels RH. Endoscope-assisted supraorbital craniotomy for lesions of the interpeduncular fossa. Neurosurgery. 1999;44(1):106–10. https://doi.org/10.1097/00006123-199901000-00062; discussion 110–2. PMID: 9894970.

Far Lateral Approach: "Trans-tumor Approach" on Huge Dumbbell-Shape Neurofibroma of Anterior Foramen Magnum Without Craniectomy—Anatomical Consideration and New Trend

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1 Introduction

Tumors of the foramen magnum remained a surgical challenge above all those located anteriorly or anterolaterally [1]. Several approaches have been described such as transoral, midline suboccipital, far lateral approach and its variants. The first techniques did not gain wide acceptance [2, 3] due to a higher risk of CSF leakage and inadequate exposure of lateral margins of the tumors, as well as unsuitable proximal control of the vertebral artery [2, 3]. In contrast, the far lateral approach appears to be a revolutionary solution to cope with tumors arising from this region. Roberto Heros and Bernard George originally introduced it in 1986 to treat vertebrobasilar lesions and in 1987 to remove tumors located in the anterior portion of the foramen magnum, respectively [4, 5]. This approach combines two steps: the cervical posterolateral approach corresponding to muscular dissection with vertebral artery exposure; and posterolateral craniectomy, including an opening of the foramen magnum with or without occipital condyle drilling [5, 6]. Here, we describe the trans-tumor approach after cervical posterolateral dissection without craniectomy for removal of the anterior foramen magnum extradural neurofibroma arising from the right C2 nerve root.

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2 Case Presentation

A 63 year-old woman without a medical past history was admitted to our department for a progressive quadriplegia. It was a long duration evolution till her admission and had begun with right arm numbness, then her right leg, then her left leg and finally her left arm. She also complained about a suboccipital headache. A few months after quadriplegia, swallowing disorders appeared. On neurological examination, the muscular strength was 1/5 on the right side and 2/5 on the left side with hyperreflexia. Gag reflex was negative. Magnetic resonance imaging (MRI) revealed a process of the inferior third of the clivus with an important compression on the medulla oblongata and the spinal cord. The process was also extended into the spinal canal till the level of C2 (Fig. 1). This lesion was hypointense on T1 weighted images and iso to slightly hyperintense on T2 weighted images. The process showed an enhancement after Gadolinium injection. There was neither a genuine hyperintensity surrounding the process on FAILR weighted images nor a compression of vertebral artery on MR angiography. Due to a progressive impairment of her condition with swallowing disorders, a trans-tumor resection through a cervical step of far lateral approach achieved a near total resection of the process. The postoperative period showed a resolution of swallowing disorders and a progressive improvement of muscular strength. At 8 months follow-up she was asymptomatic and able to walk with a normal balance.

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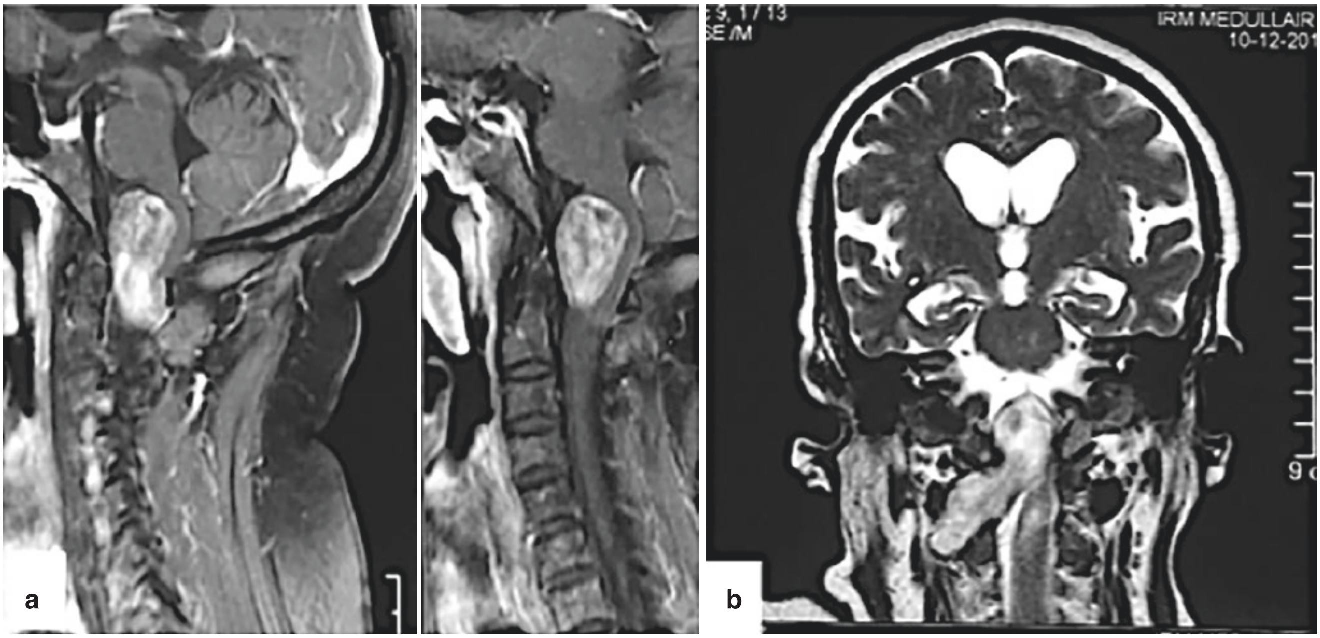

Fig. 1 Preoperative MRI: sagittal T1 post gadolinium (**a**) and coronal T2 weighted images (**b**) showing a process of foramen magnum with an important compression of medulla oblongata

3 Operative Technique and Anatomical Correlation

From a surgical view, the foramen magnum defines a space delineated anteriorly by the lower third of the clivus to the upper edge of the body of C2, laterally by the jugular tubercles to the upper aspect of C2 lamina, and posteriorly from the anterior edge of squamous occipital bone to the C2 spinous process [7]. This region contains vital neurovascular structures represented by the caudal portion of the medulla oblongata, inferior vermis with cerebellar tonsils, fourth ventricle, rostral part of spinal cord, lower cranial and upper cervical nerves [7]. The hypoglossal nerve emerges from the preolivary sulcus and courses posterior to the vertebral artery to reach the hypoglossal canal in the occipital condyle [6, 7]. The most rostral part of the dentate ligament is anchored on the dura matter at the level of foramen magnum and represents the transition point between the intradural and the extradural segment of the vertebral artery [6, 7]. Dealing with foramen magnum processes requires a perfect knowledge of the vertebral artery, above all its third segment (V3), which is divided into three portions: vertical (between the transverse process of C2 and C1), horizontal (in the sulcus arteriosus), and oblique (from this groove up to the dura mater) [8, 9]. This so-called suboccipital segment is located in the suboccipital triangle bounded medially by the rectus capitus posterior major, inferiorly by the inferior oblique muscle, and superiorly by the superior oblique muscle [6, 9]. The posterior arch of the atlas and the posterior atlantooccipital membrane forms the floor of this triangle. This space is filled with an abundant areolar tissue surrounding the horizontal portion of the third segment of vertebral artery and the dorsal ramus of C1 nerve root [9, 10] as well as the suboccipital cavernous sinus. The vertical portion of the vertebral artery is crossed posteriorly by the C2 nerve root in the inferior suboccipital triangle. This latter triangle, measuring an average of 1.89 cm^2 and where the periarterial venous plexus is less represented, is limited superiorly by the obliqus capitis inferior, inferolaterally by the posterior intertransversarii muscle, and inferomedially by C2 lamina [9]. Finally, the third segment of the vertebral artery courses posterior and medial to the occipital condyle, the hypoglossal canal, and the jugular tubercle to enter the dura mater and give the fourth segment [9]. To facilitate a preoperative surgical strategy, George et al. classified foramen magnum meningioma in three subgroups [7, 8]. Subgroup 1 relies on their compartment of origin (intradural, extradural, or intra-extradural). Subgroup 2 relies on their insertion, which can be anterior, lateral, and posterior. Subgroup 3 is according to their relationship with the vertebral artery: above, below, or both sides of the vertebral artery. In our case, the process grows from the right C2 nerve root in an anterior lateral direction, pushing the spinal cord laterally on the left side to reach the anterior surface of the medulla oblongata. This latter is pushed laterally and posteriorly. Therefore, this requires an exposition of the suboccipital and the inferior suboccipital triangles. Thus, the far lateral approach extended slightly inferior was set out.

3.1 Patient Positioning

The patient is placed in the park bench position and the head is secured using a four-pin Mayfield clamp with two pins on the contralateral side on the occipital bone and the two others pins at the ipsilateral side on the frontal bone. The incorporation of three movements is applied to the head for a proper exposure of the craniovertebral junction: anteroposterior flexion to uncover the suboccipital region and the rostral clivus, contralateral flexion to increase working space beside ipsilateral shoulder, and contralateral rotation to bring the suboccipital surface uppermost in the field. The ipsilateral shoulder is pulled toward the leg of the patient. The operative table is slightly elevated to bring the head above the heart to decrease cerebral venous congestion. Neurophysiological monitoring of cranial nerve VII to XI as well as somatosensory evoked potentials and motor evoked potential are required in such surgery but were not available in our hospital.

3.2 Skin Incision and Muscles Dissections

We chose a right C-shaped curvilinear incision, two fingers breadth above then posterior to the heart, and then turns downward along the posterior border of the sternocleidomastoid muscle (Fig. 2a). The skin flap was reflected anteriorly. Superficial muscles of the posterolateral area of the neck, namely trapezis, splenius, and semispinalis, were detached and reflected posteriorly, whereas sternocleidomastoid, longissimus capits, and the posterior belly of digastric muscle was reflected anteriorly and allowed the exposition of the

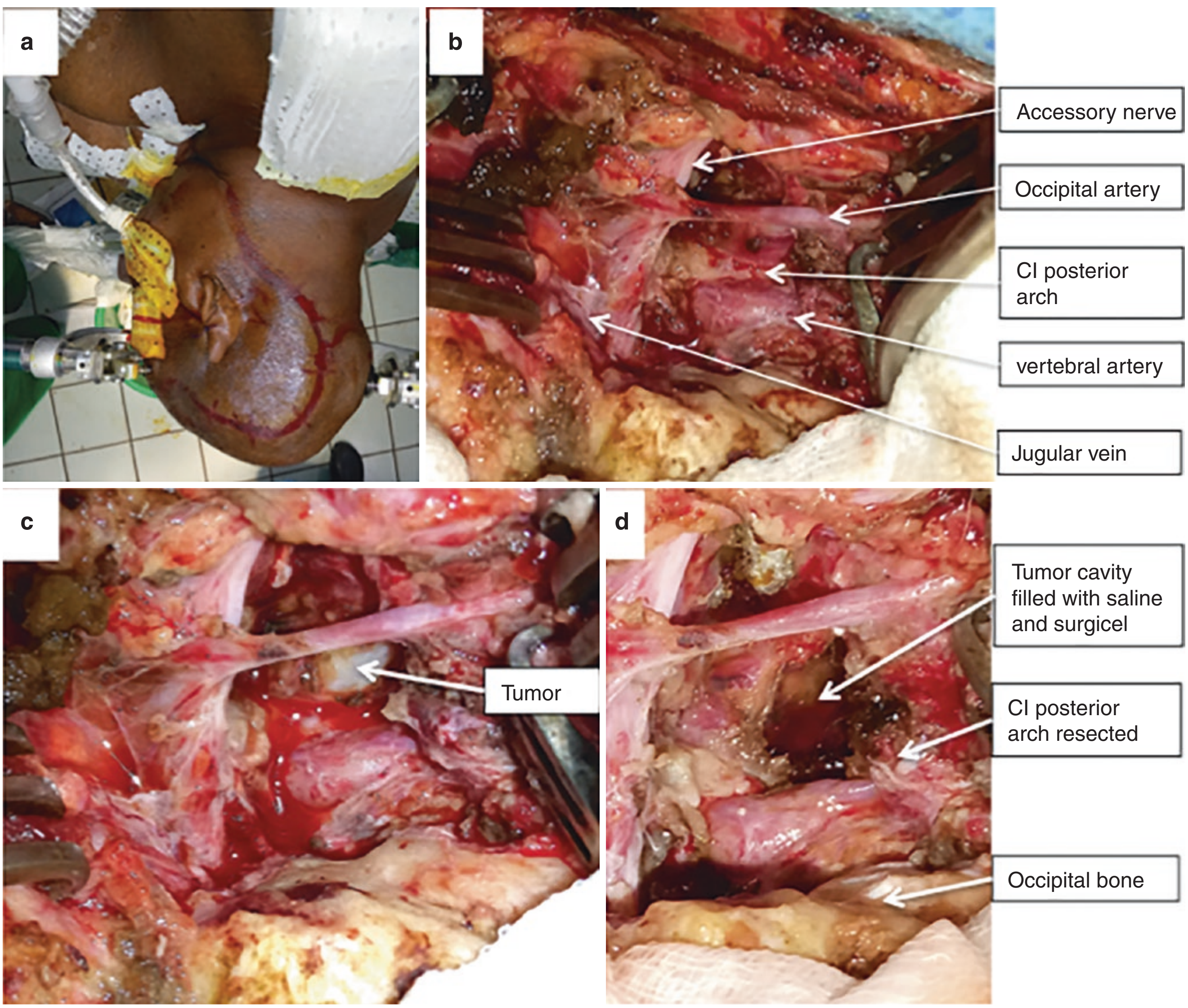

Fig. 2 Intraoperative images: (**a**) incision; (**b**) cervical step of far lateral approach with vertebral artery exposure; (**c**) tumor exposure; (**d**) tumor removal

internal jugular vein and the accessory nerve running downward on its surface. Care was taken to preserve the occipital artery for bypass if needed. The third segment of the vertebral artery was revealed after dissection of the suboccipital triangle. Bleeding from the veinous plexus of this area was controlled using surgicel. Subperiostal dissection allowed an exposition of the right posterior arch of C1 (Fig. 2b). Then, a resection of the posterior arch of C1 was achieved to enlarge the surgical field. The suboccipital dissection was brought inferiorly till the inferior suboccipital triangle where the C2 nerve root crossed the posterior surface of the vertebral artery and C1C2 join. The C2 foramen was enlarged and displayed by a firm mass with smooth surface developed from the C2 nerve root. This lesion was not hemorrhagic after the opening of its thick capsule allowing a trans-tumor debulking from the C2 foramen to the posterior third of clivius (Fig. 2c). A complete intracapsular removal was achieved. The capsule was adherent to surrounding structures, thus we did not perform its dissection. Surgicel was left in the intracapsular surgical field for hemostasis (Figs. 2d and 3a).

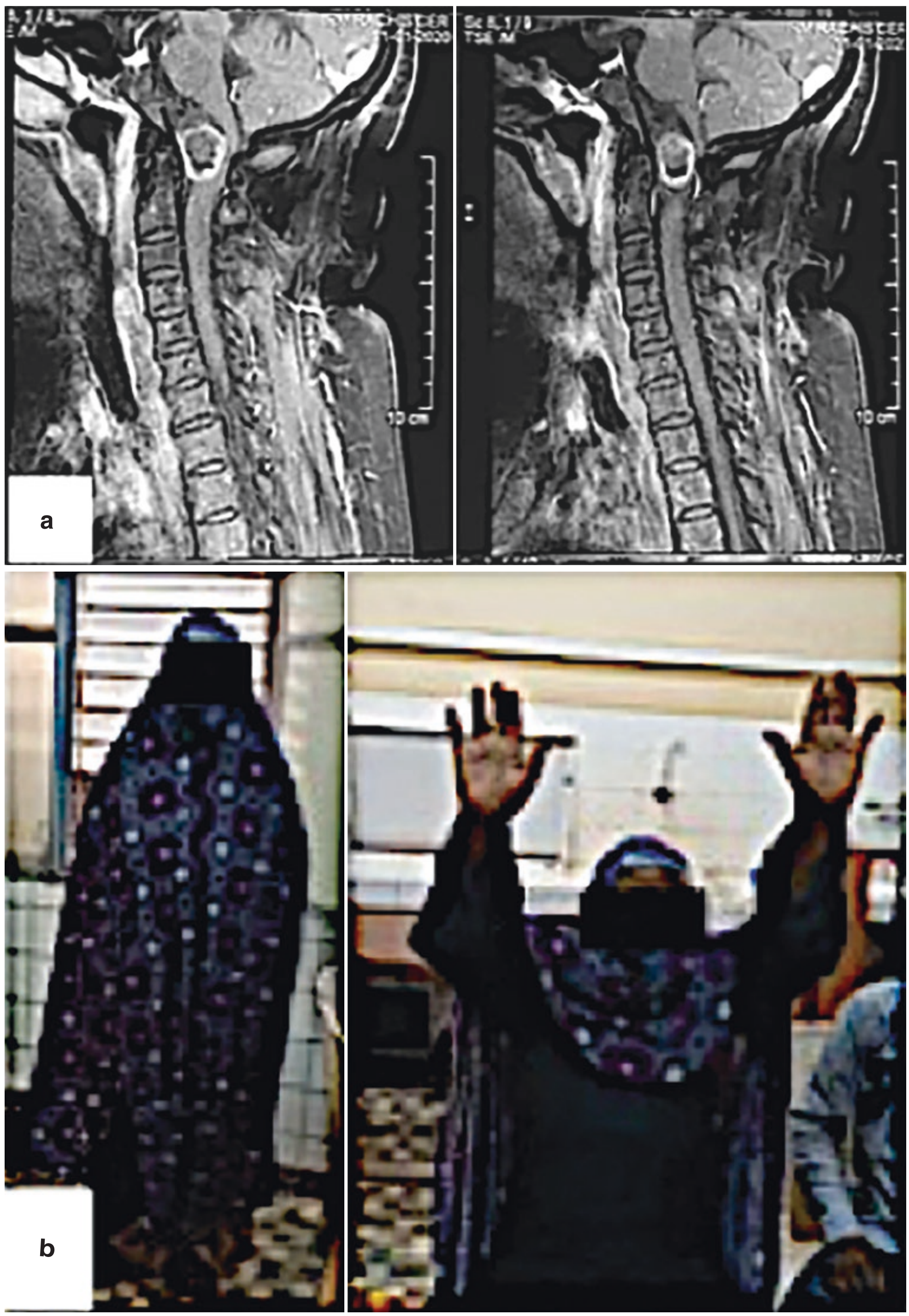

Fig. 3 (**a**) Postoperative T1 post gadolinium MRI showing a complete intracapsular removal; (**b**) patient at 8 months follow up

3.3 Operative Result

The patient was extubated at the end of surgery and transferred to the intensive care unit. Nil per os (NPO) or nothing by mouth strategy was applied and nasogastric tube was used for feeding. The daily assessment of the lower cranial nerve through gag reflex and deglutition showed an improvement of their function. The patient was thus transferred to a regular neurosurgical ward at postoperative day 5 and normal feeding by mouth with removal of the nasogastric tube was achieved. The patient was discharge from the hospital day 10 and sent to physical therapy. There was neither CSF leakage nor pseudomeningocele postoperatively.

Her condition improved dramatically, albeit gradually, and she was asymptomatic at 8 months follow-up. She was able to walk with normal balance with a complete recovery of the swallowing disorder and without sensory or motor deficit (Fig. 3b).

4 Discussion

Foramen magnum neurofibroma is rare and accounts for 13% of tumors arising in this area [11, 12]. It usual mimics degenerative spondylosis [9, 12] in the early period and then displays neurological impairment with a "U-shape" evolution [9], as in our patient. Untreated cases may progress to quadriplegia with swallowing and respiratory disorders, which can lead to death [9, 11]. In the past, foramen magnum lesions were considered inoperable and associated with high morbidity and mortality up to 29% [9]. Despite great progress in microsurgery and intraoperative neurophysiological monitoring, the management of foramen magnum tumors remains challenging. Postoperative impairment and mortality is estimated at 10% and 3%, respectively [9]. Anterior and anterolateral lesions of the lower third of the clivius extended to the foramen magnum and the superior cervical spine require a retractorless surgery on surrounding structures [11]. Thus, these vital neurovascular structures are exposed after tailored muscular dissection and bone resection. An anterior approach through the transoral route has been described for the treatment of such lesions but did not gain wide acceptance because of common associated complications such as CSF leakage and infection [9]. Moreover, inadequate proximal control of the vertebral artery and the lateral margin of the tumor result in a low rate of complete resection [9]. Therefore, the postero lateral approach appears to be a cornerstone for a proper exposition and resection of anterior and anterolateral lesions of the foramen magnum [9, 11]. This technique requires the exposition of the mastoid process, the ipsilateral posterior arch of C1, and the lamina of C2 [4]. The standard incision since the description by Heros and George in the 1980s remains the classic "reverse hockey stick" [4, 5]. However, we chose the "C-shaped" incision, which is more targeted over the lateral aspect of the inferolateral skull base [13]. This reduces the amount of muscle dissection, thus preventing postoperative pseudomeningocele and CSF leakage, which occurs in 16–20% [9, 13]. A general surgical principle stipulates that tumors displace the surrounding anatomical structures and provide a surgical path to their own resection [14]. In this way, after the cervical step of the far lateral approach consisting of muscles dissection, vertebral artery exposition, and C1 posterior arch resection, we decided to skip the craniectomy step and immediately begin tumor resection via a trans-tumor corridor. This strategy enabled us a complete intracapsular debulking. We used neither fat graft to augment closure nor lumbar drainage postoperatively.

5 Conclusion

Anterior and anterolateral processes of foramen magnum are properly managed through the far lateral approach [9, 15]. Two main steps constitute this surgical technique: the cervical step requiring muscular dissection from the posterolateral area of the neck to suboccipital triangle allowing exposition of the vertebral artery and resection of the posterior arch of C1; whereas the cranial steps require craniectomy with occipital condyle drilling [14, 16]. Our case demonstrates that the latter step can be skipped in well-selected anterolateral lesions of the craniovertebral junction extended to the inferior third of the clivus, above all those located partially extradural such as neurofibromas. In this case, a "trans-tumor" corridor is suitable and may achieve a total removal.

Disclosure The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

1. Chaddad-Neto F, Doria-Neto HL, De Campos-Filho JM, Reghin-Neto M, Rhoton AL Jr, De Oliviera E. Far-lateral craniectomy: tips and tricks. Arq Neuropsiquiatr. 2014;72:699–705.
2. Rhoton AL Jr. Meningiomas of the cerebellopontine angle and foramen magnum. Neurosurg Clin N Am. 1994;5:349–77.
3. Sen CN, Sekhar LN. Surgical management of anteriorly placed lesions at the craniocervical junction—an alternative approach. Acta Neurochir (Wien). 1991;108:70–7.
4. George B, Dematons C, Cophignon J. Lateral approach to the anterior portion of the foramen magnum. Application to surgical removal of 14 benign tumors: technical note. Surg Neurol. 1988;29:484–90.
5. Heros RC. Lateral suboccipital approach for vertebral and vertebrobasilar artery lesions. J Neurosurg. 1986;64:559–62.
6. Rothon AL Jr. Foramen magnum. Neurosurgery. 2000;47:S155–93.

7. George B, Lot G, Boissonnet H. Meningioma of the foramen magnum: a series of 40 cases. Surg Neurol. 1997;47:371–9.
8. Bruneau M, George B. Foramen magnum meningiomas: detailed surgical approaches and technical aspects at Lariboisière Hospital and review of the literature. Neurosurg Rev. 2008;31:19–33.
9. Flores BC, Boudreaux BP, Klinger DR, Mickey BE, Barnett SL. The far-lateral approach for foramen magnum meningiomas. Neurosurg Focus. 2013;35:E12.
10. Nanda A, Vincent DA, Vannemreddy PS, Baskaya MK, Chanda A. Far-lateral approach to intradural lesions of the foramen magnum without resection of the occipital condyle. J Neurosurg. 2002;96:302–9.
11. Bernard F, Lemee JM, Delion M, Fournier HD. Lower third clivus and foramen magnum intradural tumor removal: the plea for a simple posterolateral approach. Neurochirurgie. 2015;62:86–93.
12. Meyer FB, Ebersold MJ, Reese DF. Benign tumors of foramen magnum. J Neurosurg. 1984;61:136–42.
13. Lau T, Reintjes S, Olivera R, Van Loveren HR, Siviero A. C-shaped incision for far-lateral suboccipital approach: anatomical study and clinical correlation. J Neurol Surg B Skull Base. 2015;76:117–21.
14. Au K, Richarson AM, Morcos J. Far lateral approach and its variants. In: Skull base surgery of posterior fossa. Berlin: Springer International Publishing; 2017. p. 65–73.
15. Moscovici S, Umansky F, Spektor S. “Lazy” far-lateral approach to the anterior foramen magnum and lower clivus. Neurosurg Focus. 2015;38:E14.
16. Rocca GL, Altieri R, Ricciardi L, Olivi A, Pepa GMD. Anatomical study of occipital triangles: the ‘inferior’ suboccipital triangle, a useful vertebral artery landmark for safe postero-lateral skull base surgery. Acta Neurochir (Wien). 2017;159:1887–91.

Use of BoneScalpel Ultrasonic Bone Dissector in Anterior Clinoidectomy and Posterior Fossa Surgery: Technical Note

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1 Introduction

First popularized by Dolenc [1], who introduced the high-speed drill clinoidectomy for paraclinoid region surgeries, the utility of the clinoidectomy has been reported in literature [2–12]. Surgical exposure is the mainstay of skull base, vascular, and microneurosurgery. There are anatomical structures that limit exposure: the anterior clinoid process (ACP) in anterior skull base surgeries needs to be removed to obtain proximal vascular control, to devascularize skull base tumors, and to obtain a radical removal. ACP removal exposes the clinoidal and ophthalmic segments of the internal carotid artery (ICA), the ophthalmic artery, as well as the optic nerve. The ACP is the extreme medial portion of the sphenoid wing, and it presents variable pneumatization, shape, and dimensions. Anterior clinoidectomies were performed with rongeurs, before the adoption of modern high-speed drills, which allow an appropriate microsurgical APC removal, thanks to the employment of the microscope and burr holes of different sizes. Nevertheless, the high-speed drill presents the risk of damage to eloquent structures due to the heat or direct mechanical injury, which probably is underestimated [13]. A minor limitation is represented by bone dust creation and the need to remove it through continuous suction and irrigation, also reducing heat. Finally, the high-speed drill can damage neuromuscular structures with its shaft's rotation and move cottonoids [14]. We describe a novel application of the piezoelectric BoneScalpel™ in anterior skull base and posterior fossa surgeries, reporting our initial experience on a case series of 12 patients.

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2 Materials and Methods

We reported a total of 12 patients, 8 affected by posterior fossa tumors and 4 treated for anterior skull base oncologic and vascular pathologies (Table 1). In all patients, an ultrasonic bone dissector (BoneScalpel™ – Misonix) was used to perform anterior clinoidectomy (AC) and craniotomy. This study aims to assess the safety and efficacy of the piezoelectric osteotomy in skull base and posterior fossa surgeries. An extradural clinoidectomy was performed in three out of four patients, while an intradural clinoidectomy only in one case, to complete tumor removal. The high-speed drill, in these selected clinoidectomies, was used only to perform the first step of pterional craniotomy; also, the posterior fossa craniotomies were conducted using the BoneScalpel™ for the duration of the procedure.

2.1 Surgical Instruments

The BoneScalpel™ system was designed to resect bone tissue ultrasonically with extreme precision (0.5 mm narrow), sparing the underlying soft tissue, thus reducing risks of a dural tear and/or vascular injury. The console produces an electrical signal that is fed into the handpiece and its piezo-

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Table 1 Patients' demographics

Patients	Age (years)	Sex	Pathology	BoneScalpel® related complications	Osteotomy type	Craniotomy time (min)
#1	34	F	Pinealoma	None	Supra-subtentorial craniotomy	25
#2	54	F	Cerebellar renal cell metastasis	Dural tear	Suboccipital craniotomy	13
#3	71	F	Posterior fossa meningioma	None	Craniotomy	12
#4	68	F	Right cavernous sinus meningioma	None	Clinoidectomy	27
#5	40	F	Right MCA aneurysm	None	Clinoidectomy	32
#6	73	M	Left anterior clinoid meningioma	None	Clinoidectomy	29
#7	43	F	Pineal cyst	None	Supra-subtentorial craniotomy	20
#8	16	F	Medulloblastoma	None	Craniotomy	10
#9	53	F	Left vestibular schwannoma	None	Craniotomy	8
#10	56	F	Right vestibular schwannoma	None	Craniotomy	7
#11	47	F	Left carotid-ophthalmic aneurysm	None	Clinoidectomy	31
#12	12	M	Cerebellar hemangioblastoma	None	Suboccipital craniotomy	7

Table 2 BoneScalpel™ technical specifications in comparison to the SONOPET® Ultrasonic Aspirator – Stryker and the PIEZOSURGERY® – Mectron

	BONESCALPEL™ – Misonix	SONOPET® Ultrasonic Aspirator – Stryker	PIEZOSURGERY® – Mectron
Frequency	22.5 kHz	25 kHz	24–36 kHz
Irrigation	Internal coaxial and proximal to the tip	Distal to the tip	Distal to the tip
Tip size	1.3 × 1.8 mm	2.5 × 2.0 mm	1.7–2.9 mm

electric transducer. The transducer converts the electrical signal into mechanical vibrations. A peristaltic pump, integrated into the BoneScalpel™ console, provides irrigation of the operative site during its use. The instrument causes compression damage to the bone and the cutting tip oscillates a small distance at a rate of 22.500 times/s, while preserving soft tissues. Moreover, the device heats the bone, which stops bleeding. Table 2 shows BoneScalpel™ technical specifications and the comparison with the SONOPET® Ultrasonic Aspirator – Stryker. Furthermore, other than by the BoneScalpel™ – Misonix, the piezoelectric technology in neurosurgery is used by the PIEZOSURGERY® – Mectron and the SONOPET® – Stryker.

2.2 Surgical Technique

In the posterior fossa craniotomies, a piezoelectric osteotome was used to perform the entire craniotomy, both for the median suboccipital approach and the retrosigmoid approach. In the median suboccipital approach group, the craniotomy crossed the posterior third of the superior sagittal sinus (SSS) and transverse sinuses (TS) (Fig. 1a–c). No burr hole was performed, but we used the blade of the BoneScalpel™ (Fig. 1b) to cut the bone flap. We documented one dural tear and no dural venous sinus injuries. The tumor removal was accomplished as usual, and the bone flap was repositioned and fixed with titanium miniplates (Fig. 1d).

In the anterior skull base group, the piezoelectric osteotome was used after performing the first step of the pterional craniotomy (Fig. 2a). We used a 4.4 mm BoneScalpel™ diamond shaver to microsurgically remove bone from the posterior orbital roof and sphenoid wing, accomplishing the anterior clinoidectomy also with a microhook shaver (Fig. 2b–d). Microsurgical instruments (e.g., pituitary instruments, microdissectors) were used to gently dissect the dural elements from the anterior clinoid process and to remove the final bone lamina of the remnants of the ACP, optic canal roof, and optic strut. The vector of the instrument's pressure should always be directed from the inside out, to avoid damage to the periorbita and surrounding structures. Once the ACP is removed, the optic canal is removed with the same technique. The dura is opened in a typical semicircular manner. With the operating microscope, the Sylvian fissure is routinely opened in a distal-to-proximal manner, identifying the M2 branches of the MCA and then the main middle cerebral artery trunk on the way down to the ICA. After placing cotton patties to gently keep the Sylvian fissure open, the optic-carotid recess is approached to section the falciform ligament and the dura of the optic nerve sheath, to facilitate the mobilization of the optic nerve as indicated by clinical circumstances.

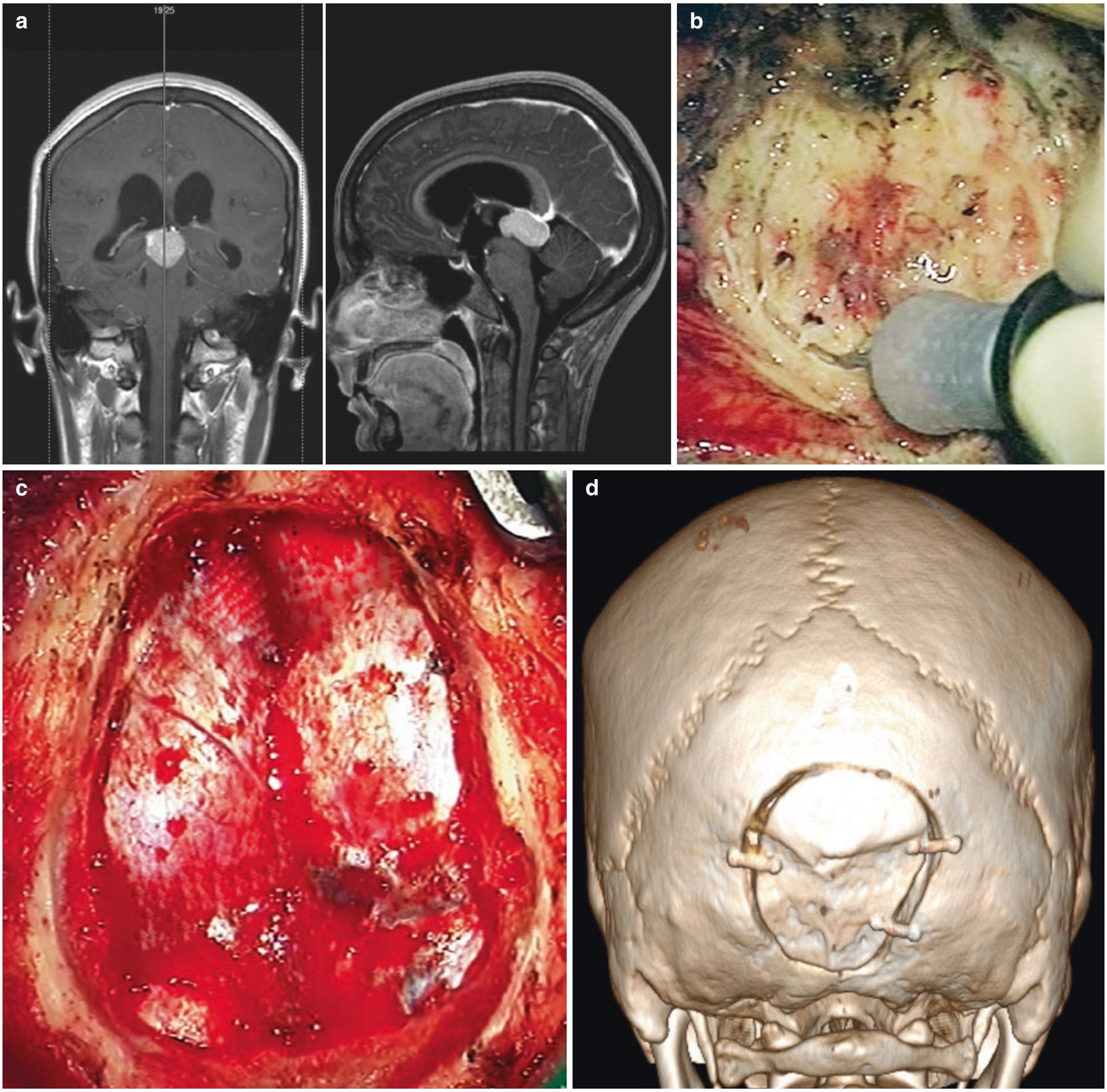

Fig. 1 Coronal and sagittal T1-weighted brain MRI images with Gadolinium showing a pinealoma. (**a**) Occipital craniotomy performed using the BoneScalpel™ blade shaver (**b**) that crossed the posterior third of the superior sagittal sinus and transverse sinuses (**c**). The bone flap was repositioned and fixed with titanium miniplates as shown in the post-operative head CT scan with 3D reconstruction (**d**)

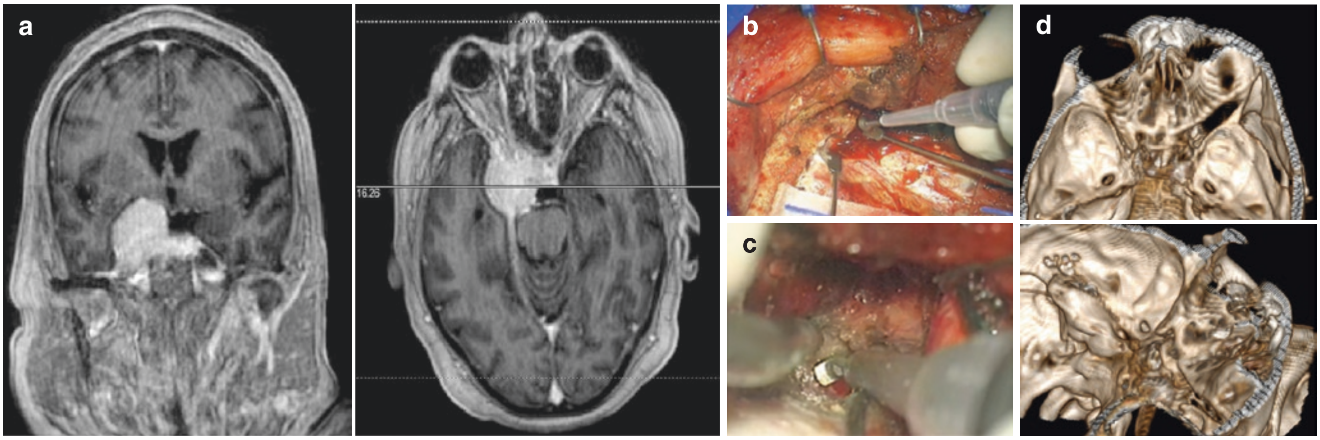

Fig. 2 Coronal and sagittal T1-weighted brain MRI images with Gadolinium showing a clinoidal meningioma. (**a**) Extradural clinoidectomy performed with 4.4 mm BoneScalpel™ diamond shaver (**b**) and microhook shaver (**c**). Post-operative head CT scan with 3D reconstruction showing anterior clinoidectomy (**d**)

3 Results

We retrospectively reviewed a total of 12 patients, 10 females and 2 males with a female/male ratio of 5/1. The mean age was 47.25 years (range 12–73 years). A successful clinoidectomy was performed in 4 out of 12 patients (33.3%). We did not document any heat damage to the surrounding soft tissue in critical areas such as the paraclinoid structures (e.g., optic nerve, oculomotor nerves, ICA). The mean surgical time for the anterior clinoidectomy was approximately 22 min (range 18–25 min), depending on the patient's specific anatomy. The mean intraoperative blood loss was 156 mL (range 43–270 mL). The mean follow-up period was 21 months (range 3 months to 6 years). The postoperative course was uneventful. We documented only a small ischemia in the right caudate nucleus without clinical consequences in one patient affected by right anterior clinoidal meningioma. Uneventful posterior fossa craniotomies were carried out in 7 out of 11 patients. We documented only one durotomy in an oncologic patient, while no lesions of the SSS or TS were detected. In these cases, the mean intraoperative blood loss was 150 mL (range 75–300 mL). The mean follow-up period was 13.5 months (range 3 months to 2 years). The postoperative course was characterized by the persistence of Parinaud syndrome in one patient affected by pinealoma, and hydrocephalus requiring ventriculoperitoneal shunt (VPS) in another patient with posterior fossa meningioma. The patient affected by cerebellar renal cell carcinoma metastasis died after 2.5 months because of tumor progression and sepsis. One patient affected by vestibular schwannoma presented severe peripheral facial nerve paralysis, which partially improved after 1 year. No cerebrospinal fluid (CSF) leaks were detected. Adjuvant therapy was performed in one patient affected by vestibular schwannoma to treat a small intrameatal remnant with gamma-knife radiosurgery (GKRS). We compared the surgical times reported in the literature of posterior fossa craniotomies and anterior clinoidectomies using BoneScalpel™, standard osteotome, and PIEZOSURGERY®; thus, we documented a slightly increased operation time in the PIEZOSURGERY® and BoneScalpel™ group to perform craniotomies, but no time difference in performing the clinoidectomy between BoneScalpel™ and a conventional high-speed drill (Table 3). SONOPET® results are not included because the instrument has been used to accomplish tumor removal or focal bone removal and not to perform craniotomies. In literature, to date, there is no mention of anterior clinoidectomies performed with piezosurgical devices.

Table 3 Surgical times comparing that reported in the literature for posterior fossa craniotomies and anterior clinoidectomies using BoneScalpel™, standard osteotome (high-speed drill for clinoidectomy), and PIEZOSURGERY®

Type approach	Standard osteotome	Bonescalpel™ (min)	Piezosurgery®
Clinoidectomy	19–25 min (high-speed drill)	18–25	–
Supratentorial + suboccipital craniotomy	16–21 min	20–25	–
Retrosigmoid craniotomy	12–16 min	15–18	17–45 min

4 Discussion

In literature, piezosurgery has been widely reported in maxillofacial surgery [5, 15–18], while only a few neurosurgical reports are present about retrosigmoid craniotomy, in the supraorbital keyhole approach and lateral orbitotomy [19], as summarized in Table 4 [16, 17, 20–34]. To our knowledge, there are no reports about the use of piezosurgery in anterior clinoidectomy. One of the main advantages of piezosurgery is related to the absence of spinning instruments, thus avoiding the risk of damage to surrounding soft tissue or of grabbing cottonoids during craniotomy, clinoidectomy, or skull base bone removal. The handpiece is comfortable and offers good operative visualization, which however can be limited in narrow spaces and require adjustments of the microscope's light direction. The continuous irrigation helps in reducing excessive heat but sometimes requires additional suction by the assistant. The literature reports experiences using PIEZOSURGERY® in brain surgery [23–28], which presents several important differences with BoneScalpel™. Other piezosurgical devices accomplish two tasks: tumor removal and bone cutting, while BoneScalpel™ has been created only to perform bone cuts. The adjustments to technical specifications allow optimizing the bone cut, which becomes more effective. Specific blades allow performing craniotomies sparing the dura mater, and we accomplished the anterior clinoidectomy with rounded tools for focal osteotomies. In our experience, we found that performing anterior clinoidectomies with BoneScalpel™ reduces the heat, as no spinning instruments such as a high-speed drill are used. However, we have documented that the irrigation of the device must be carefully set, to avoid the risk of overheating the tip, thus transmitting heat to the bone. Another disadvantage is represented by the presence of the distal cover of the tip, which may limit the view during microsurgical bone removal; this issue can be overcome by modifying the microscope's direction. In the posterior fossa group, we found it advantageous to perform thin cuts that, along with a meticulous dural closure, help to prevent CSF leakage. Moreover, we performed supra-subtentorial craniotomies across the main venous sinuses that were spared and uninjured. In the retrosigmoid craniotomy, the anatomy can be unfavorable for the standard osteotome, which needs to be used perpendicular to the bone surface, whereas the possibility to use BoneScalpel™ with smaller angles helps to operate in narrow corridors. PIEZOSURGERY® has already been reported in the pediatric population for the treatment of craniosynostosis, and the authors documented an increase in surgical times, stating that the device hardly adapts to the needs of emergency surgery [22]. As other authors have documented concerning other piezoelectric devices, we confirm that BoneScalpel™ has proven safe and effective in skull base surgery. We have documented shorter times than the other authors [34], and in this article, we report the first experience using the piezoelectric osteotome in anterior clinoidectomy. Despite BoneScalpel™ being faster than other piezosurgery scalpels, probably thanks to frequency optimization, it remains slower than the conventional osteotome in performing craniomoties, but there is no time difference in performing the clinoidectomy with a conventional high-speed drill.

Table 4 Summary of the main studies reported in the literature regarding piezosurgical devices use in neurosurgery

Authors (year)	Patients	Osteotomy type	Complications	Piezosurgery device
Acharya and Rajan (2015) [20]	10	Bone harvesting and graft	None	PIEZOSURGERY® – Mectron
Chaichana et al. (2013) [21]	13	Endoscopic osteotomies	Dural tears 23%, short operative times	BONESCALPEL™ – Misonix/ PIEZOELECTRIC SYSTEM - Depuy Synthes
Gleizal et al. (2007) [22]	30	Osteotomies and bone graft	Dural tears (6.5%), minimal soft tissue damage	PIEZOSURGERY® – Mectron
Grauvogel et al. (2011) [23]	8	Opening of internal acoustic canal	None	PIEZOSURGERY® – Mectron
Grauvogel et al. (2017) [24]	14	Orbital decompression	None	PIEZOSURGERY® – Mectron
Grauvogel et al. (2018) [25]	1	Retrosigmoid approach	None	PIEZOSURGERY® – Mectron
Grauvogel et al. (2018) [26]	22	Lateral suboccipital craniotomy	Dural tears (27%), sinus injury (13%)	PIEZOSURGERY® – Mectron
Iacoangeli et al. (2013) [17]	1	Lateral orbitotomy	None	PIEZOSURGERY® – Mectron
Iacoangeli et al. (2015) [16]	20	Supraorbital keyhole approach	None	PIEZOSURGERY® – Mectron
Kotrikova et al. (2006) [27]	2	Bone harvesting and splitting	None	PIEZOSURGERY® – Mectron
Kramer et al. (2006) [28]	15	Osteotomies	None	PIEZOSURGERY® – Mectron
Martini et al. (2017) [29]	18	Osteotomies	Dural injury (22%), periorbital injury (27%)	PIEZOSURGERY® – Mectron
Massimi et al. (2019) [30]	90	Craniotomies and laminotomies	Dural tears (3.3%)	PIEZOSURGERY® – Mectron
Ramieri et al. (2015) [31]	27	Osteotomies	None, quick orbitotomy	Not available
Shen et al. (2017) [32]	9	Osteotomies	None	Not available
Spinelli et al. (2015) [33]	13	LeFort III/IV osteotomies	CSF leakage (15%)	Not available
Vetrano et al. (2018) [34]	197	Supra and infratentorial craniotomy	Dural tears (4.3%)	PIEZOSURGERY® – Mectron
Umana et al. (2021)—present study	12	Anterior clinoidectomy, posterior fossa craniotomies	Dural tear (8.3%)	BONESCALPEL™ – Misonix

5 Conclusions

To the best of our knowledge, we report the first experience with BoneScalpel™ in anterior clinoidectomy and posterior fossa surgery, and above all, the first report on anterior clinoidectomy with piezosurgery. There is no difference in performing the clinoidectomy between BoneScalpel™ and a conventional high-speed drill, and this is an undoubted advantage in critical contexts such as clinoid-paraclinoid surgeries, where the risk of dural sinuses tears is common.

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Patient Consent Patient's consent not required as patient's identity is not disclosed or compromised.

Ethics Approval There is no ethical issue in this paper. The described technique does not present important variations from the classical one and does not involve additional risks for the patient.

References

1. Dolenc VV. A combined epi- and subdural direct approach to carotid-ophthalmic artery aneurysms. J Neurosurg. 1985;62:667–72.
2. Andaluz N, Beretta F, Bernucci C, Keller JT, Zuccarello M. Evidence for the improved exposure of the ophthalmic segment of the internal carotid artery after anterior clinoidectomy: morphometric analysis. Acta Neurochir. 2006;148:971–6.
3. Couldwell WT, Kan P, Liu JK, Apfelbaum RI. Decompression of cavernous sinus meningioma for preservation and improvement of cranial nerve function. Technical note. J Neurosurg. 2006;105:148–52.
4. De Jesús O, Sekhar LN, Riedel CJ. Clinoid and paraclinoid aneurysms: surgical anatomy, operative techniques, and outcome. Surg Neurol. 1999;51:477–88.
5. Huynh-Le P, Natori Y, Sasaki T. Surgical anatomy of the anterior clinoid process. J Clin Neurosci. 2004;11:283–7.
6. Krisht AF, Krayenbühl N, Sercl D, Bikmaz K, Kadri PA. Results of microsurgical clipping of 50 high complexity basilar apex aneurysms. Neurosurgery. 2007;60:242–52.
7. Kumon Y, Sakaki S, Kohno K, Ohta S, Ohue S, Oka Y. Asymptomatic, unruptured carotid-ophthalmic artery aneurysms. Surg Neurol. 1997;48:465–72.
8. Lee JH, Sade B, Park BJ. A surgical technique for the removal of clinoidal meningiomas. Neurosurgery. 2006;59:108–14.
9. Noguchi A, Balasingam V, Shiokawa Y, McMenomey SO, Delashaw JB Jr. Extradural anterior clinoidectomy. Technical note. J Neurosurg. 2005;102:945–50.

10. Smith RR, Al-Mefty O, Middleton TH. An orbitocranial approach to complex aneurysms of the anterior circulation. Neurosurgery. 1989;24:385–91.
11. Takahashi JA, Kawarazaki A, Hashimoto N. Intradural en bloc removal of the anterior clinoid process. Acta Neurochir. 2004;146:505–9.
12. Yonekawa Y, Ogata N, Imhof HG, Olivecrona M, Strommer K, Kwak TE, Roth P, Groscurth P. Selective extradural anterior clinoidectomy for supra- and parasellar processes. Technical note. J Neurosurg. 1997;87:636–42.
13. Xu D, Pollock M. Experimental nerve thermal injury. Brain. 1994;117:375–84.
14. Chang DJ. The "no-drill" technique of anterior clinoidectomy: a cranial base approach to the paraclinoid and parasellar region. Neurosurgery. 2009;64:96–105.
15. Hadeishi H, Suzuki A, Yasui N, Satou Y. Anterior clinoidectomy and opening of the internal auditory canal using an ultrasonic bone curette. Neurosurgery. 2003;52:867–70.
16. Iacoangeli M, Di Rienzo A, Nocchi N. Piezosurgery as a further technical adjunct in minimally invasive supraorbital keyhole approach and lateral orbitotomy. J Neurol Surg A. 2015;76:112–8.
17. Iacoangeli M, Neri P, Balercia P. Piezosurgery for osteotomies in orbital surgery: our experience and review of the literature. Int J Surg Case Rep. 2013;4:188–91.
18. Itro A, Lupo G, Carotenuto A, Filipi M, Cocozza E, Marra A. Benefits of piezoelectric surgery in oral and maxillofacial surgery. Review of literature. Minerva Stomatol. 2012;61:213–24.
19. Tirelli G, Tofanelli M, Bullo F, Bianchi M, Robiony M. External osteotomy in rhinoplasty: piezosurgery vs osteotome. Am J Otolaryngol. 2015;36:666–71.
20. Acharya AN, Rajan GP. Piezosurgery for the repair of middle cranial fossa meningoencephaloceles. Otol Neurotol. 2015;36:444–7.
21. Chaichana KL, Jallo GI, Dorafshar AH, Ahn ES. Novel use of an ultrasonic bone-cutting device for endoscopic-assisted craniosynostosis surgery. Childs Nerv Syst. 2013;29:1163–8.
22. Gleizal A, Bera JC, Lavandier B, Beziat JL. Piezoelectric osteotomy: a new technique for bone surgery: advantages in craniofacial surgery. Childs Nerv Syst. 2007;23:509–13.
23. Grauvogel J, Scheiwe C, Kaminsky J. Use of piezosurgery for internal auditory canal drilling in acoustic neuroma surgery. Acta Neurochir. 2018;153:1941–7.
24. Grauvogel J, Scheiwe C, Masalha W, Jarc N, Grauvogel T, Beringer A. Piezosurgery in modified pterional orbital decompression surgery in Graves' disease. World Neurosurg. 2017;106:422–9.
25. Grauvogel J, Scheiwe C, Masalha W, Grauvogel T, Kaminsky J, Vasilikos J. Piezosurgery-, neuroendoscopy-, and neuronavigation-assisted intracranial approach for removal of a recurrent petrous apex cholesteatoma: technical note. J Neurosurg Pediatr. 2018;21:322–8.
26. Grauvogel J, Masalha W, Heiland DH, Jarc N, Grauvogel TD, Scheiwe C. Piezosurgery: a safe technique to perform lateral suboccipital craniotomy? Oper Neurosurg (Hagerstown). 2018;15:664–71.
27. Kotrikova B, Wirtz R, Krempien R. Piezosurgery—a new safe technique in cranial osteoplasty? Int J Oral Maxillofac Surg. 2006;35:461–5.
28. Kramer FJ, Ludwig HC, Materna T, Gruber R, Merten HA, Schliephake H. Piezoelectric osteotomies in craniofacial procedures: a series of 15 pediatric patients. J Neurosurg. 2006;104:68–71.
29. Martini M, Röhrig A, Reich RH, Messing-Jünger M. Comparison between piezosurgery and conventional osteotomy in cranioplasty with fronto-orbital advancement. J Craniomaxillofac Surg. 2017;45:395–400.
30. Massimi L, Rapisarda A, Bianchi F, Frassanito P, Tamburrini G, Pelo S, Caldarelli M. Piezosurgery in pediatric neurosurgery. World Neurosurg. 2019;126:625–33.
31. Ramieri V, Saponaro G, Lenzi J. The use of piezosurgery in cranial surgery in children. J Craniofac Surg. 2015;26:840–2.
32. Shen W, Cui J, Chen J, Ji Y, Kong L. Internal distraction osteogenesis with piezosurgery oblique osteotomy of supraorbital margin of frontal bone for the treatment of unilateral coronal synostosis. Ann Plast Surg. 2017;78:511–5.
33. Spinelli G, Mannelli G, Zhang YX. Complex craniofacial advancement in paediatric patients: piezoelectric and traditional technique evaluation. J Craniomaxillofac Surg. 2015;43:1422–7.
34. Vetrano IG, Prada F, Perin A, Casali C, DiMeco F, Saini M. Piezosurgery for infra- and supratentorial craniotomies in brain tumor surgery. World Neurosurg. 2019;122:1398–404.

Chiari Malformation Type 1 and Syringomyelia: Why Do Patients Claim for International Guidelines? Commentary on the 2021 Chiari and Syringomyelia Consensus Document

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1 Introduction

Chiari malformation type 1 (CM1) and Syringomyelia (Syr) are classified as "rare diseases" even though, in recent years, their diagnosis has become more and more common, also thanks to the widespread availability of MRI. At the same time, the body of literature on these topics is growing, although randomized controlled studies on significant case series to drive guidelines are missing both in the pediatric and adult populations. On these grounds, the relevance of CM1-Syr associations has increased worldwide by enhancing CM1-Syr awareness, identifying referral specialists, and promoting the debate among the scientific community, as reported on their dedicated websites. As a result of the different opinions about surgical indications and techniques raised by CM1-Syr, an increasing number of well-informed but disoriented patients is emerging.

To bridge this gap, an International Consensus Conference was held in Milan in November 2019 to find a consensus among international experts (IE) to produce a shared document as a base for future guidelines. The present article aims to comment on the recently published Consensus Document focusing on the most relevant recommendations about diagnosis, treatment, and follow-up of CM1-Syr patients [1, 2].

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2 Materials and Methods of the Consensus Process

The Consensus Document was obtained through three different phases: (1) Literature review: an extensive review of the literature was done by the members of the Chiari and Syringomyelia Consortium [3] looking for the primary and controversial topics on Classifications, Definitions, Diagnostic Criteria, Surgical Indications and Techniques, Outcome, Failure, and Re-intervention. The other details of this step as well as the next two steps are reported elsewhere [1, 2, 4]; (2) Questionnaire elaboration: based on the evidence from the literature review, a panel of experts of the Consortium formulated 63 draft statements on CM1 and Syr on adult patients and 57 on children. Finally, the statements were collected in three different questionnaires, the General Addendum (including definitions, classifications, diagnostic criteria), the Pediatric and Adulthood Sections; (3) Delphi Consensus Study: a panel of 30 IE coming from European and extra European Countries plus two members of Patients' Associations answered the questionnaire. The jury of IE was

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composed of neurosurgeons, neurologists, and neuroradiologists with a cumulative experience of 27,000 patients (18,200 adults and 8,800 children), more than 40% of them being operated on patients. Each member of the jury answered the statements of the questionnaire, providing a score between 0 (strongly disagree) and 4 (strongly agree), according to the Delphi method [5]. In case of agreement, the statements were submitted to the working group for the final approval and subsequent drafting of the ultimate document. In case of disagreement (lower than 75%), alternative text and notes were proposed and, if no agreement was reached, the statements were returned to the authors with comments for necessary changes and were resubmitted to the experts involved. Once the Delphi process was completed, the preliminary version of the document was submitted to the Jury for the final discussion during the Chiari Consensus Conference held in Milan in November 2019, where the final version of the document was produced.

3 Results and Comments

The surgical indications, techniques, outcome, and indications for reoperation are summarized in Tables 1, 2, and 3, respectively.

3.1 Definitions

Before addressing these three sections, it is worth mentioning that IE reached a general agreement on the radiological and clinical definition of CM1. Accordingly, CM1 is defined as one or both cerebellar tonsils caudal descent on the midline sagittal T1-MRI, ≥5 mm below the basion-opisthion line. A 3–5 mm ectopia is considered pathologic only if syrinx and/or peg-like deformation of the tonsillar profile is associated. The application of such an old and apparently banal definition is mandatory to reassure many patients with a "missing" CM1 and avoid stress or even improper treatments. CM1 definition necessarily needs certain posterior fossa hypoplasia or overcrowding (therefore, tonsillar descent ≥5 mm and/or peg-like deformation of the tonsils) and/or impaired CSF dynamics at the level of its subarachnoid spaces (therefore, syringomyelia) to be satisfied.

The CM1 syndrome is characterized by: (a) Headache, usually occipital or suboccipital, of short duration (less than 5 min) and provoked/precipitated by cough or other Valsalva-like maneuvers; (b) Symptoms and signs of the brainstem (i.e., nystagmus, dysphagia, sleep apnea), cerebellar (ataxia) and/or cervical cord dysfunction (such as muscles hypotrophy, sensory and motor deficits); (c) Otoneurogical symptoms and/or signs (e.g. dizziness, disequilibrium, sensations of alteration in ear pressure, hypoacusis or hyperacusis, nystagmus, oscillopsia); (d) Scoliosis (optional criterion). Also, these clarifications must be considered, especially about the definition of headache, to avoid wrong indications to surgery. In patients with radiological evidence of CM1, particularly in the absence

Table 1 Indications to surgery

1	There is **no indication** for surgery in **asymptomatic children** with isolated CM1 and **no syringomyelia**, independently from the extent of tonsillar ectopia[a]	*Agreement: >90%*
	They should be followed by whole neuraxis MRI	[a]*Agreement: **88.2%***
2	**Neuro-pediatric evaluation** is mandatory in all children with **CM1 and Symptoms** (headache**,** symptoms and/or signs of the brainstem, cerebellar and/or cervical cord dysfunction) to identify co-pathologies.	*Agreement:**>90%***
3	**Epilepsy** and **cognitive** and/or **behavioral** disorders should not be considered CM-related symptoms, and surgery is not indicated to improve the clinical picture.	*Agreement: **>90%***
4	In asymptomatic children with **CM1 and Syringomyelia**, surgery is indicated in cases of **syrinx larger than 5–8 mm**, and smaller syrinx increasing in size.	*Agreement: **>90%***
6	In **CM1 children with Craniosynostosis** (Syndromic and Non-Syndromic sagittal or lambdoid synostosis, oxicephaly), the craniosynostosis is better treated before the CM1.	*Agreement: **>90%***
7	There is **no indication** for surgery in **asymptomatic adults with CM1 without** Syringomyelia	*Agreement: **100%***
8	In **symptomatic CM1 without Syringomyelia**, surgery is **indicated** in **adults** with headache (typical, invalidating, and resistant to therapy) and auditory/cerebellar/bulbar/spinal signs at neurological examination	*Agreement: **100%***
9	In **adults with CM1 and Syringomyelia** surgery is **indicated** for holocord syringomyelia, clinical/MRI worsening, central syringe and Vaquero Index >0.5 or eccentric syringe, syringomyelia-syringobulbia with spinal/bulbar signs	*Agreement: **>95%***
10	In symptomatic **children and adults** with **CM1 and Hydrocephalus**, it is recommended to treat hydrocephalus firstly, and CM1 can be treated afterwards if symptoms do not disappear.	*Agreement: **>90%***
11	**CM1 is rarely associated with tethered cord syndrome,** and the detethering is recommended just to treat tethered cord syndrome, and it plays no role in the management of a possible CM1 syndrome.	*Agreement: **100%***
12	The **extradural section** of the filum terminale in CM1 children **is not recommended** either to treat tethered cord syndrome nor for the management of a possible CM1 syndrome.	*Agreement: **100%***

[a]Indications to surgery: the percentage of agreement between IE in children and adults are summarized in this table; the statements that pertain just adults are with indicated

Table 2 Surgical techniques for CM1-Syr

1	In **symptomatic CM1 children without Syringomyelia**, the **bony decompression** of the posterior fossa alone could be performed for the low complication rate if the family accepts the perspective of possible second surgery.	*Agreement: >80%*
2	In **CM1 children with Syringomyelia**, **bony decompression + duraplasty** is preferable.	*Agreement: >80%*
3	In **CM1 adults with Syringomyelia**, **bony decompression + duraplasty** is preferable regardless of symptoms	*Agreement: 100%*
4	**CVJ fixation**, with or without posterior decompression, **is not indicated** in CM1 children and adults **without a documented CVJ instability**.	*Agreement: 100%*
5	The extent of the bony decompression of the posterior fossa should be wide on the foramen, always **including C1 laminectomy and never extended to C2** for the risk of CVJ instability, **both in children and in adults**[a]	*Agreement: >85%* [a]*>80%*
6	In **CM1 children and adults**[a] **without arachnoiditis**, it is indicated to **preserve the arachnoid** membrane to avoid CSF leakage and delayed scarring.	*Agreement: >85%* [a]*75%*
7	**Cerebellar tonsils coagulation/resection** is indicated in cases of very low-lying tonsils and recurrent or residual syringomyelia.	*Agreement: >85%*
8	**A watertight dural suture** helps preventing CSF leakage, by non-resorbable stitches, together with a strict muscle and soft tissue closure, **both in children and in adults**[a]	*Agreement: >95%* [a]*>90%*

[a]Indications to surgery: the percentage of agreement between IE in children and adults are summarized in this table; the statements that pertain just adults are with indicated

Table 3 Surgery for CM1: outcomes, failure, re-intervention

1	**Postoperative CSF leakage** is a predisposing factor for infections and surgical failure due to arachnoiditis.	*Agreement: >95%*
2	In case of **symptomatic CSF leakage**, a new operation is necessary, both in children and in adults[a].	*Agreement: >90%* [a]*>85%*
3	**Children with persistent symptoms and unchanged MRI** (no tonsils ascent and absent flow) at 6- or 12-months follow-up should be re-operated on.	*Agreement: >85%*
4	**CM1 operated adults with persistent symptoms and syringomyelia** and no MRI improvement (tonsils descent with FM obliteration, absent CSF flow, unchanged syrinx) at 6 or 12 months follow up should be re-operated on.	*Agreement: >85%*
5	In case of **success of surgery**, the **long-term postoperative follow-up in children** is performed by a clinical examination and whole neuraxis MRI for at least 10 years, or until the end of growth, with a timetable depending on clinical and MRI patterns.	*Agreement: >85%*
6	In case of **success of surgery**, the **long-term postoperative follow-up in adults** is performed by a clinical examination and whole neuraxis MRI for at least 10 years, with a timetable depending on clinical and MRI patterns.	*Agreement: >85%*

[a]Indications to surgery: the percentage of agreement between IE in children and adults are summarized in this table; the statements that pertain just adults are with indicated

of neurological signs, a careful clinical characterization of the headache (according to the International Headache Society criteria) is advised because of the high prevalence of migraine reported in CM1 patients (34–43%) [6].

3.2 Indications to Surgery

A first, clear, and important statement about asymptomatic patients without Syr is provided. Indeed, no surgical indication should be proposed in this instance, both in children and adults (Table 1, points 1 and 7). As known, asymptomatic poorly symptomatic CM1 patients tend to remain clinically unchanged over time [2, 7, 8], and there are no significant risks during physical or sports activities [9–11]. Thus, these patients should be reassured and followed up over time according to their characteristics.

On the other hand, CM1-related Syr and, in particular, syringobulbia are largely accepted as criteria to formulate an indication to surgery, differently from isolated Syr or hydromyelia [4, 12, 13]. In children, it is considered for treatment if progressively enlarging or if symptomatic or larger than 5–8 mm (maximum axial diameter) (Table 1, point 4); in adults, if holocord or eccentric or with Vaquero index >0.5 or if clinically or radiologically worsening, especially in the case of syringobulbia (Table 1, point 9).

Symptomatic patients without Syr should undergo surgery if presenting typical and invalidating headache and associated neurological symptoms (Table 1, point 8). This is considered a crucial point due to the large number of patients affected by migraine or other headaches where CM1 is also (incidentally) diagnosed by MRI. Migraine, tension headache, and chronic daily headache are common in the general pediatric and adult population, and their incidence can largely overcome, even in CM1 subjects, that of the typical couch-headache [14, 15]. Once again, this must be taken into account to avoid wrong surgical indications. Therefore, a multidisciplinary preoperative evaluation, aiming at properly characterizing the type of headache, is mandatory in this subset of patients. Such a need is particularly felt in children, where the diagnosis of headache and the presence of comorbidities may be difficult to assess because of the young age and the variable clinical aspects (Table 1, point 9). Such a preoperative work-up is also mandatory to correctly assess some possible comorbidities, such as epilepsy and cognitive and/or behavioral problems (Table 1, point 3), which are widely demonstrated to be etio-pathologically unrelated to CM1/Syr, which, in turn, should be addressed separately [16, 17]. Of course, as demonstrated in children with autism operated on for CM1-related pain, surgery for CM1 can improve the performance of these children by relieving from pain but not because of a direct effect on the behavioral problem [18]. Similarly, the cognitive problems resulting from the stress related to a chronic disease or from the CM1 surgical sequelae, which are relatively frequent, should be considered as distinct entities compared with the cognitive impairment resulting from CM1 (which has not been demonstrated yet but could be hypothesized, at least in some cases, according to the cognitive functions of the cerebellum) [19].

The final part of this section addressed some debated conditions. The first one is represented by craniosynostosis. In this instance, CM1 is secondary to the premature sutural fusion and, therefore, it should be addressed only after an adequate skull expansion if symptoms or Syr are present (Table 1, point 6). In many cases, the cranial expansion is actually proved to resolve or improve the clinical/radiological CM1/Syr picture [20]. If it does not occur, or in the case of adult patients with stabilized cranial growth, CM1/Syr can be addressed separately. In children with persistent CM1/Syr, the effectiveness of the previous cranial expansion should be carefully evaluated before proposing surgery for the posterior fossa.

A relevant agreement was also obtained about associated hydrocephalus. Although hydrocephalus is the consequence of CM1, it is recommended to treat it in advance because it is usually more symptomatic than CM1 and eliminate the raised intracranial pressure that could worsen CM1 or affect its surgical correction [21]. Endoscopic third ventriculostomy is the best surgical option since it is about obstructive hydrocephalus [22]. Should symptoms of CM1/Syr persist after the treatment of hydrocephalus, which occurs in about 30% of cases, their management is indicated [21]. This knowledge could allow avoiding a useless or even risky operation in most cases.

The agreement on the tethered cord was universal (Table 1, points 11 and 12). A manifest tethered cord is sporadically associated with CM1, and no etio-pathological relationships between the two conditions are demonstrated yet [23]. The spinal cord untethering has no relevant effects on the CM1 [8]. Thus, the management of the two conditions should be addressed separately, according to the patient's characteristics: usually, the most symptomatic one is approached first; or, if a prevalence of symptoms is not evident, the choice could be driven by the radiological picture. Finally, according to the panelists of this and other Consensus Conferences [24], as well as according to the current meta-analyses of the literature [25], the extradural section of the terminal filum does not have enough evidence to be proposed for CM1/Syr management. Despite this statement, this surgical option remains largely used in clinical practice. As other techniques performed in the past and currently abandoned because they were ineffective (e. g., plugging of the obex), such an operation will be discontinued over time since the number of "unchanged" patients is increasing.

3.3 Surgical Techniques

Hopefully, this section will contribute to giving a final word on the eternal dilemma of surgery for CM1, that is posterior fossa bony decompression alone versus duraplasty. The literature meta-analyses almost invariably showed that bony decompression alone is a safer but less effective operation. At the same time, the duraplasty (with or without coagulation of the tonsils) is more effective but also riskier and with a more extended hospitalization (mainly because of CSF leakage-related complications) [7, 26–32]. On these grounds, a "targeted" surgical strategy is recommended for CM1/Syr patients: (a) in symptomatic children without Syr, bony decompression alone is indicated. It is effective because of the residual growth of the posterior fossa and the greater elastic properties of the pediatric meninges (which favors the re-creation of the cisterna magna). The only prospective study on CM1/Syr in children available in the literature shows superior effectiveness and lower complication rate of bony decompression alone versus duraplasty in the pediatric population [33]. The main limit of the bony decompression is the potentially long time passing between surgery and symptoms disappearance; thus, this limitation must be explained to patients and their families (Table 2, point 1); (b) if symptoms are relevant, as generally happens in Syr, duraplasty is also preferable in children (Table 2, point 2). A discussion could be opened for asymptomatic children with Syr. Although this aspect was not discussed in detail at the Consensus Conference, a bony decompression seems to be a reasonable choice also in this instance as long as Syr is thinner than 5 mm and not progressing, and neurophysiological studies are normal; otherwise, duraplasty should be better performed; (c) due to the stabilized cranial growth, adults with Syr should always undergo duraplasty (Table 2, point 3). The literature and the clinical experience supporting this are robust [28].

A second final word could be provided about another discussed topic: the craniovertebral junction micro-instability. Such a phenomenon is advocated by some authors as an etiologic mechanism of CM1, thus justifying the use of cervical fixation even if a proven instability is missing [34, 35]. Once again, the clinical evidence does not support this choice, and the provided results are not superior to those obtained by posterior fossa decompression [36–38]. Therefore, a craniovertebral junction fixation should be adopted only in documented instability (Table 2, point 4). Craniometric measurement-based protocols designed to refine this type of surgical indication are welcome [39].

Some specific surgical steps raised further technical considerations. The first one concerned bony decompression. Since in CM1, the maximal compression point is at the level of the foramen magnum and C1, a large lateral opening of the foramen should be carried out, and the posterior C1 arch should be removed (Table 2, point 5). Instead, the rostro-caudal decompression should not be excessive because an extensive removal of the occipital squama increases the risk of dural tears and could favor cerebellar ptosis [40], while the C2 (and C3) laminectomy increases the risk of postoperative pain, kyphosis, and instability [41, 42].

The intradural manipulation was another issue for discussion (Table 2, points 6 and 7). Indeed, based on the cumulative experience of IE and the literature, showing that the intradural manipulation increases the risk of complications and symptoms recurrence [43, 44], it was recommended to attempt to leave the arachnoid unviolated unless clear arachnoiditis is already present. Arachnoid adhesions or veils, indeed, can be found during the first surgery and are considered a risk factor for Syr formation [45]. However, the management of postoperative arachnoiditis remains debated, especially in the case of multiple recurrences, because the repeated lysis is not associated with a better long-term outcome. Similarly, the coagulation of the tonsils should be limited to cases of very low tonsils herniation or recurrent Syr. A matter for further discussion could be represented by the relatively frequent indication of tonsils shrinkage in children, where the narrow surgical field can reduce in some cases the room for an adequately large duraplasty [32].

Finally, a watertight dural closure was advised, together with proper suture of the muscular and soft tissue layers, to reduce as much as possible the CSF leakage (Table 2, point 8). Even if postoperative CSF leakage or collections or pseudomeningocele represent a significant and feared complication, the missed universal agreement on this topic could reflect the strategy to leave the dura opened, which is still reported for CM1 surgery [46].

3.4 Outcome, Failures, Re-intervention

The goal of this last section was to provide some practical advice on the management of failures or complications. When addressing this issue, the most critical limitation is the lack of standardized methods to assess the outcome, which may significantly vary according to each center [47]. To promote cooperative studies or further Consensus Meetings to provide a shared definition of the clinical and radiological CM1/Syr outcome should be a priority for the Scientific Community in the following years.

As far as CSF-related complications were concerned, the agreement on their management was elevated. In particular, postoperative CSF collections were always thought to deserve a surgical repair if symptomatic (Table 3, point 2). However, the discussion could go beyond this statement because CSF collections are possible sources of infection and arachnoiditis (Table 3, point 1), thus raising the need to operate on asymptomatic patients. Once again, the answer could come from cooperative studies.

A time ranging from 6 to 12 months was considered realistic to declare the failure of surgery in children or adults with persistent symptoms and an unchanged radiological picture (Table 3, points 3 and 4). Such timing results from a compromise between the hypothetical time necessary for surgery to be effective (12 months) and the period considered acceptable for a patient to keep on tolerating the symptoms (6 months). This rule cannot have an absolute value, but it must be modulated according to each patient [48]. Its real message is actually to avoid being precipitous in considering a redo posterior fossa decompression but, at the same time, not to prolong an unfavorable postoperative course if the postoperative picture fails to improve.

Also, the last two points reflect a compromise between a successful treatment and two unpredictable conditions, such as CM1 and Syr (Table 3, points 5 and 6). Indeed, the need for an adequately extended postoperative follow-up is felt because of the evidence of late recurrences in the clinical practice and because the follow-up period reported in the literature is often too short to deduce a conclusion on the final outcome [7, 30]. At the same time, however, it is a shared opinion not to prolong the follow-up of healthy and cured patients. Therefore, a 10-year long clinical and radiological follow-up is considered reasonable to prevent these two risks. Such a period should be prolonged conveniently up to the end of physical development in children. Moreover, the timetable of the clinical and radiological check-ups should be tailored to the characteristics of each pediatric or adult patient.

4 Conclusions

The main goal of the previous Consensus Conference was not to provide conclusive statements about CM1/Syr but to suggest some recommendations that, in the near future, could lead to guidelines. This commentary aimed to underline some of the most "urgent" issues that should be addressed first by the scientific community. The Consensus Document focused on the diagnosis for CM1 (almost 5 mm of tonsils descent on the midline), the indication for surgery (associated Syringomyelia and CM Syndrome), and the endpoint for surgery (syringomyelia shrinkage and/or resolution of symptoms). Reviewing large series with this Consensus grid for diagnosis, indications, and outcomes will yield comparable data for different techniques.

As shown, indeed, some "wrong" indications or techniques, although widely disapproved by the IE and negatively experienced by many patients, remain in use (e.g., sectioning of the filum). The assignment of current studies and meetings should highlight that there is not enough evidence for certain management choices and start proposing proper solutions based on the "positive" results obtained so far.

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References

1. Ciaramitaro P, Massimi L, Bertuccio A, et al. Diagnosis and treatment of Chiari malformation and syringomyelia in adults: international consensus document. Neurol Sci. 2022;43(2):1327–42.
2. Massimi L, Peretta P, Erbetta A, et al. Diagnosis and treatment of Chiari malformation type 1 in children: the International Consensus Document. Neurol Sci. 2022;43(2):1311–26.
3. Ciaramitaro P, Garbossa D, Peretta P, et al. Syringomyelia and Chiari Syndrome Registry: advances in epidemiology, clinical phenotypes and natural history based on a North Western Italy cohort. Ann Ist Super Sanita. 2020;56(1):48–58.
4. Saletti V, Farinotti M, Peretta P, Massimi L, Ciaramitaro P, Motta S, Solari A, Valentini LG. The management of Chiari malformation type 1 and syringomyelia in children: a review of the literature. Neurol Sci. 2021;42(12):4965–95.
5. Adler M, Ziglio E. Gazing into the oracle: the Delphi method and its application to social policy and public health. London: Jessica Kingsley Publishers; 1996.
6. Bolognese PA, Brodbelt A, Bloom AB, Kula RW. Chiari I malformation: opinions on diagnostic trends and controversies from a panel of 63 international experts. World Neurosurg. 2019;130:e9–16.
7. Lin W, Duan G, Xie J, Shao J, Wang Z, Jiao B. Comparison of results between posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation type I: a systematic review and meta-analysis. World Neurosurg. 2018;110:460–474.e5.
8. Massimi L, Peraio S, Peppucci E, Tamburrini G, Di Rocco C. Section of the filum terminale: is it worthwhile in Chiari type I malformation? Neurol Sci. 2011;32(Suppl 3):S349–51.
9. Meehan WP III, Jordaan M, Prabhu SP, Carew L, Mannix RC, Proctor MR. Risk of athletes with Chiari malformations suffering catastrophic injuries during sports participation is low. Clin J Sport Med. 2015;25(2):133–7.
10. Spencer R, Leach P. Asymptomatic Chiari Type I malformation: should patients be advised against participation in contact sports? Br J Neurosurg. 2017;31(4):415–21.
11. Strahle J, Geh N, Selzer BJ, Bower R, Himedan M, Strahle M, Wetjen NM, Muraszko KM, Garton HJL, Maher CO. Sports participation with Chiari I malformation. J Neurosurg Pediatr. 2016;17(4):403–9.
12. Klekamp J. How should syringomyelia be defined and diagnosed? World Neurosurg. 2018;111:e729–45.
13. Shen J, Shen J, Huang K, Wu Y, Pan J, Zhan R. Syringobulbia in patients with Chiari malformation type I: a systematic review. Biomed Res Int. 2019;2019:4829102.
14. Mehta A, Chilakamarri P, Zubair A, Kuruvilla D. Chiari headache. Curr Pain Headache Rep. 2018;22(7):49.
15. Victorio MC, Khoury CK. Headache and Chiari I malformation in children and adolescents. Semin Pediatr Neurol. 2016;23(1):35–9.
16. Granata T, Valentini LG. Epilepsy in type 1 Chiari malformation. Neurol Sci. 2011;32(Suppl 3):S303–6.
17. Riva D, Usilla A, Saletti V, Esposito S, Bulgheroni S. Can Chiari malformation negatively affect higher mental functioning in developmental age? Neurol Sci. 2011;32(Suppl 3):S307–9.
18. Jayarao M, Sohl K, Tanaka T. Chiari malformation I and autism spectrum disorder: an underrecognized coexistence. J Neurosurg Pediatr. 2015;15(1):96–100.
19. Rogers JM, Savage G, Stoodley MA. A systematic review of cognition in Chiari I malformation. Neuropsychol Rev. 2018;28(2):176–87.
20. Tamburrini G, Caldarelli M, Massimi L, Gasparini G, Pelo S, Di Rocco C. Complex craniosynostoses: a review of the prominent clinical features and the related management strategies. Childs Nerv Syst. 2012;28(9):1511–23.
21. Massimi L, Pennisi G, Frassanito P, Tamburrini G, Di Rocco C, Caldarelli M. Chiari type I and hydrocephalus. Childs Nerv Syst. 2019;35(10):1701–9.
22. Massimi L, Pravatà E, Tamburrini G, Gaudino S, Pettorini B, Novegno F, Colosimo C, Di RC. Endoscopic third ventriculostomy for the management of Chiari I and related hydrocephalus: outcome and pathogenetic implications. Neurosurgery. 2011;68(4):950–6.
23. Valentini LG, Selvaggio G, Visintini S, Erbetta A, Scaioli V, Solero CL. Tethered cord: natural history, surgical outcome and risk for Chiari malformation 1 (CM1). Neurol Sci. 2011;32(3):353–6.
24. Canheu AC, Santos MV, Furlanetti LL, Salomão JFM, de Oliveira RS. The Brazilian Society for Pediatric Neurosurgery: consensus on Chiari I deformity. Childs Nerv Syst. 2020;36(1):17–8.
25. Milano JB, Barcelos ACES, Onishi FJ, et al. The effect of filum terminale sectioning for Chiari 1 malformation treatment: systematic review. Neurol Sci. 2020;41(2):249–56.
26. Chai Z, Xue X, Fan H, Sun L, Cai H, Ma Y, Ma C, Zhou R. Efficacy of posterior fossa decompression with duraplasty for patients with Chiari malformation type I: a systematic review and meta-analysis. World Neurosurg. 2018;113:357–365.e1.
27. Durham SR, Fjeld-Olenec K. Comparison of posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation Type I in pediatric patients: a meta-analysis. J Neurosurg Pediatr. 2008;2(1):42–9.

28. Förander P, Sjåvik K, Solheim O, Riphagen I, Gulati S, Salvesen Ø, Jakola AS. The case for duraplasty in adults undergoing posterior fossa decompression for Chiari I malformation: a systematic review and meta-analysis of observational studies. Clin Neurol Neurosurg. 2014;125:58–64.
29. Hankinson T, Tubbs RS, Wellons JC. Duraplasty or not? An evidence-based review of the pediatric Chiari I malformation. Childs Nerv Syst. 2011;27(1):35–40.
30. Lu VM, Phan K, Crowley SP, Daniels DJ. The addition of duraplasty to posterior fossa decompression in the surgical treatment of pediatric Chiari malformation Type I: a systematic review and meta-analysis of surgical and performance outcomes. J Neurosurg Pediatr. 2017;20(5):439–49.
31. Xu H, Chu LY, He R, Ge C, Lei T. Posterior fossa decompression with and without duraplasty for the treatment of Chiari malformation type I—a systematic review and meta-analysis. Neurosurg Rev. 2017;40(2):213–21.
32. Zhao JL, Li MH, Wang CL, Meng W. A systematic review of Chiari I malformation: techniques and outcomes. World Neurosurg. 2016;88:7–14.
33. Jiang E, Sha S, Yuan X, Zhu W, Jiang J, Ni H, Liu Z, Qiu Y, Zhu Z. Comparison of clinical and radiographic outcomes for posterior fossa decompression with and without duraplasty for treatment of pediatric Chiari I malformation: a prospective study. World Neurosurg. 2018;110:e465–72.
34. Goel A. Basilar invagination, syringomyelia and Chiari formation and their relationship with atlantoaxial instability. Neurol India. 2018;66(4):940–2.
35. Goel A, Kaswa A, Shah A. Atlantoaxial fixation for treatment of Chiari formation and syringomyelia with no craniovertebral bone anomaly: report of an experience with 57 cases. Acta Neurochir Suppl. 2019;125:101–10.
36. Deora H, Behari S, Sardhara J, Singh S, Srivastava AK. Is cervical stabilization for all cases of Chiari-I malformation an overkill? Evidence speaks louder than words! Neurospine. 2019;16(2):195–206.
37. Salunke P, Karthigeyan M, Malik P, Panchal C. Changing perception but unaltered reality: how effective is C1-C2 fixation for Chiari malformations without instability? World Neurosurg. 2020;136:e234–44.
38. Wagner A, Grassner L, Kögl N, Hartmann S, Thomé C, Wostrack M, Meyer B. Chiari malformation type I and basilar invagination originating from atlantoaxial instability: a literature review and critical analysis. Acta Neurochir. 2020;162(7):1553–63.
39. Ho WSC, Brockmeyer DL. Complex Chiari malformation: using craniovertebral junction metrics to guide treatment. Childs Nerv Syst. 2019;35(10):1847–51.
40. Holly LT, Batzdorf U. Management of cerebellar ptosis following craniovertebral decompression for Chiari I malformation. J Neurosurg. 2001;94(1):21–6.
41. Riew KD, Raich AL, Dettori JR, Heller JG. Neck pain following cervical laminoplasty: does preservation of the C2 muscle attachments and/or C7 matter? Evid Based Spine Care J. 2013;4(1):42–53.
42. Tatter C, Fletcher-Sandersjöö A, Persson O, Burström G, Grane P, Edström E, Elmi-Terander A. Incidence and predictors of kyphotic deformity following resection of cervical intradural tumors in adults: a population-based cohort study. Acta Neurochir. 2020;162(11):2905–13.
43. Guan J, Riva-Cambrin J, Brockmeyer DL. Chiari-related hydrocephalus: assessment of clinical risk factors in a cohort of 297 consecutive patients. Neurosurg Focus. 2016;41(5):E2.
44. Heidary M, Respondek M, Klekamp J. Histological and intraoperative evaluations of the arachnoid in patients with Chiari I malformation. Acta Neurochir. 2021;163(1):219–25.
45. Dlouhy BJ, Dawson JD, Menezes AH. Intradural pathology and pathophysiology associated with Chiari I malformation in children and adults with and without syringomyelia. J Neurosurg Pediatr. 2017;20(6):526–41.
46. Kurzbuch AR, Jayamohan J, Magdum S. Decompressive surgery for Chiari I malformation in children without dural repair: a still effective and safe procedure? Childs Nerv Syst. 2019;35(10):1839–46.
47. Greenberg JK, Milner E, Yarbrough CK, Lipsey K, Piccirillo JF, Smyth MD, Park TS, Limbrick DD. Outcome methods used in clinical studies of Chiari malformation type I: a systematic review. J Neurosurg. 2015;122(2):262–72.
48. Chotai S, Chan EW, Ladner TR, Hale AT, Gannon SR, Shannon CN, Bonfield CM, Naftel RP, Wellons JC. Timing of syrinx reduction and stabilization after posterior fossa decompression for pediatric Chiari malformation type I. J Neurosurg Pediatr. 2020;26(2):193–9.

Evaluation of Adult and Pediatric Chiari Type 1 Malformation Patients: Do Consensus Documents Fit Everyday Practice?

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1 Introduction

The Chiari malformation type 1 (CM1) represents a heterogeneous group of congenital malformations affecting children and adults. Since the first description of Chiari malformation in 1891 [1], the spectrum of the disease has been dramatically expanded. The main characteristic of CM1 is the caudal cerebellum ptosis through the foramen magnum, leading to obstruction of cerebrospinal fluid (CSF) outflow. Whereas the estimated prevalence of cerebellar tonsils descent at magnetic resonance imaging (MRI) has been estimated between 1.9 and 8.4/100,000 [2, 3], most individuals with radiologically defined CM1 remain asymptomatic. However, various neurological signs and symptoms can be reconducted to the malformation. Despite often being nonspecific, the clinical presentation of CM1 comprises headache, ocular and otoneurologic alterations, ataxia, and lower cranial nerves disturbances [4].

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Moreover, CM1 could determine or be associated with Syringomyelia (Syr) or syringobulbia, represented by single or multiple fluid-filled cavities within the spinal cord and/or the bulb. The degree of clinical manifestation of a Syr is variable, but many patients present neurological damages and progressive disability, according to the extent, location, and severity of spinal cord compression. The therapeutic management of CM1 and Syr often comprises suboccipital craniectomy and foramen magnum opening, associated with posterior C1 arch laminectomy, with or without enlargement duraplasty, arachnoid dissection, and tonsillar reduction [5–9]. Nevertheless, considering the wide range of clinical presentations and the surgical strategies proposed during the past years, it has been challenging to evaluate the best outcome according to the techniques performed. More recently, the neurosurgical and neurological community committed to CM1 management planned to analyze the contemporary state of the art and find conduct uniformity. In 2021, according to the "experts" agreement obtained at the Chiari and Syringomyelia Consensus Conference held in Milan in 2019, an international document was produced to reach a consensus on controversial topics in children and adult patients with CM1 [10, 11]. The results of a Delphi process allowed the authors to summarize as a consensus document (CD) some indications about the management of CM1.

Some debate points with less accordance among experts were the role of bone decompression alone, the integrity of the arachnoid membrane, and the use of autologous and allograft dural patches instead of artificial grafts. This study aims to evaluate, in a large, monocentric surgical series of adult and pediatric CM1 patients, if the daily clinical practice reflects what was achieved in the CD. To strengthen the value of international recommendations, we would support and highlight the degree of consensus or difference based on a homogenous series analysis, using evaluation grids derived CD to quote the accordance of a large series with the indications for surgery and reoperation, and calculating a comparable outcome rate.

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2 Materials and Methods

The main statements about diagnosis, indications for treatment, surgical technique, evaluation of surgical results, and indication for reoperation were summarized (Tables 1, 2, and 3). A retrospective analysis was performed on a prospectively collected database, reporting data about consecutive CM1 adults and children admitted at our Institution between 2000 and 2021. The malformation was documented, in all patients, with a sagittal midline T1-weighted MRI showing the ptosis of one or both cerebellar tonsils for more than 5 mm beyond the basion-opisthion, or McRae, line. In all cases, a whole spine MRI was also performed to detect syrinx, and a flow study in the posterior fossa was done to con-

Table 1 Indications to surgery

In asymptomatic children with **CM1 and Syringomyelia**, surgery is indicated in cases of **syrinx larger than 5–8 mm**, and smaller syrinx increasing in size.					*Agreement:* ***>90%***
Neuro-pediatric evaluation is mandatory in all children with **CM1 and Symptoms** (headache**,** symptoms and/or signs of the brainstem, cerebellar and/or cervical cord dysfunction) to identify co-pathologies. **Surgery is indicated if symptoms are related to CM1.**					*Agreement:* ***>90%***
Children series	Nb %	Symptoms	Syringomyelia	Just headache	Accordance to CD
Males	89 46.8%				
Females	101 53.2%				
Mean age (9 months to 18 years)	10.8				
Very young <= 6 years	44 23.2%				
Total	190	55 29%	132 69.5%	3 1.5%	**100%**
In symptomatic **children** with **CM1 and Hydrocephalus**, it is recommended to treat hydrocephalus first, and CM1 can be treated afterward if symptoms do not disappear.					*Agreement:* ***>90%***
In **CM1 children with Craniosynostosis** (Syndromic and Non-Syndromic sagittal or lambdoid synostosis, oxycephaly), the craniosynostosis is better treated before the CM1.					*Agreement:* ***>90%***
CM1 is rarely associated with tethered cord syndrome, and untethering is recommended just to treat tethered cord syndrome, and it plays no role in the management of a possible CM1 syndrome.					*Agreement:* ***100%***
Children series	Nb %	Op. before	Op. after	Not operated	Accordance to CD
CM 0	0				
CM 1	155				
CM 1.5	35 18.4%				
Ass. hydrocephalus	25 13.1%	15	3	7	**60%**
Ass. craniosynostosis	40 21%				
Simple	31	4	1	26	**12.9%**
Complex	9	7	–	2	**77%**
Ass. tethered cord	4 2.1%	2	2	–	**100%**
In **symptomatic CM1 without Syringomyelia**, surgery is **indicated** in **adults** with headache (typical, invalidating, and resistant to therapy) and auditory/cerebellar/bulbar/spinal signs at neurological examination					*Agreement:* ***100%***
In **adults with CM1 and Syringomyelia** surgery is **indicated** for holocord Syringomyelia, clinical/MRI worsening, central syringe and Vaquero Index >0.5 or eccentric syringe, syringomyelia-syringobulbia with spinal/bulbar signs					*Agreement:* ***>95%***
Adult series	Nb %	Symptoms	Syringomyelia	Just headache	Accordance to CD
Males	65 29.5%				
Females	155 70.5%				
Mean age	41 (18–77)				
Total	220	46 20.9%	171 77.2%	3 1.4%	**100%**
In symptomatic **adults** with **CM1 and Hydrocephalus**, it is recommended to treat hydrocephalus first, and CM1 can be treated afterward if symptoms do not disappear.					*Agreement:* ***>90%***
Adult series	Nb %	Op. before	Op. after	Not operated	Accordance to CD
CM 0	5				
CM 1	193				
CM 1.5	22 10%				
Ass. hydrocephalus	18 8.1%	13	3	2	**72%**
Ass. tethered cord	0				**100%**

Table 2 Surgical techniques for CM1-Syr

In **symptomatic CM1 children without Syringomyelia**, the **bony decompression** of the posterior fossa alone could be performed for the low complication rate if the family accepts the perspective of possible second surgery.					*Agreement:* ***>80%***
In **CM1 children with Syringomyelia**, **bony decompression + duraplasty** is preferable.					*Agreement:* ***>80%***
CVJ fixation, with or without posterior decompression, **is not indicated** in CM1 children and adults **without a documented CVJ instability**.					*Agreement:* ***100%***
Children series	Laminect. C1	Laminect. C2	PFD	PFDD	CVJ fixation
CM1	57	–		49	
CM1 + Syr	130	–	4	126	
+CVJ instability	1	–	7/12 craniosynostosis	1	1
Accordance CD	**100%**	**100%**	**96.7%**	**100%**	**100%**
In **CM1 adults with Syringomyelia**, **bony decompression + duraplasty** is preferable regardless of symptoms					*Agreement:* ***100%***
The extent of the bony decompression of the posterior fossa should be wide on the foramen, always **including C1 laminectomy and never extended to C2,** for the risk of CVJ instability, **both in children and in adults**					*Agreement:* ***>85% >80%***
CVJ fixation, with or without posterior decompression, **is not indicated** in CM1 children and adults **without a documented CVJ instability**.					*Agreement:* ***100%***
Adult series	Laminect. C1	Laminect. C2	PFD	PFDD	CVJ fixation
CM1	25	–	2	23	–
CM1 + Syr	195	–	1	194	–
+CVJ instability	1				1
Accordance CD	**100%**	**100%**	**99%**	**100%**	**100%**
In **CM1 children and adults without arachnoiditis**, it is indicated to **preserve the arachnoid** membrane to avoid CSF leakage and delayed scarring.					*Agreement:* ***>85% 75%***
Cerebellar tonsils coagulation/resection is indicated in very low-lying tonsils and recurrent or residual Syringomyelia cases.					*Agreement:* ***>85%***
A watertight dural suture helps prevent CSF leakage, by non-resorbable stitches, together with a strict muscle and soft tissue closure, **both in children and in adults**					*Agreement:* ***>95% >90%***
Global series	Nb		Intact arachnoid		Tonsils coagulation
DCV + duroplasty	392		97 (24.7%)		125 (31.9%)
Accordance CD			**100%**		**100%**

firm the constraint to CSF passage posteriorly. All patients had neurological symptoms attributable to the CM1 (i.e., Chiari-type headache, bulbar or cerebellar dysfunction) as evaluated preoperatively by a pediatric or adult neurologist or harbored progressive Syr. The data collected were related to the tonsil descent measured in cervical vertebra level (C1, C2, C3), the syrinx presence, and extension (medullar, cervical, dorsal, holochord), the association with hydrocephalus or previous CSF shunting. The clinical presentation, the headache characteristics (typical, atypical, both), and the presence of other associated diseases were also analyzed. Finally, we evaluated all results for the accordance with the CD, using specific grids.

2.1 Surgery and Postoperative Management

All patients were submitted to a standard preoperative evaluation, including blood tests, general and neurological clinical assessment. At our center, posterior fossa decompression with duraplasty (PFDD) is the treatment of choice on all patients, except rare cases, mainly children, in which the associated malformation (hydrocephalus, craniosynostosis, tethered cord) was treated before/concomitantly/after. After general anesthesia, the patients were placed prone with the head secured in a Mayfield clamp, with a 15–30-degree flexion. A midline incision was made from inion to the spinous process of C2. After the suboccipital bone and C1 arches were exposed, the bony decompression was performed with a high-speed drill and bony rongeurs. There was no standard rule regarding the extent of the resection, but we tend to set the bone removal to avoid a cerebellar slump. The arch of C1 was always removed. The dura is then sharply dissected with a longitudinal incision, starting caudally and proceeding cranially. The arachnoid may be left intact or opened depending on the intraoperative findings, such as important adhesions or CSF flow obstruction. The same thought process was applied to whether or not to perform the tonsillar coagulation via bipolar cautery. After assessing cerebellar pulsations as a sign of restored CSF flow, the duraplasty was performed by using allograft patches, such as bovine or equine pericar-

Table 3 Surgery for CM1: outcomes, failure, re-intervention

Postoperative CSF leakage predisposes to infections and surgical failure due to arachnoiditis.				*Agreement: >95%*
In case of **symptomatic CSF leakage**, a new operation is necessary, both in **children and in adults**				*Agreement*: ***>90%>85%***
Global series	Nb %	Evacuated		Reoperated
CSF collection	28	22		6
CSF leakage	15	12		3
Global complication rate	43 10.9%	24		9 **2.3%**
Children with persistent symptoms and unchanged MRI (no tonsils ascent and absent flow) at 6- or 12-month follow-up should be re-operated on.				*Agreement: >85%*
CM1 operated adults with persistent symptoms and Syringomyelia and no MRI improvement (tonsils descent with FM obliteration, absent CSF flow, unchanged syrinx) at 6 or 12 months follow up should be re-operated on.				*Agreement: >85%*
Global FINCB series	Early success	Failures	Failures reoperated	Accordance to CD
Syringomyelia	216	10	9	
Symptoms	314	16	**16**	
Operated elsewhere	–	–	**36**	
Persistent symptoms			1	
Persistent syringomyelia			35	
Total reoperations			**52**	**100%**
In case of **success of surgery**, the **long-term postoperative follow-up in children** is performed by a clinical examination and whole neuraxis MRI for at least 10 years, or until the end of growth, with a timetable depending on clinical and MRI patterns.				*Agreement: >85%*
In case of **success of surgery**, the **long-term postoperative follow-up in adults** is performed by a clinical examination and whole neuraxis MRI for at least 10 years, with a timetable depending on clinical and MRI patterns.				*Agreement: >85%*

dium. A watertight closure was the dural closure goal, which was reinforced by collagen or fibrin sheets. Postoperatively, patients were closely monitored for complications, such as CSF leaks, hematomas, wound infections and dehiscence, hydrocephalus, pseudomeningocele, or general complications. A non-contrast CT scan was also performed before the patients' discharge. A clinical and neuroradiological follow-up (brain MRI and, when necessary, spinal MRI) was indicated at 3 months and 1 year from surgery. Afterward, the follow-up was repeated every 1–3 years, depending on the outcome.

3 Results

3.1 Pediatric Series Characteristics

From 2000 to 2021, 190 pediatric Chiari patients underwent surgery at our Institution, mainly due to the first author. There was a slight predominance of females (53.2%) on males (46.8%). The mean age at surgery was 10.8 years, ranging from 9 months to 18 years, whereas 23.2% of the whole cohort (44 patients) were younger than 6 years. The indication for surgery was mainly represented by the presence of Syr, as it happened in 132 patients (69.5%); 29% of patients had, nevertheless, symptoms related to CM1. Only in 3 patients (1.5%), the surgical indication was headache only. Considering that aspect, our series presents accordance with the CD in 100% of the surgically treated cases (Table 1). There were no CM0, and in 35 cases, the radiological diagnosis was CM 1.5 (18.4%).

A total of 25 patients (13.1%) presented associated hydrocephalus. The CD showed an agreement greater than 90% in treating hydrocephalus first and CM1 later if symptoms do not disappear. In our series, 15/25 children received a specific treatment before surgery, 3 afterward, while 7 were never treated.

Finally, the CD indicates to treat craniosynostosis before CM1 (agreement >90%): among our pediatric series, 40 children (21%) presented associated craniosynostosis, largely isolated forms (39 children); only 11 of them were submitted to cranioplasty before CVD, mainly the complex forms. A smaller percentage of children (2.1%) presented an associated tethered cord, with the conus lying lower than L3; an untethering procedure was performed according to the neurourological presentation (specifically, 2 cases before and another 2 after the PFD). It is worth noting that we never performed any extradural sectioning of the filum terminalis, with 100% accordance with the CD.

3.2 Adult Population

The cohort of 220 adult patients was composed of 65 males (29.5%) and 155 females (70.5%), thus with a significant predominance of females. The mean age was of 41 ± 9.9 years (range 18–77 years). Also, in this case, as it happens for the pediatric cohort, the main indication for surgical treatment was the Syr, affecting 171 (77.2%) patients; among the 220 patients in total, 46 (20.9%) presented symptoms, but headache alone was the indication for surgery only in 3 patients. Again, the concordance with the CD indications was 100%.

Preoperative MRI findings showed that out of 220 patients, 193 (87.7%) had CM1, 22 (10%) had CM1.5, and 5 were diagnosed as CM0. Every patient had a tonsillar herniation >5 mm, apart from the 5 CM0 patients; the average tonsil descent was 12.6 ± 4.45 mm, ranging from 5 to 33.85 mm. CM1-associated hydrocephalus occurred in 18 (8.1%) patients; however, only 13 underwent a preoperative shunting procedure (Table 1).

3.3 Surgical Findings and Long-Term Outcome

Among children, 178 patients underwent PFDD, while the other 12 were submitted to bone decompression only. In 188 children, C1 laminectomy was also performed. In particular, 7 out of 12 bone decompression only were indicated in craniosynostosis patients. The posterior arch of C2 was never removed. Almost all these findings were in total accordance with the CD indications (Table 2). In the adult population, PFDD was performed on 217 patients (98.6%); only 3 patients underwent posterior fossa decompression without duraplasty (PFD); only 1 patient received craniovertebral junction fixation. Every patient underwent C1 laminectomy; the C2 arch was partially eroded in 130 patients due to significant tonsillar descent. Nevertheless, we tried to preserve the muscular and ligamentous system to guarantee stability in such cases (Fig. 1).

Regarding the whole series, isolated or bilateral tonsil coagulation, due to severe stenosis or tonsils' herniation, was carried out in 125 cases (31.8%), mainly upon intact arachnoid. The average length of stay was 4.5 days. The overall complication rate was 10.9%, principally due to CSF leakage and collection, but a surgical treatment for this specific issue was necessary only in 9 cases (2.3%). Other minor complications, such as partial wound dehiscence, were rapidly resolved. No deaths, respiratory failures, or intracranial infections occurred.

The average follow-up duration was 4.5 ± 3.3 years, with a minimum of 0.33 years (4 months) and a maximum of 21 years. Symptoms disappeared early in 314 cases, and Syr showed a favorable evolution (progressive and persistent reduction or disappearance) in 216 affected patients. However, a late second surgery was proposed in 52 cases due to the persistence of symptoms or Syr secondary to reactive arachnoiditis. Among these patients, 36 represented a re-do surgery of patients previously treated at different centers (Table 3). These results overcome the agreement obtained about the statement indicating that CM1 adults with persistent symptoms and Syr, and without MRI improvement at 6- or 12-month follow-up, should be submitted to a second surgery.

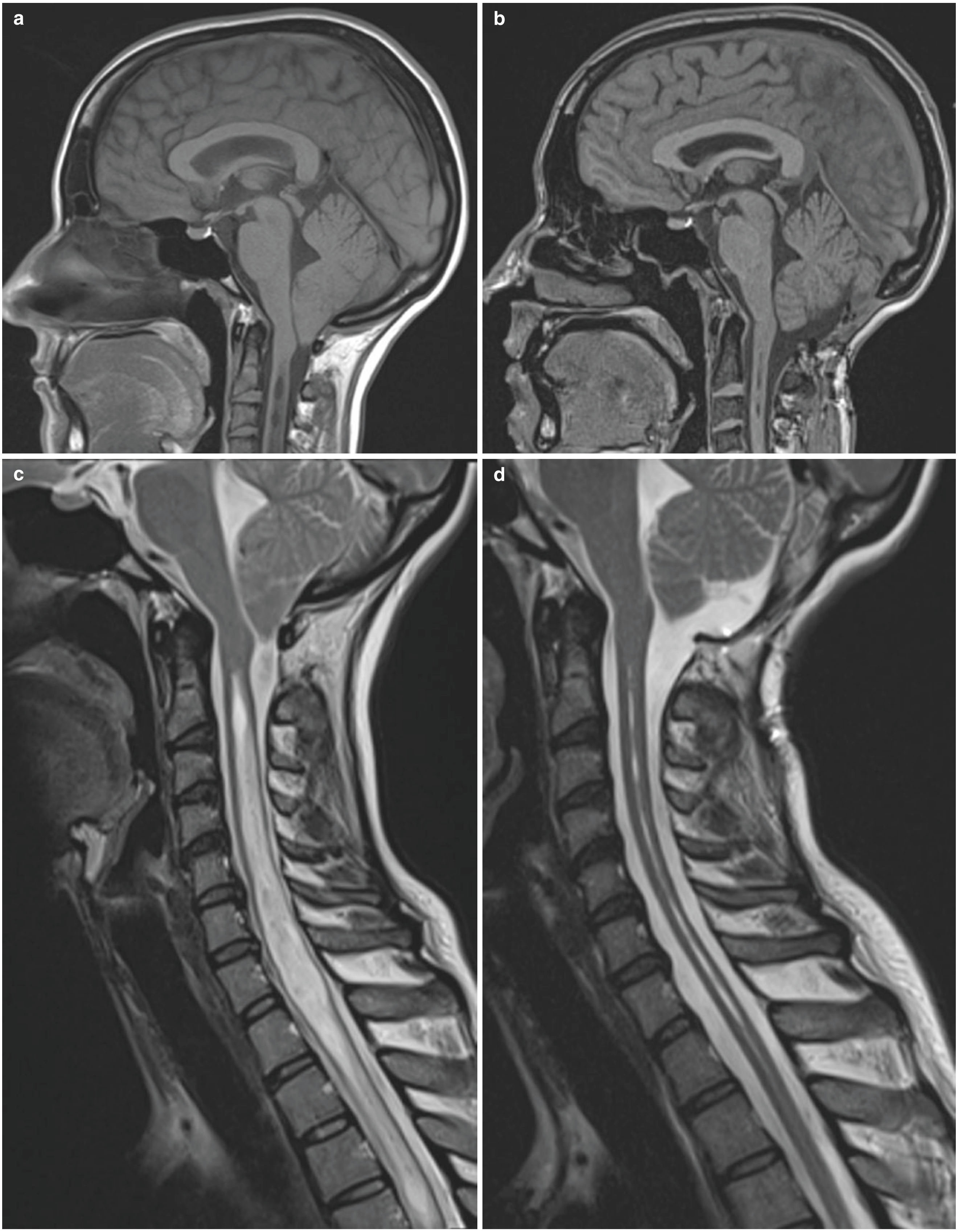

Fig. 1 Indications for surgery: the preoperative MRI scans show a CM1 (T1-weighted sagittal scan) in (**a**) with associated cervico-dorsal syringomyelia (T2-weighted sagittal scans) in (**c**); the 3-months after PFDD imaging depicts the degree of posterior decompression (**b**) with syringomyelia reduction (**d**)

4 Discussion

Our retrospective analysis showed homogeneity in the management and treatment of CM1 patients, both for adults and children. Nevertheless, we aimed to evaluate whether our results were comparable to other reported series and experts' opinions [6, 12]. Considering the difference among neurosurgeons involved in CM1, the CM1-Syr Consensus Conference (Milan, 2019) proposed a CD. This document reported shared indications by 47 international experts, coming from 27 centers pooling 27,000 cases, based on the experience of high-volume referral units for the CM1-Syr associations' network. The CD produced, by using the Delphi method in 3 rounds, 121 detailed recommendations on CM1-Syr regarding diagnosis, treatment, outcome, and follow-up. Besides answering the patients' questions on the correct therapeutic and diagnostic pathway, the main advantage of CD was to create a common language between clinicians for CM1-Syr diagnosis, symptoms, surgical outcomes, and failures, also allowing a comparison between series treated by different techniques. Some statements obtained a very high consent among experts. The first one is related to adult CM1 with syringomyelia [10]: despite the presence of symptoms, with or without symptoms, patients should undergo surgery if a holocord syringomyelia is present, or in case of clinical or radiologically worsening progression over time, or if the Vaquero index is greater than 0.5 (defined by syrinx/canal ratio) [13], or in syringobulbia [14, 15]. This statement had an agreement higher than 95% among experts, and our series fully reflect this statement. Almost all adults with Syr underwent PFDD, except for one case belonging to the early period of the series. Moreover, there is a complete agreement about treating symptomatic CM1 in adult patients without Syr in the case of persistent headache (typical, invalidating, and resistant to therapy) associated with cerebellar, auditory, bulbar, or spinal signs. The surgical statements were more complex in pediatric CM1 [11]. In symptomatic CM1 children without Syr, there was 80% agreement to suggest bony decompression only (but after a detailed discussion with patients and relatives), with the perspective of a possible second surgery; on the other hand, the agreement was always >80% in CM1 with Syr children to perform PFDD. The CD had a higher consent >90% on the need for a pediatric neurology definition of CM1 symptoms to indicate surgery; our series shows a complete agreement with all such statements.

The management of CM1 associated with craniosynostosis is not following the CD, which suggests (with an agreement >90%) to treat the craniosynostosis before the CM1. Our series comprises a high percentage of associated craniosynostosis (21%), mainly isolated (31 children), usually discovered after CM1 because actively searched by 3D-CT. As a result, only in 12.9% of cases, surgery for craniosynostosis was performed before CM1 treatment. During the last years, we paid more attention, also in older children, to the association among the two diseases to better recognize secondary CM1 [16], and we experienced no need for PFD after Cranial Vault expansion in two cases. On the contrary, in the nine cases with complex synostosis, well known before CM1, the accordance with CD was good

In the case of concomitant hydrocephalus, our current operative approach includes a shunting procedure such as VPS or ETV prior to PFDD; however, it is not a firm rule, and the decision depends on the clinical decision and radiological presentation. PFDD is then accomplished in patients who have not improved after the shunting operation. Despite these premises, the series analysis shows that associated hydrocephalus in children was present in 25 cases (13.1%), but only 15 of them underwent a shunting procedure before posterior fossa decompression. This low agreement (60%) with CD can present some speculative hypotheses, mainly related to the previous hypothesis that PFDD may solve a ventricular dilatation, improving CSF circulation; the higher complication rate experienced in these cases led us recently to a stricter adherence to this Consensus statement.

Four children underwent an intradural untethering procedure (two children before and two after PFD) for a true tethered cord, associated with CM1. Patients submitted to untethering depicted no relief of CM1 symptoms and no radiological improvement of tonsil descent, reinforcing the hypothesis that this quite rare association has a polimalformative rather than a causative relation. Some groups have advocated this procedure as a potential, less invasive approach to the CM1; however, considering the lack of robust scientific evidence for this procedure, especially in case of the absence of tethered cord syndrome, such technique plays no role in the treatment of CM1, due to complete different pathophysiology [17, 18]. There is a total agreement among experts about the lack of usefulness of untethering procedures to manage a possible CM1 syndrome, and our series followed and confirmed this statement.

About the surgical technique, our series shows a significant concordance with the CD statements but considering that the general indications should be shaped around the single institution or surgeons. For example, it is accepted that an excessive craniectomy may cause cerebellar ptosis, but we do not follow a strict measurement rule, and we determine the extension of the decompression based on intraoperative findings, mainly occurrence of dural pulsations. C1 laminectomy was always carried out, with a partial C2 posterior arch erosion due to significant tonsillar herniation and obstruction. The issues regarding C2-laminectomy are secondary to the possible postoperative onset of kyphotic deformity and secondary craniovertebral junction (CVJ) instability

[19]; however, no such complications occurred in our study. This may depend on the careful preservation of the C2 muscular and ligamentous complex.

Concerning the risks and benefits of duraplasty or tonsil coagulation, the surgical experience and the results of some meta-analyses [6, 7, 9, 20–23] led us to utilize PFDD in CM1 patients with Syr due to the better symptomatic and syrinx results. We did not run into any complications such as scar tissue or neurological deficits by cerebellar tonsils reduction. PFDD is also associated with a higher risk of CSF-related complications: in a recent meta-analysis [22], CSF leak rates were reported to be around 8%, ranging from 3.44% to 11.23%; our results did not differ significantly, with CSF leaks occurring in 10% of the patients, despite that it drops down to 2.3% considering just the cases deserving surgical revision.

Regarding the type of duraplasty, we tend to use pericardium-based heterologous products, mainly equine or less frequently bovine pericardium. The patch is then sewn in a waterproof fashion with non-resorbable stitches to prevent CSF leaks. This point was reached during the years, while previously we used adsorbable sutures, and most of the CSF leaks or collection requiring surgery were related to the old approach. Furthermore, we prefer to leave the arachnoid membrane intact in the absence of significant arachnoid scarring. In contrast, spontaneous arachnoid interruption with arachnoiditis was identified after dural opening, mainly in patients with the longest history or extended descendants of tonsils [10].

Finally, about the postoperative management, we agree with the statement indicated by CD: in case of effective surgery, the long-term postoperative follow-up in children and adults is performed by a clinical examination and whole neuraxis MRI for at least 10 years, or until the end of growth, with a timetable depending on clinical and MRI patterns.

In conclusion, the CM1 has been known for more than 100 years; however, many debates are still ongoing, in the present time, about the exact definition and treatment options. When, if, and how to treat CM1 patients often depends on the different surgeons and centers' thinking, but the introduction of the CD (based upon experts' agreement) could reduce this variability and obtain comparable series. The present series analysis on 446 consecutive patients, treated according to the CD, confirms that PFD is a safe surgical option for the treatment of CM1, in particular for Valsalva-exacerbated symptoms; the addition of duraplasty, in our hands, showed an overall better outcome, especially in patients with Syr, at the low cost of CSF-related complications rate (2.3%). This effectiveness was confirmed by the few cases (7.6%) requiring additional surgeries due to recurrent symptoms, postoperative complications, or Syr persistence.

Disclosure Statement The authors have no conflicts of interest to declare.

References

1. Chiari H. Ueber Veränderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns. Dtsch Medizinische Wochenschrift. 1891;17(42):1172–5.
2. Kahn EN, Muraszko KM, Maher CO. Prevalence of Chiari I Malformation and syringomyelia. Neurosurg Clin N Am. 2015;26(4):501–7.
3. Milhorat TH, Chou MW, Trinidad EM, Kula RW, Mandell M, Wolpert C, Speer MC. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery. 1999;44(5):1005–17.
4. Beretta E, Vetrano IG, Curone M, Chiapparini L, Furlanetto M, Bussone G, Valentini LG. Chiari malformation-related headache: outcome after surgical treatment. Neurol Sci. 2017;38(Suppl 1):95–8.
5. Durham SR, Fjeld-Olenec K. Comparison of posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation Type I in pediatric patients: a meta-analysis. J Neurosurg Pediatr. 2008;2(1):42–9.
6. Förander P, Sjåvik K, Solheim O, Riphagen I, Gulati S, Salvesen Ø, Jakola AS. The case for duraplasty in adults undergoing posterior fossa decompression for Chiari I malformation: a systematic review and meta-analysis of observational studies. Clin Neurol Neurosurg. 2014;125:58–64.
7. Hankinson T, Tubbs RS, Wellons JC. Duraplasty or not? An evidence-based review of the pediatric Chiari I malformation. Childs Nerv Syst. 2011;27(1):35–40.
8. Hoffman H, Bunch KM, Paul T, Krishnamurthy S. Comparison of pericranial autograft and AlloDerm for duraplasty in patients with Type I Chiari malformation: retrospective cohort analysis. Oper Neurosurg. 2021;21(6):386–92.
9. Lin W, Duan G, Xie J, Shao J, Wang Z, Jiao B. Comparison of results between posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari Malformation Type I: a systematic review and meta-analysis. World Neurosurg. 2018;110:460–474.e5.
10. Ciaramitaro P, Massimi L, Bertuccio A, et al. Diagnosis and treatment of Chiari malformation and syringomyelia in adults: international consensus document. Neurol Sci. 2022;43(2):1327–42.
11. Massimi L, Peretta P, Erbetta A, et al. Diagnosis and treatment of Chiari malformation type 1 in children: the International Consensus Document. Neurol Sci. 2022;43(2):1311–26.
12. Saletti V, Farinotti M, Peretta P, Massimi L, Ciaramitaro P, Motta S, Solari A, Valentini LG. The management of Chiari malformation type 1 and syringomyelia in children: a review of the literature. Neurol Sci. 2021;42(12):4965–95.
13. Vaquero J, Martinez R, Arias A. Syringomyelia-Chiari complex: magnetic resonance imaging and clinical evaluation of surgical treatment. J Neurosurg. 1990;73(1):64–8.
14. Chavez A, Roguski M, Killeen A, Heilman C, Hwang S. Comparison of operative and non-operative outcomes based on surgical selection criteria for patients with Chiari I malformations. J Clin Neurosci. 2014;21(12):2201–6.
15. Ciaramitaro P, Garbossa D, Peretta P, et al. Syringomyelia and Chiari Syndrome Registry: advances in epidemiology, clinical phenotypes and natural history based on a North Western Italy cohort. Ann Ist Super Sanita. 2020;56(1):48–58.
16. Valentini LG, Saletti V, Erbetta A, Chiapparini L, Furlanetto M. Chiari 1 malformation and untreated sagittal synostosis: a new subset of complex chiari? Childs Nerv Syst. 2019;35(10):1741–53.
17. Massimi L, Peraio S, Peppucci E, Tamburrini G, Di Rocco C. Section of the filum terminale: is it worthwhile in Chiari type I malformation? Neurol Sci. 2011;32(Suppl 3):S349–51.

18. Milano JB, Barcelos ACES, Onishi FJ, et al. The effect of filum terminale sectioning for Chiari 1 malformation treatment: systematic review. Neurol Sci. 2020;41(2):249–56.
19. Rocque BG, Oakes WJ. Surgical treatment of Chiari I malformation. Neurosurg Clin N Am. 2015;26(4):527–31.
20. Chai Z, Xue X, Fan H, Sun L, Cai H, Ma Y, Ma C, Zhou R. Efficacy of posterior fossa decompression with duraplasty for patients with Chiari Malformation Type I: a systematic review and meta-analysis. World Neurosurg. 2018;113:357–365.e1.
21. Lu VM, Phan K, Crowley SP, Daniels DJ. The addition of duraplasty to posterior fossa decompression in the surgical treatment of pediatric Chiari malformation Type I: a systematic review and meta-analysis of surgical and performance outcomes. J Neurosurg Pediatr. 2017;20(5):439–49.
22. Xu H, Chu LY, He R, Ge C, Lei T. Posterior fossa decompression with and without duraplasty for the treatment of Chiari malformation type I—a systematic review and meta-analysis. Neurosurg Rev. 2017;40(2):213–21.
23. Yahanda AT, Simon LE, Limbrick DD. Outcomes for various dural graft materials after posterior fossa decompression with duraplasty for Chiari malformation type I: a systematic review and meta-analysis. J Neurosurg. 2021;1–14.

Percutaneous Balloon Compression for Trigeminal Neuralgia. A Comparative Study Between the Fluoroscope Guided and Neuronavigated Technique

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1 Introduction

Trigeminal neuralgia (TN) is a paroxysmal electric shock-like facial pain in the field distribution of the trigeminal nerve; it can involve one or more neural branches, more frequently both maxillary and mandibular, and it is usually unilateral (right in 60% of cases vs. left in 40%). Patients are typically over 50 years old. In the case of failure of medical therapy, patients can benefit from both ablative and nonablative treatments. Microvascular decompression (MVD) is the only nonablative treatment useful in cases of radiologic evidence of neurovascular conflict between aberrant arterial loops or veins and the root entry zone of the trigeminal nerve. MVD provides the better long-term outcome with the lowest rate of pain recurrence, although is an invasive procedure burdened with significant risks such as facial nerve impairment, hearing loss, stroke, and meningitis [1]. Ablative procedures consist in lesioning the trigeminal nerve or the Gasserian ganglion: they are currently applied in cases of TN related to demyelinating conditions such as multiple sclerosis [2, 3], in patients unsuitable for MVD surgery, or in whom prior MVD has failed [4]. They include percutaneous balloon compression (PBC), radiofrequency, thermocoagulation and stereotactic radiosurgery. Among these, the first three are performed through percutaneous cannulation of the foramen ovale (FO), according to the technique first described by Härtel in 1911 [5]. Traditionally, FO cannulation is accomplished with the assistance of intraoperative C-arm fluoroscopy; recently, however, several authors have reported successful application of intraoperative CT navigation as well. Reported advantages powered by navigation include better spatial orientation and successful cannulation with a lower rate of attempts and complications [6–9]. Nonetheless, these advantages should be considered in the face of concerns regarding increased radiation dose to the patient relative to traditional fluoroscopy and its possible adverse effects [10]. The aim of this study was to compare the fluoroscopic guided and neuronavigated PBC techniques in terms of efficacy and radiological exposure. We also discussed the pertinent literature.

2 Materials and Methods

We retrospectively analyzed 37 patients (18 M and 19 F) suffering for TN and submitted to PBC at our institution from January 2021 to December 2021. The mean age was 66.43 ± 12.77 years with a follow-up of at least 1 month. TN duration before the PBC was 11.08 ± 9.93 years, the pain was atypical in 7 patients and 23 patients had undergone one or more procedures before PBC. The fluoroscope guided technique was performed as previously reported [2, 4]. The neuronavigated technique was performed according to the following steps: the reference frame was placed on the patient's forehead and secured with the aid of a noninvasive Landmark Fess Strap (Medtronic, Dublin, Ireland), with the head of the patient lodged in a U-shaped headholder. After acquisition of an HD-3D head scan with the use of a Medtronic O-Arm O2, slice images were trans-

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ferred to StealthStation S8 (Medtronic) and then used to reconstruct a 3D model for the skull base. After checking accuracy and selecting the medial part of FO as the target, a surgical plan was drawn with entry point according to the Hartel technique. Guidance view and three-plane view were selected for navigation. The orange Suretrak reference frame (Medtronic) is secured on the top of a 14-G cannulated needle. After removal of the inner stylet, a 4F Fogarty catheter (Edwards Lifescience, Lucerne, Switzerland), (Iopamiro 300, Bracco Imaging Italia) is inserted in the needle 16 mm beyond needle tip until the balloon tip is fully exposed. After cannulating of FO, confirmed by neuronavigation and in some cases by tactile perception, the stylet is removed and replaced with a 4F Fogarty catheter, which was advanced beyond the needle tip into Meckel's cave and inflated with 0.8 mL of iodinated radiocontrast medium for 90–120 s under fluoroscopic lateral view provided by O-arm O2. The outcome was evaluated according to the Barrow Neurological Institute (BNI) pain scale that was assessed before PBC and at 1 month FU [11, 12]. Dosing information was recorded both from the fluoroscope and O-Arm as provided by the devices.

2.1 Statistical Analysis

Means and SD were calculated and reported when appropriate. Differences between groups were explored with *t*-Student test, $\chi 2$ test and Fisher's exact test, where appropriate. Differences were considered significant at $p < 0.05$. Statistical analyses were done using StatView version 5 software (SAS Institute Inc.).

3 Results

Clinical and outcome data are showed in Table 1 and reported according to the surgical technique used (fluoroscopy or neuronavigation). Briefly, no difference was noticed in both groups concerning the clinical features of patients. We observed a significant improvement of BNI score at 1 month FU compared with the pre-operative in both groups ($p < 0.0001$ and $p < 0.0001$, respectively, see Table 1). A significant increase in radiation exposure was found in the neuronavigated group compared with the fluoroscopy group ($p < 0.0001$, see Table 1). No complications were reported.

Table 1 Clinical and outcome data of TN patients submitted to percutaneous balloon compression according to the surgical technique used (fluoroscopy or neuronavigation)

	Fluoroscopy guided PBC	Neuronavigated PBC	*p*-Value
Age	67.44 ± 11.78	65.47 ± 13.90	n.s.
Sex (M/F)	10/8	8/11	n.s.
TN type (typical/atypical)	16/2	14/5	n.s.
TN side (right/left)	9/9	10/9	n.s.
Previous operations	11	12	n.s.
TN duration before PBC (years)	10.52 ± 8.79	11.57 ± 11.06	n.s.
BNI before PBC	4.22 ± 0.54	4.26 ± 0.56	n.s.
BNI at FU	1.38 ± 0.50	1.94 ± 1.07	n.s.
Radiation exposure (mGy)	3.24 ± 2.57	17.73 ± 13.20	$p < 0.0001$

TN trigeminal neuralgia, *PBC* percutaneous balloon compression, *FU* follow-up, *BNI* Barrow Neurological Institute, *n.s.* not significant

4 Discussion

PBC is currently considered as a safe and effective procedure in the treatment of TN, mainly because of its simplicity, low cost and the possibility of being repeated in case of pain recurrence. Many studies reported high success rates, ranging between 81% and 85%, both in patients at their first treatment and in those with previous operations, thus confirming that PBC can also be a valid option in patients with TN recurrence after previous surgical procedures [4, 13–16]. Similar to other percutaneous techniques, PBC provides a rapid pain relief, thus being preferable to delayed results of stereotactic radiosurgery. Among side effects, the most common is facial hypoesthesia, occurring in approximately 20% of patients in our experience, with an onset immediately after procedure and improving after a few weeks, usually being well tolerated by patients. However, fluoroscopy-guided cannulation of FO requires some experience and is characterized by a steep learning curve. The lateral fluoroscopic view, in fact, provides indirect guiding landmarks only, while the anteroposterior (submental) view allows direct visualization of the FO, although in some patients it might not be clearly visible. The difficult visualization of the FO using fluoroscopy might prolong the procedure, mainly in young neurosurgeons, by requesting multiple attempts and could increase the risk of complications due to the immediate proximity of critical neuro-vascular structures such as the foramen lacerum, inferior orbital fissure, carotid artery, and jugular foramen. The reported rate of unsuccessful puncture and complication in procedures guided by X-ray fluoroscopy is 5–7% [17]. Moreover, FO can exhibit wide anatomic variation between subjects and throughout the natural life, as outlined in many cadaveric studies [18, 19]. Gusmao and colleagues first reported the use of CT fluoroscopy real time guidance for cannulation of the FO, although this technique proved to be difficult to reproduce because of logistic limitations [20]. A further evolution was obtained with the introduction of the neuronavigation technique, providing a real-time link between neuroradiological images and anatomic structures, with the aim of increasing the precision and reducing the rate of complications. Navigation guided procedures are of course easier to master when compared to fluoroscopic guided ones. Moreover, the accuracy of CT images allows studying the bony details of the FO in three dimensions and its possible anatomical variations, thus allowing prevention of potential complications. Nonetheless, the advantages provided by intraoperative CT-based neuronavigation may be weakened by concerns regarding increased radiation dose to the patient and the staff when compared to traditional fluoroscopy. This aspect has been poorly investigated and definitive radiation exposure reports with both techniques are still lacking. Desai et al. investigated this topic in a cadaveric study revealing an equivalent exposure in O-arm guided procedures compared to fluoroscopy (16.55 vs. 15.2 mGys) [21]. To our knowledge, this is the first comparative study in in vivo subjects. In our experience, a significant higher radiation exposure was found in the neuronavigated group compared with the fluoroscopy group, with no significant differences in clinical outcome. Considering these data, we do not suggest routine application of CT-based neuronavigation in FO cannulation, but rather in selected cases, such as patients with multiple previous operations, in whom a difficult access can be preoperatively hypothesized.

Conflict of Interest The authors report no conflict of interest.

References

1. Montano N, Ioannoni E, Rapisarda A. The risk of mastication weakness after percutaneous balloon compression for the treatment of trigeminal neuralgia. Clin Neurol Neurosurg. 2020;195:105880.
2. Montano N, Gaudino S, Giordano C, Pignotti F, Ioannoni E, Rapisarda A, Olivi A. Possible prognostic role of magnetic resonance imaging findings in patients with trigeminal neuralgia and multiple sclerosis who underwent percutaneous balloon compression: report of our series and literature review. World Neurosurg. 2019;125:e575–81.
3. Montano N, Papacci F, Cioni B, Di Bonaventura R, Meglio M. Percutaneous balloon compression for the treatment of trigeminal neuralgia in patients with multiple sclerosis. Analysis of the potentially prognostic factors. Acta Neurochir. 2012;154(5):779–83.
4. Montano N, Papacci F, Cioni B, Di Bonaventura R, Meglio M. The role of percutaneous balloon compression in the treatment of trigeminal neuralgia recurring after other surgical procedures. Acta Neurol Belg. 2014;114:59–64.
5. Hartel F. Die Leitungsanästhesie und Injektionsbehandlung des Ganglion Gasseri und der Trigeminusstämme. Langenbecks Arch Klin Chir. 1911;100:193.
6. Bohnstedt BN, Tubbs RS, Cohen-Gadol AA. The use of intraoperative navigation for percutaneous procedures at the skull base including a difficult-to-access foramen ovale. Neurosurgery. 2012;70(2 Suppl operative):177–80.
7. Lin MH, Lee MH, Wang TC, Cheng YK, Su CH, Chang CM, Yang JT. Foramen ovale cannulation guided by intra-operative computed tomography with integrated neuronavigation for the treatment of trigeminal neuralgia. Acta Neurochir. 2011;153(8):1593–9.
8. Mandat T, Brozyna B, Krzymanski G, Podgorski JK. An image-guided, noninvasive method of cannulation of the foramen ovale for awake, percutaneous radiofrequency rhizotomy. J Neurosurg. 2009;111:1223–5.
9. Xu S, Zhang W, Chen T, Wu C, Zhou M. Neuronavigator guided percutaneous radiofrequency thermocoagulation in the treatment of intractable trigeminal neuralgia. Chin Med J (Engl). 2006;119:1528–35.
10. Greenstock CL, Trivedi A. Biological and biophysical techniques to assess radiation exposure: a perspective. Prog Biophys Mol Biol. 1994;61(2):81–130.
11. Rogers CL, Shetter AG, Fiedler JA, Smith KA, Han PP, Speiser BL. Gamma knife radiosurgery for trigeminal neuralgia: the ini-

tial experience of The Barrow Neurological Institute. Int J Radiat Oncol Biol Phys. 2000;47(4):1013–9.
12. Ruge D, Brochner R, Davis L. A study of the treatment of 637 patients with trigeminal neuralgia. J Neurosurg. 1958;15:528–36.
13. Jellish WS, Benedict W, Owen K, Anderson D, Fluder E, Shea JF. Perioperative and long-term operative outcomes after surgery for trigeminal neuralgia: microvascular decompression vs percutaneous balloon ablation. Head Face Med. 2008;2:4–11.
14. Kouzounias K, Schechtmann G, Lind G, Winter J, Linderoth B. Factors that influence outcome of percutaneous balloon compression in the treatment of trigeminal neuralgia. Neurosurgery. 2010;67:925–34.
15. Omeis I, Smith D, Kim S, Murali R. Percutaneous balloon compression for the treatment of recurrent trigeminal neuralgia: long-term outcome in 29 patients. Stereotact Funct Neurosurg. 2008;86:259–65.
16. Skirving DJ, Dan NG. A 20-year review of percutaneous balloon compression of the trigeminal ganglion. J Neurosurg. 2001;94:913–7.
17. Gokalp HZ, Kanpolat Y, Turner B. Carotidcavernous fistula following percutaneous trigeminal ganglion approach. Clin Neurol Neurosurg. 1980;82:269–72.
18. Henderson WR. The anatomy of the Gasserian ganglion and the distribution of pain in relation to injections and operations for trigeminal neuralgia. Ann R Coll Surg Engl. 1965;37:346–73.
19. Khan AA, Asari MA, Hassan A. Anatomic variants of foramen ovale and spinosum in human skulls. Int J Morphol. 2012;30:445–9.
20. Gusmão S, Oliveira M, Tazinaffo U, Honey CR. Percutaneous trigeminal nerve radiofrequency rhizotomy guided by computerized tomography fluoroscopy. Technical note. J Neurosurg. 2003;99(4):785–6.
21. Desai S, Patel VJ, Lall RR, Branch D, Patel AP, Allison RZ, Paulson D, Ortega-Barnett JR. Comparing radiation dose from conventional fluoroscopy to intraoperative cone beam CT (O-arm) during percutaneous lesioning procedures of the Gasserian ganglion. Cureus. 2015;7(10):e345.

The Key to a Successful PBC in Treatment of Trigeminal Neuralgia

Jun Zhong

1 Introduction

As a minimally invasive treatment of trigeminal neuralgia, percutaneous balloon compression (PBC) has become increasingly popular worldwide. Compared to microvascular decompression (MVD), PBC is more acceptable due to its convenience and safety regardless of the unavoidable postoperative facial paresthesia at some degree [1]. In spite of an etiological remedy, it was reported that the offending vessel had not been found in 3.1–17% of MVD cases [2–4]. According to the literature, the actual cure rate of MVD ranged from 79% to 98.7% [5–7] with 30% recurrence at 6.2 years in a large series [8]. So far as PBC is concerned, the immediate cure rate ranged from 83% to 100% without serious complications [9–12]. Therefore, PBC seems to be a good alternative, especially for those recurrent cases following MVD—due to serious arachnoid adhesion and the anatomical alteration, re-exploration of the posterior fossa may induce increasing risk and give rise to a failure. Logically, the result of PBC is supposed to be more direct, at least at the early stage, because this process has actually turned off the "main switch" of hemifacial algesthesia. However, we have not yet reached such a perfect outcome as it deserves clinically. We believe the cure or complication rates are mainly attributable to the manipulation of the operator. Although numerous neurosurgeons, e.g., Brown, Meglio, Abdennebi, et al., have advanced the process since it was first reported by Mullan in 1978 [13–16], this surgical technique can never be overemphasized.

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2 Target of PBC

2.1 The Semilunar Ganglion

Instead of the Meckel cave, the Gasserian ganglion is the target of PBC. It consists of the pseudounipolar neuron giving out a protuberance and dividing into two branches in a T shape. The peripheral branch (nerve fibers) transmits the facial and oral stimulations into the neuron and the central branch (nerve rootlets) transmits these processed impulses into the brainstem nucleus. Unlike the axon, the soma is nonrenewable. Therefore, the *ganglia* rather than the nerve fibers or the rootlets should be ablated. If the pressure was mainly focused on the rootlets instead of the ganglia, the pain relief would be unsatisfactory or an earlier recurrence might not be avoidable.

3 A Pear in Meckel Cave

3.1 The Meckel's Cave

Meckel's cave locates inferiorly on the anterior slope of the petrous apex and crosses over the ridge toward the posterior fossa. Virtually, it is a cavity between duras and does not look like a pear in a stereo image before it is filled by the balloon. To simplify, you can imagine a tetrahedron with four triangle plans pointing toward the porus through where the trigeminal rootlets converge into root and finally enters the pons. The anterior plan consists of semilunar ganglion where the three branches of the fifth cranial nerve come and the balloon catheter enters via the foramen oval. The medial plan faces the cavernous sinus. The superolateral plan is the tentorium and the bottom the petrous bone. Therefore, we should manage to concentrate the pressure on the *anterior* rather than on the medial plan or porus while the balloon is inflated (Fig. 1).

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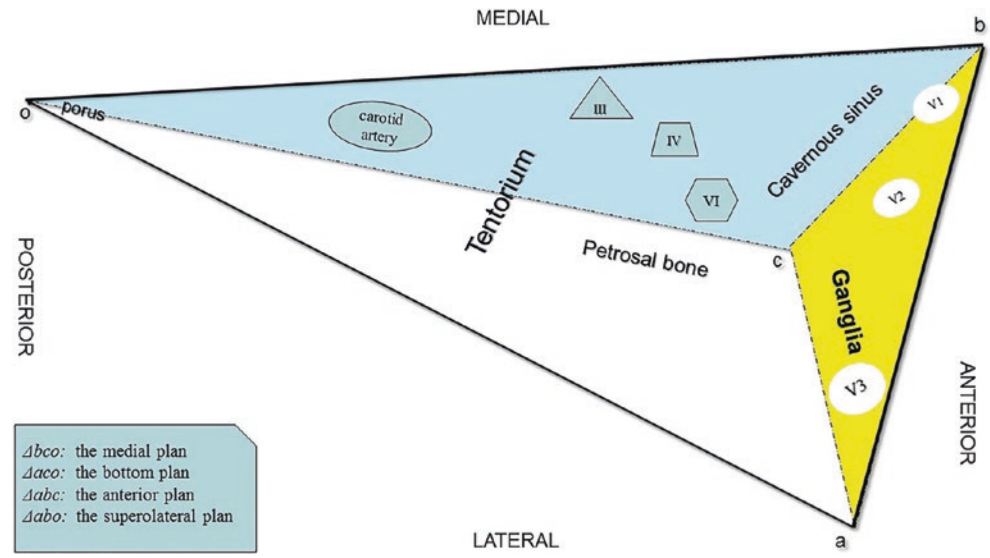

Fig. 1 An abstraction depicting the surrounding structures of Meckel's cave. A right Meckel's cave is abstracted as a tetrahedron with four triangle plans pointing toward the porus. The anterior plan (Δabc) consists of semilunar ganglion where the three branches of the fifth cranial nerve (V1, V2, and V3) converge and the balloon catheter enters via the foreman oval. The medial plan (Δbco) faces the cavernous sinus consisting of the third (III), fourth (IV), and fifth (VI) cranial nerves as well as the carotid artery. The superolateral plan (Δabo) is the tentorium and the bottom (Δaco) the petrous bone. Actually, the cavity does not present as a pear shape in a 3D image until it is filled by the balloon

3.2 Pear

When the Meckel cave is full of contrast agent, a pear shape opacity bending to the petrous bone appears in the lateral radiograph. The body of the pear outlines the main part of the cavity with a rounded bottom referring to the semilunar ganglion, the waist depicts the rootlets, the head indicates the trigeminal root going through the porus (neck), and the stalk the tip of the catheter. Because of a harder bony pedestal inferiorly and a softer celling superiorly, this pear bends stiffly to the petrous bone, while it extends supplely to the tentorium, respectively. When this figure forms in fluoroscopy, it is implied that the entirety of the ganglion is covered and an effective compression has been built (Fig. 2).

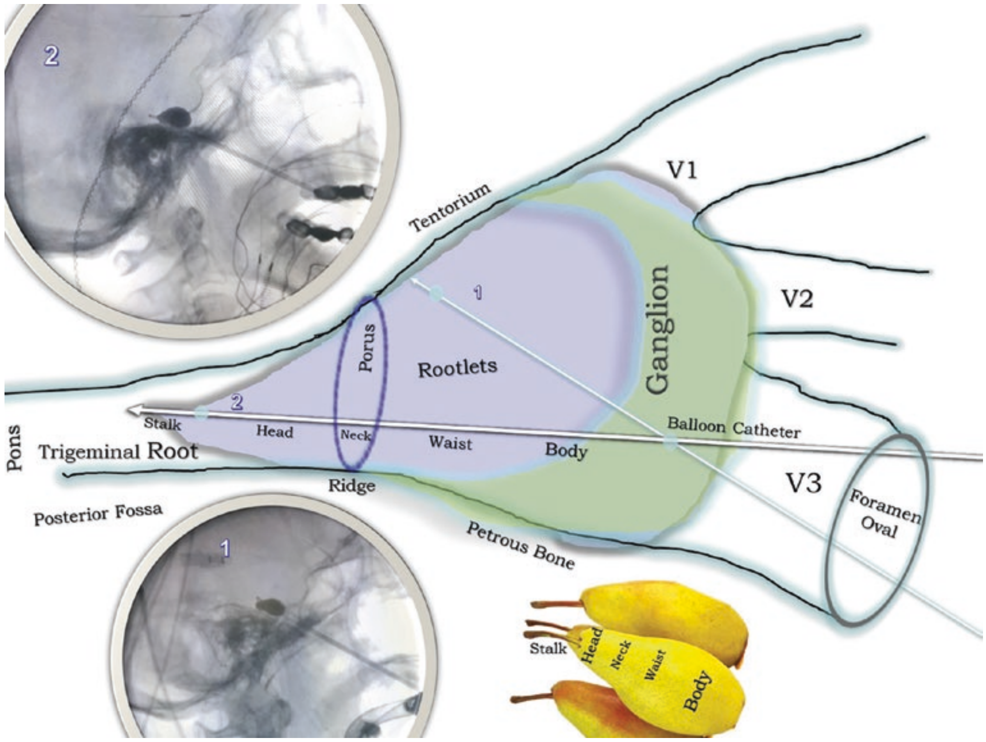

Fig. 2 A diagram illustrating the fluoroscopic appearance of a pear in Meckel's cave and the proper puncture angle. When a balloon is inflated in Meckel's cave, a pear shape opacity appears in the lateral radiograph. The body of the pear outlines the main part of the cave with a rounded bottom referring to the semilunar ganglion, the waist indicates the rootlets, the head the trigeminal root coming from the porus (neck), and the stalk the tip of the catheter. The penetrative angle is critical to achieve a satisfactory pear. The tip of the catheter as well as the puncturing points of the foramen oval and facial skin should be in a line. Sometimes, a pear with stalk rising from the neck is observed (the left bottom insert), which is caused by an upward angle of the line (1)—the tip is located in front of the porus and the head is pushed forward twistedly while inflating. Therefore, it is suggested to penetrate the upper edge of the foramen oval and advance the tip down through the porus (2) to obtain a tractable pear (the upper insert)

4 Effective Compression

The process of PBC is implemented by an effective compression against the ganglia. Therefore, first, the balloon should be positioned correctly, which is judged by a typical pear shape fluoroscopically. Second, to reach enough pressure, a certain volume of agent needs to be injected into the balloon. Third, to reduce complications, the compression time needs to be well controlled.

4.1 Shapes

A typical pear may not always be available. When an anomaly shape emerges, the balloon could be actually outside the cavity and a reposition is suggested. If the catheter is advanced too far forward, a bowling pin shape may exhibit with too much tension concentrated in the root instead of in the ganglion. While a ping-pong bat shape indicates the capsule has been excessively compressed, which may lead to an unacceptable paresthesia postoperatively. Sometimes, a bitten pear is observed. That is caused by bubbles which should have been exhausted before Omnipaque is injected in. Owing to the extraordinary compressibility of air, it will not offer enough pressure against the ganglia at the bottom. Accordingly, a tractable slim pear without defect should be expected.

4.2 Volume

The compression of the trigeminal ganglion is functioned by the volume of contrast agent injected into the balloon. However, as the volume reaches some extent, the pressure will not enhance synchronously with the dimension since Meckel's cavity is a sort of capsule with limited elasticity modulus. Contrarily, a too big balloon may conduct the pressure to the surrounding structures and threaten the cavernous sinus, especially the abducent nerve. Because the size and the elasticity vary individually, it is hard to quantify a pressure standard [17, 18]. Therefore, it is wise to stop injecting when growth of the pear becomes apparently slow.

4.3 Time

To increase cure rate and reduce complications, a minimal value of an optimized combination of volume and time should be pursued. Generally, the inflation time ranged from 1 to 4 min according to the literature [18–21]. It is suggested to maintain the effective pressure by holding the syringe continuously instead of using a triple stopcock. Corresponding to the radiographic projection and the feedback in thumb, the pressure can be well controlled in real time.

5 Tips on the Process

PBC is simple, straightforward, and does not need a complicated apparatus only a fluoroscope plus an operator's experience. Therefore, the surgical technique is essential and every single step of this process is worth further addressing.

5.1 Position

Basically, a lateral view fluoroscopy is enough to target Meckel's cave and check the inflation. To obtain clear landmarks in radiograph, the patient's head should be positioned stably to keep the projections of bilateral porions and mandibles superimposed, respectively, during the process.

5.2 Puncture

As a start leading to a correct track, the facial entry point should be emphasized. It should be aligned in the reverse extension line between the porus and the foramen oval. Basically, it is lateral to the commissure of the lips where an alcove can be felt by pressing. That is the corridor between the maxilla and the mandible. It is not necessary to put your finger into the patient's mouth to guild the puncture because the needle has already been in the corridor once entering the skin. For safety, a needle with a noncutting obturator is employed and a very tiny incision on the skin needs to be made.

5.3 Cannulate

The needle is advanced toward the ipsilateral pupil on the coronal plane and to the infra 1/3 of the line between the posterior clinoid and mandibular condyle on the lateral projection of fluoroscopy and halted as its tip just entering the foramen oval. Before withdrawing the obturator, one should make sure that the cannula is fixed well otherwise its sharp mouth rim might cut the balloon while the catheter goes by.

5.4 Penetrate

As the cannula has been steadily positioned, a sharp stylet is inserted to stab the capsule. Then a blunt stylet is used to clear the way for balloon entry. In the tunnel, the softer catheter could be advanced smoothly to an appropriate position. Otherwise, the balloon may suffer contusion as extruding tortuously from a sharp cannula's mouth and burst during inflation. To achieve a typical pear, the penetrative angle is critical—it is suggested to puncture the upper edge of the foramen oval and advance the tip down through the porus (Fig. 2).

5.5 Inflation

The balloon should not be inflated until it has been positioned appropriately, otherwise a typical slim pear may never be achieved—for the catheter tends to enter the same route with easy access. Because less contrast agent is needed to outline the head compared with the body, it is suggested to advance the catheter straight ahead to the trigeminal root—whereabouts the catheter tip appears down. If a waist begins to appear after a tentative injection, then the balloon can be slowly inflated till its body emerges. If not, it should be deflated and repositioned.

6 Conclusion

1. A pear shape with well-rounded bottom defined in fluoroscopy indicates an effective compression of the trigeminal ganglion has been built, which is crucial to a cure.
2. To attain a tractable pear, Meckel's cave needs to be tunneled in a proper penetration angle before balloon entry.
3. No full inflation before a proper position is confirmed.
4. To avoid an unacceptable postoperative paresthesia, a more than 3-min compression is not encouraged.

References

1. Cheng JS, Lim DA, Chang EF, Barbaro NM. A review of percutaneous treatments for trigeminal neuralgia. Neurosurgery. 2014;10:25–33. https://doi.org/10.1227/NEU.0000000000001687; discussion 33.
2. Cheng J, Lei D, Zhang H, Mao K. Trigeminal root compression for trigeminal neuralgia in patients with no vascular compression. Acta Neurochir. 2015;157:323–7. https://doi.org/10.1007/s00701-00014-02300-00709. Epub 2015 Jan 9.
3. Ishikawa M, Nishi S, Aoki T, Takase T, Wada E, Ohwaki H, Katsuki T, Fukuda H. Operative findings in cases of trigeminal neuralgia without vascular compression: proposal of a different mecha-

nism. J Clin Neurosci. 2002;9:200–4. https://doi.org/10.1054/jocn.2001.0922.
4. Revuelta-Gutierrez R, Lopez-Gonzalez MA, Soto-Hernandez JL. Surgical treatment of trigeminal neuralgia without vascular compression: 20 years of experience. Surg Neurol. 2006;66:32–6. https://doi.org/10.1016/j.surneu.2005.1010.1018; discussion 36.
5. Gubian A, Rosahl SK. Meta-analysis on safety and efficacy of microsurgical and radiosurgical treatment of trigeminal neuralgia. World Neurosurg. 2017;103:757–67. https://doi.org/10.1016/jwneu201710041085. Epub 2017 Apr 20.
6. Zhong J, Li ST, Zhu J, Guan HX, Zhou QM, Jiao W, Ying TT, Yang XS, Zhan WC, Hua XM. A clinical analysis on microvascular decompression surgery in a series of 3000 cases. Clin Neurol Neurosurg. 2012;114:846–51. https://doi.org/10.1016/j.clineuro.2012.1001.1021. Epub 2012 Feb 5.
7. Zhong J, Zhu J, Sun H, Dou NN, Wang YN, Ying TT, Xia L, Liu MX, Tao BB, Li ST. Microvascular decompression surgery: surgical principles and technical nuances based on 4000 cases. Neurol Res. 2014;36:882–93. https://doi.org/10.1179/1743132814Y.0000000344. Epub 2014 Mar 5.
8. Barker FG II, Jannetta PJ, Bissonette DJ, Larkins MV, Jho HD. The long-term outcome of microvascular decompression for trigeminal neuralgia. N Engl J Med. 1996;334:1077–83. https://doi.org/10.1056/NEJM199604253341701.
9. Li MW, Jiang XF, Niu CS. Efficacy of and risk factors for percutaneous balloon compression for trigeminal neuralgia in elderly patients. Br J Neurosurg. 2020;3:1–5.
10. Ni H, Wang Y, Chen X, Gu W. Outcomes of treatment for elderly patients with trigeminal neuralgia: percutaneous balloon compression versus microvascular decompression. J Craniofac Surg. 2020;31(7):e685–8.
11. Skirving DJ, Dan NG. A 20-year review of percutaneous balloon compression of the trigeminal ganglion. J Neurosurg. 2001;94:913–7. https://doi.org/10.3171/jns.2001.3194.3176.0913.
12. Ying X, Wang H, Deng S, Chen Y, Zhang J, Yu W. Long-term outcome of percutaneous balloon compression for trigeminal neuralgia patients elder than 80 years: a STROBE-compliant article. Medicine (Baltimore). 2017;96:e8199. https://doi.org/10.1097/MD.0000000000008199.
13. Belber CJ, Rak RA. Balloon compression rhizolysis in the surgical management of trigeminal neuralgia. Neurosurgery. 1987;20:908–13. https://doi.org/10.1227/00006123-198706000-198700015.
14. Brown JA, Chittum CJ, Sabol D, Gouda JJ. Percutaneous balloon compression of the trigeminal nerve for treatment of trigeminal neuralgia. Neurosurg Focus. 1996;1:e4. https://doi.org/10.3171/foc.1996.3171.3172.3111; discussion 1 p following e4.
15. Fraioli B, Esposito V, Guidetti B, Cruccu G, Manfredi M. Treatment of trigeminal neuralgia by thermocoagulation, glycerolization, and percutaneous compression of the Gasserian ganglion and/or retrogasserian rootlets: long-term results and therapeutic protocol. Neurosurgery. 1989;24:239–45. https://doi.org/10.1227/00006123-198902000-198900014.
16. Montano N, Ioannoni E, Rapisarda A. The risk of mastication weakness after percutaneous balloon compression for the treatment of trigeminal neuralgia. Clin Neurol Neurosurg. 2020;195:105880. https://doi.org/10.1016/j.clineuro.2020.
17. Unal TC, Unal OF, Barlas O, Hepgul K, Ali A, Aydoseli A, Aras Y, Sabanci PA, Sencer A, Izgi N. Factors determining the outcome in trigeminal neuralgia treated with percutaneous balloon compression. World Neurosurg. 2017;107:69–74. https://doi.org/10.1016/j.wneu.2017.1007.1132. Epub 2017 Jul 30.
18. Yadav S, Sonone RM, Jaiswara C, Bansal S, Singh D, Rathi VC. Long-term follow-up of trigeminal neuralgia patients treated with percutaneous balloon compression technique: a retrospective analysis. J Contemp Dent Pract. 2016;17:263–6. https://doi.org/10.5005/jp-journals-10024-11838.
19. Bergenheim AT, Asplund P, Linderoth B. Percutaneous retrogasserian balloon compression for trigeminal neuralgia: review of critical technical details and outcomes. World Neurosurg. 2013;79:359–68. https://doi.org/10.1016/j.wneu.2012.1003.1014. Epub 2012 Apr 2.
20. Chen JF, Tu PH, Lee ST. Long-term follow-up of patients treated with percutaneous balloon compression for trigeminal neuralgia in Taiwan. World Neurosurg. 2011;76:586–91. https://doi.org/10.1016/j.wneu.2011.1005.1021.
21. De Cordoba JL, Garcia Bach M, Isach N, Piles S. Percutaneous balloon compression for trigeminal neuralgia: imaging and technical aspects. Reg Anesth Pain Med. 2015;40:616–22. https://doi.org/10.1097/AAP.0000000000000292.

The Role of the Anesthesiologist and the Modern Intraoperative Echography in Ventriculoatrial Shunt for Hydrocephalus: From Hakim to Nowadays

R. Garra, A. Pusateri, R. Festa, Massimiliano Visocchi, and F. Tosi

Hydrocephalus is the most common disease treated by pediatric neurosurgeons, which presents a prevalence of 1/1000 births in high-income countries. The term hydrocephalus refers to a pathological accumulation of cerebrospinal fluid (CSF) in the subarachnoid space or in the cerebral ventricles, typically associated with increased intracranial pressure [1]. Understanding CSF physiology enables us to differentiate two pathophysiological mechanisms underlying the acquired and congenital causes of pediatric hydrocephalus (Table 1). The obstruction to CSF flow from its origin in the choroid plexus within the ventricles is known as hydrocephalus obstructive or non-communicating, and the obstruction of CSF absorption in the subarachnoid space is classified as communicating hydrocephalus [2].

Table 1 Causes of pediatric hydrocephalus

Acquired hydrocephalus
– Inflammatory
– Neoplastic
– Vascular
Congenital or development hydrocephalus
– Chiari II
– Myelomeningocele
– Acqueductus stenosis
– Posterior fossa malformation
– Subaracnoidal cysts
– Foramen of Monro atresia

Since the introduction of silastic tubing, in the middle of the last century, hydrocephalus treatment has been and still remains based on ventricular shunting. The technique consists in the insertion of a cranial catheter in the lateral ventricle of the head and the insertion of a catheter in a distal site (heart, peritoneum, pleura). Differential pressure (with fixed or programmable settings) or flow-regulating valve mechanisms are between the ventricular and distal catheters and are often paired with antisiphon or gravitational devices to prevent CSF over-drainage from posture-related siphoning [3]. Despite that endoscopic third ventriculostomy (ETV) has been shown as a viable alternative treatment for hydrocephalus, particularly in patients with non-communicating hydrocephalus, ventricular shunting procedures continue to be the mainstay of hydrocephalus management in children [4]. Among these, ventricular peritoneal (VP) shunting is considered the first-line option for the effectiveness of peritoneal resorption and the feasibility of catheter insertion that runs subcutaneously from the head to the abdomen. However, distal shunt failure may occur as a result of adhesions, intraperitoneal infections, ascites, and a history of necrotizing enterocolitis. Moreover, the presence of intestinal stoma after abdominal surgery contraindicates VP shunting due to the risk of infections of the peritoneal catheter [5]. Therefore, in situations where VP shunting is contraindicated or has failed, ventricular atrial (VA) shunting may be considered a valid second-line option as it provides an alternative site for the distal catheter [6].

The first Nulsen and Spitz's description of the technique, way back in 1951, involved open neck dissection to cannulate a tributary vein of the internal jugular in which to pass the catheter to the right atrium.

The less invasive method of percutaneous insertion, described by Ashker et al. in 1981, based on anatomical landmarks, has allowed the technique to be widely accepted (Fig. 1). However, even the "blind" percutaneous venipuncture has serious limitations when performed in neonates,

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Fig. 1 Anatomical landmark for the internal jugular venipuncture

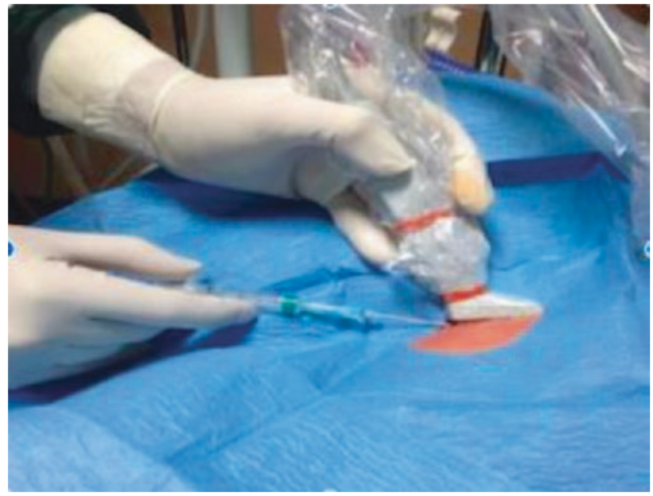

Fig. 2 Ultrasound guided venipuncture in long axis using a frequency probe of 10–14 MHz

infants, and children due to the landmarks less defined respect to adults, and the increased risk of complications, such as pneumothorax, hemothorax, secondary to accidental arterial and/or pleural puncture.

The introduction of ultrasound guided venipuncture in clinical practice has greatly facilitated the performance of the procedure, especially in neonates and children where it results in a lower technical failure rate, less time-consuming, and fewer complications compared to the traditional landmark method [7, 8]. The higher efficacy and safety of "ultrasound guidance" lies in the visualization of the needle entering the vein. This dynamic or "real time" technique has become part of the anesthetist's tools also to perform nerve blocks in loco-regional anesthesia/analgesia and for monitoring vital cardiac and pulmonary functions in the perioperative period; thus, two decades after its introduction into anesthetic practice, practitioners have achieved considerable technical expertise. This allowed anesthetists to be part of the surgical team; therefore, they are not only dedicated to inducing and maintaining general anesthesia but also to performing venipuncture of the central vein of the neck and to localizing the tip of the catheter.

The procedure is performed methodically, with the child in the supine position, the head slightly in extension and turned in the opposite site, starting with the visualization of the internal jugular in short or long axis using a frequency probe of 7–10 MHz for children, and 10–14 MHz for neonates [9–11] (Fig. 2) Under ultrasound guidance the internal jugular vein is punctured with a 22–20 gauge needle and a floppy tipped in guide wire inserted. A 3.5–4.5-Fr, peel-away sheath is inserted and the shunt catheter is passed inside it after having removed the guide wire. Then, the peel-away catheter is removed leaving the shunt catheter in situ which is attached to the cranial catheter via a connector.

The tip catheter can be localized by fluoroscopy, intracavitary ECG (IC-ECG), or by echocardiography. However, even for tip catheter localization anesthetists have borrowed the IC-ECG method used to check the tip of the central venous catheter (CVC), as it has a better cost–benefit ratio. Indeed, unlike fluoroscopy, it does not require a fluoroscope, and it does not expose the patient to radiation; while unlike transesophageal ultrasound, it is not invasive and it is more accessible [12]. The basis of the IC-ECG technique is to fill the catheter with saline solution that acts as an electrical conductor, and to use the catheter tip as an exploratory electrode or, in other words, as an endocavitary lead. In practice, if the catheter is connected to lead V1 or V2 of an electrocardiograph, the tip level can be followed "step by step" evaluating the different morphologies assumed by the P wave, in terms of deflection and amplitude, as it approaches the sinoatrial node. Thus, when the tip, acting as a scanning electrode, is at the level of the superior cava, the P wave shows a negative deflection and a low voltage. While, as the tip approaches the sinoatrial node, the atrial depolarization is always read as a negative deflection, but of greater amplitude the closer the tip approaches the nodal tissue in the atrio-caval junction. Finally, when the tip reaches the right atrium, a biphasic P wave appears, first positive of small size, then of greater amplitude, while the negative phase tends in the same time to shrink, until disappearing.

The atrio-caval junction or the atrium are the ideal locations for the placement of a VA shunting. Indeed, if the distal

Fig. 3 Subcostal scan to visualize the atrium and inferior vena cava

end of the catheter does not reach at least the lower third of the superior vena cava, the risk of thrombosis is high. Conversely, catheters that are too long, with the tip positioned in the lower part of the atrium, near the tricuspid or in the ventricle, can cause arrhythmias, thrombosis, or valve damage. Therefore, the tip of the atrial catheter must be positioned in such a way to obtain a biphasic P-wave, which corresponds to the upper-middle right atrium [13].

The subcostal ultrasound scan give, in children more than in adults, an excellent visualization of the inferior vena cava and the right atrium. This "window" allows identifying the tip of the catheter and it looks equally promising to confirm its correct position in the right atrium with the so-called bubble test, which consists in visualizing a linear flow of micro bubbles after having injected a bolus of 4.5 mL of saline solution or 0.5 of air into the distal catheter (Fig. 3).

The anesthetist's tools have allowed performing a simple and safe method, and anesthetists have become an active part of the surgical team, charged with a specific role during the placement of the ventricular atrial shunting, in addition to the well-known conventional one.

References

1. Simon TD, Riva-Cambrin J, Srivastava R, Bratton SL, Dean JM, Kestle JR, The Hydrocephalus Clinical Research Network. Hospital care for children with hydrocephalus in the United States: utilization, charges, comorbidities, and deaths. J Neurosurg Pediatr. 2008;1:131–7.
2. Kulkarni AV, Riva-Cambrin J, Butler J, et al. The Hydrocephalus Clinical Research Network. Outcomes of CSF shunting in children: comparison of Hydrocephalus Clinical Research Network cohort with historical controls: clinical article. J Neurosurg Pediatr. 2013;12:334–8.
3. Kestle JR, Walker ML, Strata I, the Strata Investigators. A multicenter prospective cohort study of the Strata valve for the management of hydrocephalus in pediatric patients. J Neurosurg. 2005;102(Suppl):141–5.
4. Kulkarni AV, Drake JM, Mallucci CL, et al. Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. J Pediatr. 2009;155:254–59.e1.
5. Kulkarni AV, Drake JM, Lamberti-Pasculli M. Cerebrospinal fluid shunt infection: a prospective study of risk factors. J Neurosurg. 2001;94:195–201.
6. Clark DJ, Derek AC, Roebuc J. Ultrasound guided placement of the distal catheter in paediatric ventriculoatrial shunts—an appraisal of efficacy and complications. Child Nerv Syst. 2016;32:1219–25.
7. Pittiruti M. Ultrasound guided central vascular access in neonates, infants and children. Curr Drug Targets. 2012;13:961–9.
8. Froehlich C, Rigby M, Rosenberg E, et al. Ultrasound-guided central venous catheter placement decreases complications and decreases placement attempts compared with the landmark technique in patients in a pediatric intensive care unit. Crit Care Med. 2009;37:1090–6.
9. Di Nardo M, Tomasello C, Pittiruti M, et al. Ultrasound-guided central venous cannulation in infants weighing less than 5 kilograms. J Vasc Access. 2011;12:318–20.
10. Jeon Y, Ryu HG, YoonD SZ, Kim JH, Bahk JH. Transesophageal echocardiographic evaluation of ECG-guided central venous catheter placement. Can J Anaesth. 2006;53(10):978–83.
11. Chu KS, Hsu JH, Wang SS, et al. Accurate central venous port. A catheter placement: intravenous electrocardiography and surface landmark techniques compared by using transesophageal echocardiography. Anesth Analg. 2004;98:910–4.
12. Serafini G, Pietrobono P, Cornara G. Location of central venous catheter in children by endocavitary ECG: a new tecnicque. Clin Nutr. 1985;4:201–2.
13. Gebhard RE, Szmuk P, Pivalizza EG, Melnikov V, Vogt C, Warters RD. The accuracy of electrocardiogram-controlled central line placement. Anesth Analg. 2007;104:65–70.

Part II

Spine

Role of Navigation in the Surgery of Spine Tumours

Marcel Ivanov and Matthias Radatz

1 Background

Computer-assisted navigation has emerged in neurosurgery as an approach to improve intraoperative orientation and achieve better surgical results with lower complication rates. While its initial use in cranial neurosurgery was focused around precise identification of the surgical target, the current applications, in particular in spine surgery, are much wider and continue to rapidly expand.

2 Methods

This is a retrospective analysis of the spinal cases operated in Sheffield Teaching Hospitals using spinal navigation between 2010 and 2020 with a focus on the analysis of benefits of computer guidance in the surgery of spinal tumours.

For intraoperative navigation, we used BrainLab Navigation with dedicated spinal software for CT-based 3D surface matching and intraoperative 3D X-ray (Siemens Arcadis and Ziehm).

3 Findings and Discussions

Widespread adoption of instrumentation in spine surgery helped to provide the necessary stability and was initially performed using anatomical landmarks. However, some of the early papers reported suboptimal screw placement in up to a third of implanted screws [1]. This was explained by several factors that include individual variations of the anatomy among patients and individual surgeon's experience.

Suboptimal screw placement prompted the need to improve accuracy and safety of the procedure. Although the conventional method, fluoroscopy, became readily available and inexpensive, it has several drawbacks. The main disadvantage is limitation provided by having only antero-posterior and lateral or oblique views with the inability to provide an axial view of the spine. The other disadvantages include poor or absent visibility in case of obesity, severe osteoporosis, cervico-thoracic junction due to shoulder obstruction, or in patients with abnormal anatomy secondary to previous surgeries, tumour/trauma destruction, degenerative and/or congenital problems.

Narrow or abnormal pedicles leave little or no room for error and the ability to accurately identify them and execute their cannulation with millimetric accuracy became crucial for the success of surgery. In addition, concerns regarding radiation exposure and the drive to provide better visual guidance spurred the development of intraoperative image-guided surgery.

Computer-assisted navigation and advanced intraoperative imaging provided numerous benefits in spine surgery. It was able to significantly increase the accuracy of screw placement up to 98–100% [2–5]. As a result of more accurate placement, the spine surgeons are now able not only to reduce the risk of iatrogenic injury secondary to suboptimally placed screws, but also to plan and achieve much more robust spinal construct from a biomechanical perspective, with optimisation of the screw length and diameter, choice of optimal trajectory, consideration of bi- and three-cortical screws with expected lower risk of screw pull-out/metalwork failure.

The ability to view the unexposed anatomy not only on the A-P and lateral view but also on axial or virtually any desired plane significantly improved the accuracy and safety of spine surgery.

This is particularly relevant for the cervical spine, which not only has a limited bone mass for screw placement but is also abundant in anatomical structures that must not be damaged during surgery (vertebral artery, nerve roots, spinal cord). In the cervical spine, with the aid of spinal navigation, the surgeon can enhance the biomechanical constructions by planning cervical pedicles screws, which offers much more

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solid construction, in particular when lateral masses are not suitable for screws due to significant degenerative/arthritic/osteoporotic changes. Although free-hand cervical pedicle screw fixation has been well described [6, 7], the majority of spine surgeons do not use this technique because of the high risks associated with the lack of reliable anatomical landmarks, narrow pedicles and proximity to important anatomical structures that should not be damaged.

In tumour surgery, in particular when a gross total tumour resection is planned, image guided surgery can help to define with high accuracy the margins of the tumour on preoperative MRI scans and merge with the intraoperative imaging, thus providing intraoperative multimodal information important for better intraoperative orientation during various steps of surgery (Figs. 1 and 2). This applies both for the tumours of the spine as well as intraspinal tumours, in particular large dumbbell nerve sheath tumours, where in addition to navigation the real-time intraoperative ultrasound can help to assess whether the dumbbell tumours are extending intradurally or are limited to the extradural compartment, avoiding unnecessary dural opening (Fig. 2C2) [8–11].

Another benefit of image-guided surgical navigation is accurate planning and execution of osteotomy in the case of primary bone tumours—with a margin of healthy tissue. The ability to see the optimal trajectory and size of osteotomy on the screen can help to maximise the chances of gross total resection of the tumour [12].

It is important to acknowledge that in intraspinal benign nerve sheath tumours with slow growth, the vertebral bodies suffer scalloping with significant narrowing or displacement of the pedicles, laminas and vertebral bodies. It frequently results in abnormal spinal alignment. To access the intraspinal tumour component which often affects several levels, the surgeon has to perform a laminectomy at several levels with further negative impact on spinal stability (Fig. 1). In such a scenario, spinal instrumented stabilisation often becomes mandated, but local anatomical changes produced by the tumour make spinal stabilisation extremely challenging and risky with no margin for error. Navigation guided surgery in such cases becomes a mandatory part of the procedure (Figs. 1 and 2). In addition to this, congenital spinal abnormalities or coexistence with other regional pathologies may add to the complexity of an already challenging surgery.

In addition to improved intraoperative orientation with millimetric accuracy, we did find spinal navigation beneficial for several other reasons.

3.1 Safe Training

It is well recognised that in spine surgery there is a steep learning curve, which may last several years. At the beginning of this learning curve, the trainees are more likely to make a mistake, with a higher risk of suboptimal screw placement. With the aid of intraoperative navigation, we developed a system when a trainee is asked during surgery to identify the usual anatomical landmarks as well as screw entry point without looking at the navigation screen first. Subsequent placement of the navigation pointer can confirm whether the anatomically identified entry points and trajectories are accurate, which would be re-assuring for the trainee, or if the anatomical knowledge has to be improved, in which case the trainee can re-adjust his knowledge of anatomical landmarks without causing a harm to the patient.

3.2 Radiation

It is well known that X-ray guided spinal stabilisation has a risk of cumulative radiation exposure to the surgeon and surgical team, which may have long-term detrimental effects. Use of navigation in our hospital reduced radiation exposure of the surgical team in spinal instrumented cases to zero, also bringing additional comfort from not needing to wear a heavy led gown during the procedure and no need for repeat X-rays during the procedure, freeing a radiographer for other tasks. For patient's registration in our spinal cases, we used either CT scans obtained preoperatively or intraoperative 3D X-ray at the beginning and, if needed, at the end of the procedure (to confirm accurate screw placement). We also find that better intraoperative orientation and no need to perform repeat X-rays had a positive impact on improvement of the overall duration of surgery.

The benefits of advanced navigation guidance during spine surgery are numerous. One of illustrative cases is described below.

Illustrative Case

A 56-year-old patient presented with clinical features of progressive myelopathy. An MRI scan showed a large intraspinal tumour extending between C2 and C6 (Fig. 1A1) with lateral displacement of the spinal cord. Further investigations with angio-CT demonstrated displacement of the right vertebral artery anteriorly, but also looping of the vertebral artery (VA)

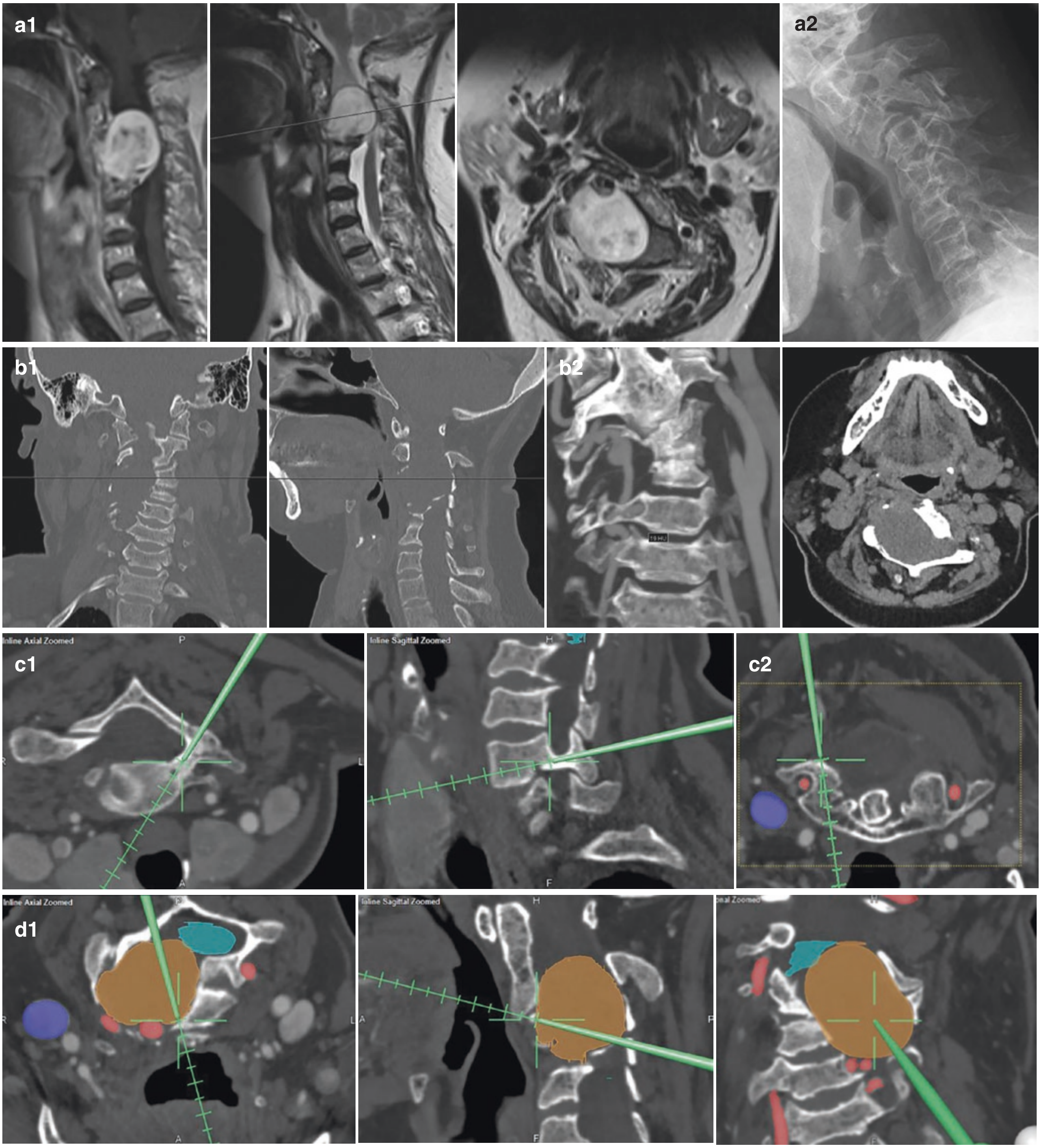

Fig. 1 (**a1**) MRI T1 with contrast and T2. Large C3–C6 dumbbell nerve sheath tumour encasing vertebral artery. (**a2**) X-ray cervical spine—inversion of normal lordosis. Anterolisthesis of C3 on C4 vertebra. (**b1**) CT cervical spine and (**b2**) angio CT demonstrating scalloping of the vertebras, abnormal looping vertebral artery with aneurysm. (**c1**) Intraoperative navigation guided screw cannulation of cervical pedicle and (**c2**) lateral mass. (**d1**) Navigation guidance during tumour debulking showing the degree of tumour removed and distance to the vertebral artery. (**e1**) Postoperative MRI shows spinal cord decompression. (**e2**) Accurate placement of the screws

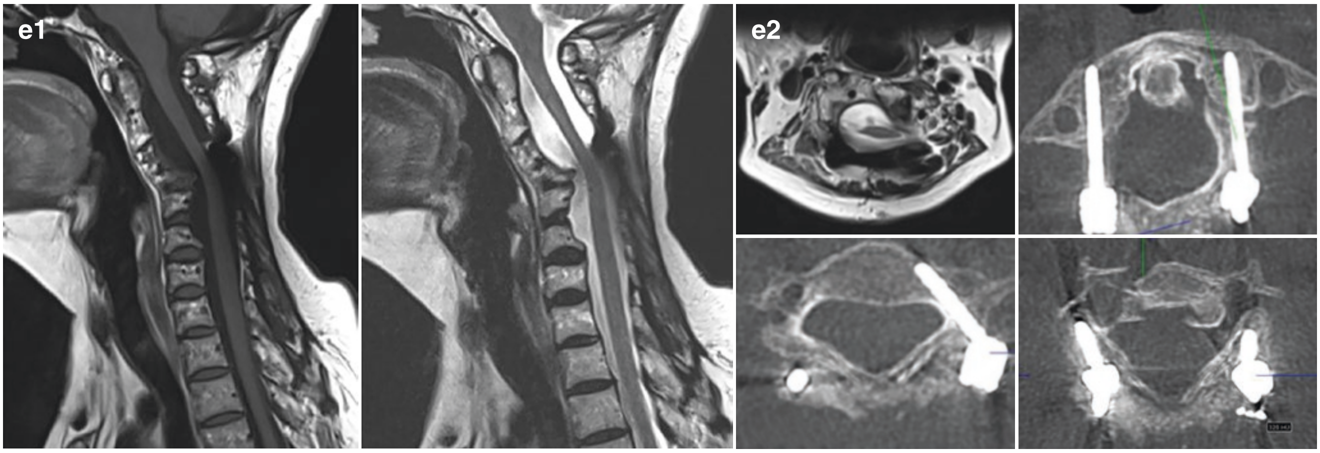

Fig. 28.1 (continued)

and an aneurysm of VA within the rostral part of the tumour (Fig. 1B2). Dynamic X-ray of the cervical spine demonstrated inversion of the normal lordosis (Fig. 1A2). It is important to note that there was significant scalloping of several vertebras affected by the tumour with abnormal lateral masses which made them unsuitable for screw insertion (Fig. 1B1).

In such a scenario, one of the surgical steps is multilevel laminectomy. Considering the inversion of the normal lordosis with listhesis of C3 on C4, such laminectomy would have a high risk of deterioration of instability/deformity, and to avoid this, spinal stabilisation is imposed. However, most of the lateral masses were anatomically not suitable for instrumentation. Another challenge in this case was the intimate relationship of the tumour with displaced abnormal vertebral artery and aneurysm, covered by the tumour.

The patient had standard posterior midline exposure. With the aid of spinal navigation, we were able to (a) accurately define the edges of the tumour and perform initial safe tumour debulking with the ability to see the exact location of the vertebral artery and aneurysm, even when covered by the tumour (Fig. 1D1); (b) pre-plan optimal trajectories for the cervical screws and achieve necessary spinal stabilisation using limited bone mass in this specific patient (Fig. 1C1, C2).

Patient recovered well without any new deficit and was discharged home within 72 h from surgery. Postoperative MRI confirmed satisfactory decompression of the spinal cord and CT scan demonstrated accurately placed spinal implants providing good spinal stability (Fig. 1E1, E2).

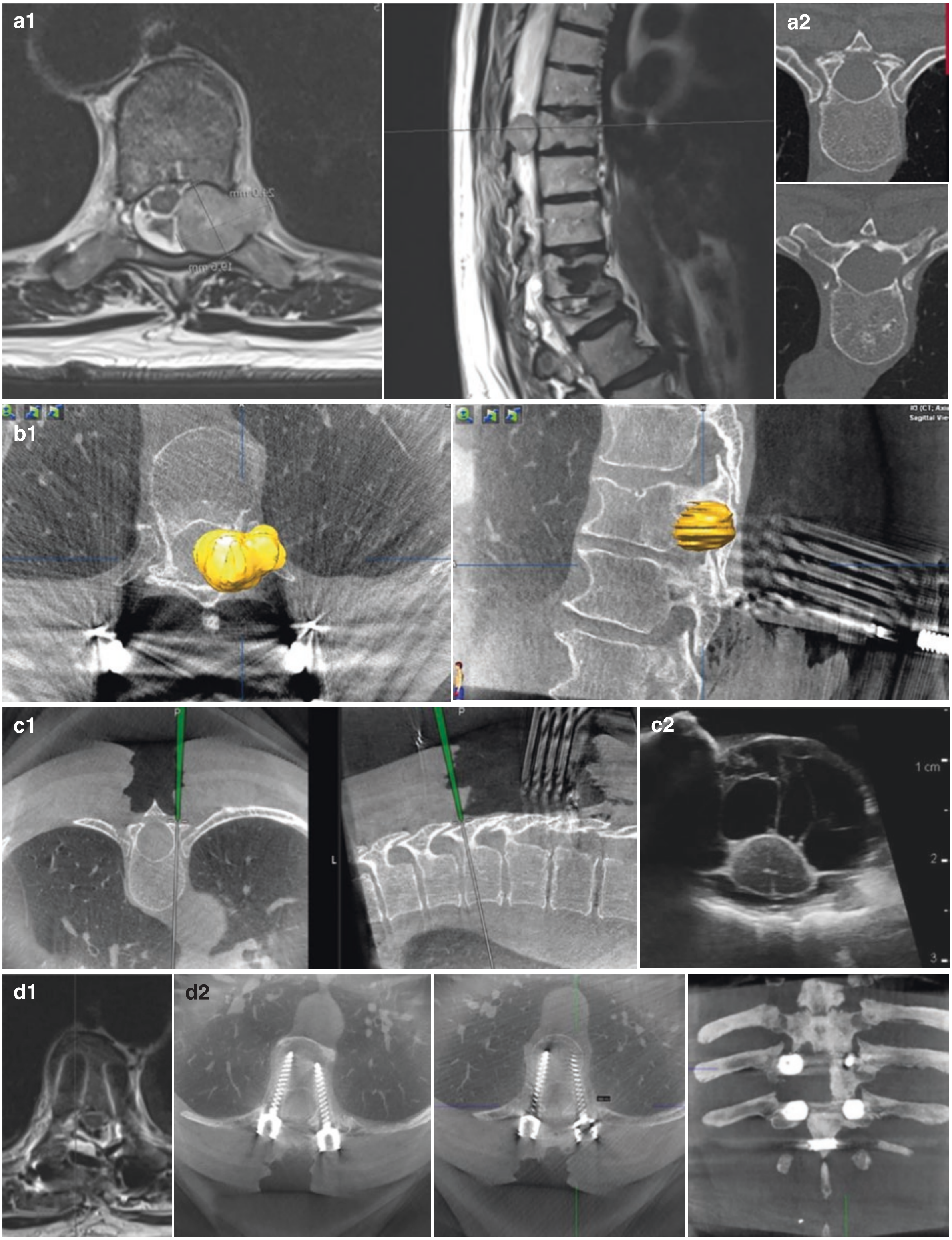

Fig. 2 (**a1**) Preoperative T2 MRI—thoracic T8 dumbbell tumour with intra and extraspinal extension. There is also old osteoporotic fracture T12 and evidence of cement augmentation T11. (**a2**) CT—narrow 'hairpin' size pedicles at T7 and T8. (**b1**) Intraoperative 3D X-ray (Ziehm) fused with preoperative imaging demonstrating tumour contour. (**c1**) Navigation guided pedicle cannulation using intraop 3D X-ray. (**c2**) Intraoperative ultrasound demonstrates no intradural extension of the tumour. (**d2**) Intraoperative 3D X-ray after pedicle screw insertion—showing accurate placement of the screws and extension of laminectomy. (**d1**) Postoperative MRI (24 h postop) confirms gross total tumour excision

4 Conclusion

Intraoperative navigation is a technology that helped us to improve intraoperative orientation to the unexposed anatomy and reduce the risk of iatrogenic complications; achieve better tumour resection; optimise the biomechanical construct; provide a safer learning environment for the spinal surgical trainees; minimise radiation exposure of the surgical team and shorten the operating time.

In our opinion, navigation was helpful not only to reduce the risk of complications but also, by providing millimetric accuracy and improving orientation, to perform procedures, which without navigation could have been considered inoperable or very high risk.

We have to emphasise that careful examination of the preoperative imaging as well as a sound knowledge of the regional anatomy remain paramount in any neurosurgical procedure. Image guidance in spine surgery, similar to more trivial navigation on the road, is an adjunct that can help to improve our results and the efficiency of our activity. However, it does not replace the basic principles of the anatomy and surgical knowledge, which should remain dominant.

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References

1. Castro WH, Halm H, Jerosch J, Malms J, Steinbeck J, Blasius S. Accuracy of pedicle screw placement in lumbar vertebrae. Spine. 1996;21:1320–4. https://doi.org/10.1097/00007632-199606010-00008.
2. Budu A, Sims-Williams H, Radatz M, Bacon A, Bhattacharyya D, Athanassacopoulos M, Ivanov M. Comparison of navigated versus fluoroscopic-guided pedicle screw placement accuracy and complication rate. World Neurosurg. 2020;144:e541–5. https://doi.org/10.1016/j.wneu.2020.08.207.
3. Ling JM, Dinesh SK, Pang BC, Chen MW, Lim HL, Louange DT, Yu CS, Wang CM. Routine spinal navigation for thoracolumbar pedicle screw insertion using the O-arm three-dimensional imaging system improves placement accuracy. J Clin Neurosci. 2014;21:493–8. https://doi.org/10.1016/j.jocn.2013.02.034.
4. Shin BJ, James AR, Njoku IU, Hartl R. Pedicle screw navigation: a systematic review and meta-analysis of perforation risk for computer-navigated versus freehand insertion. J Neurosurg Spine. 2012;17:113–22. https://doi.org/10.3171/2012.5.SPINE11399.
5. Tarawneh AM, Haleem S, D'Aquino D, Quraishi N. The comparative accuracy and safety of fluoroscopic and navigation-based techniques in cervical pedicle screw fixation: systematic review and meta-analysis. J Neurosurg Spine. 2021;1–8. https://doi.org/10.3171/2020.11.SPINE201877.
6. Jung YG, Jung SK, Lee BJ, Lee S, Jeong SK, Kim M, Park JH. The subaxial cervical pedicle screw for cervical spine diseases: the review of technical developments and complication avoidance. Neurol Med Chir. 2020;60:231–43. https://doi.org/10.2176/nmc.ra.2019-0189.
7. Xu RM, Ma WH, Wang Q, Zhao LJ, Hu Y, Sun SH. A freehand technique for pedicle screw placement in the lower cervical spine. Orthop Surg. 2009;1:107–12. https://doi.org/10.1111/j.1757-7861.2009.00023.x.
8. Ivanov M, Budu A, Sims-Williams H, Poeata I. Using intraoperative ultrasonography for spinal cord tumor surgery. World Neurosurg. 2017;97:104–11. https://doi.org/10.1016/j.wneu.2016.09.097.
9. Ivanov M, Wilkins S, Poeata I, Brodbelt A. Intraoperative ultrasound in neurosurgery - a practical guide. Br J Neurosurg. 2010;24:510–7. https://doi.org/10.3109/02688697.2010.495165.
10. Lee MT, Panbehchi S, Sinha P, Rao J, Chiverton N, Ivanov M. Giant spinal nerve sheath tumours - surgical challenges: case series and literature review. Br J Neurosurg. 2019;33:541–9. https://doi.org/10.1080/02688697.2019.1567678.
11. Mair R, Heald J, Poeata I, Ivanov M. A practical grading system of ultrasonographic visibility for intracerebral lesions. Acta Neurochir. 2013;155:2293–8. https://doi.org/10.1007/s00701-013-1868-9.
12. Ando K, Kobayashi K, Machino M, Ota K, Morozumi M, Tanaka S, Ishiguro N, Imagama S. Computed tomography-based navigation system-assisted surgery for primary spine tumor. J Clin Neurosci. 2019;63:22–6. https://doi.org/10.1016/j.jocn.2019.02.015.

Spinal Cord Stimulation Meets Them All: An Effective Treatment for Different Pain Conditions. Our Experience and Literature Review

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1 Introduction

Spinal Cord Stimulation (SCS) is an emerging minimally invasive technique which uses neuromodulation to manage different forms of intractable pain. This technique relies on the gate control theory in order to perform neuromodulation through the application of electrical stimuli [1, 2]. SCS is performed through implantation of epidural leads which are connected to a subcutaneous implantable pulse generator (IPG). Stimulation modalities and parameters can be easily modified in relation to pain location and patients' response.

As regards action mechanisms, SCS is capable of converting pain perception into different sensitive modalities. Traditionally, SCS electrical stimuli transform nociception into paresthesia. During the past few decades, technological improvement led to an extended range of stimulation modalities by the introduction of burst, high frequency, and multiple waveforms stimulation patterns [1–3].

SCS is a well-established treatment option for various pain conditions such as failed back surgery syndrome (FBSS), complex regional pain syndrome (CPRS), peripheral neuropathy (such as diabetic neuropathy), and pain related to chronic vascular ischemia (e.g., peripheral ischemia and angina pectoris). Nowadays, indications are ever increasing and SCS is used for the treatment of oncological pain, spinal cord injury, chronic back pain in "naïve" patients, neurological, genitourinary, and gastrointestinal disorders [1, 4].

In this study, we present our case series of 49 patients who underwent SCS at our Institution for the treatment of pain from different etiologies and discuss our 10-year experience with SCS. For the purpose of this study, we also performed a systematic review of current indications and new perspectives in SCS.

2 Materials and Methods

2.1 Case Series

From January 2011 to January 2021, 49 patients underwent SCS at our Institution for the treatment of pain from different etiologies. We included patients suffering from unbearable pain, with no response to drug or physical therapy, with a pre-operative NRS higher than 7/10. Exclusion criteria were presence of not stabilized psychiatric disorders and high surgical risks due to pre-existing severe diseases. Age was not considered as a criterion of exclusion, considering that spinal disorders are prevalent in elderly people. Each patient underwent implantation of a thoraco-lumbar spinal stimulator. Leads were implanted using a 16G Tuohy needle in the epidural space between T8 and L2, depending on the location and characteristics of pain; IPGs were implanted in the lumbar or abdominal region, based upon patients' skin thickness

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and body structure. All the procedures were performed by a single surgeon at our Institution. General and clinical data were recorded for each patient: location and side of pain, pre-operative drug response, pre- and post-operative pain evaluation, presence or absence of psychiatric disorders, positive or negative response to surgical treatment, complications of the SCS system, and post-operative reduction of drug use. Pain was assessed for each patient using a numeric rating scale for pain (NRS), ranging from 0 (no pain) to 10 (maximum tolerable pain). We considered the patient as a "responder" when post-operative NRS showed a reduction of three points; otherwise, we considered the patient as "not responder" to treatment.

2.2 Systematic Review

A comprehensive literature search and systematic review was performed, according to PRISMA guidelines. Queried databases were PubMed, Cochrane Review Database, Embase, and Google Scholar. A literature search was conducted in July 2021, the following medical subject headings (MeSH) and free text terms were combined: "Spinal Cord Stimulation AND failed back surgery syndrome" (499 results), "Spinal Cord Stimulation AND oncological pain" (243 results), "Spinal Cord Stimulation AND malignant pain" (174 results), "Spinal Cord Stimulation AND cancer" (600 results), "Spinal Cord Stimulation AND neoplastic pain" (10 results), "Spinal Cord Stimulation AND cancer pain" (242 results), "Spinal Cord Stimulation AND naive" (180 results), "Spinal Cord Stimulation AND naive patients" (23 results), "spinal cord stimulation AND diabetic neuropathy" (153 results). Reference lists of all publications and 2124 records were also screened. Only studies regarding the uses of SCS in different populations were included. Reviews, systematic reviews, concluded clinical trials, case series, case reports, and meta-analysis were included. Ongoing clinical trials were excluded. Exclusion criteria were lack of full text, non-English and non-Italian language, studies published prior to 10 years. Data extracted from each study were type of disease, specific application and level of evidence, size of sample (restricted to clinical trials and case series), and year of publication.

3 Results

3.1 Case Series

Our case series includes 49 consecutive patients (22 males and 27 females) who underwent SCS for the treatment of pain from different etiologies. For the purpose of this study, patients were differentiated into two different groups upon prior spinal surgery: in particular, patients who had undergone prior spinal surgery for back pain were defined as the "FBSS group," and patients suffering from different types of pain but who had never undergone surgery were defined as the "naive group". Among these patients, 36 were diagnosed with FBSS and assigned to the "FBSS group," while 13 patients with other chronic pain (diabetic neuropathy, spinal cord injury, refractory lumbar back pain without prior surgery, multiple myeloma) were assigned to the "naive group."

The "FBSS group" comprised 19 female and 17 male patients, with a median age of 60.89 years (range 36–84). Almost the totality of them underwent prior lumbar fixation, except for two patients who underwent lumbar diskectomy or decompression. FBSS was defined according to the International Association for the Study of Pain. Among them, 15 complained of back pain, 10 patients complained of leg pain, and 10 patients complained of both leg and back pain. As regards response to conservative therapy, 23 patients had undergone pain therapy without any improvement and in the totality of them pain was drug resistant. As regards mental status, five patients were affected by psychiatric comorbidities. As regards pain severity, median pre-operative NRS was 8.69 (range 7–10); while median post-operative NRS was 5.80 (range 2–10). As regards clinical response to SCS, 20 patients were classified as responders, while 16 patients were classified as "not responders" to SCS. Seven of them underwent subsequent system removal due to wound dehiscence (3 of 7), system rejection (1 of 7), subcutaneous infection (1 of 7), and displacement of the proximal electrode (1 of 7).

The "naive group" comprised 8 female and 5 male patients, with a median age of 66.15 years (range 45–79). Median pre-operative NRS was 8.23 (range 7–10); while median post-operative NRS was 4.69 (range 3–7). Ten patients were classified as responders, while two patients were classified as "not responders." Among the "not responders" group, one patient underwent system removal because of bacterial meningitis.

Patient demographics and clinical data of the case series are summarized in Table 1.

3.2 Systematic Review

A total of 2124 records were screened, and after removal of duplicates, 2037 citations were identified. We excluded ongoing clinical trials, articles lacking the full text, languages other than English and Italian, and studies published prior to 10 years.

From the literature, 359 potentially relevant studies were selected by title; 105 articles were selected by abstract screening; 73 full-text articles were assessed for eligibility; 36 studies were excluded.

Thirty-seven studies were included in the qualitative synthesis and data were retrieved in order to be summarized. Results of the literature review are summarized in Tables 2, 3, and 4.

Table 1 Summarized demographics and clinical characteristics of our case series. *NRS* numeric rating scale for pain, *QoL* quality of life, *FBSS* failed back surgery syndrome, *PDPN* painful diabetic peripheral neuropathy

Pt.	Gender age	Pathology	Lead, level	Clinical presentation	Pain localization	Previous pain therapy	Pre-op NRS	Post-op NRS	Response to SCS	QoL improvement	Reduction of opioids	Follow-up
1	M, 51 years	PDPN	1 octopolar lead, D9-D11	No previous surgery. Leg pain.	Leg, bilateral	Yes	9	4	Yes	Yes	Yes	2 years
2	F, 55 years	FBSS	2 octopolar leads, D8-D10 and D9-D11	Previous lumbar stabilization. Leg pain. History of psychiatric disorders.	Leg, unilateral	Yes	10	10	No, system removal	No	No	10 years
3	F, 52 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Leg pain.	Leg, unilateral	Yes	10	3	Yes	Yes	Yes	10 years
4	F, 55 years	FBSS	1 octopolar lead D7-D9	Previous lumbar stabilization. Leg pain.	Leg, unilateral	No	7	6	No, system removal	No	No	9 years
5	M, 69 years	FBSS	2 Octopolar leads D8-D10 and D11-L1	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	Yes	8	8	No, system removal	No	No	9 years
6	F, 36 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	No	9	8	No, system removal	No	No	9 years
7	M, 73 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back pain.	Back, unilateral	No	8	3	Yes	Yes	Yes	8 years
8	F, 60 years	FBSS	1 octopolar lead D7-D9	Previous lumbar stabilization. Back and leg pain. History of psychiatric disorders.	Back and leg, bilateral	No	9	3	Yes	Yes	Yes	7 years
9	M, 39 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	No	10	3	Yes	Yes	Yes	6 years
10	F, 48 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	Yes	8	8	No, system removal	No	No	6 years
11	F, 67 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Leg pain. History of psychiatric disorders.	Leg, unilateral	Yes	9	8	No	No	No	5 years
12	F, 77 years	FBSS	1 octopolar lead D7-D9	Previous lumbar stabilization. Leg pain.	Leg, unilateral	Yes	9	8	No	No	No	5 years
13	M, 59 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	Yes	7	7	No, system removal (wound complication)	No	No	5 years
14	F, 74 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back pain.	Back, bilateral	Yes	9	4	Yes	Yes	Yes	5 years
15	M, 62 years	FBSS	1 octopolar lead D7-D9	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	8	5	Yes	Yes	Yes	5 years
16	M, 76 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Leg pain.	Leg, unilateral	Yes	8	4	Yes	Yes	Yes	4 years

(continued)

Table 1 (continued)

Pt.	Gender age	Pathology	Lead, level	Clinical presentation	Pain localization	Previous pain therapy	Pre-op NRS	Post-op NRS	Response to SCS	QoL improvement	Reduction of opioids	Follow-up
17	F, 73 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain. History of psychiatric disorders.	Back and leg, bilateral	No	10	5	Yes	Yes	Yes	3 years
18	F, 48 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	No	9	4	Yes	Yes	Yes	3 years
19	F, 60 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	8	7	No	No	No	3 years
20	M, 80 years	FBSS	1 octopolar lead D9-D11	Previous lumbar decompression. Back pain.	Back, unilateral	Yes	8	7	No	No	No	3 years
21	F, 55 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	No	8	3	Yes	Yes	Yes	3 years
22	M, 52 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Leg pain.	Leg, bilateral	Yes	9	8	No system removal (wound complication)	No	No	3 years
23	M, 44 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	7	2	Yes	Yes	Yes	3 years
24	F, 62 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back pain.	Back, bilateral	Yes	9	9	No, system removal	No	No	4 years
25	M, 55 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back pain.	Back, unilateral	No	10	5	Yes	Yes	Yes	3 years
26	M, 67 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	8	3	Yes	Yes	Yes	3 years
27	M, 72 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back and leg pain.	Back and leg, unilateral	No	10	3	Yes	Yes	Yes	2 years
28	M, 71 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	No	8	5	Yes	Yes	Yes	2 years
29	F, 69 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	10	7	Yes	Yes	Yes	2 years
30	M, 44 years	FBSS	1 octopolar lead D8-D10	Previous lumbar discectomy. Leg pain.	Leg, unilateral	Yes	8	8	No, system removal (wound complication)	No	No	2 years
31	M, 56 years	FBSS	1 octopolar lead D8-D10	Previous lumbar stabilization. Back and leg pain.	Back and leg, bilateral	Yes	8	4	Yes	Yes	Yes	2 years
32	F, 84 years	FBSS	1 octopolar lead D6-D9	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	9	9	No, system removal	No	No	2 years
33	F, 69 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, bilateral	No	8	9	No, system removal (subcutaneous infection)	No	No	2 years

34	M, 64 years	FBSS	2 octopolar leads, D9-D1 and D10-D12	Previous lumbar stabilization. Back pain. History of psychiatric disorders.	Back, unilateral	Yes	10	6	Yes	Yes	Yes	2 years
35	F, 37 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Leg pain.	Leg, bilateral	No	10	10	No, system removal (lead migration)	No	No	1 year
36	F, 73 years	FBSS	1 octopolar lead D9-D11	Previous lumbar stabilization. Back pain.	Back, unilateral	Yes	10	4	Yes	Yes	Yes	3 years
37	M, 55 years	FBSS	1 paddle D9-D11	Previous lumbar stabilization. Leg pain.	Leg, bilateral	Yes	7	3	Yes	Yes	Yes	2 years
38	M, 71 years	Naive	1 paddle D12-L2	No previous surgery. Leg pain.	Leg, bilateral	Yes	8	4	Yes	Yes	Yes	9 years
39	M, 75 years	Naive	1 octopolar lead D8-D10	No previous surgery. Leg pain.	Leg, bilateral	Yes	9	3	Yes	Yes	Yes	5 years
40	F, 78 years	Naive	1 octopolar lead D8-D10	No previous surgery. Leg pain.	Leg, unilateral	Yes	7	3	Yes	Yes	Yes	5 years
41	M, 79 years	Naive	1 octopolar lead D9-D11	No previous surgery. Back and leg pain.	Back and leg, unilateral	Yes	9	4	Yes	Yes	Yes	2 years
42	M, 77 years	Naive	1 octopolar lead D7-D9	No previous surgery. Back and leg pain.	Back and leg, bilateral	Yes	9	4	Yes	Yes	Yes	2 years
43	F, 71 years	Naive	1 octopolar lead D9-D11	No previous surgery. Back and leg pain.	Back and leg, bilateral	Yes	10	6	Yes	Yes	Yes	2 years
44	F, 66 years	Naive	1 octopolar lead D8-D10	No previous surgery. Back and leg pain.	Back and leg, unilateral	Yes	7	7	No, system removal (meningitis)	No	No	2 years
45	F, 74 years	Naive	1 elettrodo ottopolare D6-D8	No previous surgery. Back pain.	Back, unilateral	Yes	7	7	No, system removal	No	No	1 year
46	F, 54 years	Naive	1 octopolar lead D8-D10	No previous surgery. Back pain.	Back, unilateral	Yes	8	3	Yes	Yes	Yes	1 year
47	F, 66 years	Naive	1 octopolar lead D8-D10	No previous surgery. Back and leg pain.	Back and leg, unilateral	Yes	7	7	No, system removal and following fixation	No	No	3 years
48	F, 45 years	Oncologic pain	1 octopolar lead D11-L1	No previous surgery. Back and leg pain.	Back and leg, bilateral	Yes	9	5	Yes	Yes	Yes	6 months
49	F, 53 years	Spinal cord injury	1 octopolar lead D8-D10	No previous surgery. Back and leg pain.	Back and leg, bilateral	Yes	8	4	Yes	Yes	Yes	7 years

Table 2 Summary of literature review regarding SCS for the treatment of FBSS. *NRS* numerical rating scale for pain, *VAS* visual analog scale for pain, *ODI* Oswestry Disability Index, *EQ-5D-5L* European Quality of Life–Five Dimensions, version 5L score, *SCS* spinal cord stimulation, *IPG* implantable pulse generator, *OMM* optimal medical management, *HF-SCS* high frequency SCS, *HD-SCS* high density SCS, *C-SCS* conventional SCS

Authors-year	Study design	N. of patients	Gender	Age (mean)	Pathology	Pre-op pain evaluation	Pain laterality/ localisation	Post op pain evaluation	Improvement of QoL	Opioids reduction	Follow-up
Kapural et al. 2016 [5]	Multicenter RCT	198 (101 HF10 therapy) (97 traditional SCS)	Female 62% in HF10 group, 58.6% in SCS group	54.6 in HF10 group, 55.2 in SCS group	FBSS other (see article)	Back pain VAS 7.4 in HF10 group Back pain VAS 7.8 in SCS group Leg pain VAS7.1 in HF10 group Leg pain VAS 7.6 in SCS group	Predominant back pain: 56.4% in HF10 group, 52.6% in SCS group	Back pain VAS 2.4 in HF10 group Back pain VAS 4.5 in SCS group Leg pain VAS 2.4 in HF10 group Leg pain 3.9 in SCS group	Significant improvement in ODI Score	N/A	2 years
Farber et al. 2017 [6]	Retrospective review	122.827 FBSS patients (5328 underwent SCS)	Female 53.7%, male 42.7%	58.8	FBSS	N/A	N/A	N/A	N/A	N/A	9 years
De Andres et al. 2017 [7]	Prospective RCT	60 patients randomized: 29 HF-SCS 31 C-SCS	37.9% male 62.1% female	53.79 (C-SCS group; 51.62 HF-SCS group)	FBSS	Mean NRS 7.60 (S-SCS) 7.69 (HF SCS)	N/A	20/25% reduction	ODI 4 points reduction	N/A	1 years
Scalone et al. 2018 [8]	Observational study	80	32 male	58	FBSS	9.2 NRS	Low back and/ or legs	See article	See article	N/A	4 months
Nissen et al. 2019 [9]	Retrospective Single Center Case Series	224	Male 52% Female 48%	48 years	FBSS	N/A	Back and/or legs	N/A	7% complete recover 62% substantial improvement 25% little improvement 3% no change 2% substantial decline 2% total failure	N/A	5 years

Rigoard et al. 2019 [10]	Multicenter RCT	278	Female 60.6%	53.9 years	FBSS	Back pain 7.5 NPRS Leg pain 5.3 NPRS	Back or leg neuropathic pain	≥2-point NPRS reduction in LBP In 43.0% of SCS patients	EQ-5D-5L, ODI, SF-36 improvement at 12 and 24 months (see article)	N/A	2 years
Harman et al. 2020 [11]	Retrospective Single Center Case Series	16	Female 12 (75%) Male 4 (25%)	50 (35–80)	FBSS	Back pain 8 NPRS Leg pain 8 NPRS	Leg and back neurophatic pain	Significant improvement in NPRS score	Significant improvement in ODI score	N/A	2 years
De Jaeger et al. 2020 [12]	Multicentric retrospective case series	78	Male 25 (32.1%) Female 53 (67.9%)	56	Refractory FBSS (already treated with S-SCS)	Low back pain NRS 7 Leg pain 7 NRS	Leg and low back pain	Conversion from standard SCS to HD-SCS is effective in a subgroup of refractory SCS (see article)	Significant improvement of EQ5D-3L	N/A	1 years
Remacle et al. 2020 [13]	Observational single-center study	62	35 female 27 male	54	FBSS refractory to OMM	Back VAS 9, leg VAS 7	Back and/or legs	See article	See article	See article	5 years
Do et al. 2021 [14]	Monocenter prospective serie	208	127 female (61%)	52	FBSS	Back VAS 8.1 Leg VAS 8.6	Back pain, leg pain, back + leg pain	At 24 months back VAS 4.7, leg VAS 4.9	EQ5D score halved and ODI duplicated in 24 months	N/A	2 years
Goudman et al. 2020 [15]	Retrospective cohort study	119	78 female 41 male	51.5	FBSS	Severe back pain 88.24% Severe leg pain 63.56%	Back pain 63.02%, leg pain 17.65%, back + leg 19.33%	Severe back pain 31.10% severe leg pain	ODI and EQ5D EL significative improvement	N/A	N/A
Nissen et al. 2020 [16]	Retrospective cohort study	211 (164 SCS patients)	N/A	N/A	FBSS	N/A	N/A	N/A	N/A	N/A	2 years
De Jaeger et al. 2019 [17]	Retrospective case series	81	37 males (45.7%), 44 females (54.3%)	54.6	FBSS	Low back pain 8 NRS Leg pain 8 NRS	N/R	At 3 months LBP NRS 4 and leg NRS 3	ODI value halved at 3 months	N/A	3 months
Benyamin et al. 2020 [18]	Open-label, prospective, multicenter study	64 (32 with IPG implant)	53% female 47% male	57.5	FBSS	NRS overall 7.5	Back and legs	Overall NPRS 3.8 at 3 months	EQ5D5L 0.58 ODI 51.5	N/A	3 months

(continued)

Table 2 (continued)

Authors-year	Study design	N. of patients	Gender	Age (mean)	Pathology	Pre-op pain evaluation	Pain laterality/ localisation	Post op pain evaluation	Improvement of QoL	Opioids reduction	Follow-up
Kapural et al. 2020 [19]	Retrospective clinical assessment	105	Female 58.1% Male 41.9%	60	Refractory FBSS	VAS 8.3	N/A	VAS 3.32	N/A	Reduction from 60.3 to 32.1 mg	2 years
Kallewaard et al. 2021 [20]	Prospective, multicenter, open-label study	70	43 female 27 male	51.5	Chronic intractable back and leg pain (63 pts.) Chronic intractable leg pain (7 pts.)	Leg pain VAS 7.7 Back pain VAS 5.6	Leg pain: unilateral 36 patients bilateral 34 patients	At 12 months 68% leg pain remitters and 80% back pain remitters	Significant improvement in ODI Score (62% pts); improvement in HADS depression and anxiety scale	Significant reduction in opioids intake	1 years
Motov et al. 2021 [21]	Single center experience	39	53% female 47% male	69	FBSS	VAS back 8.1 VAS leg 4.9	Neuropathic back and leg pain, LBP without neuropathic pain	VAS back 2.9 VAS leg 2.2	N/A	N/A	10 months
Breel et al. 2021 [22]	Multicenter, randomized, double blinded, crossover clinical study	32	19 female	49	FBSS	VAS 6.8	Unilateral neuropathic pain	VAS	EQ 5D 3L 0.843; improvement of SF36 and sleep	N/A	12 months
Witkam et al. 2021 [23]	Case series patients interview	13	4 female 9 male	54	FBSS	NRS 6.38	N/A	NRS 3.76	31% significant pain relief (≥50%). 54% improvement of enjoyment of life (≥50%).	N/A	2.8 years

Table 3 Summary of literature review regarding SCS for the treatment of oncological pain. *PTN* Posttorachotomy neuralgia, *VAS* visual analog scale for pain, *ADL* activities of daily living, *QoL* quality of life

Authors-year	Study design	No. pts	Gender	Age (mean)	Pathology	Pre-op. pain evaluation	Treatment	Pain laterality	Clinical presentation	Post-op. pain evaluation	Improvement of QoL	Reduction of opioids use	Follow-up
Maeda et al. 2020 [24]	Case report	1	Male	66	Malignant Pleural Mesothelioma (MPM)	NRS = 8	Burst SCS	Unilateral	Pain from the left lower scapula to the left axilla and lower edge of the breast	NRS = 4	Significant increase in his daily life activities; decrease in sleep disturbance	Reduction of 180 mg total oral morphine equivalents	9 months
Yakovlel et al. 2008 [25]	Case report	2	1 Male	51	Squamous cell carcinoma of the anus	VAS (rest) = 2–4 VAS (activities) = 8	Conventional SCS	Unilateral	Burning pain at the left groin site of inguinal metastases	VAS = 1–2	Significant increase in his daily life activities	Stop using all pain medications	12 months
			1 Female	43	Metastatic colon carcinoma (radiation-induced pain)	VAS = 5–9	Conventional SCS	Unilateral	Burning, throbbing, and shooting pain in low back and right lower extremity	VAS = 1	Increase level of functioning, improved sleep and ADL's	Totally stop using of opioids medications	12 months
Yakovlel et al. 2012 [26]	Retrospective study	15	M/F = 9/6	56	Colon, anal cancer, or angiosarcoma of the sacrum (no evidence of local recurrences or metastases)	VAS = 7 (range from 6 to 9)	Conventional SCS	Bilateral	Burning, aching, throbbing, sharp and shooting stabbing pain over the low back, intermittently radiating to lower extremities	VAS = 1.8 (range from 1 to 4)	N/A	8 stop 5 decrease use of opioid medications 2 unchanged	12 months
Nouri et al. 2011 [27]	Case report	1	Male	57	Prostate carcinoma (after prostatectomy)	VAS = 5	Conventional SCS	Unilateral	Progressive burning and stabbing left scrotal and inguinal pain	VAS = 1	N/A	Stop all oral analgesics	6 weeks
Mirpuri et al. 2015 [28]	Case report	1	Female	65	Hereditary multiple osteochondromas (HMO)	VAS = 5 (at rest). VAS = 9 (during activities)	Conventional SCS	Bilateral	Pain in the lumbar, pelvis, femur, and tibial regions	VAS = 1–2	Increased ADL such as being able to climb steps more easily	Complete discontinuation of opioids medications	6 months

(continued)

Table 3 (continued)

Authors-year	Study design	No. pts	Gender	Age (mean)	Pathology	Pre-op. pain evaluation	Treatment	Pain laterality	Clinical presentation	Post-op. pain evaluation	Improvement of QoL	Reduction of opioids use	Follow-up
Cata et al. 2004 [29]	Case report	2	Male	65	Melanoma (pain-related chemiotherapy)	VAS = 4.5 (Med-on). VAS = 9.3 (Med-off)	Conventional SCS	Bilateral	Bilateral constant and burning pain in lower extremities	VAS = 2	N/A	Decrease use of opioids	4 months
				46	Ewing Sarcoma (pain-related chemioterapy)	VAS = 8.8	Conventional SCS	Bilateral	Burning, dull pain at lower extremites.	VAS = 3	N/A	Decrese use of opioids	3 months
Wininger et al. 2012 [30]	Case report	1	Female	58	Squamous cell carcinoma of the lung (PTN):	VAS = 8–9/10	Conventional SCS	Unilateral	Persistent pain in the chest wall on right side. Sharp jabbing pain along the right rib, traversing to below right breast. Pain exacerbated with all upper limb movements and coughing.	VAS = 1–2/10 (reduction of almost 75% of pain)	Increased ADL (continued tolerance for daily activities, including leisure time and social activities and the ability to relax, as well as a feeling of increased independence)	Complete discontinuation of analgesic medications	24 months
Yakovlel et al. 2010 [31]	Case Series	14	10 male 4 female	54	N/A	VAS = 7.5 (mean value)	Conventional SCS	Bilateral	Constant burning, aching, stabbing pain over the chest wall	VAS = 2 (mean value)	N/A	4: decrease use of opioid 10: stop opioids	12 months
Viswanathan et al. 2010 [32]	Case Series	4	3 male 1 female	38.7	Hemangiomatosis, Rhabdosarcoma, Spindle cell carcinoma, Chondrosarcoma	N/A	Conventional SCS	Unilateral	Phantom limb pain	Reduction of >80%	N/A	N/A	8–66 months

Elahi et al. 2013 [33]	Case report	1	Male	59	Stage IV prostate cancer (pain-related radiotherapy)	VAS = 8	Conventional SCS	Unilateral	Deep, aching, and sharp with an occasional burning quality pain in the left pelvic and perineal region with intermittent radiation to the testicles and the left groin.	VAS = 1	Great improvement in QoL	Discontinued use of opioids	10 months
Yakovlel et al. 2012 [34]	Case report	1	Male	55	Right upper lobe lung carcinoma + lumbar laminectomy	N/A	Conventional SCS	Bilateral	Intractable right chest wall pain, chronic low back pain, and bilateral lower extremity pain	Reduction of >50%	N/A	Discontinued use of opioids	12 months
Abd Elsayed et al. 2016 [35]	Case report	1	Female	30	Breast cancer (pain-related chemotherapy)	VAS = 8	Conventional SCS	Bilateral	Nonradiating, constant, sharp, burning, and stabbing pain on bilateral lower extremity	Reduction of about 95%	Marked improvement in ability to perform daily activities; less dependent on others to help; improvement in sleep pattern	Discontinued use of opioids	24 months
Hutson et al. 2017 [36]	Case report	1	Female	69	History of breast cancer and thyroid cancer with a metastatic lesion in the sacrum	N/A	Conventional SCS	Unilateral	Low back pain with radicular pain of the right thigh along the S1 and S2 distribution	Reduction of >60%	Walking without pain, in great spirits.	Discontinued use of opioids	1 month
Lee et al. 2009 [37]	Case report	1	Female	40	Spinal T5 meningioma	VAS = 9	Conventional SCS	Unilateral	Right posterior calf and sole dull pain in resting state and aggravated when walking	VAS = 1	Increased QoL and improve sleep	Important reduction of analgesic drugs assumption	8 months

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Table 4 Summary of literature review regarding SCS for the treatment of back and leg pain in "naïve" patients. *HF-SCS* high frequency spinal cord stimulation, *HD-SCS* high density spinal cord stimulation, *VAS* visual analog scale for pain, *ADL* activities of daily living, *QoL* quality of life, *LBP* lumbar back pain

Authors-year	Study design	No of patients	Gender	Age (mean)	Pathology	Pre-op. pain evaluation	Treatment	Pain laterality	Clinical presentation	Post-op. pain evaluation	Improvement of QoL	Reduction of opioids use	Follow up
Ahmadi et al. 2017 [38]	Prospective single-center study	8	4 male 4 female	60.0	LBP alone or in conjunction with leg pain	NRS = 8.8 (back pain) and 8.1 (leg pain)	HF-SCS	Unilateral/bilateral	Radicular and non radicular pain	NRS = 4.75 (back pain) and 2.36 (leg pain)	N/A	N/A	306 days (mean value)
Al Kaisy et al. 2017 [39]	Prospective, open-label study	21	12 male 9 female	43.0	LBP alone or in conjunction with leg pain	Back VAS = 7.9 ± 1.3. Leg VAS = 3.3 ± 2.1	HD-SCS	Unilateral/bilateral	N/A	Back VAS = 2.3 leg VAS = 1.9	Significant increasing in QoL	64% of reduction in opioid use	12 months
Al Kaisy et al. 2020 [40]	Prospective study	27	9 male 18 female	50.3	LBP alone or in conjunction with leg pain	Back VAS = 7.7 ± 0.2. Leg VAS = 7.3 ± 0.3	HF-SCS	Unilateral/bilateral	Radicular and non radicular pain	Reduction of 62% in back pain and 68% in leg pain	Great improvement in QoL and ADL	Important reduction of opioid intake	12 months
Baranidharan et al. 2020 [41]	Prospective study	21	7 male 14 female	46.2	Lumbar back pain alone or in conjunction with leg pain	Back pain VAS = 8 Leg pain VAS = 5	HF-SCS	Unilateral/bilateral	N/A	Back pain VAS = 3 Leg pain VAS = 2.8	Significant increasing in QoL	6/14-stop opioid medications; 1/14 reduce opioid medications; 7/14—no change	12 months

4 Discussion

Spinal Cord Stimulation is a well-established option for the treatment of various pain conditions such as FBSS, CPRS, and pain from chronic vascular ischemia. It has been shown to be a clinically effective intervention for intractable pain that has been refractory to conventional medical management [42]. The aim of this article is to highlight the potential beneficial role of SCS not only for the treatment of FBSS but also for the treatment of "naive" non-surgical cases, such as CPRS, peripheral neuropathy, vascular ischemic pain, oncological pain, spinal cord injury, chronic back pain in non-surgical patients, neurological, genitourinary, and gastrointestinal disorders. This technique may be a therapeutic alternative for patients who have exhausted all available treatments or who have an increased risk for or prefer not to have more invasive interventions.

4.1 SCS for FBSS

FBSS is a frequent condition, affecting between 10 and 40% of patients after lumbar back surgery [3, 43, 44]. It is defined by the "International Association for the Study of Pain (IASP)" as "*Lumbar spinal pain of unknown origin either persisting despite surgical intervention or appearing after surgical intervention for spinal pain originally in the same topographical location"* [13, 45].

FBSS does not necessarily define a failed surgical procedure, but rather a technically successful procedure that has not been able to produce improved, long-term clinical outcomes in terms of pain reduction and improvements in QoL and ADLs. Remarkably, the rate of success drops exponentially with each subsequent surgery [46, 47].

Chronic pain caused by failed back surgery syndrome is typically associated with a higher pain score, increased opioid use, lower health-related quality of life (HRQoL), and higher functional disability when compared to the general population and to other pain etiologies [14, 43].

The etiology of FBSS may be determined by a large variety of pre-operative and post-operative risk factors. Among the pre-operative ones: the lack of an accurate diagnosis of the patient's etiology of pain (which should influence the type of surgery); economic factors; behavioral factors such as smoking, obesity, and psychological attitude of the patient. Postoperative factors include altered biomechanics from spinal surgery and progression of degenerative changes [45, 48–50].

Treatments for FBSS range over a large variety of options, from the less invasive and conservative management to the most invasive surgical procedure [8, 45, 46, 49, 51].

Conservative management for FBSS include exercise, physical therapy, rehabilitation and medical management [41]. Unfortunately, patients affected by chronic pain often become refractory to conventional medical treatment. Overall drug resistance may be as high as 5% of cases [52–54].

Invasive procedures for treating FBSS include interventional techniques (such as epidural steroid injections, nerve blocks, adhesiolysis for treatment of postoperative scar formation, radiofrequency ablation of nerves), neuromodulation and neurostimulation (through spinal cord stimulation, dorsal root ganglion stimulation), and revision surgery [45, 46].

Surgical revision for FBSS patients is often associated with a high morbidity and corresponding low rates of success. For these reasons, surgical options for the treatment of FBSS should be limited to last line therapy [45].

Spinal Cord Stimulation (SCS) is an effective therapy for several chronic and neuropathic pain conditions, such as failed back surgery syndrome (FBSS) [42]. SCS is delivered through electrodes placed in the dorsal epidural space in order to interfere with nociceptive pathway arising from the painful area. Since its introduction in clinical practice, standard SCS with 30–80 Hz electrical stimulation has undergone several technical innovations and over time the implantable pulse generators (IPGs) became more efficient, rechargeable, smaller, with several output capabilities, giving the possibility to adapt the treatment to the need of each individual patient [12, 45, 46, 55–58]. Furthermore, SCS is one of the few operative treatments that is not only reversible but allows patients to try clinical effects prior to moving forward with the definitive implantation [6].

As regards the economic impact of SCS, implantation of an SCS system results in short-term costs increase; but the annual cumulative costs decrease during the following years after implantation, when compared to the costs of conventional management [6].

Nowadays, a large variety of SCS techniques have become available in clinical practice. They differ by typology and localization of leads (dorsal root ganglion electrode, multicolumn or monocolumn, octopolar or 16-polar), and by stimulation parameters (frequency, waveform, amplitude) [55]. The so-called paresthesia free techniques adopt higher electrical frequency than conventional SCS (up to 10 kHz). Other frequently used "paresthesia free" SCS modalities are "burst stimulation" and high density (HD) stimulation [3, 52].

Some multicentric clinical trials and literature reviews have shown "non inferior" or rather "superior" results when compared to the conventional SCS technology. This is related to the greater possibilities of neuromodulation and the evidence that many patients prefer the absence of paresthesia allowed by these new modalities of SCS [22, 59]. In our case series, the results are really promising, showing 52.8% of patients responding to treatment. Among the remaining patients, 8 patients (47% of the not responder group) were obliged to remove systems due to complications.

4.2 SCS for "Naive Patients" and Other Indications

Beyond the application for the treatment of FBSS, SCS has also been used for the treatment of other types of chronic non-oncological pain such as neuropathic pain and chronic back pain ineligible for surgical intervention. This evidence paved the way to establishing the potential role of SCS also for the treatment of oncological pain. However, the effectiveness and relative safety of SCS for cancer-related pain has not yet been adequately established [60].

Oncological pain represents an important burden for the public health care system. The mainstay of therapy relies on opioid medication and many patients develop drug resistance, with progressive intractable pain in up to 38% of cancer patients and decreased QoL [25, 61, 62]. Additionally, adverse effects from pain-related medications represent a considerable challenge for clinicians and patients [63].

Causes of cancer pain are multifactorial and complex [59, 64]. Moreover, the etiology of pain may be related to primary or metastatic disease in two-thirds of patients, whereas other causes including surgery, chemotherapy, radiation, immobility, osteoporosis, and infection may lead to pain in a third of patients [63]. Owing to its complex pathophysiology, oncological pain may favorably respond to SCS [64–67]. According to this, SCS may be considered as an early treatment in case of medical refractory pain to prevent the chronicity of the neuropathic component of oncological pain.

One of the first retrospective studies aimed to demonstrate the effectiveness of SCS in the treatment of cancer-related pain was conducted by Shimoji et al. in 1993. In this study, 52 consecutive oncological patients with intractable pain underwent SCS with a reduction of pain of at least 50% [68]. These results were confirmed by Yakovlev et al., who showed how SCS is able to relieve painful symptoms in patients with various types of cancer, with a marked improvement in QoL and significant reduction in opioid usage [26, 31]. Other evidence about the effectiveness of SCS for the treatment of oncological pain in various cancer patients came from several singular experiences. In particular, the persistent effectiveness of SCS in terms of pain reduction, opioid termination, and improved daily activities and QoL has been reported in cases of spinal meningiomas [37], hemangiomatosis, rhabdosarcoma, spindle cell carcinoma, chondrosarcoma [32], hereditary multiple osteochondromas [28], melanoma, Ewing sarcoma [29], and breast cancer [35].

Radiation therapy and chemotherapy may be a cause of severe neuropathy in cancer patients. Even in the case of neuropathic pain, it has been reported that SCS may be effective for the treatment of primary or secondary neuropathy [33, 63, 69]. As regards post-surgical pain in cancer patients, it has been reported that SCS is a valuable treatment also for post-surgical neuralgia [27, 30], and even for phantom limb pain [32].

Nowadays, literature about SCS in cancer-related pain conditions is still scarce. However, based on the evidence of SCS for the treatment of FBSS and other non-cancer condition, it seems likely that SCS can be a useful and effective therapy in many of the challenging cancer-related pain syndromes such as post radiation neuropathic pain, chemotherapy-induced peripheral neuropathies, and post-surgical pain syndromes [63]. In this regard, in our case series, we have successfully treated a patient affected by multiple myeloma; achieving a marked and sustained improvement of pain during the entire follow-up and a reduction of opioid usage.

Given the abovementioned evidence of SCS effectiveness for the treatment of FBSS and oncological pain in cancer patients, the treatment of pain in non-oncological and "naive" surgery patients represents a recent field of application. We previously defined "naive patients" as those patients suffering from different types of pain but who had never undergone surgery. Among the etiologies which have been treated by SCS, chronic neuropathic pain may be effectively treated by new stimulation modalities.

Indeed, preliminary evidence suggests that 10 kHz SCS (also known as high-frequency—HF, or high-dose stimulation) can improve symptoms in back pain patients who never underwent surgery [39, 40, 70]. HF-SCS employs higher frequencies than common SCS (60–200 Hz). Potential mechanisms of action for pain relief with high-frequency stimulation include axonal conduction block, desynchronization of axonal activity, and glial-neuronal interactions [3, 52, 71].

In a prospective study, Ahmadi et al. demonstrated the efficacy of HF-SCS in reducing pain, with a sustained clinical improvement up to 1 year during follow-up [38]. Another prospective study conducted by Baranidharan et al. highlighted the clinical benefit related to the use of HF-SCS in treating lumbar back pain alone or in conjunction with leg pain in a cohort of 21 naïve patients [41]. Taken together, these findings suggest that short-term use of 10 kHz SCS may confer benefits to patients with non-surgical low back pain.

According to this evidence, HF-SCS therapy may significantly reduce chronic low back pain and associated disability in non-surgical medically refractory patients with no past history of surgery, increasing their physical function and quality of life up to 1 year from the SCS implant. According to literature results, we treated eight naïve patients, with medical-refractory lumbar or/and leg pain and five of them showed a marked and sustained reduction of pain. The dogma that considers SCS for chronic lower back pain as a treatment option only in cases of FBSS should be revisited if these results are confirmed through an appropriately designed randomized controlled trial [40].

Noteworthy, two other possible etiologies of medical refractory pain in naïve patients are painful diabetic peripheral neuropathy (PDPN) and pain related to chronic vascular ischemia. There is a growing body of literature suggesting that SCS may be effective in treating PDPN, though the role of spinal stimulation remains under debate [2]. As a matter of fact, in a prospective multicenter clinical trial which assessed the SCS long-term outcomes and complications in PDPN patients, it has been shown that an SCS success rate was observed in nearly 55% of the patients after 5 years, underlying that SCS is effective in reducing chronic pain in lower limbs related to PDPN also in long-term follow-up, with an odd of success indirectly related to the severity of PDPN-related pain [72]. In our experience, a single patient with PDPN has been successfully treated by SCS, with a marked reduction of pain and a sustained improvement of symptoms up to 2-years follow-up. In other prospective multicenter RCT assessing the effectiveness of SCS in combination with the best medical treatment (BMT) (SCS group) compared with BMT only (BMT group) in patients with PDPN, a success rate of 59% in SCS patients compared to patients treated with BMT only has been demonstrated. However, this study highlighted how SCS is not a risk-free procedure and it should be applied as a last resort treatment, given the invasiveness of this procedure [73]. Also, claudication and pain from untreatable chronic ischemia seems to be well responsive to spinal cord stimulation and this is relevant when revascularization cannot be completed due to patient comorbidities. In these patients, SCS may be considered as a lower morbidity and lower cost option rather than CABG, with good pain relief outcomes [74]. Nevertheless, both for PDPN and angina-related pain, further randomized clinical trials are mandatory.

5 Conclusions

Spinal Cord Stimulation is a well-established option in FBSS treatment FBSS, and SCS has also been used for the treatment of “naive” patients, suffering from other types of chronic, non-oncological, and medical-refractory pain such as neuropathic pain and chronic back pain ineligible for surgical intervention.

In the emerging field of employment, SCS may also be effective for the treatment of oncological pain. In fact, SCS may be considered as an early treatment in case of medical refractory pain to prevent the chronicity of the neuropathic component of oncological pain.

As regards “naive” patients, HF-SCS may significantly reduce chronic low back pain and associated disability in non-surgical medically refractory patients with no past history of surgery, increasing their physical function and quality of life up to 1 year from the SCS implant.

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Harmsen IE, Hasanova D, Elias GJB, Boutet A, Neudorfer C, Loh A, Germann J, Lozano AM. Trends in clinical trials for spinal cord stimulation. Stereotact Funct Neurosurg. 2021;99(2):123–34.
2. Rock AK, Truong H, Park YL, Pilitsis JG. Spinal cord stimulation. Neurosurg Clin N Am. 2019;30(2):169–94.
3. Sdrulla AD, Guan Y, Raja SN. Spinal cord stimulation: clinical efficacy and potential mechanisms. Pain Pract. 2018;18(8):1048–67.
4. Graziano F, Gerardi RM, Lo Bue E, Basile L, Brunasso L, Somma T, Maugeri R, Nicoletti G, Iacopino DG. Surgical back risk syndrome and spinal cord stimulation: better safe than sorry. World Neurosurg. 2020;133:e658–65.
5. Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz high-frequency and traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain 24-month results from a multicenter, randomized, controlled pivotal trial. Neurosurgery. 2016;79(5):667–77.
6. Farber SH, Han JL, Elsamadicy AA, Hussaini Q, Yang S, Pagadala P, Parente B, Xie J, Lad SP. Long-term cost utility of spinal cord stimulation in patients with failed back surgery syndrome. Pain Physician. 2017;20(6):E797–805.
7. De Andres J, Monsalve-Dolz V, Fabregat-Cid G, Villanueva-Perez V, Harutyunyan A, Asensio-Samper JM, Sanchis-Lopez N. Prospective, randomized blind effect-on-outcome study of conventional vs high-frequency spinal cord stimulation in patients with pain and disability due to failed back surgery syndrome. Pain Med (United States). 2017;18(12):2401–21.
8. Scalone L, Zucco F, Lavano A, et al. Benefits in pain perception, ability function and health-related quality of life in patients with failed back surgery syndrome undergoing spinal cord stimulation in a clinical practice setting. Health Qual Life Outcomes. 2018;16(1):1–14.
9. Nissen M, Ikäheimo T-M, Huttunen J, Leinonen V, von und zu Fraunberg M. Long-term outcome of spinal cord stimulation in failed back surgery syndrome: 20 years of experience with 224 consecutive patients. Neurosurgery. 2019;84(5):1011–8.
10. Rigoard P, Basu S, Desai M, et al. Multicolumn spinal cord stimulation for predominant back pain in failed back surgery syndrome patients: a multicenter randomized controlled trial. Pain. 2019;160(6):1410–20.
11. Harman F, Aydin S, Sencan S, et al. Percutaneous spinal cord stimulation for failed back surgery syndrome: a retrospective study. Turk Neurosurg. 2020;30(5):739–45.
12. De Jaeger M, Goudman L, Brouns R, De Smedt A, Linderoth B, Eldabe S, Moens M. The long-term response to high-dose spinal cord stimulation in patients with failed back surgery syndrome after conversion from standard spinal cord stimulation: an effectiveness and prediction study. Neuromodulation. 2020;24:546. https://doi.org/10.1111/ner.13138.

13. Remacle T, Mauviel S, Renwart HJ, Ghassempour K, Belle F, Lückers O, Bex V, Remacle JM, Bonhomme V. Long-term multicolumn-lead spinal cord stimulation efficacy in patients with failed back surgery syndrome: a six-year prospective follow-up study. World Neurosurg. 2020;142:e245–52.
14. Do TT, Smet I, Jerjir A, Vandamme K, Devos M, Van Buyten JP. Real-world analysis: long-term effect of spinal cord stimulation with different waveforms for patients with failed back surgery syndrome. Pain Pract. 2021;21(2):215–25.
15. Goudman L, Van Buyten J-P, De Smedt A, Smet I, Devos M, Jerjir A, Moens M. Predicting the response of high frequency spinal cord stimulation in patients with failed back surgery syndrome: a retrospective study with machine learning techniques. J Clin Med. 2020;9(12):4131.
16. Nissen M, Ikäheimo T-M, Huttunen J, Leinonen V, Jyrkkänen H-K, von Und Zu Fraunberg M. Higher preimplantation opioid doses associated with long-term spinal cord stimulation failure in 211 patients with failed back surgery syndrome. Neuromodulation. 2021;24(1):102–11.
17. De Jaeger M, Goudman L, Eldabe S, Van Dongen R, De Smedt A, Moens M. The association between pain intensity and disability in patients with failed back surgery syndrome, treated with spinal cord stimulation. Disabil Rehabil. 2019;43(15):2157–63. https://doi.org/10.1080/09638288.2019.1694084.
18. Benyamin R, Galan V, Hatheway J, et al. Options: a prospective, open-label study of high-dose spinal cord stimulation in patients with chronic back and leg pain. Pain Physician. 2020;23(1):87–98.
19. Kapural L, Sayed D, Kim B, Harstroem C, Deering J. Retrospective assessment of salvage to 10 kHz spinal cord stimulation (SCS) in patients who failed traditional SCS therapy: RESCUE study. J Pain Res. 2020;13:2861–7.
20. Kallewaard JW, Gültuna I, Hoffmann V, et al. 10 kHz spinal cord stimulation for the treatment of failed back surgery syndrome with predominant leg pain: results from a prospective study in patients from the Dutch healthcare system. Pain Pract. 2021;21(5):490–500.
21. Motov S, Aftahy K, Jörger A-K, Wagner A, Meyer B, Shiban E. High-frequency spinal cord stimulation in failed back surgery syndrome patients with predominant low back pain—single-center experience. Neurosurg Rev. 2021;2021:1–10.
22. Breel J, Wille F, Wensing AGCL, Kallewaard JW, Pelleboer H, Zuidema X, Bürger K, de Graaf S, Hollmann MW. A comparison of 1000 Hz to 30 Hz spinal cord stimulation strategies in patients with unilateral neuropathic leg pain due to failed back surgery syndrome: a multicenter, randomized, double-blinded, crossover clinical study (HALO). Pain Ther. 2021;10:1189. https://doi.org/10.1007/s40122-021-00268-7.
23. Witkam RL, Kurt E, van Dongen R, Arnts I, Steegers MAH, Vissers KCP, Henssen DJHA, Engels Y. Experiences from the patient perspective on spinal cord stimulation for failed back surgery syndrome: a qualitatively driven mixed method analysis. Neuromodulation. 2021;24(1):112–25.
24. Maeda A, Watanabe M, Saigano C, Nakayama S, Yamaura K. Spinal cord stimulation alleviates intractable pain due to malignant pleural mesothelioma: a case report. JA Clin Rep. 2020;6:78. https://doi.org/10.1186/s40981-020-00386-9.
25. Yokovlev AE, Ellias Y. Spinal cord stimulation as a treatment option for intractable neuropathic cancer pain. Clin Med Res. 2008;6:103. https://doi.org/10.3121/cmr.2008.813.
26. Yakovlev AE, Resch BE. Spinal cord stimulation for cancer-related low back pain. Am J Hosp Palliat Med. 2012;29(2):93–7.
27. Nouri KH, Brish EL. Spinal cord stimulation for testicular pain. Pain Med. 2011;12(9):1435–8.
28. Mirpuri RG, Brammeier J, Chen H, Hsu FPK, Chiu VK, Chang EY. Spinal cord stimulation for treatment of the pain associated with hereditary multiple osteochondromas. J Pain Res. 2015;8:557. https://doi.org/10.2147/JPR.S86790.
29. Cata JP, Cordella JV, Burton AW, Hassenbusch SJ, Weng HR, Dougherty PM. Spinal cord stimulation relieves chemotherapy-induced pain: a clinical case report. J Pain Symptom Manag. 2004;27(1):72–8.
30. Wininger KL, Bester ML, Deshpande KK. Spinal cord stimulation to treat postthoracotomy neuralgia: non-small-cell lung cancer: a case report. Pain Manag Nurs. 2012;13(1):52–9.
31. Yakovlev AE, Resch BE, Karasev SA. Treatment of cancer-related chest wall pain using spinal cord stimulation. Am J Hosp Palliat Med. 2010;27(8):552–6.
32. Viswanathan A, Phan PC, Burton AW. Use of spinal cord stimulation in the treatment of phantom limb pain: case series and review of the literature. Pain Pract. 2010;10(5):479–84.
33. Elahi F, Callahan D, Greenlee J, Dann TL. Pudendal entrapment neuropathy: a rare complication of pelvic radiation therapy. Pain Physician. 2013;16(6):793–8.
34. Yakovlev AE, Resch BE. Treatment of multifocal pain with spinal cord stimulation. Neuromodulation. 2012;15:210. https://doi.org/10.1111/j.1525-1403.2012.00435.x.
35. Abd-Elsayed A, Schiavoni N, Sachdeva H. Efficacy of spinal cord stimulators in treating peripheral neuropathy: a case series. J Clin Anesth. 2016;28:74–7.
36. Hutson N, Hung JC, Puttanniah V, Lis E, Laufer I, Gulati A. Interventional pain management for sacroiliac tumors in the oncologic population: a case series and paradigm approach. Pain Med. 2017;18:959. https://doi.org/10.1093/pm/pnw211.
37. Lee MG, Choi SS, Lee MK, Kong MH, Lee IO, Oh HR. Thoracic spinal cord stimulation for neuropathic pain after spinal meningioma removal: a case report. Clin J Pain. 2009;25(2):167–9.
38. Ahmadi SA, Vesper J, Schu S, Slotty PJ. High-frequency spinal cord stimulation in surgery-naïve patients—a prospective single-center study. Neuromodulation. 2017;20(4):348–53.
39. Al-Kaisy A, Palmisani S, Smith TE, Pang D, Lam K, Burgoyne W, Houghton R, Hudson E, Lucas J. 10 kHz high-frequency spinal cord stimulation for chronic axial low back pain in patients with no history of spinal surgery: a preliminary, prospective, open label and proof-of-concept study. Neuromodulation. 2017;20(1):63–70.
40. Al-Kaisy A, Van Buyten JP, Kapural L, Amirdelfan K, Gliner B, Caraway D, Subbaroyan J, Edgar D, Rotte A. 10 kHz spinal cord stimulation for the treatment of non-surgical refractory back pain: subanalysis of pooled data from two prospective studies. Anaesthesia. 2020;75:775. https://doi.org/10.1111/anae.15036.
41. Baranidharan G, Feltbower R, Bretherton B, Crowther T, Cooper L, Castino P, Radford H. One-year results of prospective research study using 10 kHz spinal cord stimulation in persistent nonoperated low back pain of neuropathic origin: maiden back study. Neuromodulation. 2021;24(3):479–87.
42. Pouratian N, Sheth SA. Stereotactic and functional neurosurgery - principles and applications. Berlin: Springer Nature; 2020. https://doi.org/10.1007/978-3-030-34906-6.
43. De Jaeger M, Goudman L, Putman K, De Smedt A, Rigoard P, Geens W, Moens M. The added value of high dose spinal cord stimulation in patients with failed back surgery syndrome after conversion from standard spinal cord stimulation. J Clin Med. 2020;9(10):3126.
44. Maugeri R, Graziano F, Giugno A, Iacopino DG. A new concept to treat lumbar spine stenosis in a mini invasive way. J Neurosurg Sci. 2021;61:347. https://doi.org/10.23736/s0390-5616.16.03277-x.
45. Baber Z, Erdek MA. Failed back surgery syndrome: current perspectives. J Pain Res. 2016;9:979–87.
46. Amirdelfan K, Webster L, Poree L, Sukul V, McRoberts P. Treatment options for failed back surgery syndrome patients with refractory

chronic pain: an evidence based approach. Spine (Phila Pa 1976). 2017;42:S41–52.
47. Giugno A, Gulì C, Basile L, Graziano F, Maugeri R, Visocchi M, Iacopino DG. Spinal cord stimulation: an alternative concept of rehabilitation? Acta Neurochir Suppl. 2017;124:15–8.
48. Brunasso L, Basile L, Iacopino DG, Gulì C, Graziano F, Pino MA, Nicoletti GF, Tumbiolo S, Maugeri R. All that glitters is not gold: a spinal epidural empyema following epidural steroid injection. Surg Neurol Int. 2020;11:240. https://doi.org/10.25259/SNI_340_2020.
49. Daniell JR, Osti OL. Failed back surgery syndrome: a review article. Asian Spine J. 2018;12(2):372–9.
50. Waszak PM, Modric M, Paturej A, Malyshev SM, Przygocka A, Garnier H, Szmuda T. Spinal cord stimulation in failed back surgery syndrome: review of clinical use, quality of life and cost-effectiveness. Asian Spine J. 2016;10(6):1195–204.
51. Cho JH, Lee JH, Song KS, Hong JY, Joo YS, Lee DH, Hwang CJ, Lee CS. Treatment outcomes for patients with failed back surgery. Pain Physician. 2017;20(1):E29–43.
52. Giammalva GR, Iacopino DG, Azzarello G, Gaggiotti C, Graziano F, Gulì C, Pino M, Maugeri R. End-of-life care in high-grade glioma patients. The palliative and supportive perspective. Brain Sci. 2018;8(7):125.
53. Isagulyan E, Slavin K, Konovalov N, Dorochov E, Tomsky A, Dekopov A, Makashova E, Isagulyan D, Genov P. Spinal cord stimulation in chronic pain: technical advances. Korean J Pain. 2020;33(2):99–107.
54. Moisset X, Bouhassira D, Avez Couturier J, et al. Pharmacological and non-pharmacological treatments for neuropathic pain: systematic review and French recommendations. Rev Neurol (Paris). 2020;176(5):325–52.
55. Caylor J, Reddy R, Yin S, et al. Spinal cord stimulation in chronic pain: evidence and theory for mechanisms of action. Bioelectron Med. 2019;5(1):1–41.
56. Hamm-Faber TE, Gültuna I, van Gorp EJ, Aukes H. High-dose spinal cord stimulation for treatment of chronic low back pain and leg pain in patients with FBSS, 12-month results: a prospective pilot study. Neuromodulation. 2020;23(1):118–25.
57. Mekhail N, Visnjevac O, Azer G, Mehanny DS, Agrawal P, Foorsov V. Spinal cord stimulation 50 years later: clinical outcomes of spinal cord stimulation based on randomized clinical trials - a systematic review. Reg Anesth Pain Med. 2018;43(4):391–406.
58. Peeters JB, Raftopoulos C. Tonic, burst, high-density, and 10-kHz high-frequency spinal cord stimulation: efficiency and patients' preferences in a failed back surgery syndrome predominant population. Review of literature. World Neurosurg. 2020;144:e331–40.
59. Maugeri R, Graziano F, Basile L, Gulì C, Giugno A, Giammalva GR, Visocchi M, Iacopino DG. Reconstruction of vertebral body after radiofrequency ablation and augmentation in dorsolumbar metastatic vertebral fracture: analysis of clinical and radiological outcome in a clinical series of 18 patients. Acta Neurochir Suppl. 2017;124:81–6. https://doi.org/10.1007/978-3-319-39546-3_13.
60. Zejun Z, Lihua P, Ke W, Su M, Bennett MI. Spinal cord stimulation for cancer-related pain in adults. Cochrane Database Syst Rev. 2011. https://doi.org/10.1002/14651858.cd009389.
61. Bhaskar A. Interventional pain management in patients with cancer-related pain. Postgrad Med. 2020;132(Suppl 3):13–6.
62. Tapias Pérez JH. Spinal cord stimulation: beyond pain management. Neurol (Engl Ed). 2021. https://doi.org/10.1016/j.nrleng.2019.05.007.
63. Hagedorn JM, Pittelkow TP, Hunt CL, D'Souza RS, Lamer TJ. Current perspectives on spinal cord stimulation for the treatment of cancer pain. J Pain Res. 2020;13:3295. https://doi.org/10.2147/JPR.S263857.
64. Chwistek M. Recent advances in understanding and managing cancer pain. F1000Research. 2017;6:945. https://doi.org/10.12688/f1000research.10817.1.
65. Burchiel KJ, Raslan AM. Contemporary concepts of pain surgery. J Neurosurg. 2019;130(4):1039–49.
66. Maugeri R, Giammalva GR, Cicero G, De Luca R, Gulì C, Graziano F, Basile L, Giugno A, Iacopino DG. Unusual case of dorsal vertebral metastases from a male breast cancer. Acta Medica Mediterr. 2017;2017:1157–61. https://doi.org/10.19193/0393-6384_2017_6_181.
67. Maugeri R, Giugno A, Giammalva RG, Gulì C, Basile L, Graziano F, Iacopino DG. A thoracic vertebral localization of a metastasized cutaneous Merkel cell carcinoma: case report and review of literature. Surg Neurol Int. 2017;8:190. https://doi.org/10.4103/sni.sni_70_17.
68. Shimoji K, Hokari T, Kano T, Tomita M, Kimura R, Watanabe S, Endoh H, Fukuda S, Fujiwara N, Aida S. Management of intractable pain with percutaneous epidural spinal cord stimulation: differences in pain-relieving effects among diseases and sites of pain. Anesth Analg. 1993;77(1):110–6.
69. Hamid B, Haider N. Spinal cord stimulator relieves neuropathic pain in a patient with radiation-induced transverse myelitis. Pain Pract. 2007;7(4):345–7.
70. Maugeri R, Basile L, Gulì C, Banco A, Giordano G, Giugno A, Graziano F, Giammalva RG, Iacopino DG. Percutaneous pedicle-lengthening osteotomy in minimal invasive spinal surgery to treat degenerative lumbar spinal stenosis: a single-center preliminary experience. J Neurol Surg A Cent Eur Neurosurg. 2018;79(5):365–71.
71. Graziano F, Scalia G, Cammarata G, Lo Bue E, Brunasso L, Maugeri R, Umana GE, Gerardi RM, Iacopino DG, Nicoletti GF. Letter to the Editor regarding "First report of extraspinal lead migration along a thoracic spinal nerve after spinal cord stimulation". World Neurosurg. 2021;145:536–7. https://doi.org/10.1016/j.wneu.2020.09.024.
72. Van Beek M, Geurts JW, Slangen R, Schaper NC, Faber CG, Joosten EA, Dirksen CD, Van Dongen RT, Van Kuijk SMJ, Van Kleef M. Severity of neuropathy is associated with long-term spinal cord stimulation outcome in painful diabetic peripheral neuropathy: five-year follow-up of a prospective two-center clinical trial. Diabetes Care. 2018;41:32. https://doi.org/10.2337/dc17-0983.
73. Slangen R, Schaper NC, Faber CG, Joosten EA, Dirksen CD, Van Dongen RT, Kessels AG, Van Kleef M. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. Diabetes Care. 2014;37:3016. https://doi.org/10.2337/dc14-0684.
74. Eldabe S, Thomson S, Duarte R, Brookes M, Debelder M, Raphael J, Davies E, Taylor R. The effectiveness and cost-effectiveness of spinal cord stimulation for refractory angina (RASCAL study): a pilot randomized controlled trial. Neuromodulation. 2016;19:60. https://doi.org/10.1111/ner.12349.

Rheumatoid Diseases Involving the Cervical Spine I. History, Definition, and Diagnosis: New Trends and Technologies

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1 Cervical Spine Anatomy

Understanding the anatomy of the cervical spine is of outmost importance to understand its involvement in inflammatory rheumatic diseases. The craniovertebral junction (CCJ) separates the skull base from the subaxial cervical spine and provides cranial flexion, extension, and axial rotation functions. The components that make up the CCJ are responsible for support and protection of the cervicomedullary structures within. Ligaments and articulation of the occipitoatlantoaxial complex control the mobility and restriction of movement. The ring of atlas (C1) articulates with the skull base through to the occipital condyle and it is confined by the tectorial membrane. The atlas is also connected to the skull by the atlantooccipital membrane, which connects the C1 anterior arch to the anterior margin of the foramen magnum.

The anterior arch of C1 articulates with the odontoid process of C2 in a synovial joint that is constrained by the transverse ligament, which holds the dens to the anterior arch of C1 via a "strap-like" mechanism and avoids anterior translation of C1 relative to C2 [1].

Injuries to the cervical spine are namely atlanto-axial instability (AAI), atlanto-axial subluxation (AAS), vertical axis subluxation (VS) (also known as cranial settling), and subaxial subluxation (SAS).

The AAS is characterized by a weakening or rupture of ligaments and subchondral bone erosion in the atlanto-axial joints. It can be visualized on a plain radiograph by an anterior atlantodental interval (AADI) >3 mm and a posterior atlantodental interval (PADI) <14 mm.

Cranial settling is the vertical translocation of dens into the foramen magnum and is defined as a migration of the odontoid process >4.5 mm above the McGregor line. The SAS is defined by a subluxation in the joints C3–7 due to destruction of the joint surface and the ligaments between the processes spinosis. On a plain radiograph there is a horizontal displacement of vertebrae with an irreducible translation >3.5 mm [2].

Cervical spine disease may be seen in rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), and spondyloarthritis (SpA), especially psoriatic arthritis (PsA) [3], as shown in the following paragraphs.

2 Rheumatoid Arthritis

The prevalence of RA worldwide is approximately 0.5–1% of the population with a women to men ratio of a 3:1 [4]. Male incidence rises dramatically with age, whereas female incidence keeps on rising until the age of 45, has its plateau at the age of 75, and eventually falls in the elderly [5, 6]. Neck pain is the most frequent symptom of spinal involvement in RA; it occurs in 40–80% of patients and is mostly localized at the craniocervical junction [7]. Risk factors for cervical involvement are male sex, presence of rheumatoid factor and anti-citrullinated protein antibodies (ACPA), rheumatoid nodules, severe peripheral disease with early and extensive development of erosive damages, intense systemic inflammatory response at onset, long-term disease and prolonged use of corticosteroids. Moreover, a relationship between cervical arthritis and peripheral erosive disease has been established [8, 9]. In these patients, inflammation of the atlanto-axial joint produces odontoid erosion and ligamentous laxity [10]. Moreover, facet joint, uncovertebral joints, retrodental bursa, interspinous ligament, and ligament around the atlas involvement can be appreciated leading to cervical spine instability and subsequent myelopathy [11].

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Anterior AAS is the most common presentation, followed by lateral AAS (20%) and posterior AAS (7%). Posterior AAS takes place when the anterior arc of the atlas has shifted to the odontoid process. SAS can be found in 20% of cases.

Vertical subluxation (VS) occurs in 20% of patients with cervical spine involvement. VS is more common in patients with erosive or mutilating disease than those with minimal peripheral disease [12, 13].

Despite that most patients are asymptomatic [14], joint arthropathy, muscle wasting, decreased range of motion, compressive neuropathy, or a combination of these factors might be experienced and shall be promptly recognized to allow timely diagnosis. Neck pain may be present, and it occurs with the involvement of the craniovertebral-junction [15]. The latter takes place at atlanto-axial instability (AAI) or cranial settling which can compress occipital nerves between atlas and axis.

Compression of the C2 spinal nerve or greater auricular nerve can determine migraine or neck, mastoid, ear or facial pain [16].

Compression of brainstem and vertebral artery leads to tinnitus, vertigo, visual disturbance, diplopia, and dysphagia [14].

Compression of the vagus and glossopharyngeal nerve provokes dysphagia, compression of the hypoglossal nerve dysarthria, compression of the spinal trigeminal tract facial dysesestesia [16], and compression of the superior spinal cords and cervicomedullary junction the Lhermitte's sign (an electric shock sensation with forward flection of the head) [14, 16].

Spinal cord compression brings about myelopathy and its symptomatology: muscle weakness and atrophy, gait impairment, limb paresthesia, hyperreflexia, spasticity, lack of proprioception, bladder and bowel disorders.

In extreme cases paralysis can be present for syringomyelia or locked-in syndrome [8].

3 Spondyloarthritis

This group includes seronegative diseases (negative rheumatoid factor), such as ankylosing spondylitis (AS), PsA, reactive arthritis, arthritis associated with inflammatory bowel disease, and undifferentiated SpA. SpA do not frequently involve the cervical spine, while PsA tends to involve the cervical spine early in the disease, AS involves the cervical spine in advanced disease [17]. In SpA, instabilities are rare, probably due to new bone formation, as the characteristic lesions of the disease are syndesmophytes, parasyndesmophytes, and ankylosis [17].

AS occurs in 0.02% of the population [18] and affects the spine and the sacroiliac joints, while extra-axial manifestations include acute uveitis, peripheral arthritis, enthesitis, psoriasis, aortic root, and gut inflammation. Although once believed to affect men predominantly, recent evidence suggests women are affected equally but experience milder symptoms.

In the most severe forms, the condition is associated with macroscopic changes such as the progressive ossification of the spinal ligaments and ankylosis of the facet joints eventually leading to a totally stiff spine (the so-called "bamboo spine" appearance on the radiographs) [19].

The primary symptom in AS is inflammatory back pain, usually dull and insidious in onset and felt deep in the lower back or buttocks. It is frequently associated with morning rigidity (lasting for 30 min or more), fatigue, enthesitis, and peripheral arthritis. The fused spinal column is associated with stiffness, restricted spinal movements, and osteoporosis which increases the risk of fractures of the spine in these patients with devastating neurological complications [20]. Although atlantoaxial instability can occur in patients with AS, it is not as common as in patients with RA [17].

Among the different types of cervical injuries, anterior atlanto-axial subluxation (AAS) is present in up to 21% of cases, while vertical AAS is only found in 2%, and it has been found to correlate with high levels of C reactive protein (CRP), peripheral arthritis, the degree of sacroiliitis, uveitis, and the use of biological treatment [21]. Clinically significant spontaneous AAS can lead to spinal cord compression if it is not recognized and stabilized. In 16% of the AS population ossification of the posterior longitudinal ligament is seen and it may lead to myelopathy [22].

The study by Maas et al. [23] showed that cervical facet joints were frequently involved in AS: 52% of AS patients had syndesmophytes and 25% had ankylosis of the facet joints. Interestingly, in this study, 26% and 13% of patients who underwent biological treatment developed new syndesmophytes and facet joint ankylosis, respectively, within 4 years. Among the predisposing conditions linked to the destruction of the facet joints a longer disease duration, presence of uveitis, psoriasis, or inflammatory bowel diseases, as well as high disease activity, a high modified stroke ankylosing spondylitis spinal score (mSASSS), the presence of syndesmophytes, and an increased occiput to wall distance measured at clinical assessment were included.

PsA is an inflammatory musculoskeletal disease associated with cutaneous psoriasis. Psoriasis has a prevalence of 2–4% in Western adults [24] and 20–30% of psoriatic patients will develop PsA [24].

Men and women are almost equally affected between the ages of 40 and 50 years. Cervical spine involvement in psoriatic arthritis is observed in 35–75% of cases and it occurs most frequently in severe psoriatic arthritis with a long-standing disease [17], especially in patients with the polyarticular subtype of PsA [25].

In a previous study, the duration of psoriatic arthritis and the presence of radiocarpal erosions were prognostic factors for cervical spine disease, but no correlation was found regarding the severity of skin or nail disease [26].

Blau et al. categorized C-spine involvement in PsA into two heterogeneous groups: ankylosing and rheumatoid-like. While the first group is more commonly encountered and is characterized by the presence of ankylosis, syndesmophytes, and ligamental calcification, rheumatoid-like PsA tends to be erosive and is associated with AAS [27].

In a study conducted by Laiho et al., inflammatory cervical spine changes were not commonly seen in patients with PsA. The most common change was apophysial joint ankylosis, accounting for 11% of patients, followed by anterior AAS, seen in 8% of patients [28].

A recently reported case of a PsA patient presenting with four limb paresthesia and gain difficulty caused by C1–C2 instability was successfully treated with instrumented posterior arthrodesis C1, C2, C3, C4, and C5 associated with laminectomy C3, C4, and C5 [29], suggesting that C1–C2 instability should be systematically checked on the dynamic cervical spine X-ray, in the case of neurological symptoms.

In the Van Tilt et al. study [30] three PsA patients with increasing cervical pain and loss of mobility were described. Each of them showed specific radiographic characteristics, suggesting that in psoriatic arthritis different mechanisms underlie the cervical involvement. Specifically, two patients reported bone edema at MRI, while one patient showed new bone formation around the odontoid process with ossification of the ligamentum transversum. These findings suggest a possible entheseal involvement as seen in spondyloarthropathies in general, underscoring a different nature from the one occurring in RA.

4 Juvenile Idiopathic Arthritis

JIA is the most common idiopathic inflammatory arthritis affecting children younger than 16 years of age and lasting 6 weeks or longer [31]. JIA is a heterogeneous group of arthritis characterized primarily by peripheral joint arthritis. Although chronic arthritis is mandatory for all subtypes, the extraarticular and the systemic manifestations characterized every specific subtype [31]. Disease complications of JIA can vary from growth retardation and osteoporosis secondary to treatment and disease activity, to life-threatening macrophage activation syndrome with multi-organ insufficiency. In the JIA, the cervical spine can be affected in up to 80% of patients, most commonly in those with the polyarticular subtype, followed by enthesitis-related arthritis group. Rate of occurrence in seronegative and seropositive patients is similar [32]. In JIA, early apophyseal bone ankylosis is characteristic, in addition to impaired spinal growth [16].

According to a recent review [17], the most striking features of JIA are early cervical spine apophyseal joint ankyloses, observed in up to 41% of patients, accompanied by bone growth developmental disturbances, such as vertebral or disc hypoplasia caused by chronic inflammation and long-term steroid use. Fusion typically begins at the C2/C3 level, and patients with early-onset JIA are at increased risk. Erosions and subluxations, similar to those observed in RA, also occur. Other less specific features include ligamental calcifications.

Regarding subluxations, anterior AAS has been observed in up to 33% of seropositive patients which were predisposed to severe anterior AAS. Dens erosions were seen in up to 19% of cases, while SAS was seen in up to 7% [33].

5 Imaging Modalities

The first line imaging modality for assessing cervical involvement in the above mentioned inflammatory arthropathies is radiography, both static and dynamic. Classic radiography is relatively effective in the detection of bone lesions and C-spine alignment. The most used views include lateral and anteroposterior (AP) projections, with the latter used for alignment and Luschka joint assessment. On the other hand, in rheumatology settings, functional lateral projections are often requested to assess subluxations, especially at the C1, C2 level. The significant limitation of plain radiography of the craniovertebral junction is the superimposition of anatomical structures, which is especially common when rotational instability is present. The lack of functional views and reliance only on lateral neutral projection leads to failed radiological diagnosis in almost 50% of cases [34].

Plain radiographs are indeed limited to appreciate visualization of bony erosions, craniocervical junction, cervicothoracic junction, and pannus and spinal cord compression.

The indication to repeat such imaging comes every 2 years or upon arrival of new symptomatology [33]. CT and MRI are suggested to patients when cervical spine disease is confirmed or when neurological symptomatology is detected [12].

Computed tomography (CT) is mainly used preoperatively; although it is superior in the assessment of soft tissue involvement when compared to radiography, it is still inferior to MRI, especially in the context of spinal cord and nerve root imaging. CT scans on one hand provide valuable information concerning erosions, assessment of ankylosis or pseudoarthrosis, but on the other hand, it must be taken into account that CT scans provide little soft tissue information at a price of high radiation dosage [33].

MRI allows for a more precise diagnosis of C-spine lesions, especially in terms of early diagnosis. MRI is the most sensitive imaging technique to establish cervical spine involvement [35, 36]. It is considered the gold standard for brainstem, spinal cord, or nerve root involvement. MRI shows cysts, erosions of the dens or spinous processes, or vertebral endplates and spinal cord involvement in the cervical spine. Typical MRI protocols include sagittal T1 and T2-weighted sequences, T2 STIR (short tau inversion recovery), and axial T2-weighted images. Optionally, the coronal T2-weighted sequence can be used, primarily to evaluate lateral subluxation. Furthermore, sagittal post contrast T1-weighted images can be used to assess active inflammatory lesions, mainly synovitis. Fluid sensitive sequences with fat saturation are preferred for visualizing bone marrow edema [37]. Drawbacks of MRI include that it is expensive, time-consuming, and not eligible for carriers of ferromagnetic implants and pacemakers [38].

6 Rheumatoid Arthritis

Myelopathy can be classified according to the Ranawat classification. It is useful in evaluating patients, deciding treatment and assessing results. Class I patients have no neural deficit, Class II patients have subjective weakness with hyperreflexia and dysesthesia, and Class III has been subdivided into IIIA for ambulatory patients and IIIB for the remnants [8].

According to Zoli et al., conventional radiography allowed detection of 41.3% of patients with craniocervical involvement, but only in advanced stages of the disease. However, MR imaging had the unique potential of direct and detailed synovial visualization, especially in the gadolinium enhanced axial images, resulting in the early diagnosis of craniocervical RA [35]. The same concept is underlined by Di Gregorio et al. who carried out a study where 38 patients affected by RA were screened for craniocervical involvement by conventional radiography, unenhanced Computed Tomography (CT) and Gadolinium-enhanced Magnetic Resonance Imaging (MRI) of the cervical spine. Eventually, the cervical spine involvement was assessed in 25/38 (66%) patients (20 women and 5 men). In particular, in 13 of them (mean disease duration 12.7 years), the diagnosis was made by radiography which showed atlantoaxial and subaxial subluxations and/or erosions. Of the 12 patients with negative conventional radiography (mean disease duration 2.5 years), 4 were identified with both CT and MRI (synovial pannus and erosions), 3 with MRI only (joint effusion/hypervascularized synovial pannus), and five exhibited questionable CT findings which were clarified only by MR demonstration. This study strengthen the idea that MRI is the most sensitive imaging tool [39].

A great-deal of information can be derived by imaging but precious data is also gained by bioptical specimen. Interestingly O'Brien et al. have undergone a histologic review of surgical specimens of dens in 33 myelopathic chronic RA patients. The histologic specimens suggested that ligamentous destruction was followed by replacement of the rheumatoid synovium with fibrous tissue, whereas the osseous structures revealed severe destruction secondary to mechanical instability, rather than to an acute inflammatory process. Therefore, this study was in line with the idea that early, preemptive surgical intervention can prevent the development of spinal cord injuries caused by instability [10]. Moreover, two different histologic patterns were determined. Type I synovium had a recognizable synovial structure without no hyperplastic synovial layer, no significant inflammatory cell population, and no lymphocytic infiltration typical of early active rheumatoid synovium. Type II synovium was a bland, fibrous, hypercellular and hypovascular tissue with little synovium and few inflammatory cells. Patients with Type II synovium were older and presented with more advanced neurologic involvement caused by spinal cord compression [10].

The former study agrees with the concept later expressed by Shen FH et al. according to which if such patients are left untreated a large percentage of them will progress toward complex instability patterns resulting in significant morbidity and mortality. Moreover, it was underlined that once myelopathy occurs, prognosis for neurologic recovery and long-term survival is poor [40].

7 Juvenile Inflammatory Arthritis

A very recently published study [41] aimed to assess the frequency of cervical spine lesions on radiographs and MRI in JIA patients with clinical signs of cervical spine involvement and to verify if with the addition of MRI, the use of radiographs could be abandoned. This retrospective study evaluated 34 children with JIA and with clinical involvement of cervical spine. In each patient, both radiographs and MRI of the cervical spine were performed. Authors concluded that the cervical spine lesions are still a frequent complication affecting up to 35% of JIA patients. Most of them develop serious complications, such as AAS and ankylosis. Despite advantages of MRI in terms of the imaging of the atlantoaxial region, radiography shows superiority in diagnosis of AAS and SAS.

8 Conclusions

Cervical involvement in inflammatory rheumatic diseases is still frequent and quite disabling, yet few data are present in the recent literature. However, such involvement may lead to severe acute complications that might be masked by the chronic pain frequently experienced by these patients.

Therefore, cervical spine involvement should always be investigated by the physician to avoid the dramatic neurological consequences that it could bring about.

References

1. Gillick JL, Wainwright J, Das K. Rheumatoid arthritis and the cervical spine: a review on the role of surgery. Int J Rheumatol. 2015;2015:252456. https://doi.org/10.1155/2015/252456. Epub 2015 Aug 17. PMID: 26351458; PMCID: PMC4553335.
2. Janssen I, Nouri A, Tessitore E, Meyer B. Cervical myelopathy in patients suffering from rheumatoid arthritis—a case series of 9 patients and a review of the literature. J Clin Med. 2020;9(3):811. https://doi.org/10.3390/jcm9030811. PMID: 32191997; PMCID: PMC7141180.
3. Sudoł-Szopińska I. Diagnostyka obrazowa zapalnych chorób reumatycznych. Warszawa: PZWL Wydawnictwo Lekarskie; 2016.
4. Magarelli N, Simone F, Amelia R, Leone A, Bosello S, D'Antona G, Zoli A, Ferraccioli G, Bonomo L. MR imaging of atlantoaxial joint in early rheumatoid arthritis. Radiol Med. 2010;115(7):1111–20. https://doi.org/10.1007/s11547-010-0574-4. English, Italian. Epub 2010 Jul 31. PMID: 20680496.
5. De Lorenzis E, Crudo F, Fedele AL, Fiorita A, Bruno D, Paludetti G, Alivernini S, Giraldi L, Picciotti PM, Zoli A, Cadoni G. Postural control and disability in patients with early rheumatoid arthritis. Clin Exp Rheumatol. 2021;39(6):1369–77. Epub 2021 Jan 7. PMID: 33427617.
6. Krauss WE, Bledsoe JM, Clarke MJ, Nottmeier EW, Pichelmann MA. Rheumatoid arthritis of the craniovertebral junction. Neurosurgery. 2010;66:A83–95.
7. Ferrante A, Ciccia F, Giammalva GR, Iacopino DG, Visocchi M, Macaluso F, Maugeri R. The craniovertebral junction in rheumatoid arthritis: state of the art. Acta Neurochir Suppl. 2019;125:79–86. https://doi.org/10.1007/978-3-319-62515-7_12. PMID: 30610306.
8. Nguyen HV, Ludwig SC, Silber J, Gelb DE, Anderson PA, Frank L, Vaccaro AR. Rheumatoid arthritis of the cervical spine. Spine J. 2004;4:329–34.
9. Salaffi F, Carotti M, Di Carlo M, Sessa F, Malavolta N, Polonara G, Giovagnoni A. Craniocervical junction involvement in musculoskeletal diseases: an area of close collaboration between rheumatologists and radiologists. Radiol Med. 2020;125(7):654–67. https://doi.org/10.1007/s11547-020-01156-4. Epub 2020 Feb 22. PMID: 32088810.
10. O'Brien MF, Casey AT, Crockard A, Pringle J, Stevens JM. Histology of the craniocervical junction in chronic rheumatoid arthritis: a clinicopathologic analysis of 33 operative cases. Spine (Phila Pa 1976). 2002;27(20):2245–54. https://doi.org/10.1097/00007632-200210150-00012. PMID: 12394902.
11. Oláh C, Kardos Z, Kostyál L, et al. Assessment of cervical spine involvement in rheumatoid arthritis patients in the era of biologics: a real-life, cross-sectional MRI study. Rheumatol Int. 2020;40:915–21.
12. Shlobin NA, Dahdaleh NS. Cervical spine manifestations of rheumatoid arthritis: a review. Neurosurg Rev. 2021;44(4):1957–65. https://doi.org/10.1007/s10143-020-01412-1. Epub 2020 Oct 10. PMID: 33037539.
13. Terashima Y, Yurube T, Hirata H, Sugiyama D, Sumi M. Predictive risk factors of cervical spine instabilities in rheumatoid arthritis: a prospective multicenter over 10-year cohort study. Spine. 2017;42:556–64.
14. Gillick JL, Wainwright J, Das K. Rheumatoid arthritis and the cervical spine: a review on the role of surgery. Int J Rheumatol. 2015;2015:1–12.
15. Zoli A, Bosello S, Magarelli N, D'Antona G, Amelia R, Fedele A, Peluso G, Bonomo L, Ferraccioli G. Atlantoepistrophic magnetic resonance imaging involvement in early rheumatoid arthritis: an aggressive tight control therapy not fully arresting the disease. Arthritis Care Res (Hoboken). 2011;63(11):1629–33. https://doi.org/10.1002/acr.20573. PMID: 21954100.
16. Dreyer SJ, Boden SD. Natural history of rheumatoid arthritis of the cervical spine. Clin Orthop Relat Res. 1999;366:98–106.
17. Kotecki M, Sotniczuk M, Gietka P, et al. Imaging of cervical spine involvement in inflammatory arthropathies: a review. Pol J Radiol. 2021;86:e620–9.
18. Younes M, Belghali S, Kriâa S, et al. Compared imaging of the rheumatoid cervical spine: prevalence study and associated factors. Joint Bone Spine. 2009;76:361–8.
19. Zochling J, Smith EU. Seronegative spondyloarthritis. Best Pract Res Clin Rheumatol. 2010;24(6):747–56.
20. Mundwiler M, Siddique K, Dym J, et al. Complications of the spine in ankylosing spondylitis with a focus on deformity correction. Neurosurg Focus. 2008;24:1–9.
21. Lee JS, Lee S, Bang SY, et al. Prevalence and risk factors of anterior atlantoaxial subluxation in ankylosing spondylitis. J Rheumatol. 2012;39:2321–6.
22. Ramos Remus C, Gomez-Vargas A, Guzman-Guzman JL, et al. Frequency of atlantoaxial subluxation and neurologic involvement in patients with ankylosing spondylitis. J Rheumatol. 1995;22:2120–5.
23. Maas F, Spoorenberg A, Brouwer E, et al. Radiographic damage and progression of the cervical spine in ankylosing spondylitis patients treated with TNFα inhibitors: facet joints vs. vertebral bodies. Semin Arthritis Rheum. 2017;46:562–8.
24. Ocampo DV, Gladman D. Psoriatic arthritis. F1000Res. 2019;8:1665. F1000 Faculty Rev-1665.
25. Tan S, Wang R, Ward MM. Syndesmophyte growth in ankylosing spondylitis. Curr Opin Rheumatol. 2015;27(4):326–32.
26. Jenkinson T, Armas J, Evison G, et al. The cervical spine in psoriatic arthritis: a clinical and radiological study. Br J Rheumatol. 1994;33:255–9.
27. Blau RH, Kaufman RL. Erosive and subluxing cervical spine disease in patients with psoriatic arthritis. J Rheumatol. 1987;14:111–7.
28. Laiho, et al. The cervical spine in patients with psoriatic arthritis. Ann Rheum Dis. 2002;61:650–2.
29. Maher T, et al. C1-C2 instability in psoriatic arthritis. Pan Afr Med J. 2020;36(217):217.
30. Van Tilt I, Lories RJ, Westhovens R, de Vlam K. Unusual cervical spine involvement in psoriatic arthritis: a case series. Clin Rheumatol. 2009;28(11):1343–6.
31. Thatayatikom A, Modica R, De Leucio A. Juvenile idiopathic arthritis. Treasure Island, FL: StatPearls Publishing; 2021.
32. Martini A, Ravelli A, Avcin T, et al. Pediatric Rheumatology International Trials Organization (PRINTO) toward new classification criteria for juvenile idiopathic arthritis: first steps, Pediatric Rheumatology International Trials Organization International Consensus. J Rheumatol. 2019;46(2):190–7.
33. Joaquim AF, Ghizoni E, Tedeschi H, Appenzeller S, Riew KD. Radiological evaluation of cervical spine involvement in rheumatoid arthritis. Neurosurg Focus. 2015;38(4):E4. https://doi.org/10.3171/2015.1.FOCUS14664. PMID: 25828498.
34. Kauppi M, Neva MH. Sensitivity of lateral view cervical spine radiographs taken in the neutral position in atlantoaxial subluxation in rheumatic diseases. Clin Rheumatol. 1998;17:511–4.
35. Zoli A, Priolo F, Galossi A, Altomonte L, Di FG, Cerase A, Mirone L, Magaro M. Craniocervical junction involvement in rheumatoid arthritis: a clinical and radiological study. J Rheumatol. 2000;27:1178–82.
36. Zoli A, Priolo F, Galossi A, Altomonte L, Di Gregorio F, Cerase A, Mirone L, Magarò M. Craniocervical junction involvement in

rheumatoid arthritis: a clinical and radiological study. J Rheumatol. 2000;27(5):1178–82. PMID: 10813284.

37. Colebatch AN, Edwards CJ, Østergaard M, Van Der Heijde D, Balint PV, D'Agostino M-A, Forslind K, Grassi W, Haavardsholm EA, Haugeberg G. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Ann Rheum Dis. 2013;72:804–14.
38. Mańczak M, Gasik R. Cervical spine instability in the course of rheumatoid arthritis–imaging methods. Reumatologia. 2017;55:201.
39. Di Gregorio F, Priolo F, Cerase A, Belli P, Galossi A, Magarò M, Marano P. Ruolo integrato della Tomografia Computerizzata e della Risonanza Magnetica nel rilievo delle alterazioni precoci dell'artrite reumatoide della giunzione cranio-cervicale [Integrated role of computerized tomography and magnetic resonance imaging in identifying the early changes in rheumatoid arthritis of the craniocervical junction]. Radiol Med. 1997;93(1–2):18–26. Italian. PMID: 9380862.
40. Shen FH, Samartzis D, Jenis LG, An HS. Rheumatoid arthritis: evaluation and surgical management of the cervical spine. Spine J. 2004;4(6):689–700. https://doi.org/10.1016/j.spinee.2004.05.001. PMID: 15541704.
41. Kotecki M, Gietka P, Posadzy M, Sudoł-Szopinska I. Radiographs and MRI of the cervical spine in juvenile idiopathic arthritis: a cross-sectional retrospective study. J Clin Med. 2021;10:5798.

Spinal Cord High-Frequency Stimulation. The Current Experience and Future Directions

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1 Introduction

Spinal cord stimulation (SCS) is a minimally invasive treatment option for neuropathic intractable pain [1]. Traditional SCS produces paraesthesia, which is experienced by the patient as a variable sensation overlapping the target area. A randomized control trial of traditional low-frequency SCS compared with conservative management or repeat spinal surgery showed benefits for leg pain but not for low back pain (LBP) [2, 3]. New waveforms of stimulation in SCS, including using a frequency of 10 kHz, have instead showed effectiveness against LBP [4, 5]. These paraesthesia-free stimulations produce safe and effective pain relief. Most of these observations have been collected from patients who have had unsuccessful spinal surgery and LBP for many years, as a rescue strategy in the treatment of the heterogeneous clinical conditions known as failed back surgery syndrome (FBSS) [6]. Strong efforts predominate the literature and present SCS as a potential treatment for patients with other rare conditions, such as patients experiencing chronic LBP who have not had prior spinal surgery (known as virgin-back patients) [7], patients affected by multiple sclerosis (MS) or patients with central neuropathic pain secondary to myelopathy. In particular, although SCS revealed more than 50 years ago a possible effect on motor function recovery, over the past decade, many clinical challenges have arisen in targeting motor circuits [8]. The aim of our work is to report our clinical experiences on spinal cord high-frequency (HF) stimulation. We also report two unusual clinical cases and discuss the potential future indications of this technique.

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2 Materials and Methods

We retrospectively reviewed the clinical and outcome data of 20 patients (M/F, 4/16) who underwent an HF SCS for different clinical indications between January 2016 and December 2021. The mean age was 55.5 ± 14.9 years, and the mean follow-up (FU) was 13.6 ± 9.3 months. All patients were submitted to a trial before the definitive implantation. As outcome indicators, we evaluated their NRS (numerical rating scale) scores before the procedure, after the clinical trial and at the latest FU.

2.1 Statistical Analysis

The means and standard deviations (SDs) were calculated and reported when appropriate. The differences between groups were explored by using the Wilcoxon signed rank test, the Mann–Whitney U test, the $\chi 2$ test, and/or the Fisher's exact test, where appropriate. Differences were considered significant at $p < 0.05$. Statistical analyses were conducted by using StatView version 5 software (SAS Institute Inc.).

3 Results

Clinical and outcome data are reported in Table 1. Briefly, we observed significant improvements in NRS scores after the trial and the latest FU (9.4 ± 0.6, 3.1 ± 1.2 and 3.7 ± 1.8, respectively; $p < 0.0001$ and $p < 0.0001$) compared with the preoperative scores. The different factors studied, namely

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Table 1 Clinical and outcome data of patients submitted to spinal cord high-frequency stimulation

Patients	20
Sex (M/F)	4/16
Mean age (years)	55.5 ± 14.9
Mean follow-up (months)	13.6 ± 9.3
Trial duration (days)	42.5 ± 18.8
Diagnosis	
FBSS	5
Myelopathy	7
Arachnoiditis	2
SM	3
Virgin low back pain	3
Hybrid system (yes/no)	5/15
Lead level	
Cervical	3
Dorsal (T8-T9)	16
Double	1
NRS	
Preoperative	9.4 ± 0.6
After the trial	3.1 ± 1.2
At latest follow-up	3.7 ± 1.8

sex, age, trial duration, diagnosis and lead level, did not significantly affect the clinical outcomes of patients.

We report on two unusual cases as follows.

Case 1

A 53-year-old woman came with a history of surgeries for lumbosacral lipoma asportation, complicated by cerebrospinal fluid (CSF) leakage, meningitis and hydrocephalus to our attention. Owing to the development of a chronic adhesive arachnoiditis with a septate arachnoid cist at the C6-T4 level and a consequent mass effect on the cord, she underwent spinal cord decompression, arachnoid cyst fenestration and the lysis of adhesions. The magnetic resonance imaging (MRI) findings after these operations are reported in Fig. 1. Because of the persistence of severe spasticity and neuropathic pain despite maximal medical therapy (a combination of nonsteroidal anti-inflammatory drugs, tapendatol, pregabalin and baclofen) and the evidence of a neurogenic bladder and severe paraparesis, the patient was submitted to SCS with octopolar lead, with a distal extremity placed at the T8 level. During the trial period (1 month), we conducted a tonic stimulation with a comfortable paresthesia fully covering the painful area and multiple HF programs using different dipoles of stimulation. The best response was obtained from a frequency-pairing stimulation of a program combining 10 kHz therapy with the tonic spinal cord stimulation. The patient experienced a level of pain relief >60% and significant improvement in lower-limb hypertonia. Accordingly, she underwent the definitive implantation with an MRI-compatible lead system (Nevro Senza Omnia). After 8 months of follow-up, the patient reported a stable clinical improvement of pain and spasticity with no need for multiple drugs (she was taking only the pregabalin at latest FU).

Case 2

A 37-year-old man with a 5-year history of MS and experiencing LBP and lower extremity pain with relevant spasticity came to our attention. These symptoms affected his deambulation, with gait disturbances and the progressive reduction of walking speed and walking distance despite the best medical therapy. The MRI showed multiple cerebral and spinal cord lesions without significant neural foraminal stenosis or spinal canal narrowing. A SCS was carried out with the octopolar lead placed at the top of T8. During the trial (1 month), the patient did not tolerate the paresthesia associated with tonic stimulation, so an HF stimulation was attempted, which led to significant improvements in LBP and leg pain, a decrease in spasticity and a correspondingly improvement in walking. Thus, the patient underwent a definitive implantation of an MRI-compatible lead system (Nevro Senza Omnia). At a 3-month FU, the patient reported stable improvements in his clinical conditions.

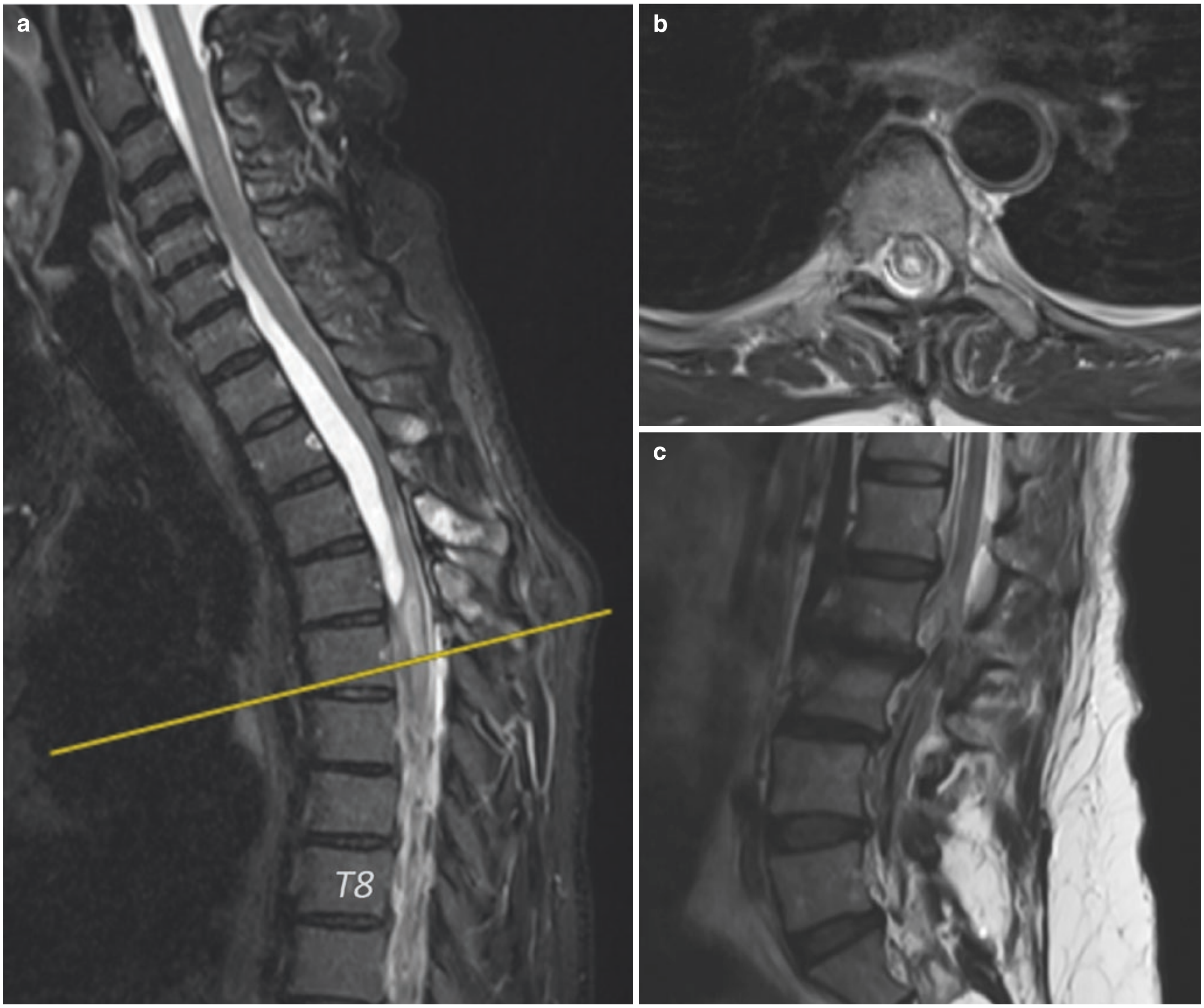

Fig. 1 Radiological finding of the last MRI before SCS trial. (**a**) sagittal images and (**b**) axial images showing a cervicothoracic septated arachnoid cyst and a caudal area of myelopathy. (**c**) Lumbosacral findings are the results of lipoma asportation and CSF leakage repair

4 Discussion

SCS is strongly recommended in FBSS and complex regional pain syndrome [9]. HF SCS using 10 kHz frequencies might expand the utility of SCS, particularly for mixed nociceptive-neuropathic or axial pain components [10]. HF SCS has been proved efficient in reducing LBP and leg pain, improving quality of life and reducing medication use, and it may also result in cost savings for public health systems [11]. As reported in our study, after a standardized trial period, HF SCS results in significant stable pain relief with well-preserved improvements in both radicular and central axial back pain during the FUs in all subjects. Prospective studies and a randomized control trial provided evidence to support the use of HF SCS in subjects with predominant chronic back pain [5]. SCS is now being applied as a potential therapy for a wide range of indications, including neurological, cardiac, and gastrointestinal disorders [11]. Potential effects on the outcomes of ischemic and traumatic brain injuries have also been reported. SCS has been able to to increase cerebral blood flow and induce modification in cerebral microcirculation [12, 13].

Regarding motor disorders, early studies exploring the use of SCS on spasticity were carried out in 1980 [14], but they were obscured by the extensive use of botulinum toxin and intrathecal baclofen therapy with a programmable pump.

Over the past decade, the widespread application of SCS brought a renewed interest in spasticity treatment and further insights into the mechanisms of action for SCS. Epidural

SCS seems to modify lower-limb electromyography (EMG) activity in patients with a spinal cord injury and spasticity. As proved in other pathologic models, variation in stimulation protocols could modify clinical and electrophysiological outcomes [15, 16]. In detail, stimulation frequency, amplitude and electrode configuration could induce different patterns of EMG activity (rhythmic, tonic, or continuous), potentially achieving different motor outputs during standing and stepping [17]. Davis et al. described the effects of SCS on 101 patients, most of whom had MS, and Koulousakis et al. reported epidural stimulation in paraplegic patients [18, 19]. Most of the major effects have been reported in spinal spasticity because the benefits in cerebral spasticity have been less impressive. However, some results have been collected on supraspinal spasticity. Cioni et al. reported on 13 patients affected by spastic hemiparesis following a stroke [20]. As reported by Dekapov et al., chronic SCS may be a potential treatment for patients with moderate spinal and cerebral spasticity with predominant spastic lower paraparesis. In patients with spastic tetraparesis, SCS therapy has not proved to be effective [21].

A recent meta-analysis showed considerable variability in using SCS on motor disfunction in MS patients, stressing the needing for a better selection of cases and the implementation of stimulation protocols [22]. In this paper, we presented two unusual clinical cases of neuropathic pain associated with the spasticity of lower limbs caused by different aetiologies. In both cases, HF SCS has resulted in stable and significant pain control, according to the reported NRS scores. The patients showed reductions in medication use and higher levels of quality of life. The consequences of SCS on their spasticity levels offer interesting points of view on the potential different effects gained by varying frequency stimulation. In fact, the patient with the MS diagnosis (Case 2) reported a considerable improvement in motor function using HF stimulation, and in Case 1, a pairing stimulation was required. Even in the presence of a similar clinical pattern, the etiopathogenesis and the pathophysiology sustaining the motor disfunctions are profoundly different. Different hypotheses have been reported in the literature to explain the potential mechanisms of action for SCS in muscle hypertonia. SCS seems to facilitate the processing of sensory information, restore some supraspinal control in order to produce movement and stimulate medullary neuroplasticity [23]. Our paper has several limitations, including its retrospective design and small sample analysed. During the follow-up, no quality-of-life scores were collected, and we did not perform a walking and gait computerized analysis for patients with spasticity or motor disorders. Nonetheless, our results confirm the efficacy of HF SCS in controlling LBP and leg pain and highlight the potential role of HF SCS in patients with different motor conditions.

Conflicts of Interest The authors declare no conflicts of interest.

References

1. Turner JA, Loeser JD, Bell KG. Spinal cord stimulation for chronic low back pain: systematic literature synthesis. Neurosurgery. 1995;37:1088–95.
2. Nagel SJ, Wilson S, Johnson MD, Machado A, Frizon L, Chardon MK, Reddy CG, Gillies GT, Howard MA 3rd. Spinal cord stimulation for spasticity: historical approaches, current status, and future directions. Neuromodulation. 2017;20(4):307–21.
3. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery. 2005;56(1):98–107.
4. Al-Kaisy A, Van Buyten JP, Kapural L, Amirdelfan K, Gliner B, Caraway D, Subbaroyan J, Edgar D, Rotte A. 10 kHz spinal cord stimulation for the treatment of non-surgical refractory back pain: subanalysis of pooled data from two prospective studies. Anaesthesia. 2020;75(6):775–84.
5. Al-Kaisy A, Van Buyten JP, Smet I, Palmisani S, Pang D, Smith T. Sustained effectiveness of 10 kHz high-frequency spinal cord stimulation for patients with chronic, low back pain: 24-month results of a prospective multicenter study. Pain Med. 2014;15(3):347–54.
6. Mazzucchi E, Auricchio AM, Stifano V, Montano N. Unrecognized failed back surgery syndrome: a paradigmatic case in a very young patient. Acta Neurol Belg. 2018;118(3):523–5.
7. Al-Kaisy A, Palmisani S, Smith TE, Carganillo R, Houghton R, Pang D, Burgoyne W, Lam K, Lucas J. Long-term improvements in chronic axial low Back pain patients without previous spinal surgery: a cohort analysis of 10-kHz high-frequency spinal cord stimulation over 36 months. Pain Med. 2018;19(6):1219–26.
8. Harmsen IE, Hasanova D, Elias G, Boutet A, Neudorfer C, Loh A, Germann J, Lozano AM. Trends in clinical trials for spinal cord stimulation. Stereotact Funct Neurosurg. 2021;99(2):123–34.
9. Deer TR, Mekhail N, Provenzano D, Pope J, et al. The appropriate use of Neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the neuromodulation appropriateness consensus committee. Neuromodulation. 2014;17:515–50.
10. Van Buyten JP, Al-Kaisy A, Smet I, Palmisani S, Smith T. High-frequency spinal cord stimulation for the treatment of chronic back pain patients: results of a prospective multicenter European clinical study. Neuromodulation. 2013;16:59–66.
11. Tiede J, Brown L, Gekht G, Vallejo R, Yearwood T, Morgan D. Novel spinal cord stimulation parameters in patients with predominant back pain. Neuromodulation. 2013;16(4):370–5.
12. Visocchi M, Della Pepa GM, Esposito G, Tufo T, Zhang W, Li S, Zhong J. Spinal cord stimulation and cerebral hemodynamics: updated mechanism and therapeutic implications. Stereotact Funct Neurosurg. 2011;89(5):263–74.
13. Visocchi M, Giordano A, Calcagni M, Cioni B, Di Rocco F, Meglio M. Spinal cord stimulation and cerebral blood flow in stroke: personal experience. Stereotact Funct Neurosurg. 2001;76(3–4):262–8.
14. Siegfried J, Lazorthes Y, Broggi G. Electrical spinal cord stimulation for spastic movement disorders. Appl Neurophysiol. 1981;44(1–3):77–92.

15. Meglio M, Cioni B, Visocchi M. Cerebral hemodynamics during spinal cord stimulation. Pacing Clin Electrophysiol. 1991;14(1):127–30.
16. Zhong J, Huang DL, Sagher O, Visocchi M. Parameters influencing augmentation of cerebral blood flow by cervical spinal cord stimulation. Acta Neurochir. 2004;146:1227–34.
17. Rejc E, Angeli CA. Spinal cord epidural stimulation for lower limb motor function recovery in individuals with motor complete spinal cord injury. Phys Med Rehabil Clin N Am. 2019;30(2):337–54.
18. Davis R, Emmonds SE. Spinal cord stimulation for multiple sclerosis: quantifiable benefits. Stereotact Funct Neurosurg. 1992;58(1–4):52–8.
19. Koulousakis A, Buchhaas U, Nittner K. Application of SCS for movement disorders and spasticity. Acta Neurochir Suppl. 1987;39:112–6.
20. Cioni B, Meglio M, Prezioso A, Talamonti G, Tirendi M. Spinal cord stimulation (SCS) in spastic hemiparesis. Pacing Clin Electrophysiol. 1989;12(4 Pt 2):739–42.
21. Dekopov AV, Shabalov VA, Tomsky AA, Hit MV, Salova EM. Chronic spinal cord stimulation in the treatment of cerebral and spinal spasticity. Stereotact Funct Neurosurg. 2015;93(2):133–9.
22. Rapisarda A, Ioannoni E, Izzo A, D'Ercole M, Montano N. Is there a place for spinal cord stimulation in the management of patients with multiple sclerosis? A systematic review of the literature. Minim Invasive Surg. 2021;2021:9969010.
23. Courtine G, van den Brand R, Musienko P. Spinal cord injury: time to move. Lancet. 2011;377(9781):1896–8.

Spontaneous Intracranial Hypotension: Controversies in Treatment

Francesco Signorelli and Massimiliano Visocchi

1 Introduction

Spontaneous intracranial hypotension (SIH) is a disorder of low cerebrospinal fluid (CSF) volume secondary to CSF leakage through a dural defect along the neuraxis [1, 2]. The estimated incidence of SIH is 5 people per 100,000 [3], but the true incidence is expected to be higher because it is frequently misdiagnosed initially.

Patients usually present with bilateral subdural hygromas or subdural hematomas (SDHs) and orthostatic headache, which generally starts within 15 min of assuming an upright position, predominantly in the back of the head. This can be explained by the sagging of the brain secondary to the low CSF volume and the resulting tension on the cranial nerves and dura mater, which is especially tension sensitive in the posterior fossa [4]. Other symptoms may include nausea, vomiting, disorientation, memory impairment, diplopia, gait disturbance, cranial nerve palsies, sinus thrombosis, large-vessel strokes, and comas [5–9]. Auditory disturbances such as ringing in the ears, or tinnitus—a pressure sensation in the ear—can seldom coexist, and some patients are initially treated for sudden hearing loss or suspected Ménière disease [10].

Neuroimaging techniques need to be directed toward the brain, to assess the consequences of CSF hypotension, and toward the spinal column, to localize the leakage and possibly guide diagnosis if a targeted treatment is pursued. The best tool to diagnose SIH is magnetic resonance imaging (MRI), which usually shows the triad of diffuse dural thickening/enhancement, the downward displacement of the brain ("slumping" midbrain), and subdural hematomas or hygromas [11–13].

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Great debate persists on the optimal treatment of this pathology, and clinical results are often contradictory.

Our group recently performed a systematic review and meta-analysis of the literature to evaluate the role of different factors that possibly affect the efficacy of the EBP procedure, by analyzing comparative studies reporting a clear description of patients experiencing good and poor responses to EBP [14].

2 Pathogenesis

SIH is caused by spontaneous CSF leaks from the spinal meningeal diverticula or dural rents along nerve sleeves [15]. Mechanical factors and several connective tissue disorders, such as Marfan syndrome, Ehlers-Danlos syndrome type 2, and autosomal dominant polycystic kidney disease, can determine dural weakness, leading to one or more CSF leaks. Ventral dural tears by disk herniation and CSF–venous fistulas are other possible underlying etiologies.

According to the Monro–Kellie doctrine, the loss of volume secondary to CSF leaks increases blood volume, ultimately leading to the enlargement of dural arteries, the dilatation of cortical/medullary veins, and the dilatation of dural venous sinuses.

Conversely, the neurophysiological hypothesis arises from observing an abnormally low spinal epidural pressure in patients affected by SIH. This would act as an aspiration force applied to the entire dural surface, thus determining a CSF transdural "steal" in predisposed patients, such as those with connective disorders.

3 Diagnosis

Diagnostic criteria include a CSF pressure < 60 mm H_2O and/or radiological evidence of a CSF leak [2]. However, only one-third of SIH patients have low CSF opening pres-

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sure; moreover, lumbar puncture is an invasive procedure. Therefore, performing MRIs on the head and the spine is mandatory [16]. Myelography with iodinated contrast followed by the thin-cut computed tomography (CT) of the entire spine (or with gadolinium followed by MRI) has been shown to be the study of choice to accurately define the location and extent of a CSF leak when it is required. The majority of CSF leaks are at the cervicothoracic junction or along the thoracic spine. Multiple simultaneous CSF leaks can coexist.

4 Therapeutic Options

SIH may be initially approached via conservative measures, such as bed rest often supplemented with hydration, caffeine, and theophylline [17], which overall relieve symptoms in a small subset of patients at 6 months [18].

Epidural blood patching (EBP) is generally the next consideration in management. It is the most commonly performed intervention for spinal CSF leaks, as the first option or following a failure of conservative treatment [9, 19]. EBP consists of the injection of a variable volume of autologous blood in the epidural space (ranging from 10 to 55 mL) [20, 21], where the patient lies supine in the postprocedural setting to help with epidural blood redistribution along the neuraxis.

There is no consensus on how to perform a blood patch ("loss of resistance," fluoroscopy guided, CT guided, blood, or fibrin glue). Controversy exists regarding the optimal site of EBP delivery, which can be targeted to the site of the CSF leak on imaging when aiming to seal it, or it can be blindly delivered into the lumbar region, thus raising the pressure in the epidural space. To date, no prospective randomized trials have demonstrated the superiority of one technique over the other. IN more detail, Yoon et al. and Choi et al. [22, 23] compared the results of blind and targeted EBP in responders and nonresponders: however, significant differences between the two groups have not been demonstrated. Some other authors have reported better results following targeted EBP when comparing results with those of nontargeted patching [23, 24], but this finding was not confirmed by our recently performed meta-analysis on this topic. Apart from the chosen technique, the ideal volume of injected blood is still a matter of debate. Higher volumes are correlated with better therapeutic outcomes [21].

The response rate to initial EBP significantly varies among investigations, ranging from 36% to 90% [5, 9, 25]. A patient is generally defined as a good responder if a persistent reduction in a VAS score of at least 50% for at least 6 months is achieved within 48 hours of the EBP [20].

Further procedures may be performed in the case of a partial or temporary response to EBP and if the spinal CSF leak has been definitively localized [26]. In those cases, if the CSF leak is well localized, the surgical closure of the spinal CSF leak may be considered. Surgical procedures may include clipping the leaking root sleeve (for leaks associated with nerve root sleeve diverticula), epidural packing, or primary dural repair, which may prove technically challenging if the leak is ventrally located [10].

Lateral meningeal diverticulae at the nerve root, CSF–venous fistulas, and laterally and ventrally located dural tears can be reached through a dorsal approach and closed safely and with minimal invasiveness through an interlaminar fenestration or a hemilaminectomy [10, 26]. Ventral dural tears require a transdural approach that detaches the denticulate ligaments so that the spinal cord can be mobilized under intraoperative neuromonitoring.

A therapeutic algorithm is schematized in Fig. 1.

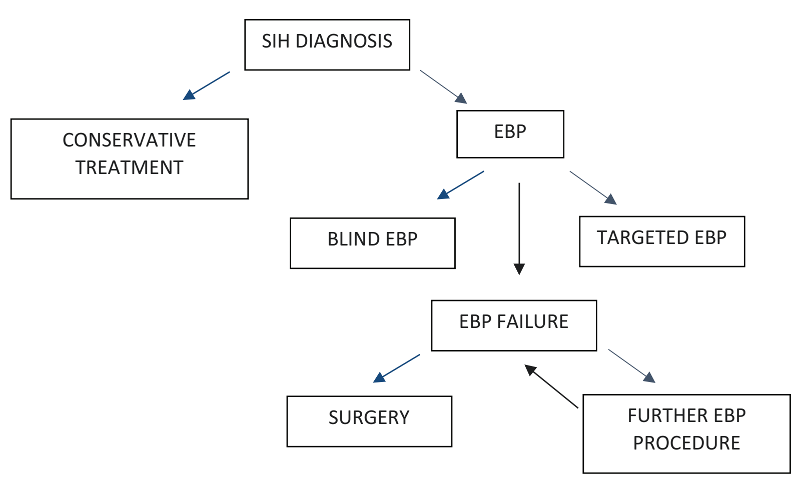

Fig. 1 Therapeutic algorithm for SIH

5 Conclusion

SIH is a complex but treatable CSF disorder. Despite recent advances in the field of neuroimaging and the various therapeutic options available, the most-appropriate management remains controversial and should be tailored to the patient.

References

1. Schievink WI, Meyer FB, Atkinson JLD, Mokri B. Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. J Neurosurg. 1996;84:598–605.
2. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders. Cephalalgia. 2018;38:1–211.
3. Kranz PG, Gray L, Amrhein TJ. Spontaneous intracranial hypotension: 10 myths and misperceptions. Headache. 2018;58(7):948–59. https://doi.org/10.1111/head.13328. Epub 2018 May 24.
4. Schievink WI. Misdiagnosis of spontaneous intracranial hypotension. Arch Neurol. 2003;60:1713–8.
5. Ferrante E, Savino A, Sances G, Nappi G. Spontaneous intracranial hypotension syndrome: report of twelve cases. Headache. 2004;44:615–22.
6. Loya JJ, Mindea SA, Yu H, Venkatasubramanian C, Chang SD, Burns TC. Intracranial hypotension producing reversible coma: a systematic review, including three new cases. J Neurosurg. 2012;117(3):615–28. https://doi.org/10.3171/2012.4.JNS112030.
7. Nowak DA, Rodiek SO, Zinner J, Guhlmann A, Topka H. Broadening the clinical spectrum: unusual presentation of spontaneous cerebrospinal fluid hypovolemia. Case report. J Neurosurg. 2003;98:903–7.
8. Pakiam AS, Lee C, Lang AE. Intracranial hypotension with parkinsonism, ataxia, and bulbar weakness. Arch Neurol. 1999;56:869–72.
9. Paldino M, Mogilner AY, Tenner MS. Intracranial hypotension syndrome: a comprehensive review. Neurosurg Focus. 2003;15(6):1. ECP2 Published 2003 Dec 15.
10. Luetzen N, Dovi-Akue P, Fung C, Beck J, Urbach H. Spontaneous intracranial hypotension: diagnostic and therapeutic workup. Neuroradiology. 2021;63(11):1765–72. https://doi.org/10.1007/s00234-021-02766-z. Epub 2021 Jul 23. PMID: 34297176; PMCID: PMC8528761.
11. Atkinson JL, Weinshenker BG, Miller GM, et al. Acquired Chiari I malformation secondary to spontaneous spinal cerebrospinal fluid leakage and chronic intracranial hypotension syndrome in seven cases. J Neurosurg. 1998;88:237–42.
12. Chiapparini L, Ciceri E, Nappini S, Castellani MR, Mea E, LeoneM B, Savoiardo M. Headache and intracranial hypotension: neuroradiological findings. Neurol Sci. 2004;25(Suppl 3):S138–41.
13. Schick U, Musahl C, Papke K. Diagnostics and treatment of spontaneous intracranial hypotension. Minim Invasive Neurosurg. 2010;53:15–20.
14. Signorelli F, Caccavella VM, Giordano M, Ioannoni E, Caricato A, Polli FM, Olivi A, Montano N. A systematic review and meta-analysis of factors affecting the outcome of the epidural blood patching in spontaneous intracranial hypotension. Neurosurg Rev. 2021;44(6):3079–85.
15. Hyun SH, Lee KH, Lee SJ, Cho YS, Lee EJ, Choi JY, Kim BT. Potential value of radionuclide cisternography in diagnosis and management planning of spontaneous intracranial hypotension. Clin Neurol Neurosurg. 2008;110(7):657–61. https://doi.org/10.1016/j.clineuro.2008.03.014. Epub 2008 May 23. PMID: 18457913..
16. Kranz PG, Tanpitukpongse TP, Choudhury KR, Amrhein TJ, Gray L. How common is normal cerebrospinal fluid pressure in spontaneous intracranial hypotension? Cephalalgia. 2016;36:1209–17.
17. Kong DS, Park K, Nam DH, Lee JI, Kim JS, Eoh W, Kim JH. Clinical features and long-term results of spontaneous intracranial hypotension. Neurosurgery. 2005;57:91–6.
18. Davidson B, Nassiri F, Mansouri A, Badhiwala JH, Witiw CD, Shamji MF, Peng PW, Farb RI, Bernstein M. Spontaneous intracranial hypotension: a review and introduction of an algorithm for management. World Neurosurg. 2017;101:343–9.
19. Kranz PG, Gray L, Malinzak MD, Amrhein TJ. Spontaneous intracranial hypotension: pathogenesis, diagnosis, and treatment. Neuroimaging Clin N Am. 2019;29(4):581–94.
20. Levi V, Di Laurenzio NE, Franzini A, et al. Lumbar epidural blood patch: effectiveness on orthostatic headache and MRI predictive factors in 101 consecutive patients affected by spontaneous intracranial hypotension. J Neurosurg. 2019;8:1–9.
21. Wu JW, Hseu SS, Fuh JL, Lirng JF, Wang YF, ChenWT CSP, Wang SJ. Factors predicting response to the first epidural blood patch in spontaneous intracranial hypotension. Brain. 2017;140(2):344–52.
22. Yoon SH, Chung YS, Yoon BW, Kim JE, Paek SH, Kim DG. Clinical experiences with spontaneous intracranial hypotension: a proposal of a diagnostic approach and treatment. Clin Neurol Neurosurg. 2011;113(5):373–9.
23. Choi H, Lee MJ, Choi HA, Cha J, Chung CS. Intracranial structural alteration predicts treatment outcome in patients with spontaneous intracranial hypotension. Cephalalgia. 2018;38(2):323–31.
24. Cho KI, Moon HS, Jeon HJ, Park K, Kong DS. Spontaneous intracranial hypotension: efficacy of radiologic targeting vs blind blood patch. Neurology. 2011;76:1139–44.
25. Sencakova D, Mokri B, McClelland RL. The efficacy of epidural blood patch in spontaneous CSF leaks. Neurology. 2001;57(10):1921–3.
26. Beck J, Ulrich CT, Fung C, Fichtner J, Seidel K, Fiechter M, Hsieh K, Murek M, Bervini D, Meier N, Mono ML, Mordasini P, Hewer E, Z'Graggen WJ, Gralla J, Raabe A. Diskogenic microspurs as a major cause of intractable spontaneous intracranial hypotension. Neurology. 2016;87:1220–6.

Pedicle Screw Placement Aided by C-Arm Fluoroscopy: A "Nevermore without" Technology to Pursue Optimal Spine Fixation

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1 Introduction

Spinal pedicle screw placement has consistently evolved over the past decades, thanks to its proven effectiveness in and consequent favorable outcomes after treating post-traumatic injuries, deformity, and degenerative and neoplastic diseases. By guaranteeing control over the three columns and allowing the fusion of few segmental levels, independently from eventual facet and laminar damage, pedicle screw fixation is now considered an established technique that neurosurgeons have become familiar with [1]. Obviously, the learning curve requires increasing confidence in anatomical landmarks, and this general concept is particularly true at the thoracic levels, where minimal misplacements may produce catastrophic consequences, including life-threatening ones.

Technological development has brought a dramatic decrease in the misplacement rate of pedicle screws, in particular for procedures assisted by computer-aided navigation [2, 3]. In our experience, the shift from using traditional bidimensional fluoroscopic intraoperative imaging to using a tridimensional C-arm has dawned a new era in screw-placement effectiveness, greatly reducing misplacement rates at every level of the spine and consequently improving surgeon confidence during the procedure and, most of all, patient outcomes. Daily advances in healthcare technology have enriched the imaging acquisition pool by introducing intraoperative assisting methods like volumetric image-based navigation. However, each technology has its counterpart and economic impacts from its acquisition and maintenance to take into account. In this context, we herein report our experience in performing pedicle screw fixation at all spinal levels with the assistance of the intraoperative 3D C-arm fluoroscopy for the treatment of a wide range of diseases.

2 Materials and Methods

The authors retrospectively recorded a series of 329 patients affected by post-traumatic spine fractures, spinal stenosis, or vertebral instability, over 5 years (2016–2020). The case series was restricted to patients over 18 years of age treated by the spine pedicle screw fixation (PSF) of the cervical, thoracic, or lumbosacral spine tract. All the procedures were performed using intraoperative C-arm fluoroscopy to assess and optimize screw trajectory and to promptly identify eventual screw mispositioning. A postoperative computed tomography (CT) scan was routinely performed after each case and at follow-up, whose minimal length was 12 months, in order to confirm correct screw positioning, quantify fusion grade, and detect possible late procedural complications. A descriptive statistical analysis was conducted to compare the pedicle screw insertion accuracy rate between cervical, thoracic, and lumbosacral segments.

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3 Results

In total, 329 surgical procedures were performed, as follows: 70 cervical (21.3%), 78 thoracic (23.7%), and 181 lumbar spine (55%); 634 screws were positioned. In specific, 19 patients underwent C0-C1-C2 fixation (27.1%), 12 anterior odontoid screw fixation (17.1%), 2 C3-C4 fixation (2.8%), 10 C4-C5 fixation (14.3%), 13 C5-C6 fixation (18.6%), 11 C6-C7 fixation (15.7%), 3 C7-Th1 fixation (4.3%), 31 Th2-Th4 pedicle screw fixation (39.7%), 27 Th5-Th8 fixation (34.6%), 20 Th9-Th12 fixation (25.6%), 13 L1-L2 fixation (7.2%), 5 L2-L3 fixation (2.8%), 30 L3-L4 fixation (16.6%), 98 L4-L5 fixation (54.1%), and 35 L5-S1 fixation (19.3%). An optimal overall pedicle screw positioning was obtained, with slight differences between the cervical (98.6%), thoracic (100%), and lumbar (98.9%) tracts. Accordingly, only three patients required a revision surgery owing to mispositioning (0.91%). Intraoperative 3D C-arm fluoroscopy significatively improved the accuracy of thoracic screw positioning, as shown by postoperative CT scan. Neither hardware failure nor neurovascular injury was demonstrated on follow-up. Two illustrative cases are shown in Figs. 1 and 2.

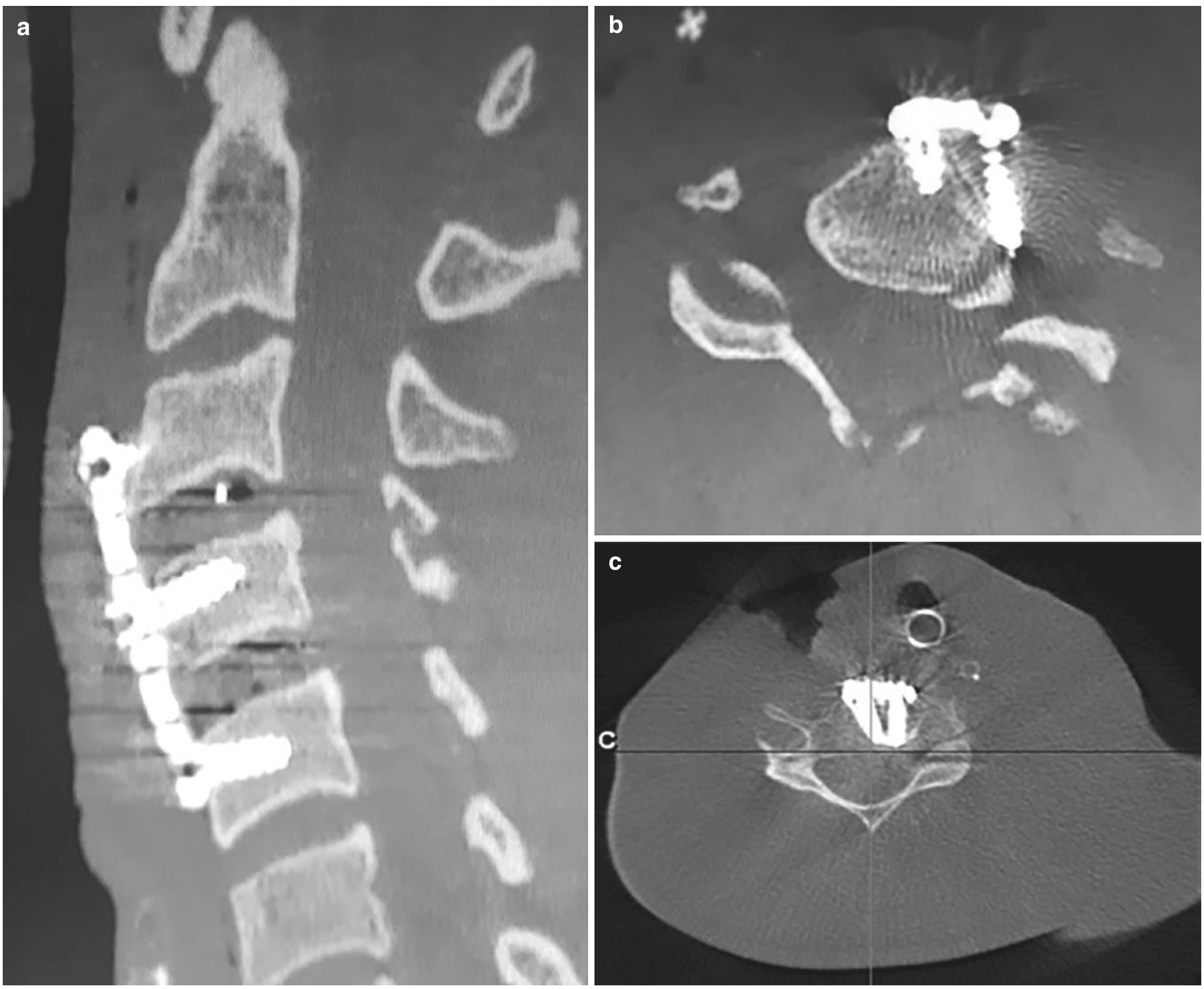

Fig. 1 Case example of misplacement using 2D C-arm: A 35-year-old man presented with spinal cord injury secondary to cervical compression after a road accident. A multilevel cervical anterior cervical discectomy and fusion (ACDF) was performed between C3 and C5, followed by screw placements at the same levels. A satisfactory intraoperative screw placement with 2D radiological control was achieved, and no postoperative neurological deficit appeared. Nonetheless, postoperative cervical CT scans documented screw misplacement as shown in sagittal (**a**) and axial (**b**) captures. The patient was promptly escorted to the operating room again, and the procedure was reviewed (**c**)

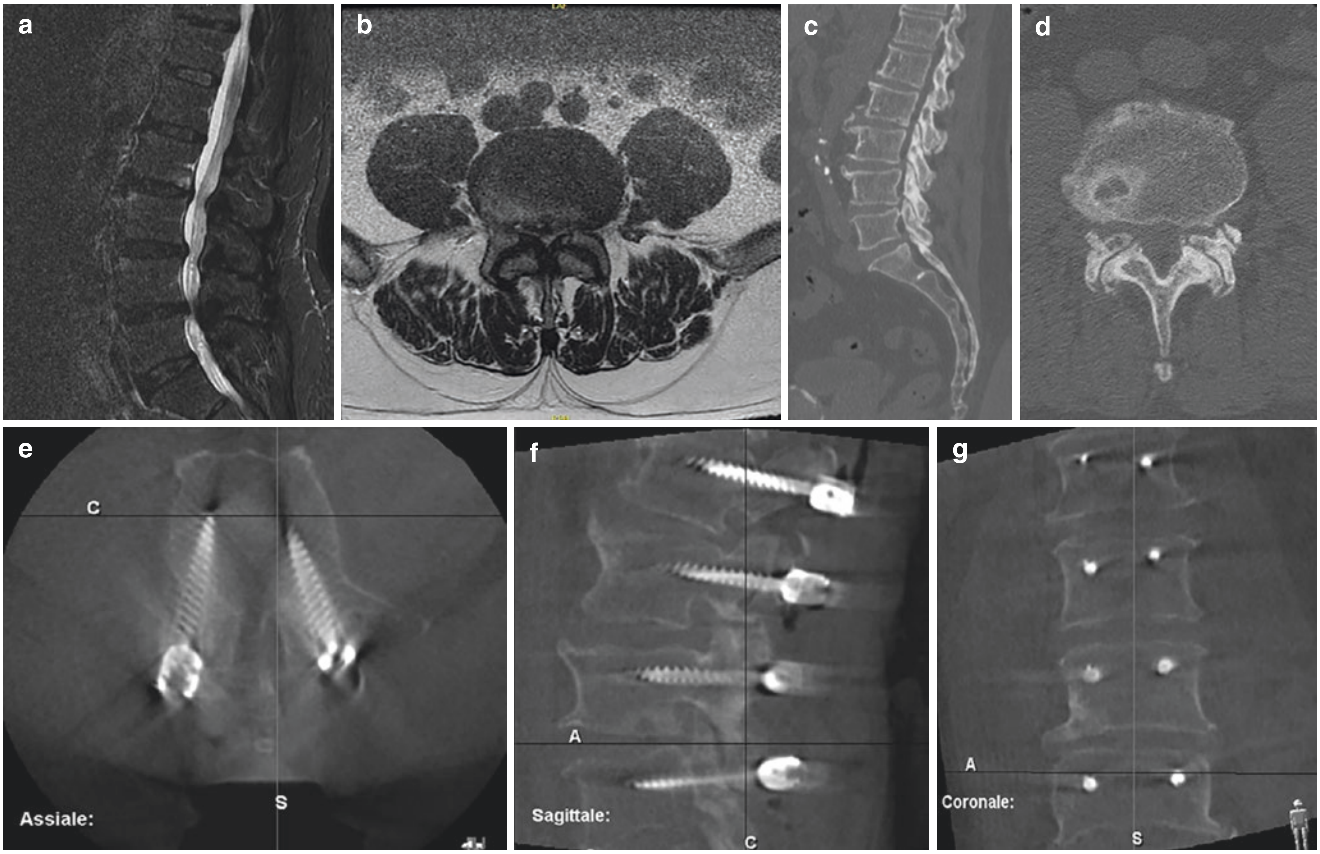

Fig. 2 Case example of screw placement using 3D C-arm: A 58-year-old man had diffuse degenerative lumbar disease that caused lumbar spondylosis with hypertrophy of the facet joints and the narrowing of the lumbar spinal canal and had intense lumbar back pain and neurogenic claudication. Lumbar MRI (**a**, **b**) and CT scan (**c, d**) are shown. The patient underwent the decompression of the lumbar spinal canal and spinal fusion, and intraoperative 3D radiological control showed the correct placement of the lumbar screws (**e**, **f**)

4 Discussion

The increased aging of the worldwide population has gone hand in hand with the increase in age-related diseases, such as degenerative spinal conditions, thus boosting the diffusion of spinal instrumentation surgery, which is also used to treat a wide range of conditions, such as post-traumatic fractures and neoplastic and spinal infectious disease. The technical armamentarium counts several alternative methods to achieve spinal fixation and fusion, among which are the transpedicle, the transarticular, the lateral mass, and the extrapedicular screw fixation methods. Indeed, the transpedicle screw fixation method has become one of the most favored spinal surgical procedures currently performed [4]. Pedicle violation resulting from a mispositioned screw leads to causing potential harm to nearby vital and neural structures and correlates with postoperative neurological deterioration and poor patient outcomes. Using freehand placement, the rate of misplaced pedicle screws has been reported to be from 5% to 41% in the lumbar spine and from 3% to 55% in the thoracic spine, with almost 7% of these resulting in neurological injuries [4, 5]. Moreover, a number of studies described pedicle violations in relation to the spinal segment, such as cervical and thoracic, where the size, shape, and orientation of their pedicles make it more challenging [4, 6]. For this reason, surgeons showed marked interest in reaching a reproducible strategy for screw placement accuracy by employing several various preoperative and intraoperative supporting methods to act as a virtual "roadmap" [3] of a patient's anatomy in relation to the position of surgical instruments. Intraoperative neurophysiological monitoring, preoperative planning by anatomical markers, and spinal navigation are routine basilar strategies in surgeons' hands. In addition, intraoperative assisting methods include volumetric image-based navigation (such as CT, O-arm, and MRI), fluoroscopic navigation, C-arm navigation (such as two- or three-dimensional (2D or 3D) fluoroscopic images), and potentially imageless navigation [3]. Even today, none of the reported methods has been determined as the best and safest intraoperative assisting method in guiding pedicle screw placement in all spinal segments, and comparing all the techniques remains a focus of clinical research and published literature. Many studies in the literature have suggested that the incidence of pedicle violation among the cases with the navigation assistance was statistically significantly less [7] when comparing the accuracy of pedicle screw placement with and without the assistance of the navigation system [3]. These findings have confirmed that C-arm fluoroscopic imaging has been a traditional navigation technique used for years for guidance in spine surgery, with satisfactory results. Accordingly, the comparison between the freehand technique and the navigation-guided procedure has been widely investigated in the pertinent literature. The advent of the O-arm imaging technique exceeded the limits of the conventional C-arm system [8–10], for which additional artificial correction of the arm trajectory is intraoperatively required for the patient's position and involved spinal segment [2], leading to longer and potentially less-accurate screw positioning during surgical procedures. Spinal instrumentation using active fluoroscopy is cumbersome because it needs to use heavy protective lead shielding, although it has demonstrated the absence of radiation exposure to the personnel of the operating room by using cone-beam CT-guided imaging systems [11]; moreover, the patient may not require further imaging in the postoperative period once intraoperative imaging has confirmed appropriate implant insertion [4]. The development of 3D fluoroscopy appeared to combine the advantages of CT and 2D fluoroscopy-based assistance. Likewise, CT navigation provides intraoperative 3D images without the prohibitive characteristics typical of the pre- and perioperative preparation, such as the paired-point matching in using anatomical fiducials or the more difficult and less employed material fiducials, imaging time, and radiation dosage. A randomized clinical trial [12] studied the pedicle screw insertion accuracy with and without the assistance of 3D fluoroscopy, and it revealed a markedly lower screw misplacement score, even in thoracic deformity correction surgery, compared with the freehand placement subgroup; these results were also confirmed in the case of percutaneous pedicle screw insertion [13]. Large patient cohort studies analyzing the outcome of screw placement assisted by either CT-based or 3D fluoroscopy-based navigation did not show any statistically relevant difference in breach rates between these two groups [13–16]. Moreover, some studies even reported remarkable advantages of using 3D fluoroscopy assistance not only in guiding pedicle screw insertion when compared with CT navigation, including strictly procedure-related features like radiation exposure [9], but also in perioperative outcomes, such as surgical times, surgeons' learning curves and expertise levels, patients' blood losses, and patients' functional outcomes [3, 17]. Although 3D fluoroscopy and 2D fluoroscopy have the same fluoroscopic intraoperative assisting method, 3D fluoroscopy can reduce the radiation running time more than conventional 2D fluoroscopy can because the former does not need the repeated intraoperative movement of the C-arm [3].

The result of the present study and the conclusions on the accuracy of pedicle screw insertion by using 3D fluoroscopy intraoperative assistance are based on our retrospective study on a single-center experience. We clearly demonstrate that the 3D fluoroscopic navigation technique results in high pedicle screw accuracy, especially in the thoracic region, that is superior to conventional fluoroscopy or freehand screw placement, which is in agreement with the most recent data in the literature. Placing pedicle screws in the upper thoracic spine is a challenge, and the accuracy of thoracic screw placement reportedly ranges from 27.6% to 91.5%, even in the hands of experienced surgeons [18]. The short and triangular vertebral bodies and the thin and medially oriented pedicles from T1 to T6 are the major factors responsible for these difficulties [2] and knowing in real time the safe margins of cortical violation with 3D view is paramount given that routine anteroposterior and lateral views are inadequate to evaluate screw position in all directions, especially for medial violations. According to our study and our literature search, we claim that all the factors implicated in the analysis of pedicle screw placement data could be particularly difficult to understand in confirming the superiority of one technique over another if removed from the hospital and the surgeon's point of view. The results of this study cannot be interpreted as confirming the validity of 3D C-arm's benefit over other imaging systems.

5 Limitations

This study reports a single-institution experience, basically exploring how the instrumented surgery of the spine changed in terms of safety and surgeons' confidence in pedicle screw positioning after shifting from traditional fluoroscopic imaging to C-arm visualization. A further comparison of the present results with other series could provide stronger evidence of the point of view herein, which is nevertheless based on solid rates of successful screw positioning at all spine levels.

6 Conclusion

Image-guided spinal surgery is a significant tool in the armamentarium of the spine surgeon in increasing accuracy in screw placement and reducing the risk of neurological injuries. The results of this analysis suggest a significantly high rate of pedicle screw placement accuracy in the cervical, thoracic, and lumbosacral spine procedures when intraoperative 3D fluoroscopy navigation is used. In the ongoing search for the next technological tool in neurosurgery, we believe that 3D C-arm fluoroscopy can still be a reasonable compromise between the imperative to pursue the best outcome and the need for updated and affordable technological equipment.

Conflicts of Interest The authors declare no conflicts of interest.

References

1. Tian NF, Huang QS, Zhou P, Zhou Y, et al. Pedicle screw insertion accuracy with different assisted methods: a systematic review and meta-analysis of comparative studies. Eur Spine J. 2011;20(6):846–59.
2. Braga BP, De Morais JV, Vilela MD. Free-hand placement of high thoracic pedicle screws with the aid of fluoroscopy: evaluation of positioning by CT scans in a four-year consecutive series. Arq Neuropsiquiatr. 2010;68(3):390–5.
3. Rahmathulla G, Nottmeier EW, Pirris SM, Deen HG, et al. Intraoperative image-guided spinal navigation: technical pitfalls and their avoidance. Neurosurg Focus. 2014;36(3):E3.
4. Nottmeier EW, Seemer W, Young PM. Placement of thoracolumbar pedicle screws using three-dimensional image guidance: experience in a large patient cohort. J Neurosurg Spine. 2009;10(1):33–9.
5. Ishikawa Y, Kanemura T, Yoshida G, Matsumoto A, et al. Intraoperative, full-rotation, three-dimensional image (O-arm)-based navigation system for cervical pedicle screw insertion. J Neurosurg Spine. 2011;15(5):472–8.
6. Feng W, Wang W, Chen S, Wu K, et al. O-arm navigation versus C-arm guidance for pedicle screw placement in spine surgery: a systematic review and meta-analysis. Int Orthop. 2020;44(5):919–26.
7. Holly LT, Foley KT. Three-dimensional fluoroscopy-guided percutaneous thoracolumbar pedicle screw placement. Technical note. J Neurosurg. 2003;99(3 Suppl):324–9.
8. Verma SK, Singh PK, Agrawal D, Sinha S, et al. O-arm with navigation versus C-arm: a review of screw placement over 3 years at a major trauma center. Br J Neurosurg. 2016;30(6):658–61.
9. Banat M, Wach J, Salemdawod A, Bahna M, et al. The role of intraoperative image guidance systems (three-dimensional C-arm versus O-arm) in spinal surgery: results of a single-center study. World Neurosurg. 2021;146:e817–21.
10. Rajasekaran S, Vidyadhara S, Ramesh P, Shetty AP. Randomized clinical study to compare the accuracy of navigated and non-navigated thoracic pedicle screws in deformity correction surgeries. Spine (Phila Pa 1976). 2007;32(2):E56–64.
11. Mason A, Paulsen R, Babuska JM, Rajpal S, et al. The accuracy of pedicle screw placement using intraoperative image guidance systems. J Neurosurg Spine. 2014;20(2):196–203.
12. Gruetzner PA, Waelti H, Vock B, et al. Navigation using fluoro-CT technology. Eur J Trauma. 2004;30:161–70. https://doi.org/10.1007/s00068-004-1328-6.
13. Kosmopoulos V, Schizas C. Pedicle screw placement accuracy: a meta-analysis. Spine (Phila Pa 1976). 2007;32(3):E111–20.
14. Zeiller SC, Lee J, Lim M, Vaccaro AR. Posterior thoracic segmental pedicle screw instrumentation: evolving methods of safe and effective placement. Neurol India. 2005;53(4):458–65.
15. Chang CC, Chang HK, Wu JC, Tu TH, et al. Comparison of radiation exposure between O-arm navigated and C-arm guided screw placement in minimally invasive transforaminal lumbar interbody fusion. World Neurosurg. 2020;139:e489–95.
16. Nakashima H, Sato K, Ando T, Inoh H, et al. Comparison of the percutaneous screw placement precision of isocentric C-arm 3-dimensional fluoroscopy-navigated pedicle screw implantation and conventional fluoroscopy method with minimally invasive surgery. J Spinal Disord Tech. 2009;22(7):468–72.
17. Nottmeier EW, Bowman C, Nelson KL. Surgeon radiation exposure in cone beam computed tomography-based, image-guided spinal surgery. Int J Med Robot. 2012;8(2):196–200.
18. Annoni E, Joedicke H, et al. The 3D O-arm surgical imaging system with navigation effectively and economically addresses the challenges of spina stabilization procedures. Value Health. 2013;16:556.

Comparison Between Ventricular and Spinal Infusion Tests in Suspected Normal Pressure Hydrocephalus

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1 Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is an often-overlooked or misdiagnosed brain disorder characterized by overt ventriculomegaly and associated with gait disturbances, cognitive impairment, and urinary incontinence. If correctly diagnosed, it is considered the only form of dementia treatable with surgery, namely through a ventriculoperitoneal or ventriculoatrial shunt with programmable valves. Despite having several diagnostic tools available, the selection of patients who will benefit from shunting still represents the main clinical challenge, as other neurological disorders can mimic iNPH or can coexist with it [1–5].

Apart from the well-known radiological signs (i.e., increased Evan's ratio, disproportionally effaced superior frontal sulci, and reduced callosal angle), functional information on perfusion, glucose metabolism, and amyloid deposit provided by positron emission tomography could be predictive of outcomes in iNPH patients, as reported in a recent review by our group [6].

Among the invasive tests to predict shunt responses, Katzman's infusion test evaluates cerebrospinal fluid (CSF) hydrodynamics [7, 8]. CSF outflow resistance (Rout) is generally regarded as the most significant parameter investigated in order to predict shunt-related neurological improvement [9]. Nonetheless, different Rout thresholds have been reported, and in 2013, a multicenter study concluded that it should not be used as a parameter to exclude patients from treatment [5].

In 2010, our group summarized 30 years of experience in the treatment of iNPH, showing that an intracranial elastance index (IEI) above 0.3 is a reliable predictor of a positive response after shunting [10]. This index is calculated by a dedicated software program developed at our institution during an intraventricular infusion test by measuring the slope of the linear regression between the diastolic intracranial pressure (ICP) values and the corresponding amplitude of each CSF pulse pressure wave.

More recently, we tried to verify the accuracy of IEI at predicting responses to shunts at both short- and long-term follow-ups in 64 patients with suspected iNPH who underwent ventricular shunting for iNPH on the basis of a positive ventricular infusion test (IEI $\geq$ 0.3 and $R^2 > 0.8$) [11].

Historically, our group has performed both ventricular and lumbar infusion tests. The intraventricular infusion test (IVKT) has been considered more reliable than the Spinal Katzman Test (SKT) [5] and has allowed for obtaining deeper insights into the pathophysiology of iNPH [1].

In this study, we compare the relationship between EI and Rout in two groups (IVKT and SKT), aiming to investigate the reliability of both procedures.

2 Methods

Among the 856 spinal and ventricular infusion tests performed from 2001 to 2017 at our institution, we analyzed 106 cases selected for suspected normotensive hydrocephalus. In all cases, EI and Rout values were calculated (Fig. 1). Infusion tests performed on patients with secondary normal pressure hydrocephalus (NPH) (e.g., post-traumatic, posthemorrhagic,

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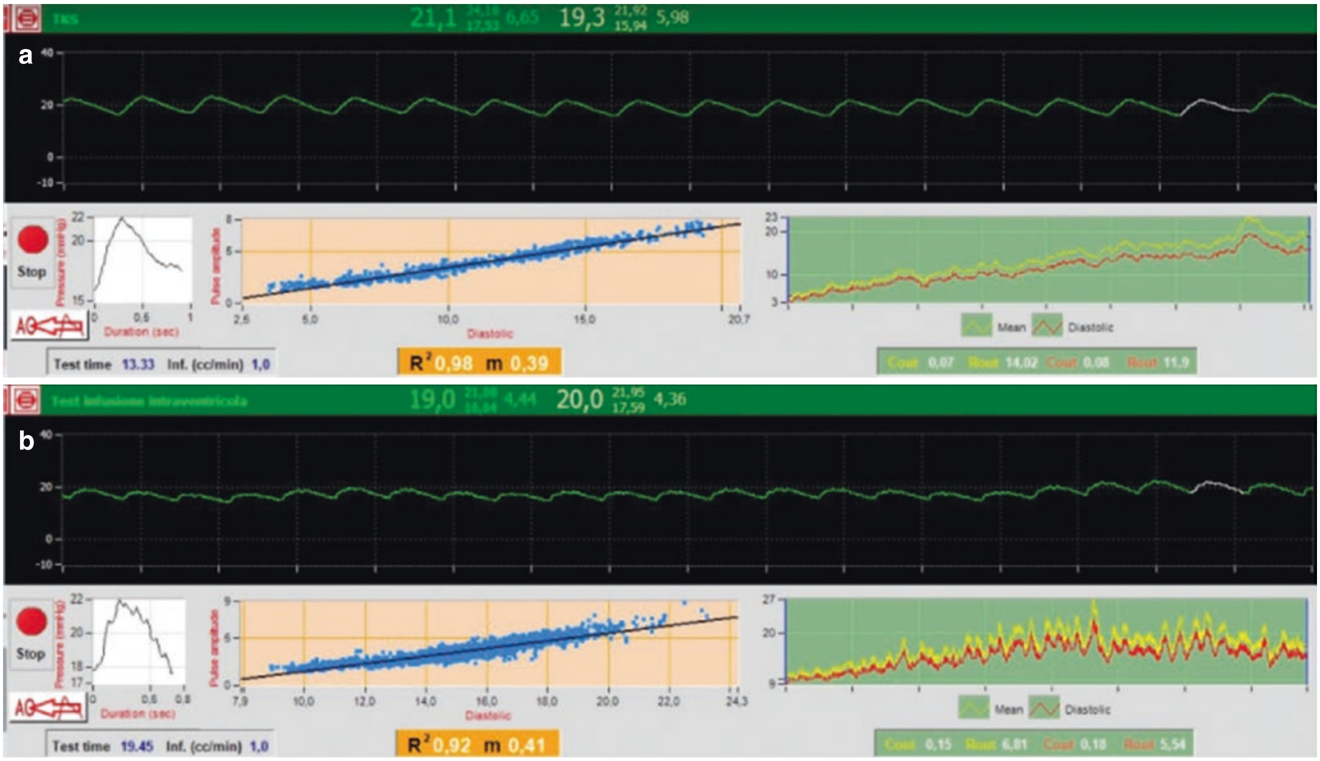

Fig. 1 Examples of SKT (**a**) and IVKT (**b**) performed at our institution

or postinfective) or who showed evidence of long-standing overt ventriculomegaly (LOVA) were excluded.

The method used for the infusion test has been previously described [10]. All patients gave written informed consent for the analysis of clinical data. All iNPH patients were selected for the infusion test according to the evidence from partial or complete clinical trials and the radiological evidence of ventriculomegaly with increased Evan's ratios, disproportionally effaced superior frontal sulci, and reduced callosal angles at brain high-field MRI (≥ 1.5 tesla). All the patients also underwent preadmission neuropsychological testing conducted by dedicated neurologists. The decision to perform either a ventricular or a spinal infusion test was at the discretion of the neurosurgeon.

3 Data Collection

All the infusion tests were reviewed, and the following parameters were collected—opening pressure, closing pressure, IEI, Rout, and ICP wave morphology before infusion and at the end of infusion—according to the four classes. Classification was based on changes in the relations between the three ICP peaks (percussion, tidal, and dicrotic peaks) previously reported by our group [12].

4 Results

We analyzed 106 cases selected for suspected normotensive hydrocephalus: 52 patients underwent SKT, and the remaining 54 underwent IVKT (Table 1). Of the 40 patients in the SKT group with pathological elastance (71%), 17 also had a Rout >12 mmHg and 23 a Rout <12 mmHg. Of the 50 patients in the IVKT group with pathological elastance (92%), 38 also had a Rout >12 mmHg and 12 a Rout <12 mmHg. We have found a statistically significant difference between the presence of elastance and pathological Rout values, on one hand, and the presence of pathological elastance and nonpathological We have found a statistically significant difference between the presence of both pathological elastance and Rout values, on one hand, and the presence of pathological elastance and nonpathological Rout. Of the 12 patients in the SKT group with normal elastance (29%), four had a Rout >12 mmHg and eight a Rout <12 mmHg. Of the four patients in the IVKT group with normal elastance (8%), one had a Rout >12 mmHg and three a Rout <12 mmHg. In this case, we did not find a statistically significant difference between the presence of nonpathological elastance and Rout and the presence of nonpathological elastance and pathological Rout between the SKT group and the IVKT group ($p = 0.755$ Fisher exact test).

Table 1 Results of both tests in patients with pathological values of IEI

	IEI > 0.3	IEI > 0.3 Rout >12	IEI > 0.3 Rout <12	*P*-value
IVKT	50	38	12	0.001
SKT	40	23	17	

5 Discussion

The role of CSF dynamics, characterized by resistance to CSF outflow (Rout) and other pressure–volume compensatory parameters, is still controversial in NPH, partially reflecting the insufficiently understood regulatory mechanism of CSF production [13], making the diagnosis and management of idiopathic NPH a complicated issue.

The diagnosis of iNPH is primarily clinical and radiological. However, because the literature reported a percentage of shunt nonresponders, ranging between 20% and 40% of patients [14], some ancillary, invasive tests have been developed to help clinicians to select patients who are more likely to improve after surgical treatment [8, 14, 15].

The ancillary tests can be divided into two categories: subtraction tests, namely the tap test or prolonged lumbar drainage, and infusion tests, either lumbar or ventricular. Several studies have previously addressed the predictive role of these invasive tests: When specificity and positive predictive values are elevated, low-sensitivity and negative predictive values are generally reported [5, 15–18].

Whether lumbar tests and intraventricular tests are equally reliable or supplementary in providing the baseline CSF dynamic data of interest in patients with suspected iNPH is debated. A previous study [19] demonstrated that a lumbar infusion test equals the intraventricular one in the selection of shunt-responsive patients.

In other studies, an intraventricular infusion test was deemed more reliable than a lumbar infusion test [5] and allowed for obtaining deeper insights into the pathophysiology of iNPH [1].

Among the parameters studied during Katzman's infusion test, the CSF outflow resistance (Rout) is generally regarded as the most significant one to predict improvement after shunt placement [2, 3, 9]; however a multicenter study concluded that Rout should not be used as a parameter to exclude patients from treatment [5].

In 2010, our group summarized 30 years of experience in the treatment of iNPH, showing that an intracranial elastance index (IEI) above 0.3 was a robust predictor of a positive response after shunting [10]. This index was automatically computed by a dedicated software program developed at our institution by measuring the slope of the linear regression between each diastolic intracranial pressure (ICP) value and the corresponding amplitude of each CSF pulse pressure wave during an intraventricular infusion test. The test was considered as reliable if the coefficient of determination (R^2) was >0.8. All the patients who were selected for shunting using a threshold of IEI ≥ 0.3 showed clinical improvements at 6- and 12-month follow-ups. On the other hand, patients with an IEI < 0.3 did not improve at the same follow-up time points. In the same series, Rout values did not correlate with clinical outcomes.

More recently, we retrospectively reviewed 64 patients undergoing ventriculoperitoneal shunting for iNPH on the basis of a positive ventricular infusion test (IEI ≥ 0.3), and we found that an IEI ≥ 0.3 predicts both short-term and long-term outcomes, where more than 50% of patients were able to look after themselves 6 years after treatment [11].

IVKT, although more invasive than the SKT, allows a more reliable analysis of the CSF dynamics [20]. Our study, based on an analysis of instrumental data, highlights that in cases of IVKT, pathological elastance values are significantly related to the pathological ones of Rout, unlike the cases of the SKT group. This matching, not found for nonpathological values of elastance and Rout, could be considered a more reliable index of the overall significance of the test rather than a separate analysis of the same, thus providing evidence of the superiority of the IVKT.

6 Limitations

Our study could be prone to the biases associated with a retrospective research method. The limited number of cases further limits the strengths of this study. Moreover, the present study deals only with technical aspects of infusion tests; we did not consider clinical aspects or the predictive values of the test in terms of the outcomes of shunt procedures, so our findings should be analyzed with caution.

7 Conclusions

IVKT and SKT to date represent two useful tools in the diagnosis of normal pressure hydrocephalus. Despite being more invasive, IVKT, including both IEI and Rout analysis, could be considered more reliable than SKT and therefore could be reserved for the most controversial cases.

References

1. Andersson J, Rosell M, Kockum K, Söderström L, Laurell K. Challenges in diagnosing normal pressure hydrocephalus: evaluation of the diagnostic guidelines. eNeurologicalSci. 2017;7:27–31.
2. Halperin JJ, Kurlan R, Schwalb JM, Cusimano MD. Practice guideline: idiopathic normal pressure hydrocephalus: response to shunting and predictors of response. Published online: 9. 2015.

3. Hellström P, Klinge P, Tans J, Wikkelsø C. The neuropsychology of iNPH: findings and evaluation of tests in the European multicentre study. Clin Neurol Neurosurg. 2012;114(2):130–4. https://doi.org/10.1016/j.clineuro.2011.09.014.
4. Raneri F, Zella MAS, Di Cristofori A, Zarino B, Pluderi M, Spagnoli D. Supplementary tests in idiopathic Normal pressure hydrocephalus: a single-center experience with a combined lumbar infusion test and tap test. World Neurosurg. 2017;100:567–74.
5. Wikkelsø C, Hellström P, Klinge PM, Tans JTJ. European iNPH multicentre study group. The European iNPH multicentre study on the predictive values of resistance to CSF outflow and the CSF tap test in patients with idiopathic normal pressure hydrocephalus. J Neurol Neurosurg Psychiatry. 2013;84(5):562–8.
6. Mattoli MV, Treglia G, Calcagni ML, Mangiola A, Anile C, Trevisi G. Usefulness of brain positron emission tomography with different tracers in the evaluation of patients with idiopathic normal pressure hydrocephalous. Int J Mol Sci. 2020;21(18):6523.
7. Hussey F, Schanzer B, Katzman R. A simple constant-infusion manometric test for measurement of CSF absorption. II Clinical studies. Neurology. 1970;20(7):665–80.
8. Katzman R, Hussey F. A simple constant-infusion manometric test for measurement of CSF absorption. Rationale and method. Neurology. 1970;20(6):534–44.
9. Kahlon B. Comparison between the lumbar infusion and CSF tap tests to predict outcome after shunt surgery in suspected normal pressure hydrocephalus. J Neurol Neurosurg Psychiatry. 2002;73(6):721–6. https://doi.org/10.1136/jnnp.73.6.721.
10. Anile C, De Bonis P, Albanese A, Di Chirico A, Mangiola A, Petrella G, Santini P. Selection of patients with idiopathic normal-pressure hydrocephalus for shunt placement: a single-institution experience. J Neurosurg. 2010;113:64–73.
11. Trevisi G, Signorelli F, de Waure C, Stifano V, Sturdà C, Rapisarda A, Pompucci A, Mangiola A, Anile C. Intraventricular infusion test accuracy in predicting short- and long-term outcome of iNPH patients: a 10-year update of a three-decade experience at a single institution. Neurosurg Rev. 2021;44(6):3323–34.
12. Nucci CG, De Bonis P, Mangiola A, Santini P, Sciandrone M, Risi A, Anile C. Intracranial pressure wave morphological classification: automated analysis and clinical validation. Acta Neurochir. 2016;158:581–8.
13. Trevisi G, Frassanito P, Di Rocco C. Idiopathic cerebrospinal fluid overproduction: case-based review of the pathophysiological mechanism implied in the cerebrospinal fluid production. Croat Med J. 2014;55(4):377–87.
14. Giordan E, Palandri G, Lanzino G, Murad MH, Elder BD. Outcomes and complications of different surgical treatments for idiopathic normal pressure hydrocephalus: a systematic review and meta-analysis. J Neurosurg. 2018:1–13.
15. Junkkari A, Luikku AJ, Danner N, Jyrkkänen HK, Rauramaa T, Korhonen VE, Koivisto AM, Nerg O, Kojoukhova M, Huttunen TJ, Jääskeläinen JE, Leinonen V. The Kuopio idiopathic normal pressure hydrocephalus protocol: initial outcome of 175 patients. Fluids Barriers CNS. 2019;16:21.
16. Czosnyka Z, Owler B, Keong N, Santarius T, Baledent O, Pickard JD, Czosnyka M. Impact of duration of symptoms on CSF dynamics in idiopathic normal pressure hydrocephalus: duration of symptoms and CSF dynamics. Acta Neurol Scand. 2011;123:414–8. https://doi.org/10.1111/j.1600-0404.2010.01420.x.
17. Eide PK. The correlation between pulsatile intracranial pressure and indices of intracranial pressure-volume reserve capacity: results from ventricular infusion testing. J Neurosurg. 2016;125:1493–503. https://doi.org/10.3171/2015.11.JNS151529.
18. Eide PK, Sorteberg W. Outcome of surgery for idiopathic Normal pressure hydrocephalus: role of preoperative static and pulsatile intracranial pressure. World Neurosurg. 2016;86:186–193.e1. https://doi.org/10.1016/j.wneu.2015.09.067.
19. Bech-Azeddine R, Gjerris F, Waldemar G, Czosnyka M, Juhler M. Intraventricular or lumbar infusion test in adult communicating hydrocephalus? Practical consequences and clinical outcome of shunt operation. Acta Neurochir. 2005;147(10):1027–35. discussion 1035-6.
20. Halperin JJ, Kurlan R, Schwalb JM, Cusimano MD, Gronseth G, Gloss D. Practice guideline: Idiopathic normal pressure hydrocephalus: Response to shunting and predictors of response: report of the guideline development, dissemination, and implementation subcommittee of the american academy of neurology. Neurology. 2015;85(23):2063–71. https://doi.org/10.1212/WNL.0000000000002193. Erratum in: Neurology. 2016 Feb 23;86(8):793. PMID: 26644048; PMCID: PMC4676757.

Spinal Dural Arteriovenous Fistulas: A Retrospective Analysis of Prognostic Factors and Long-Term Clinical Outcomes in the Light of the Recent Diagnostic and Technical Refinements

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Abbreviations

dAVFs	Spinal dural arteriovenous fistulas
DSA	Digital subtraction angiography
mALS	Modified Aminoff–Logue Disability Scale
MRI	Magnetic resonance imaging
SEPs	Somatosensorial evoked potentials
TIVA	total intravenous anaesthesia

1 Introduction

Spinal dural arteriovenous fistulas (dAVFs) are acquired abnormal connections between one or more meningeal branches of a segmental artery and a radiculomedullary vein within the dural sleeve of a nerve root. Differently from a true arteriovenous malformation, dAVFs do not present an interposed nidus [1]. The resulting venous hypertension in the perimedullary coronal venous plexus is responsible for the progressive congestive myelopathic condition known as Foix–Alajouanine syndrome [2]. They show a pretty rare incidence at only 5–10 new cases per million people per year [3]. Finally, dAVFs may lead toward a progressive severe neurological impairment over time when they are not timely diagnosed and treated. Aminoff and Logue reported the progression of disability from 19% at 6 months up to 50% after 3 years from clinical onset [4].

The two main diagnostic pitfalls are as follows:

1. A late clinical suspicion, especially at onset, when the symptoms can be faded
2. The difficulty of making a correct diagnosis on the basis of magnetic resonance imaging (MRI), which, in the absence of medullary oedema is limited to recognising a perimedullary venous congestion, in turn will suggest performing a digital subtraction angiography (DSA)

Once the diagnosis has been made, the treatment is pretty straightforward in that it consists of the surgical disconnection or endovascular obliteration of the origin of the dAVF venous drainage.

The surgical approach usually has a high rate of success and virtually no risk of recurrence or incomplete treatment [1], and the main difficulty among expert neurovascular surgeons is considered finding the fistula itself.

According to a recent meta-analysis, about 89% of patients showed improvement or stabilisation of symptoms after treatment. However, a not negligible outcome variability does exist among patients, and although several studies have addressed the problem of factors connected with outcome, their understanding is not yet exhaustive. In this paper, we analyse the long-term clinical outcomes for our recent institutional series of patients treated for a dAVF, exploring some demographic, angioarchitectural and clinical characteristics potentially connected with outcome.

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2 Materials and Methods

We retrospectively reviewed all consecutive patients admitted to our department from January 2015 to December 2021 for a diagnosis of dAVF located in the cervical and thoracolumbar regions. We collected all demographic and angioarchitectural characteristics, including the topography of the involved nerve root sleeve and the origin of the Adamkiewicz artery.

According to the most frequent location of the great radicular artery of Adamkiewicz, which usually originates from a low left (sometimes right) intercostal artery between T8 and T12 and less often from an upper lumbar artery (L1 or L2), we grouped the dAVFs into three main topographies: (a) above T7, (b) between T7 and T12 and (c) below T12. Similarly, we determined the location of the Adamkiewicz artery in the same three categories.

We also reviewed and scored the clinical presentation according to the modified Aminoff–Logue Disability Scale (mALS). Further, mALS points were collected for three categories according to gait function (G-score), urinary disturbances (U-score) and faecal continence (F-score) and then grouped into three score intervals (0–3; 4–7; 8–11) that represent clinical severity (moderate, intermediate and severe). Clinical improvement was defined as a decrease of at least one point in the mALS score at follow-up compared with baseline assessment.

We also assessed the time between clinical onset and treatment as well as the type of treatment. Moreover, we evaluated the most important preoperative neuroradiological features, including the number of medullar neuromers presenting oedema, the presence of syringomyelia, its extension, and the presence of multiple dural feeders on the digital subtraction angiography (DSA). Also, we assessed the baseline intraoperative somatosensorial evoked potentials (SEPs) under total intravenous general anaesthesia (TIVA) to measure their variation in width and latency. Next, we evaluated all the neuroradiological and clinical changes in these features observed at last follow-up. Finally, we compared patients who showed and patients who did not show clinical improvements in all the available demographic, angioarchitectural and treatment-related variables, including surgical timing and intraoperative neurophysiological monitoring parameters in order to explore their prognostic value.

Quantitative variables were expressed as mean ± standard deviation, and the Student's *t*-test was used to compare their means. The Fisher exact test (two sided) was used to compare the categorical variables with the outcomes.

The statistical analysis was conducted by using Microsoft Excel v. 16 (Microsoft, Redmond, WA, USA) and R software (version 4.0).

3 Results

Between January 2015 and December 2021, we collected 30 patients with a diagnosis of dAVFs.

Demographic and preoperative clinical characteristics of the included patients are listed in Table 1.

The mean age was 62.6 ± 12.0 years old, with a clear prevalence of male sex (83.3%).

More than half of dAVFs originated among T7 and T12 (53.3%), equally distributed between the two sides, followed by those at level of the lumbar roots (30%) and then by those that originated above the T7 level (16.7%).

A similar distribution was observed for the origin of the Adamkiewicz artery, which branched from a T7-T12 intercostal artery in 18/30 (60%) out of patients (mainly on left side in 13 out of 18 cases), followed by lumbar arteries below T12 in 13.3% and upper cervico-thoracic spine in 6.7%; the Adamkiewicz artery was instead not visualized in 20% of cases. In no cases did the great radicular artery originate from the same segmental artery whose meningeal branches fed the dAVF.

According to the modified Aminoff–Logue scale, most patients (25/30, or 83.3%) showed a motor deficit starting from a restricted exercise tolerance (G2), to a progressive requirement of a support (G3), and up to crutches or two sticks for walking (G4), with a mean G-score of 3.1 ± 1.2 points.

Urinary tract disturbances were present in 70% of cases, with a prevalence for urge incontinence or occasional incontinence or retention in about 57% of cases, and a persistent deficit was present in about 13%, with a mean U-score of 1.2 ± 1.02.

Finally, bowel symptoms were present only in 50% of patients: In particular, 26.7% showed only mild constipation, whereas more-severe incontinence was present only in just over 23%, with a mean F-score of 0.8 ± 0.9.

At preoperative diagnostic valuation, MRI showed the presence of spinal oedema in all cases, with a mean number of 5.5 ± 3.3 involved neuromers, whereas a true syringomyelia was present in 40% of patients. The DSA assessment was able to identify the precise site of the draining vein's origin in all cases, also showing the presence of multiple dural feeders coming from different segmental arteries in more than half of cases.

In our series, 26 out of 30 cases (86.7%) were treated with microsurgery and 13.3% with endovascular occlusion. The mean interval between clinical onset and intervention was 10.8 ± 14.2 months. After the induction of total intravenous general anaesthesia (TIVA), SEP measurements showed a significantly reduced width and/or augmented latency in 26 patients (86.7%).

Table 1 Demographic and preoperative clinical characteristics of 30 included patients with spinal dAVFs

Characteristics (n = 30)			N. (%)
Mean age ± SD			62.6 ± 12.0
Male sex			25 (83.3)
Topography of the fistula		Above T7	5 (4R + 1 L) (16.7)
		T7-T12	16 (8R + 8 L) (53.3)
		Below T12	9 (4R + 5 L) (30)
Origin of the Adamkiewicz artery		Above T7	2 (0R + 2 L) (6.7)
		T7-T12	18 (5R + 13 L) (60)
		Below T12	4 (3R + 1 L) (30)
		Not visualized	6 (20)
Preoperative mALS score	G-score	0	0
		1	2 (6.7)
		2	7 (23.3)
		3	10 (33.3)
		4	8 (26.7)
		5	3 (10)
		mean ± SD	3.1 ± 1.2
	U-score	0	9 (30)
		1	9 (30)
		2	8 (26.7)
		3	4 (13.3)
		mean ± SD	1.2 ± 1.02
	F-score	0	15 (50)
		1	8 (26.7)
		2	5 (16.7)
		3	2 (6.7)
		mean ± SD	0.8 ± 0.9
Preoperative mALS groups	moderate	0–3	10 (33.3)
	intermediate	4–7	13 (43.3)
	severe	8–11	7 (23.3)
Preoperative MRI		Oedema: no. of involved levels – mean ± SD	5.5 ± 3.3
		Presence of Syrinx: no. of patients (%)	12 (40)
Preoperative DSA		Presence of multiple dural feeders no. (%)	16 (53.3)
Intraoperative SEP under TIVA		Reduced width and/or augmented latency	26 (86.7)
Treatment		Surgery	26 (86.7)
		Endovascular	4 (13.3)
Interval between symptoms and treatment in months mean ± SD			10.8 ± 14.2

No. number, *SD* standard deviation, *MRI* magnetic resonance imaging, *DSA* digital subtraction angiography, mALS modified Aminoff and Logue's Scale, *SEPs* somatosensory evoked potentials, *TIVA* total intravenous anaesthesia

Table 2 Postoperative clinical and radiological outcomes of 30 included patients with spinal dAVFs

Characteristics (n = 30)			No. of patients (%)
Postoperative MRI		Reduced oedema	22 (73.3)
		Reduced dorsal venous system congestion	22 (73.3)
		Reduced Syrinx	12 (40)
Postoperative DSA		Closed fistula at first intervention	29 (96.7) (1 retreatment)
Intraoperative SEP change after dAVF ligation (under TIVA)		Improvement of width and latency	0
Postoperative clinical improvement (mALS score)	G-score	0	6 (20)
		1	6 (20)
		2	7 (23.3)
		3	7 (23.3)
		4	2 (6.7)
		5	2 (6.7)
		mean ± SD	1.9 ± 1.4
	U-score	0	14 (46.7)
		1	12 (40)
		2	1 (3.3)
		3	3 (10)
		mean ± SD	0.7 ± 0.9
	F-score	0	21 (70)
		1	6 (20)
		2	2 (6.7)
		3	1 (3.3)
		mean ± SD	0.4 ± 0.7
Postoperative clinical severity (mALS groups)	mild	0–3	19 (63.3)
	intermediate	4–7	9 (30)
	severe	8–11	2 (6.7)
Clinical follow-up (months)		mean ± SD	105.89 ± 191.9
Radiological follow-up (months)		mean ± SD	60.77 ± 180.3

Postoperative clinical and radiological outcomes are reported in Table 2. All patients had an immediate postoperative DSA, showing the complete dAVF occlusion in all cases except one, which was microsurgically re-explored with dAVF identification and closure 2 days later. At a follow-up MRI, we observed the reduction of the oedema and the dorsal venous system congestion in almost three-quarters of patients, while no significant changes were observed in the immediate post-dAVF closure in SEP, in terms of neither width nor latency. The mean radiological follow-up was 105.89 ± 191.9 months.

A significant clinical improvement was observed at follow-up in 24 of 30 (80%) patients, with a reduction in mean G-score from 3.1 ± 1.2 to 1.9 ± 1.4 ($p < 0.01$) in the mean G-score, from 1.2 ± 1.02 to 0.7 ± 0.9 ($p = 0.04$) in the mean

U-score and from 0.8 ± 0.9 to 0.4 ± 0.7 (p = 0.05) in the mean F-score, with a mean follow-up time of 105.89 ± 191.9 months (Table 3). Finally, we compared the principal demographic, clinical and radiological characteristics of patients who showed a clinical improvement after surgery and those who did not (Table 4). However, none of them showed significant prognostic value to the clinical improvement observed at follow-up.

Table 3 Comparison between preoperative and follow-up mean mALS

n = 30		Preop	Postop	p-Value
mALS score mean ± SD	G-score	3.1 ± 1.2	1.9 ± 1.4	< 0.01
	U-score	1.2 ± 1.02	0.7 ± 0.9	0.04
	F-score	0.8 ± 0.9	0.4 ± 0.7	0.05

Table 4 Comparison between the demographic, clinical and neuroradiological features of patients with and without clinical improvement after surgery

	Variable	Patients with clinical improvement (tot. = 24) (%)	Patients with no clinical improvement (tot. = 6) (%)	p-Value
Age	≤ 30 years	0	0	1.00
	> 30 years	24 (100)	6 (100)	
	≤ 60 years	11 (45.8)	3 (50)	1.00
	> 60 years	13 (54.2)	3 (50)	
Sex	Man	19 (79.2)	5 (83.3)	1.00
	Woman	5 (20.8)	1 (16.7)	
Interval between symptoms onset and treatment	< 1 months	7 (29.2)	3 (50)	0.37
	> 1 months	17 (70.8)	3 (50)	
	< 6 months	14 (58.3)	3 (50)	1.00
	> 6 months	10 (41.7)	3 (50)	
Location	Above T7	8 (33.3)	1 (16.7)	0.63
	T7-T12	8 (33.3)	4 (66.7)	0.18
	Below T12	8 (33.3)	1 (16.7)	0.63
Treatment	Clipping	20 (83.3)	6 (100)	0.55
	Endovascular	4 (16.7)	0	
Preoperative MRI	Oedema: no. of involved levels mean ± SD	5.1 ± 3.4	7.4 ± 2.5	0.13
	Presence of Syrinx	10 (41.7)	2 (33.3)	0.65
Preoperative DSA	Multiple dural feeders	13 (54.2)	3 (50)	1.00
Preoperative SEP	Reduced width and/or augmented latency	20 (83.3)	6 (100)	0.55
Preoperative mALS groups	Mild (0–3)	9 (37.5)	1 (16.7)	0.63
	Intermediate (4–7)	9 (37.5)	4 (66.7)	0.35
	Severe (8–11)	6 (25)	1 (16.7)	1.00

4 Discussion

Overall, dAVFs are the most common types of spinal cord vascular malformations that can be challenging to promptly diagnose and treat. Although the existence of progressive neurological damage due to vascular spinal disorders has been known for more than half a century, only the advent of the selective spinal catheter DSA has allowed the documentation of the different types of spinal cord vascular malformations, identifying dAVFs as Type I. These are abnormal connections between a radicular feeding artery and the coronal venous plexus of the spine, and the fistula site is localised within the dural sleeve of the nerve root.

The subsequent arterialisation of the venous plexus, along with the obstruction of the outflow, leads to venous congestion, hypertension and progressive ascending myelopathy (Fig. 1). Further, dAVFs represent approximately more than 2/3 of all the spinal arteriovenous malformations, with an incidence of 5–10 cases per million people annually [5, 6]. Although they seem to be acquired conditions that affect mainly middle-aged men, their aetiology remains unknown.

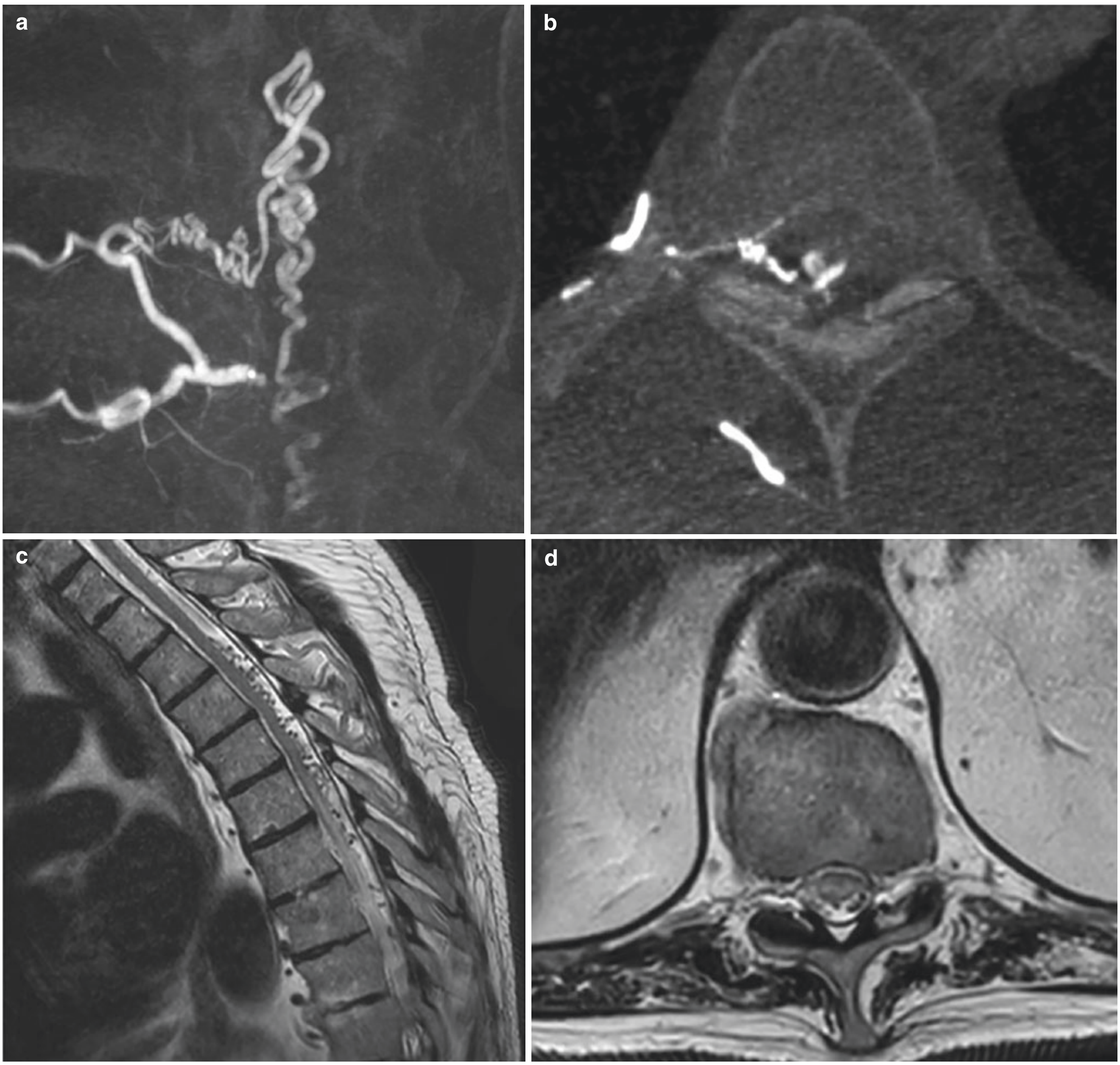

Fig. 1 Coronal (**a**) and axial (**b**) 3D DynaCT-scan reconstruction showing the fistula site within the dural sleeve of the right T8 nerve root along with the congestion of the perimedullary coronal venous plexus. Same aspects appear visible at sagittal (**c**) and axial (**d**) T2-MRI sequences, also showing a thoracic spine hydromielia

The presenting clinical symptoms and signs are nonspecific and insidious at onset. The majority of patients develop myelopathic symptoms that gradually progress over time or that sometimes occur in a stepwise fashion. Most of them commonly present gait impairment and lower-extremity weakness associated with sensory disturbances, pain and sphincter incontinence [5].

In 1926, Foix and Alajouanine first described two young men with progressive myelopathy who showed a clinical trend of acute or subacute neurological deterioration attributed to a venous origin [7]. Although at that time dAVFs were not yet known, some speculated that the patients in the original report by Foix and Alajounaine were affected by this vascular disorder [8].

Establishing accurate predictors before dAVF treatment has been challenging in past studies and has been limited by the small sizes of most published series. In general, clinical characteristics, rather than radiological findings, have seemed to have had the most predictive value [5], and patients with preoperative mild gait disability were reported to have improved more than those in other grade categories [9, 10].

Some other studies also reported a different prognostic significance in dAVF location, showing that patients with low thoracic fistulas had the best improvement in functional recovery over time compared with the other levels [11, 12]. However, all these results appear inconsistent among studies.

On the other hand, analyses of a large cohort study of surgically treated dAVF patients with myelopathy showed continuous improvement after hospital discharge for a long time [13].

In our study, we did not find a correlation between age, sex, duration of symptoms, location of fistula and outcome at follow-up. We observed that more than 50% of patients had a dAVF located in the low thoracic spine, but we did not find a better long-term outcome among different locations. Moreover, unlike previous studies [14], we observed a better outcome neither in younger patients (<30 years old) nor in older (>60). Instead, in agreement with what other authors have observed, we did not find correlation between symptom duration before the intervention and long-term outcome [12, 14–16].

Regarding treatment choice, both surgical and endovascular approaches primarily aim to interrupt the dAVF at the level of the draining vein's origin (Fig. 2). A meta-analysis published in 2004 attested to the superiority of surgery over embolisation in terms of both immediate dAVF obliteration and the inferior rate of clinical and radiological recurrence, with a success rate less than 50% for the endovascular group [17]. The transarterial endovascular approach, in fact, may fail to obliterate the venous compartment, which implies that there is a risk of the medium- to long-term recurrence of the fistula [18].

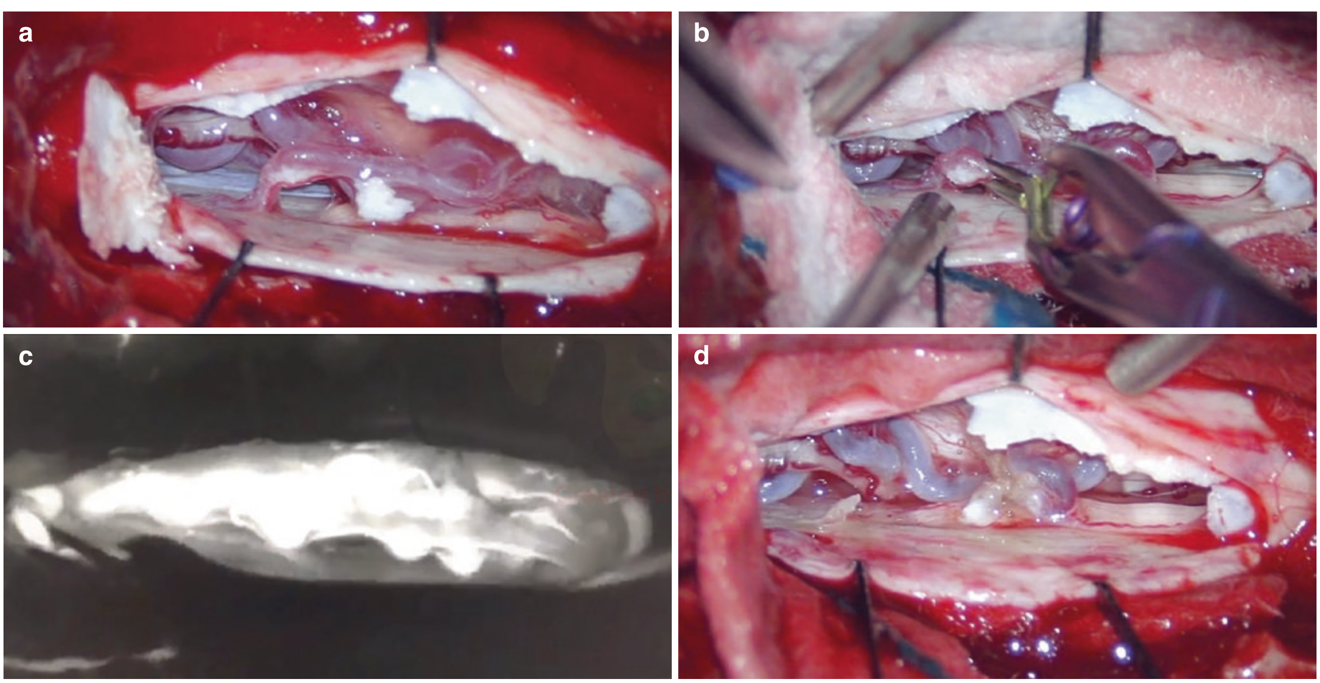

Fig. 2 Intraoperative view of dAVF microsurgical ligation, showing the abnormal connection between a perimedullay vein and a meningeal arterial branch (**a**); the origin of the venous drainage is temporary clipped under neurophysiological monitoring (**b**), and indocyanine green (ICG) videoangiography and microdoppler are performed to obtain the hemodynamic confirmation of the fistula (**c**); next, the vein origin is coagulated and sectioned if neurophysiological monitoring shows stability (**d**)

However, the endovascular approach has shown a tremendous evolution over the past two decades, in terms of both techniques and tools. A more recent meta-analysis, in fact, attested to a rate of success for endovascular closure of dAVFs that has improved up to more than 70%, although surgery still showed its clear superiority, with a success rate of more than 96% [19]. In our series, about 13.3% of cases were treated endovascularly, with a 100% success rate at the current follow-up, while the remaining 26 cases were treated with surgery, with a rate of the immediate closure of 25 of 26 cases (96.1%). One patient with a doubtful intraoperative finding was microsurgically re-explored on the second postoperative day; after that, a new DSA confirmed the persistence of the fistula.

Notably, no major complications were observed in our series owing to the approach that was usually performed through a minimally invasive laminotomy with posterior element preservation while taking particular care during the dissection and closure of the muscular and superficial layers to achieve the best aesthetic result [20, 21]. Finally, in our recent experience, we always kept in mind the observation that a condition of acute paraplegia due to dAVFs could be induced by corticosteroid administration in misdiagnosed patients and could also be exacerbated by hydrostatic forces resulting from erect posture, abnormal compression and the Valsalva manoeuvre [22, 23].

5 Conclusions

Although our study appears to be limited by its small sample size, in agreement with the inconsistency in the relevant literature, our data do not support the absolute paradigm that patients with a more severe clinical picture have no chance to recover. Furthermore, as no prognostic factors have proved to be unquestionably definitive, none of these can be considered to support the scenario of not offering treatment to a patient once an angiographic diagnosis has been made.

Funding Not applicable.

Conflicts of Interest/Competing Interests The authors declare no conflicts if interest.

Ethics Approval IRB approval was not required for the retrospective collection of anonymous data.

Consent to Participate Informed consent was provided by every patient participating in this study.

Consent for Publication Not applicable.

Author Contributions Conception and design, CLS; data collection, CLS, AAu, IV, and AP; data analysis, CLS, AAu, and RM; drafting, CLS; helping with drafting, AAu, RM, and AA; approval of final version, CLS and AA.

References

1. Ghadirpour R, Nasi D, Iaccarino C, Romano A, Motti L, Farneti M, Pascarella R, Servadei F. Intraoperative neurophysiological monitoring in surgical treatment of spinal dural arteriovenous fistulas: technique and results. Asian J Neurosurg. 2018;13(3):595–606.
2. Sadighi N, Tajmalzai A, Salahshour F. Spinal arteriovenous malformations causing Foix-Alajouanine syndrome, a case report and review of the literature. Radiol Case Rep. 2021;16(8):2187–91.
3. Thron A. Spinal dural arteriovenous fistulas. Radiologe. 2001;41(11):955–60.
4. Aminoff MJ, Logue V. The prognosis of patients with spinal vascular malformations. Brain. 1974;97(1):211–8.
5. Fugate JE, Lanzino G, Rabinstein AA. Clinical presentation and prognostic factors of spinal dural arteriovenous fistulas: an overview. Neurosurg Focus. 2012;32(5):E17.
6. Koch C. Spinal dural arteriovenous fistula. Curr Opin Neurol. 2006;19(1):69–75.
7. Linoli O. Foix-Alajouanine disease (subacute necrotic myelitis). I. Anatomoclinical aspects. Rass Studi Psichiatr. 1957;46(5):607–30.
8. Ferrell AS, Tubbs RS, Acakpo-Satchivi L, Deveikis JP, Harrigan MR. Legacy and current understanding of the often-misunderstood Foix-Alajouanine syndrome. Historical vignette. J Neurosurg. 2009;111(5):902–6.
9. Atkinson JL, Miller GM, Krauss WE, Marsh WR, Piepgras DG, Atkinson PP, Brown RD, Lane JI. Clinical and radiographic features of dural arteriovenous fistula, a treatable cause of myelopathy. Mayo Clin Proc. 2001;76(11):1120–30.
10. Westphal M, Koch C. Management of spinal dural arteriovenous fistulae using an interdisciplinary neuroradiological/neurosurgical approach: experience with 47 cases. Neurosurgery. 1999;45(3):451–7. discussion 457-458.
11. Cenzato M, Debernardi A, Stefini R, D'Aliberti G, Piparo M, Talamonti G, Coppini M, Versari P. Spinal dural arteriovenous fistulas: outcome and prognostic factors. Neurosurg Focus. 2012;32(5):E11.
12. Cenzato M, Versari P, Righi C, Simionato F, Casali C, Giovanelli M. Spinal dural arteriovenous fistulae: analysis of outcome in relation to pretreatment indicators. Neurosurgery. 2004;55(4):815–22. discussion 822-823.
13. Saladino A, Atkinson JLD, Rabinstein AA, Piepgras DG, Marsh WR, Krauss WE, Kaufmann TJ, Lanzino G. Surgical treatment of spinal dural arteriovenous fistulae: a consecutive series of 154 patients. Neurosurgery. 2010;67(5):1350–7. discussion 1357-1358.
14. Nagata S, Morioka T, Natori Y, Matsukado K, Sasaki T, Yamada T. Factors that affect the surgical outcomes of spinal dural arteriovenous fistulas. Surg Neurol. 2006;65(6):563–8. discussion 568
15. Cecchi PC, Musumeci A, Faccioli F, Bricolo A. Surgical treatment of spinal dural arterio-venous fistulae: long-term results and analysis of prognostic factors. Acta Neurochir. 2008;150(6):563–70.
16. Wakao N, Imagama S, Ito Z, et al. Clinical outcome of treatments for spinal dural arteriovenous fistulas: results of multivariate analysis and review of the literature. Spine (Phila Pa 1976). 2012;37(6):482–8.
17. Steinmetz MP, Chow MM, Krishnaney AA, Andrews-Hinders D, Benzel EC, Masaryk TJ, Mayberg MR, Rasmussen PA. Outcome after the treatment of spinal dural arteriovenous fistulae: a contemporary single-institution series and meta-analysis. Neurosurgery. 2004;55(1):77–87. discussion 87-88
18. Oh Y, Heo Y, Jeon SR, Roh SW, Park JH. Microsurgery versus endovascular treatment—which is adequate for initial treatment of spinal dural arteriovenous fistula: a case series. Neurospine. 2021;18(2):344–54.

19. Bakker NA, Uyttenboogaart M, Luijckx GJ, Eshghi OS, Mazuri A, Metzemaekers JDM, Groen RJM, Van Dijk JMC. Recurrence rates after surgical or endovascular treatment of spinal dural arteriovenous fistulas: a meta-analysis. Neurosurgery. 2015;77(1):137–44. discussion 144
20. Ricciardi L, Stifano V, Sturiale CL, D'Onofrio GF, Olivi A, Montano N. Minimally invasive decompression with posterior elements preservation versus laminectomy and fusion for lumbar degenerative spondylolisthesis: a systematic review and meta-analysis of surgical, clinical and radiological outcomes. Surg Technol Int. 2020;36:457–63.
21. Ricciardi L, Sturiale CL, Pucci R, et al. Patient-oriented aesthetic outcome after lumbar spine surgery: a 1-year follow-up prospective observational study comparing minimally invasive and standard open procedures. World Neurosurg. 2019;122:e1041–6.
22. O'Keeffe DT, Mikhail MA, Lanzino G, Kallmes DF, Weinshenker BG. Corticosteroid-induced paraplegia—a diagnostic clue for spinal dural arterial venous fistula. JAMA Neurol. 2015;72(7):833–4.
23. Sato K, Terbrugge KG, Krings T. Asymptomatic spinal dural arteriovenous fistulas: pathomechanical considerations. J Neurosurg Spine. 2012;16(5):441–6.

Vertebral Candidiasis, the State of the Art: A Systematic Literature Review

Dario Candura, Andrea Perna, Sara Calori, Francesco Ciro Tamburrelli, Luca Proietti, Maria Concetta Meluzio, Calogero Velluto, Amarildo Smakaj, and Domenico Alessandro Santagada

1 Introduction

Candida species are typically considered commensal organisms and either part of the normal human flora or associated with clinically benign infections. The increased incidence of invasive candidiasis has led to the identification of risk factors for invasive *Candida* infections, such as antimicrobial exposure, central catheter placement, immunocompromised status, prolonged neutropenia, and injection drug use [1].

Vertebral osteomyelitis (VO) is one of the invasive infections that *Candida* can lead to. VO is a bone infection characterized by osteolysis, deformity of the intervertebral discs, and collections of purulent material in the epidural space, resulting in continuous and progressive back pain, fever, and, in a smaller percentage of cases, neurological deficits [2].

The diagnosis of *Candida* vertebral osteomyelitis begins with a high clinical index of suspicion, followed by appropriate radiographic studies and confirmation with microbiological tests. Plain radiographs frequently show erosive and destructive vertebral changes, but these may not be visible for weeks to months. Instead, computer tomography (CT) may show early changes in the bone and any vertebral and paravertebral collections, even if no characteristic signs have been found that distinguish osteomyelitis from *Candida* and those caused by other pathogens [3].

In contrast, some studies in the literature have reported several characteristic magnetic resonance imaging (MRI) findings in cases of fungal VO that distinguished those cases from bacterial VO.

MRI should be considered the imaging modality of choice for vertebral osteomyelitis [4], but the definitive diagnosis of *Candida* vertebral osteomyelitis requires culturing a biopsy specimen.

Bone infections by *Candida* are rare. Scant data concern *Candida* VO, which accounts for approximately 1% of infectious spondylodiscitis [2]. Therefore, the aim of this study is to systematically review the literature for the epidemiology, clinical-radiological aspects, treatment protocols, and outcomes of *Candida* VO and to report our center's experience with a case of *Candida* VO in a nonimmunocompromised patient who injects drugs.

2 Materials and Methods

2.1 Study Setting and Design

In this study, a systematic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). Institutional experience for *Candida* VO was also reported.

2.2 Inclusion and Exclusion Criteria

In this review, the full-text articles reporting clinical and radiological characteristics of patients affected by *Candida* VO were considered eligible. Only articles written in English were included. No date limits were set on publication. Expert

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M. Visocchi (ed.), *The Funnel: From the Skull Base to the Sacrum*, Acta Neurochirurgica Supplement 135,
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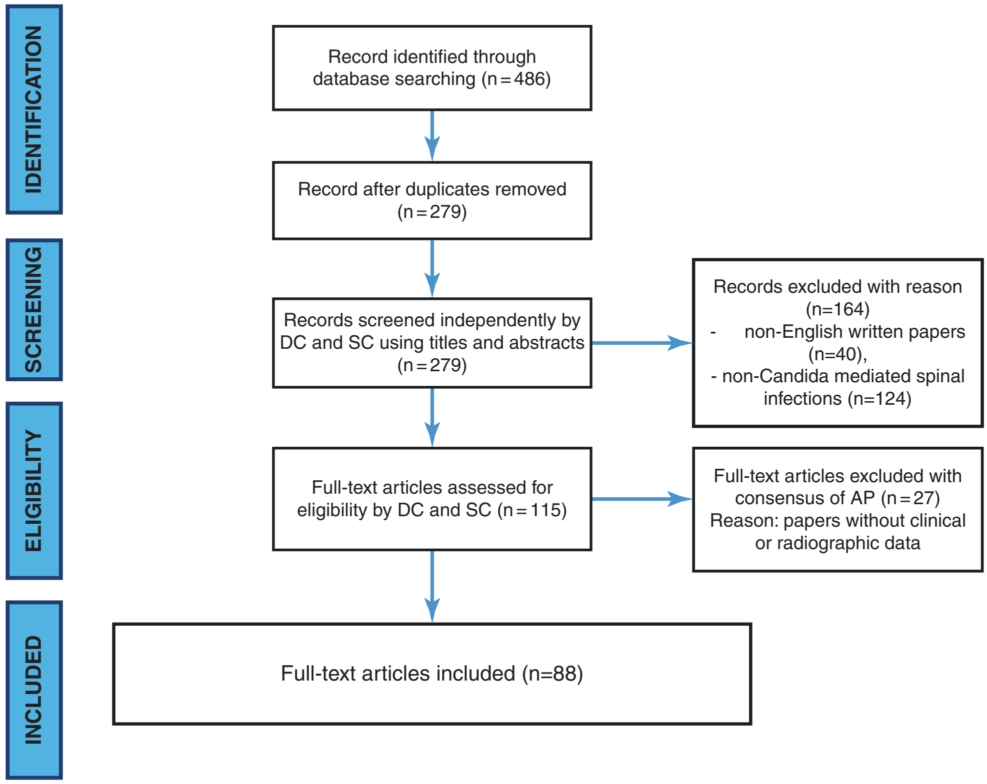

Fig. 1 PRISMA flowchart

opinions, studies on animals, unpublished reports, in vitro investigations, case reports, letters to the editor, abstracts from scientific meetings, and book chapters were excluded from this review.

2.3 Search Strategy and Study Selection

Scopus, Cochrane Library database, Medline, PubMed, and Embase were searched using the keywords "vertebral", "spinal", "infection", "spondylodiscitis", "discitis", "osteomyelitis", "Candida", and "Candidiasis" and their medical subject heading (MeSH) terms in any possible combinations using the logical operators "AND" and "OR." The reference lists of relevant studies were then screened to identify other studies of interest. The search was reiterated until February 10, 2021.

2.4 Data Extraction and Analysis

Two independent authors (D.C. and S.C.) searched and collected data from the included studies. Any discordances were resolved by consensus with a third author (A.P.). The following data were extracted: demographic data, the type of *Candida* isolated, the level of infection, antifungal treatment, surgical treatment, the duration of therapy, the presence of paravertebral/epidural abscess, the type of material sampling, and final outcome. Numbers software (Apple Inc., Cupertino, CA) was used to classify the obtained data. Categorical variables are presented as frequencies and percentages. Continuous variables are presented as means and standard deviation. Only one decimal digit was reported, and it was rounded up.

Case Report A 47-year-old man was admitted to our emergency room on December 31, 2020, because of paraplegia onset 5 days before, associated with sphincter deficiency and a marked decline in general condition. A laboratory blood test showed neutrophilic leukocytosis, C-reactive protein (CRP) 144 ng/L, and procalcitonin 2 ng/mL.

The patient's medical history presented the following: type 1 diabetes mellitus, drug addiction with heroin consumption up to 7 years ago (in therapy with methadone 10 mL/day until December 29, 2020), hepatopathy, HCV related to a picture of ascites, chronic renal failure, sarcopenia, and malnutrition. Second stage sacral ulcer. The patient was also a tobacco and cannabis smoker.

His recent pathological history began in March 2020, when worsening back pain appeared. The pain symptoms were treated with anti-inflammatory therapy without improvement. After a few months, a spinal MRI was performed, and a dorsal spondylodiscitis was diagnosed in September 2020. An empirical antibiotic therapy with azithromycin 3 days/week for 2 weeks was started. Because of his poor clinical response, he subsequently

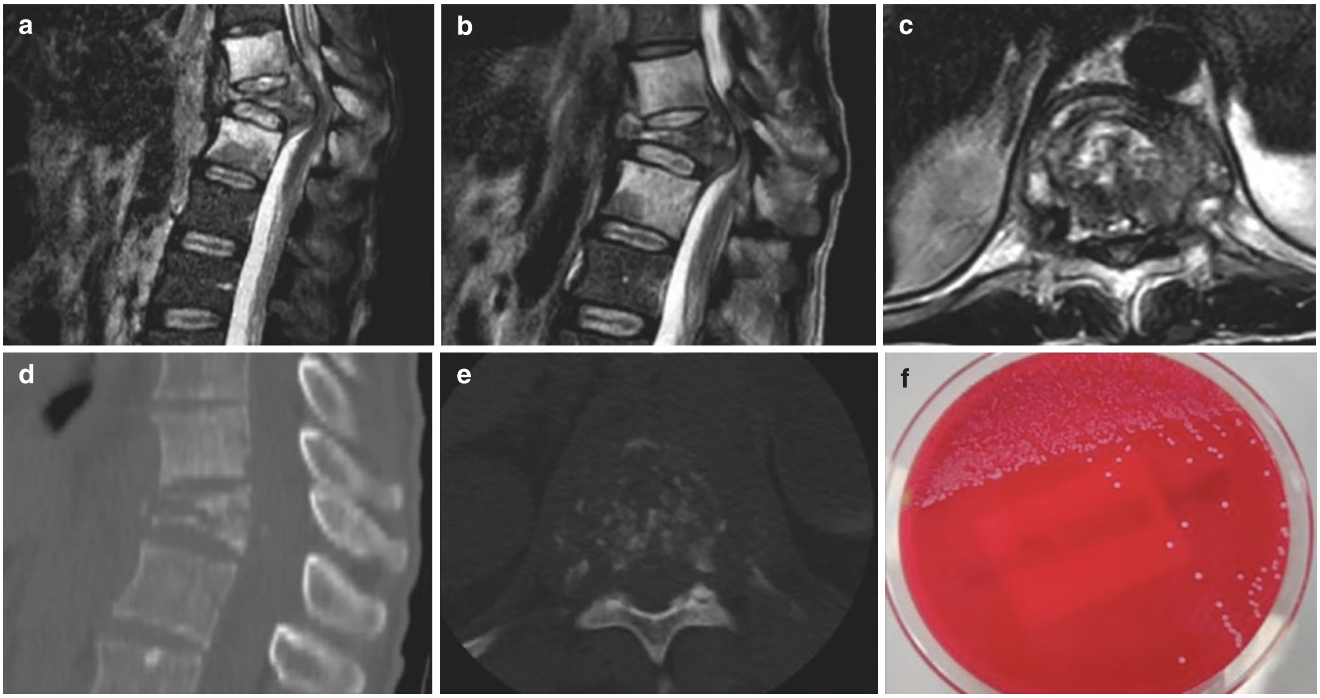

Fig. 2 (**a**–**c**) Spinal MR T2-weighted sagittal and axial images showing the complete collapse of T11 vertebral body with epidural abscess that compresses the spinal cord. d,e. Spinal CT sagittal and axial images showing extensive destruction of the soma of T11 (collapsed) with the involvement of the corresponding posterior wall. f. Biopsy sample positive for *Candida albicans*. Note the presence of characteristics such as hyphae, which have grown in the Petri dish on specific media for fungi: Candida BCG Agar+ and Saboraud Dextrose Agar+ CAF tube

started antibiotic therapy with flucloxacillin 1 g, once a day, for another 15 days. He then resumed azithromycin 3 days/week for 4 weeks (until the end of November), with a reported benefit to back pain and with a reported reduction in CRP.

For a new worsening of his back pain and because of the appearance of weakness and sensitivity deficits in the lower limbs, therapy with Co-trimoxazole and levofloxacin was performed from mid December until his return to our emergency unit.

On December 31, in the emergency room, the patient underwent a CT and an MRI examination of his preoperative spine, specifically for a T2-weighted sagittal image, which showed evidence of the collapse of T11 with an epidural abscess that compressed the spinal cord (MRI picture raise the suspicion of tuberculous spondylitis; see Fig. 2).

His chest CT showed the presence of some nonspecific micronodules, some ground glass areas, and some atelectatic areas. From December 31, he underwent antibiotic therapy with daptomicin and ceftriaxone, and multiple blood cultures (in apyrexial) were performed. On January 8, 2021, a CT-guided biopsy was performed for a histological and microbiological cultural study (common germs, fungi, and mycobacteria).

After the positive growth of *Candida* from a biopsy sample, the patient was evaluated by an infection specialist, who recommended starting therapy with fluconazole 800 mg intravenous (IV) and daptomicin 700 mg IV every 24 h and monitoring the values of β-d-glucan, blood count, CRP, creatine phosphokinase, and liver and kidney function. On January 12, the patient underwent minimally invasive decompression surgery, D8-L2 arthrodesis with the correction of angular kyphosis, and a transpedicle biopsy of D11 [5–7]. A postoperative radiograph of the dorsal spine in AP (Antero-posterior) and LL (latero-lateral) showed D8-L2 arthrodesis with the correction of angular kyphosis (Fig. 3).

The biopsy samples were grown manually by the technician in the field on specific media for fungi: Candida BCG Agar (Meus, Italy) and Saboraud Dextrose Agar + CAF tube (Meus, Italy). They were incubated for 4 days, extending the incubation for a further 7 days for samples that were negative after 4 days. Next, the incubation proceeded with identification and an antibiogram for the species grown in cultures.

Microorganisms were identified by using the MALDI BioTyper protocol: A single colony was collected with a sterile toothpick and placed in duplicate on a MALDI "target" plate: Each colony was covered with 1 μL of matrix (3 mL of alpha-cyano-4 hydroxicinnamic acid in 50% acetonitrile and 2.5% trifluoroacetyl acid). The MALDI plate was placed in the chamber of the mass spectrometer. The spots to be evaluated were hit by a laser, which causes the desorption and ionization of the microbial analytes.

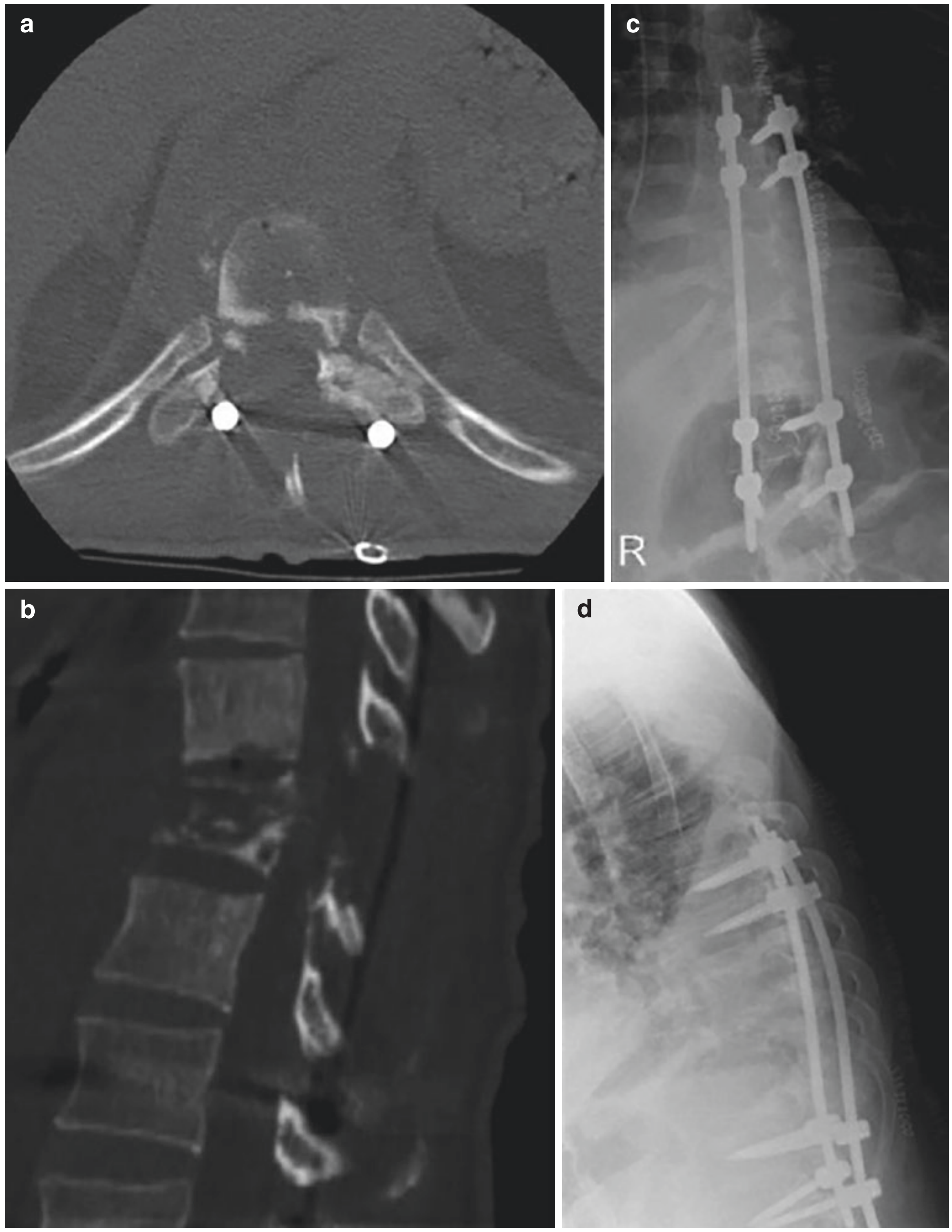

Fig. 3 (**a**) Postoperative axial CT image showing wide bilateral laminectomy performed. (**b**) Postoperative sagittal CT image showing deformity correction and wide decompression performed. (**c**, **d**) Postoperative standard X-ray of thoracic and lumbar spine in anteroposterior and lateral views showing angular kyphosis correction between the T10 and T12 levels

Three out of five biopsy samples were positive for *Candida albicans*. At this point, the infection specialist gave an indication to suspend daptomycin, continue with fluconazole 400 mg IV, and add caspofungin 50 mg with the first loading dose at 70 mg. The biopsy sample was positive for *Candida albicans*. It is possible to note the presence of characteristic hyphae that have grown in the Petri dish on specific media on fungi: Candida BCG Agar+ and Saboraud Dextrose Agar+ CAF tube (Fig. 3f).

After surgery, the patient was prescribed a rigid thoracolumbar corset to use when in a sitting position. After 40 days of medical treatment, CRP (C-reactive protein) and WBC (withe-cells blood count) counts showed decreasing trends, and back pain improved as well. At 3 months after surgery, the antifungal treatment was still in progress. The patient walked with two crutches. The corset has since been removed. On control X-rays, there were no signs of implant loosening or rupture.

After 8 months, the MRI and X-rays showed further improvement, with no signs of active inflammatory process or neurological compression. The patient was continuing the antifungal therapy, and he was pain-free, showing an improvement in the mobility of the lower limbs. The patient gave consent for scientific purp3oses, according to the institutional guidelines.

3 Discussion and Literature Review

3.1 Study Selection and Characteristics.

After the screening of 279 papers, 88 papers were considered for eligibility in the present systematic review. Thus, 191 papers were excluded, according to the exclusion criteria: non-English written papers [8], papers without *Candida*-mediated spinal infections (124), and papers without clinical or radiographic data [9]. Finally, 113 cases, including our case report, of *Candida* spondylodiscitis were included in the present review [10–97]. The mean age of included patients was 53.87 ± 17.68 years; two of these (1.8%) were pediatric (<18 years). Among the patients included, 69 (60.53%) were male and 41 (35.96%) were female. The demographic and clinical data are summarized in Table 1.

3.2 Localization, Symptoms, and Risk Factors

Vertebral candidiasis seems to involve the lumbar spine in more than a half of our cases (52.6%), followed by the thoracic segment (25.4%) and the cervical segment (10.5%). Five cases had a single localization, while multiple contiguous localizations were found in 100 patients (87.7%); finally, nine patients (79%) had multiple skipped localizations.

The presence of abscesses was reported in 93 cases: epidural abscess was found in 31 cases (27.2%), intradiscal abscess in 52 cases (45.6%), and both abscesses in two cases; also, sacral abscess was found in one case, pelvic abscess in one case, psoas abscess in two cases, and presacral phlegmon in one case.

The most frequently presented symptoms were back pain (88.6%), followed by fever (36%), weight loss (10.5%) and lower-limb numbness (3.5%).

The patients were affected by different comorbidities, such as diabetes (13.1%), cardiovascular diseases (10.5%), and gastrointestinal diseases (19.3%).

Different risk factors were identified in our cases: 14 (12.28%) patients were substance users, seven (6.14%) underwent chemotherapy for hematologic malignancies, and three (2.6%) underwent immunosuppressive therapy after organ transplantation.

Table 1. Summary of clinical features describing patients with vertebral candidiasis

Variable	Value
Mean age (yr)	53.9 ± 17.7
Sex	
Male	69 (60.5)
Female	41 (36)
Location	
Cervical	12 (10.5)
Thoracic	29 (25.4)
Lumbar	60 (52.6)
Sacral	2 (1.7)
Comorbidities	
None	7 (6.1)
Autoimmune disease	5 (4.4)
Diabetes	15 (13.2)
Cardiovascular disease	12 (10.5)
Gastrointestinal disease	22 (19.3)
Risk factors	
None	7 (6.1)
Substance abuse	14 (12.3)
Transplant recipient	3 (2.6)
Previous tuberculosis	1 (0.9)
Leukemia	7 (6.1)
Specimen isolated	
Candida albicans	64 (56.1)
Candida tropicalis	21 (18.4)
Candida glabrata	14 (12.3)
Candida parapsilosis	5 (4.4)
Candida dublinensis	3 (2.6)
Candida auris	1 (0.9)
Candida sake	1 (0.9)
Candida krusei	1 (0.9)
Candida paratropicalis	1 (0.9)
Candida fumata	1 (0.9)
Surgical treatment	
Decompression	3 (2.6)
Decompression and posterior fusion	4 (3.5)
Laminectomy	8 (7)
Debridement/curettage	27 (23.7)
No surgical treatment	42 (36.8)
Complications	
Superinfection	2 (1.7)
Neurologic sequelae	1 (0.9)
Respiratory failure	1 (0.9)
Outcome	
Cured	87 (76.3)
Not cured	9 (7.9)
Died	10 (8.7)
Follow-up (days)	395

Values are presented as mean ± standard deviation or number (%)

3.3 Etiology and Diagnosis

Vertebral candidiasis is a rare disease that has been frequently reported in immunodeficient patients. Hematogenous spread of *Candida* to the disc space seems to be the main mechanism of disease in the majority of patients, the interval between candidemia and spondylodiscitis usually ranging from 2 to 14 months [10]. The diagnostic sample was obtained usually by open biopsy (40 cases, 35.1%), drainage of the abscess (31 cases, 27.2%) or by CT-guided biopsy (27 cases, 23.7%). *Candida albicans* was the most frequent isolated pathogen with 64 cases (56.1%) followed by *Candida tropicalis* (21 cases, 18.4%), *Candida glabrata* (14 cases, 12.3%), *Candida parapsilosis* (five cases, 4.4%), *Candida paratropicalis* (four cases, 3.5%), *Candida dublinensis* (three cases, 2.6%), *Candida auris*, *Candida sake*, *Candida krusei*, and *Candida fumata* (one case, 0.9%). Etiological diagnosis was made culturing sample in 79 cases (69.2%) and by histological examination in 27 (23.7%).

The diagnosis of *Candida* spondylodiscitis is currently based on specific cultures for the growth of fungi and is confirmed through histological examination. The clinical presentation does not recognize any pathognomonic symptom or sign or pyogenic spondylodiscitis [5, 11]. The most common symptoms reported at the time of hospitalization are back pain and neurological deficits [5, 6, 11]. Gadolinium-enhanced MRI usually shows epidural abscesses, disc narrowing, the destruction of the endplates, and subjacent vertebral bones [12].

3.4 Treatment Protocols, Clinical Outcomes, and Complications

Medical treatment is generally carried out by using antifungal drugs, among which the most common are fluconazole and amphotericin. According to the revised IDSA (Infectious Diseases Society of America) guidelines, treatment with fluconazole (with or without a 2-week "induction" phase with an echinocandin or amphotericin B formulation) for 6–12 months is recommended for the treatment management of *Candida* osteomyelitis [13]. Although treatment appeared to be appropriate for the *Candida* species isolated, the duration of therapy was frequently shorter than recommended and the initiation of treatment was often delayed [13]. Some studies have shown that fluconazole is as effective as amphotericin, showing higher levels of safety and tolerability [12]. The present study showed that medical treatment alone was administered in 42 cases (36.8%), while in 66 cases (58.4%), combinations of medical and surgical treatment were described. Medical treatment was assumed as monotherapy in 37 cases (32.5%) and in a combination of multiple drugs in 69 cases (61.1%). Fluconazole and amphotericin B were the most frequently administered antifungal agents.

Surgical treatment should not be considered at the onset of the disease, but the worsening of the neurological symptoms and/or poor response to medical therapies may lead to surgical decompression. It was necessary in the case of spinal instability or vertebral collapse to ensure a solid fusion and correction of the deformity. Also, in most cases, surgery is needed to obtain an open biopsy to reach the diagnosis with cultures or histological examination [5, 7, 14, 15].

Surgery treatment principally consisted of debridement and bone grafts in 27 cases (23.7%), decompression in three (2.6%), decompression and posterior fusion in four (3.5%), and laminectomy in eight (7%). The mean duration of therapy was 145.7 days. The mean duration of the follow-up was 395 days. Finally, 87 (76.3%) cases completely recovered, 10 (8.7%) died, and 9 (7.9%) reported sequelae, such as spinal kyphosis deformity, paraplegia, and the persistence of numbness.

3.5 Limitations

The present investigation had some limitations. First of all, the included studies had a low level of evidence (IV–V). Data were reported in a nonhomogeneous way among the included papers, so it was not possible to carry out any data pooling for statistical analysis. Given the rarity of the disease examined, no date limit was set among the research parameters, so the included works were published within the past 60 years.

4 Conclusion

Candida VO is a rare disease. It is important to keep in mind the possible occurrence of *Candida* spondylodiscitis in patients presenting with subacute or chronic back pain, even in the absence of fever, if the patients have risk factors for disseminated candidiasis, such as a history of intravenous drug use or central venous access, immunosuppression, and/or prolonged antibiotic use.

MRI and biopsies with appropriate culture examination are essential for making an accurate and definitive diagnosis. Prognosis is generally good with prolonged antifungal therapy, starting initially with oral azole for susceptible *Candida* species, among which the most frequently used is fluconazole, followed by parenteral amphotericin B (Table 2).

Table 2 Antifungal therapy

Variable	Value
None or not reported	7 (6.1)
Monotherapy	37 (32.5)
Flu	18 (15.8)
AmB	14 (12.3)
CAS	1 (0.9)
ITRA	1 (0.9)
MIC	1 (0.9)
ANID	1 (0.9)
VO	1 (0.9)
Polytherapy	69 (60.5)
Fosf, Flu	1 (0.9)
Flu, AmB, ANID	2 (1.6)
VO, AmB, Flu	1 (0.9)
AmB, Flu	17 (14.9)
MIC, AmB	1 (0.9)
Cipro, COR	1 (0.9)
AmB, CAS	2 (1.6)
CAS, Flu, Mox	1 (0.9)
Flu, Cipro	1 (0.9)
Flu, Sulta	1 (0.9)
Flu, CAS, AmB	1 (0.9)
CAS, Posa	1 (0.9)
AmB, VO	1 (0.9)
Flu, CAS	1 (0.9)
AmB, Vanco	1 (0.9)
AmB, 5-fluc, Flu, ITRA	9 (7.9)
AmB, ITRA, Vanco	2 (1.6)
AmB, 5-fluc, Naf	3 (2.6)
AmB, 5-fluc	4 (3.5)
AmB, ISO	4 (3.5)

Values are presented as mean ± standard deviation or number (%)
Flu fluconazole, *AmB* amphotericin B, *CAS* caspofungin, *ITRA* itraconazole, *Mic* micafungin, *ANID* anidulafungin, *VO* voriconazole, *Fosf* fosfluconazole, *Vanco* vancomycin, *Cipro* ciprofloxacin, *COR* coriconazole, *ISO* isoniazid, *5-fluc* 5-flucytosin, *Naf* nafcillin, *Sulta* sultamicillin

Declarations Compliance with ethical standards: All procedures performed were in accordance with the 1964 Declaration of Helsinki. This research has been approved by the IRB of the authors' affiliated institutions.

Consent for publication: Written informed consent for scientific purposes and clinical data collection and publication was obtained from patients according to institutional protocols.

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References

1. McLeod N, Fisher M, Lasala PR. Vertebral osteomyelitis due to Candida species. Infection. 2019;47:475–8. https://doi.org/10.1007/s15010-019-01294-6.
2. Richaud C, De Lastours V, Panhard X, Petrover D, Fantin B, Lefort A. Candida vertebral osteomyelitis (CVO) 28 cases from a 10-year retrospective study in France. Medicine (Baltimore). 2017;96:e7525. https://doi.org/10.1097/MD.0000000000007525.
3. Miller DJ, Mejicano GC. Vertebral osteomyelitis due to Candida species: case report and literature review. Clin Infect Dis. 2001;33:523–30. https://doi.org/10.1086/322634.
4. Bruns J, Hemker T, Dahmen G. Fungal spondylitis. A case of Torulopsis glabrata and Candida tropicalis infection. Acta Orthop Scand. 1986;57:563–5. https://doi.org/10.3109/17453678609014795.
5. Cho K, Lee SH, Kim ES, Eoh W. Candida parapsilosis spondylodiscitis after lumbar discectomy. J Korean Neurosurg Soc. 2010;47:295–7. https://doi.org/10.3340/jkns.2010.47.4.295.
6. Cha JG, Hong HS, Koh YW, Kim HK, Park JM. Candida albicans osteomyelitis of the cervical spine. Skelet Radiol. 2008;37:347–50. https://doi.org/10.1007/s00256-007-0429-9.
7. Cone LA, Byrd RG, Potts BE, Wuesthoff M. Diagnosis and treatment of Candida vertebral osteomyelitis: clinical experience with a short course therapy of amphotericin B lipid complex. Surg Neurol. 2004;62:234–7; discussion 237. https://doi.org/10.1016/j.surneu.2003.11.018.
8. Jorge VC, Cardoso C, Noronha C, Simões J, Riso N, Riscado MV. Fungal spondylodiscitis in a non-immunocompromised patient. BMJ Case Rep. 2012;2012:bcr1220115337. https://doi.org/10.1136/bcr.12.2011.5337.
9. Ferra C, Doebbeling BN, Hollis RJ, Pfaller MA, Lee CK, Gingrich RD. Candida tropicalis vertebral osteomyelitis: a late sequela of fungemia. Clin Infect Dis. 1994;19:697–703. https://doi.org/10.1093/clinids/19.4.697.
10. Sebastiani GD, Galas F. Spondylodiscitis due to Candida tropicalis as a cause of inflammatory back pain. Clin Rheumatol. 2001;20:435–7. https://doi.org/10.1007/s100670170011.
11. Burton MJ, Shah P, Swiatlo E. Misidentification of Candida parapsilosis as C famata in a clinical case of vertebral osteomyelitis. Am J Med Sci. 2011;341:71–3. https://doi.org/10.1097/MAJ.0b013e3181f54dab.
12. Kulcheski AL, Graells XS, Benato ML, Del Santoro PG, Sebben AL. Fungal spondylodiscitis due to Candida albicans: an atypical case and review of the literature. Rev Bras Ortop. 2015;50:739–42. https://doi.org/10.1016/j.rboe.2015.10.005.
13. Neofytos D, Huprikar S, Reboli A, Schuster M, Azie N, Franks B, Horn D. Treatment and outcomes of Candida osteomyelitis: review of 53 cases from the PATH Alliance® registry. Eur J Clin Microbiol Infect Dis. 2014;33:135–41. https://doi.org/10.1007/s10096-013-1939-0.
14. Corso FA, Shaul DB, Wolfe BM. Spinal osteomyelitis after TPN catheter-induced septicemia. JPEN J Parenter Enteral Nutr. 1995;19:291–5. https://doi.org/10.1177/0148607195019004291.
15. Crane JK. Intrathecal spinal abscesses due to Candida albicans in an immunocompetent man. BMJ Case Rep. 2018;2018:bcr2017223326. https://doi.org/10.1136/bcr-2017-223326.
16. Ackerman G, Bayley JC. Candida albicans osteomyelitis in a vertebral body previously infected with Serratia marcescens. Spine. 1990;15:1362–3. https://doi.org/10.1097/00007632-199012000-00024.
17. Argersinger DP, Natkha VP, Shepard MJ, Thomas AA, Oler AJ, Williamson PR, Chittiboina P, Heiss JD. Intradural cauda equina Candida abscess presenting with hydrocephalus: case report. J Neurosurg Spine. 2019;30:1–4. https://doi.org/10.3171/2019.6.SPINE19271.
18. Armstrong N, Schurr M, Helgerson R, Harms B. Fungal sacral osteomyelitis as the initial presentation of Crohn's disease of the small bowel: report of a case. Dis Colon Rectum. 1998;41:1581–4. https://doi.org/10.1007/BF02237311.

19. Bogaert J, Lateur L, Baert AL. Case report 762. Torulopsis glabrata spondylodiscitis as a late complication of an infected abdominal aortic graft. Skelet Radiol. 1992;21:550–4. https://doi.org/10.1007/BF00195242.
20. Bonomo RA, Strauss M, Blinkhorn R, Salata RA. Torulopsis (Candida) glabrata: a new pathogen found in spinal epidural abscess. Clin Infect Dis. 1996;22:588–9. https://doi.org/10.1093/clinids/22.3.588.
21. Boyd B, Pratt T, Mishra K. Fungal lumbosacral osteomyelitis after robotic-assisted laparoscopic Sacrocolpopexy. Female Pelvic Med Reconstr Surg. 2018;24:e46–8. https://doi.org/10.1097/SPV.0000000000000612.
22. Brembilla C, Lanterna LA, Risso A, Bonaldi G, Gritti P, Resmini B, Viscone A. Cervical bone graft Candida albicans osteomyelitis: management strategies for an uncommon infection. Case Rep Orthop. 2014;2014:986393. https://doi.org/10.1155/2014/986393.
23. Curran MP, Lenke LG. Torulopsis glabrata spinal osteomyelitis involving two contiguous vertebrae. A case report. Spine (Phila Pa 1976). 1996;21:866–70. https://doi.org/10.1097/00007632-199604010-00019.
24. Dailey NJM, Young EJ. Candida glabrata spinal osteomyelitis. Am J Med Sci. 2011;341:78–82. https://doi.org/10.1097/MAJ.0b013e3181f6c6ea.
25. Darrieutort-Laffite C, Lassalle C, Chouet-Girard F, Perez L, Dernis E. Candida albicans diskitis after body piercing in an immunocompetent patient. Joint Bone Spine. 2013;80:226–7. https://doi.org/10.1016/j.jbspin.2012.07.013.
26. Derkinderen P, Bruneel F, Bouchaud O, Regnier B. Spondylodiscitis and epidural abscess due to Candida albicans. Eur Spine J. 2000;9:72–4. https://doi.org/10.1007/s005860050013.
27. De la Meilleure GE, Marchau MM. Candida parapsilosis vertebral osteomyelitis. Eur J Neurol. 1995;2:504–7. https://doi.org/10.1111/j.1468-1331.1995.tb00165.x.
28. De Vitis R, Passiatore M, Perna A, Tulli A, Pagliei A, Taccardo G. Modified Matti- Russe technique using a "butterfly bone graft" for treatment of scaphoid non-union. J Orthop. 2019;19:63–6. https://doi.org/10.1016/j.jor.2019.11.030.
29. Diament MJ, Weller M, Bernstein R. Candida infection in a premature infant presenting as discitis. Pediatr Radiol. 1982;12:96–8. https://doi.org/10.1007/BF00972443.
30. Dijkmans BA, Koolen MI, Mouton RP, Falke TH, van den Broek PJ, van der Meer JW. Hematogenous Candida vertebral osteomyelitis treated with ketoconazole. Infection. 1982;10:290–2. https://doi.org/10.1007/BF01640877.
31. Edwards JE, Turkel SB, Elder HA, Rand RW, Guze LB. Hematogenous candida osteomyelitis. Report of three cases and review of the literature. Am J Med. 1975;59:89–94. https://doi.org/10.1016/0002-9343(75)90325-3.
32. Eisen DP, MacGinley R, Christensson B, Larsson L, Woods ML. Candida tropicalis vertebral osteomyelitis complicating epidural catheterisation with disease paralleled by elevated D-arabinitol/L-arabinitol ratios. Eur J Clin Microbiol Infect Dis. 2000;19:61–3. https://doi.org/10.1007/s100960050013.
33. El Khoury C, Younes P, Hallit R, Okais N, Matta MA. Candida glabrata spondylodiscitis: a case report. J Infect Dev Ctries. 2018;12:32S. https://doi.org/10.3855/jidc.10062.
34. El-Zaatari MM, Hulten K, Fares Y, Baassiri A, Balkis M, Almashhrawi A, El-Zaatari FAK. Successful treatment of Candida albicans osteomyelitis of the spine with fluconazole and surgical debridement: case report. J Chemother. 2002;14:627–30. https://doi.org/10.1179/joc.2002.14.6.627.
35. Fogarty M. Candidial osteomyelitis: a case report. Aust N Z J Surg. 1983;53:141–3. https://doi.org/10.1111/j.1445-2197.1983.tb02415.x.
36. Friedman BC, Simon GL. Candida vertebral osteomyelitis: report of three cases and a review of the literature. Diagn Microbiol Infect Dis. 1987;8:31–6. https://doi.org/10.1016/0732-8893(87)90044-7.
37. Gagliano M, Suardi LR, Marchiani C, Bandini G, Palagano N, Cioni E, Pignone M, et al. On "a rare case of Candida glabrata spondylodiscitis: case report and literature review". Int J Infect Dis. 2019;80:64–5. https://doi.org/10.1016/j.ijid.2018.12.019.
38. Garbino J, Schnyder I, Lew D, Bouchuiguir-Wafa K, Rohner P. An unusual cause of vertebral osteomyelitis: Candida species. Scand J Infect Dis. 2003;35:288–91. https://doi.org/10.1080/00365540310000067.
39. Giger A, Yusuf E, Manuel O, Clerc O, Trampuz A. Polymicrobial vertebral osteomyelitis after oesophageal biopsy: a case report. BMC Infect Dis. 2016;16:141. https://doi.org/10.1186/s12879-016-1471-9.
40. Gopinathan A, Kumar A, Nagaraja Rao S, Kumar K, Karim S. Candidal vertebral osteomyelitis in the midst of renal disorders. J Clin Diagn Res. 2016;10:DD03–5. https://doi.org/10.7860/JCDR/2016/18134.7615.
41. Grimes CL, Tan-Kim J, Garfin SR, Nager CW. Sacral colpopexy followed by refractory Candida albicans osteomyelitis and discitis requiring extensive spinal surgery. Obstet Gynecol. 2012;120:464–8. https://doi.org/10.1097/AOG.0b013e318256989e.
42. Gursel T, Kaya Z, Kocak U, Erbaş G, Akyurek N, Tali ET. Candida vertebra osteomyelitis in a girl with factor X deficiency. Haemophilia. 2005;11:629–32. https://doi.org/10.1111/j.1365-2516.2005.01148.x.
43. Hashimoto Y, Tanioka H. Vertebral osteomyelitis associated with disseminated candidiasis in an oral cancer patient. J Oral Maxillofac Surg. 1991;49:901–3. https://doi.org/10.1016/0278-2391(91)90026-i.
44. Hayes WS, Berg RA, Dorfman HD, Freedman MT. Case report 291. Diagnosis: Candida discitis and vertebral osteomyelitis at L1-L2 from hematogenous spread. Skelet Radiol. 1984;12:284–7. https://doi.org/10.1007/BF00349511.
45. Hendrickx L, Van Wijngaerden E, Samson I, Peetermans WE. Candidal vertebral osteomyelitis: report of 6 patients, and a review. Clin Infect Dis. 2001;32:527–33. https://doi.org/10.1086/318714.
46. Huang A, Huang C, Kugathasan S. Vertebral osteomyelitis due to Candida parapsilosis in a child with Crohn disease while receiving anti-TNF therapy. J Pediatr Gastroenterol Nutr. 2013;56:e23–6. https://doi.org/10.1097/MPG.0b013e31827ecbda.
47. Joshi TN. Candida albicans spondylodiscitis in an immunocompetent patient. J Neurosci Rural Pract. 2012;3:221–2. https://doi.org/10.4103/0976-3147.98261.
48. Kankare J, Lindfors NC. Reconstruction of vertebral bone defects using an expandable replacement device and bioactive glass S53P4 in the treatment of vertebral osteomyelitis: three patients and three pathogens. Scand J Surg. 2016;105:248–53. https://doi.org/10.1177/1457496915626834.
49. Kashimoto T, Kitagawa H, Kachi H. Candida tropicalis vertebral osteomyelitis and discitis. A case report and discussion on the diagnosis and treatment. Spine (Phila Pa 1976). 1986;11:57–61. https://doi.org/10.1097/00007632-198601000-00016.
50. Kelesidis T, Tsiodras S. Successful treatment of azole-resistant Candida spondylodiscitis with high-dose caspofungin monotherapy. Rheumatol Int. 2012;32:2957–8. https://doi.org/10.1007/s00296-011-2121-6.
51. Khazim RM, Debnath UK, Fares Y. Candida albicans osteomyelitis of the spine: progressive clinical and radiological features and surgical management in three cases. Eur Spine J. 2006;15:1404–10. https://doi.org/10.1007/s00586-005-0038-z.

52. Liang JD, Fang CT, Chen YC, Chang SC, Luh KT. Candida albicans spinal epidural abscess secondary to prosthetic valve endocarditis. Diagn Microbiol Infect Dis. 2001;40:121–3. https://doi.org/10.1016/s0732-8893(01)00252-8.
53. Metcalfe S, Morgan-Hough C. Cervical epidural abscess and vertebral osteomyelitis following non-traumatic oesophageal rupture: a case report and discussion. Eur Spine J. 2009;18(Suppl 2):224–7. https://doi.org/10.1007/s00586-009-0889-9.
54. Moon HH, Kim JH, Moon BG, Kim JS. Cervical spondylodiscitis caused by Candida albicans in non-immunocompromised patient. J Korean Neurosurg Soc. 2008;43:45–7. https://doi.org/10.3340/jkns.2008.43.1.45.
55. Mullins RF, Still JM Jr, Savage J, Davis JB, Law EJ. Osteomyelitis of the spine in a burn patient due to Candida albicans. Burns. 1993;19:174–6. https://doi.org/10.1016/0305-4179(93)90045-a.
56. Munk PL, Lee MJ, Poon PY, O'Connell JX, Coupland DB, Janzen DL, Logan PM, Dvorak MF. Candida osteomyelitis and disc space infection of the lumbar spine. Skelet Radiol. 1997;26:42–6. https://doi.org/10.1007/s002560050189.
57. Nahra R, Hoedt C, Jagga S, Ren S, Kim TWB. Candida albicans sacral osteomyelitis causing necrosis of a sacral nerve root: a case report. JBJS Case Connect. 2017;7:e48. https://doi.org/10.2106/JBJS.CC.16.00224.
58. Neale TJ, Muir JC, Mills H, Horne JG, Jones MR. Candida albicans vertebral osteomyelitis in chronic renal failure. Postgrad Med J. 1987;63:695–8. https://doi.org/10.1136/pgmj.63.742.695.
59. Nikkanen HE, Brown DFM, Nadel ES. Low back pain. J Emerg Med. 2002;22:279–83. https://doi.org/10.1016/s0736-4679(01)00484-x.
60. Oksi J, Finnilä T, Hohenthal U, Rantakokko-Jalava K. Candida dubliniensis spondylodiscitis in an immunocompetent patient. Case report and review of the literature. Med Mycol Case Rep. 2013;13:4–7. https://doi.org/10.1016/j.mmcr.2013.11.001.
61. Owen PG, Willis BK, Benzel EC. Torulopsis glabrata vertebral osteomyelitis. J Spinal Disord. 1992;5:370–3. https://doi.org/10.1097/00002517-199209000-00018.
62. Ozdemir N, Celik L, Oğuzoğlu S, Yildirim L, Bezircioğlu H. Cervical vertebral osteomyelitis and epidural abscess caused by Candida albicans in a patient with chronic renal failure. Turk Neurosurg. 2008;18:207–10.
63. Parry MF, Grant B, Yukna M, Adler-Klein D, McLeod GX, Taddonio R, Rosenstein C. Candida osteomyelitis and diskitis after spinal surgery: an outbreak that implicates artificial nail use. Clin Infect Dis. 2001;32:352–7. https://doi.org/10.1086/318487.
64. Pennisi AK, Davis DO, Wiesel S, Moskovitz P. CT appearance of Candida diskitis. J Comput Assist Tomogr. 1985;9:1050–4. https://doi.org/10.1097/00004728-198511000-00009.
65. Perna A, Ricciardi L, Fantoni M, Taccari F, Torelli R, Santagada DA, Fumo C, Tamburrelli FC, Proietti L. Spontaneous vertebral aspergillosis, the state of art: a systematic literature review. Neurospine. 2021;18:23–33. https://doi.org/10.14245/ns.2040338.169.
66. Perna A, Luca Ricciardi L, Carmelo Lucio Sturiale CL, Massimo Fantoni M, Francesco Ciro Tamburrelli FC, Nadia Bonfiglio N, Luca Proietti L. Skipped vertebral spontaneous spondylodiscitis caused by Granulicatella adiacens: case report and a systematic literature review. J Clin Orthop Trauma. 2020;11:937–41. https://doi.org/10.1016/j.jcot.2019.07.002.
67. Perna A, Ricciardi L, Barone G, Tamburrelli FC, Proietti L, Pola E. Medical management of acute non-specific low back pain: comparison of different medical treatments, one center's retrospective analysis. J Biol Regul Homeost Agents. 2018;32(6 Suppl. 1):121–9.
68. Proietti L, Ricciardi L, Noia G, Barone G, Valenzi E, Perna A, Giannelli I, Scaramuzzo L, Visocchi M, Papacci F, Tamburrelli FC. Extensive spinal epidural abscesses resolved with minimally invasive surgery: two case reports and review of the recent literature. Acta Neurochir Suppl. 2019;125:345–53. https://doi.org/10.1007/978-3-319-62515-7_50.
69. Rambo WM Jr. Treatment of lumbar discitis using silicon nitride spinal spacers: a case series and literature review. Int J Surg Case Rep. 2018;43:61–8. https://doi.org/10.1016/j.ijscr.2018.02.009.
70. Relvas-Silva M, Rodrigues Pinho A, Vital L, Leão B, Nogueira Sousa A, Carvalho AC, Veludo V. Azole-resistant Candida albicans spondylodiscitis after bariatric surgery: a case report. JBJS Case Connect. 2020;10(3):e1900618. https://doi.org/10.2106/JBJS.CC.19.00618.
71. Rowe IF, Wright ED, Higgens CS, Burnie JP. Intervertebral infection due to Candida albicans in an intravenous heroin abuser. Ann Rheum Dis. 1988;47:522–5. https://doi.org/10.1136/ard.47.6.522.
72. Salzer HJF, Rolling T, Klupp EM, Schmiedel S. Hematogenous dissemination of Candida dubliniensis causing spondylodiscitis and spinal abscess in a HIV-1 and HCV-coinfected patient. Med Mycol Case Rep. 2015;8:17–20. https://doi.org/10.1016/j.mmcr.2015.02.001.
73. Savall F, Dedouit F, Telmon N, Rougé D. Candida albicans spondylodiscitis following an abdominal stab wound: forensic considerations. J Forensic Legal Med. 2014;23:1–3. https://doi.org/10.1016/j.jflm.2013.12.027.
74. Schiedo RM, Lavelle W, Sun MH. Lumbar spinal Candida Glabrata treated without surgical intervention: a case report. Cureus. 2017;9:e1371. https://doi.org/10.7759/cureus.1371.
75. Stolberg-Stolberg J, Horn D, Roßlenbroich S, Riesenbeck O, Kampmeier S, Mohr M, Raschke MJ, Hartensuer R. Management of destructive Candida albicans spondylodiscitis of the cervical spine: a systematic analysis of literature illustrated by an unusual case. Eur Spine J. 2017;26:1009–18. https://doi.org/10.1007/s00586-016-4827-3.
76. Storm L, Lausch KR, Arendrup MC, Mortensen KL, Petersen E. Vertebral infection with Candida albicans failing caspofungin and fluconazole combination therapy but successfully treated with high dose liposomal amphotericin B and flucytosine. Med Mycol Case Rep. 2014;6:6–9. https://doi.org/10.1016/j.mmcr.2014.07.001.
77. Supreeth S, Al Ghafri KA, Jayachandra RK, Al Balushi ZY. First report of Candida auris spondylodiscitis in Oman: a rare presentation. World Neurosurg. 2020;135:335–8. https://doi.org/10.1016/j.wneu.2019.09.021.
78. Tamburrelli FC, Meluzio MC, Masci G, Perna A, Burrofato A, Proietti L. Etiopathogenesis of traumatic spinal epidural hematoma. Neurospine. 2018;15:101–7. https://doi.org/10.14245/ns.1834938.469.
79. Tamburrelli FC, Perna A, Proietti L, Zirio G, Santagada DA, Genitiempo M. The feasibility of long-segment fluoroscopy-guided percutaneous thoracic spine pedicle screw fixation, and the outcome at two-year follow-up. Malays Orthop J. 2019;13:39–44. https://doi.org/10.5704/MOJ.1911.007.
80. Tan AC, Parker N, Arnold M. Candida glabrata vertebral osteomyelitis in an immunosuppressed patient. Int J Rheum Dis. 2014;17:229–31. https://doi.org/10.1111/1756-185X.12113.
81. Tan HY, Low GJ, Roche E, Tan HK. A case report of invasive candidiasis and fungal osteomyelitis mimicking oropharyngeal carcinoma recurrence in an immunocompetent patient following transoral robotic surgery. Int J Surg Case Rep. 2017;35:33–6. https://doi.org/10.1016/j.ijscr.2017.04.005.
82. Tokuyama T, Nishizawa S, Yokota N, Ohta S, Yokoyama T, Namba H. Surgical strategy for spondylodiscitis due to Candida albicans in an immunocompromised host. Neurol Med Chir. 2002;42:314–7. https://doi.org/10.2176/nmc.42.314.
83. Torres-Ramos FM, Botwin K, Shah CP. Candida spondylodiscitis: an unusual case of thoracolumbar pain with review of imaging findings and description of the clinical condition. Pain Physician. 2004;7:257–60.
84. Ugarriza LF, Cabezudo JM, Lorenzana LM, Rodríguez-Sánchez JA. Candida albicans spondylodiscitis. Br J Neurosurg. 2004;18:189–92. https://doi.org/10.1080/02688690410001681091.

85. Wang YC, Lee ST. Candida vertebral osteomyelitis: a case report and review of the literature. Chang Gung Med J. 2001;24:810–5.
86. Werner BC, Hogan MV, Shen FH. Candida lusitaniae discitis after discogram in an immunocompetent patient. Spine J. 2011;11:e1–6. https://doi.org/10.1016/j.spinee.2011.09.004.
87. Williams RL, Fukui MB, Meltzer CC, Swarnkar A, Johnson WD, Welch W. Fungal spinal osteomyelitis in the immunocompromised patient: MR findings in three cases. AJNR Am J Neuroradiol. 1999;20:381–5.
88. Sakayama K, Kidani T, Matsuda Y, Fujibuchi T, Miyazaki T, Takada K, Shibata T, Yamamoto H. Subdural spinal granuloma resulting from Candida albicans without immunosufficiency: case report. Spine (Phila Pa 1976). 2002;27:E356–60. https://doi.org/10.1097/00007632-200208010-00019.
89. Schilling A, Seibold M, Mansmann V, Gleissner B. Successfully treated Candida krusei infection of the lumbar spine with combined caspofungin/posaconazole therapy. Med Mycol. 2008;46:79–83. https://doi.org/10.1080/13693780701552996.
90. Seravalli L, Van Linthoudt D, Bernet C, de Torrenté A, Marchetti O, Porchet F, Genné D. Candida glabrata spinal osteomyelitis involving two contiguous lumbar vertebrae: a case report and review of the literature. Diagn Microbiol Infect Dis. 2003;45:137–41. https://doi.org/10.1016/s0732-8893(02)00497-2.
91. Shaikh BS, Appelbaum PC, Aber RC. Vertebral disc space infection and osteomyelitis due to Candida albicans in a patient with acute myelomonocytic leukemia. Cancer. 1980;45:1025–8. https://doi.org/10.1002/1097-0142(19800301)45:5<1025::aid-cncr2820450532>3.0.co;2-i.
92. Shaikh Z, Shaikh S, Pujol F, Trauber D, Sam M. Candida tropicalis osteomyelitis: case report and review of literature. Am J Med. 2005;118:795–8. https://doi.org/10.1016/j.amjmed.2004.11.027.
93. Smimmo A, Perna A, Fantoni M, De Marco D, Velluto C, Proietti L, Sali M, Tamburrelli FC. Non tuberculous mycobacteria related spondylodiscitis: a case report and systematic literature review. Infez Med. 2020;28:425–35.
94. Sugar AM, Saunders C, Diamond RD. Successful treatment of Candida osteomyelitis with fluconazole. A noncomparative study of two patients. Diagn Microbiol Infect Dis. 1990;13:517–20. https://doi.org/10.1016/0732-8893(90)90084-9.
95. Yamada T, Shindo S, Otani K, Nakai O. Candia albicans lumbar spondylodiscitis contiguous to infected abdominal aortic aneurysm in an intravenous drug user. BMJ Case Rep. 2021;14:e241493. https://doi.org/10.1136/bcr-2020-241493.
96. Yu LD, Feng ZY, Wang XW, Ling ZH, Lin XJ. Fungal spondylodiscitis in a patient recovered from H7N9 virus infection: a case study and a literature review of the differences between Candida and Aspergillus spondylodiscitis. J Zhejiang Univ Sci B. 2016;17:874–81. https://doi.org/10.1631/jzus.B1600077.
97. Yuste JR, Alfonso M, Bustos C, Quintana J, Rubio M, Villas C, Del Pozo JL. Iliac bone Candida albicans osteomyelitis in a patient with iliac crest bone autograft: a case report and review of the literature. Infection. 2012;40:445–9. https://doi.org/10.1007/s15010-012-0276-z.

Part III

Cervical

Combined Transoral Exoscope and OARM-Assisted Approach for Craniovertebral Junction Surgery. New Trends in an Old-Fashioned Approach

Massimiliano Visocchi and Francesco Signorelli

1 Introduction

Craniovertebral junction (CVJ), whether congenital or acquired from compressive pathologies, can lead to acute or chronic medullary damage. Surgical approaches to CVJ compressive pathologies have traditionally been addressed on the ventral, dorsal, and lateral aspects through a variety of 360-degree surgical corridors [1, 2].

The transoral approach (TOA) represents a direct microsurgical route to the ventral aspects of CVJ, in particular to the anterior portion of the lower clivus, the anterior arch of C1, and the odontoid and body of C2 [3–8]. The recent introduction of some innovations in the field of intraoperative imaging and neuronavigation, such as the O-arm StealthStation (Medtronic, Memphis, TN), allow for performing safer surgical procedures. As part of the improvement of surgical visual magnification and wide expansion of surgical corridors, the 3D 4 K exoscope (EX) represents a very interesting tool [9, 10].

Herein, according to our preliminary experience and the current literature, we exploit the potential offered by the simultaneous application of O-arm intraoperative neuronavigation and an imaging system, along with the 3D 4 K exoscope in TOA, for the treatment of CVJ pathologies.

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2 Methods

Our experience at the Department of Neurosurgery of Fondazione Policlinico Gemelli IRCCS, Catholic University, Rome, started in 1998 with CVJ instrumentation procedures and in 2011 with anterior decompressive transmucosal procedures, both performed with a classic operative microscope (OM), and continued with endoscopic microsurgical techniques with neurophysiological (motor evoked potentials and somasensory evoked potentials—MEPs and SSEPs, respectively) and neuroradiological (fluoroscopy and neuronavigation) monitoring.

In the past 4 years, ten patients with CVJ compressive pathologies underwent one-step combined anterior neurosurgical decompression and posterior instrumentation with the fusion technique.

After 3 days in neurosurgical Intensive Care Unit (ICU), all the patients underwent a complete preoperative radiologic workup via magnetic resonance (MR) and computed tomography (CT) scans, along with a 3D angiographic reconstruction of the epiaortic vessels and a standard/dynamic X-ray evaluation of the CVJ.

A preoperative, short-lasting percutaneous tracheostomy was performed on all the patients. The following technical armamentarium was included for all: O-arm-assisted neuronavigation (Medtronic, Memphis, TN) and EX; in detail, four cases operated with a VITOM 3D exoscope (Karl Storz GmbH, Tuttlingen, Germany) and six cases were treated with ORBEYE exoscope (OLYMPUS, Tokyo, Japan). In the same operating theater, one OM was also available for possible use in case of emergency (OPMI Pentero or Carl Zeiss and Leica), as were endoscopies at 0 and 30 degrees (Karl Stortz GmbH, Tuttlingen, Germany). Continuous intraoperative neuromonitoring by means of somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) was performed on all the patients, in both anterior and posterior procedures as well. Prophylactic antibiotics were adminis-

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tered intraoperatively and postoperatively (cefazoline 2 g/day). A nasogastric tube was used for enteral feeding for 1 week, and a percutaneous tracheostomy was removed after 10 days for all patients. All patients were discharged within 2 weeks.

The complete postoperative radiological set (MR imaging, CT scan, and X-ray assessment), obtained before discharge, was repeated every 3 months up to the complete bone fusion assessment. The anterior and posterior surgical procedures have been previously described [11].

3 Results

No intraoperative neurophysiological changes or postoperative infections occurred, but neurological improvement was evident in all patients.

A complete decompression and a stable instrumentation and fusion of the CVJ were accomplished in all cases. No dysphagia, dysphonia, or the nasal regurgitation of fluids were present at the latest follow-up, except the progressive disappearance of nasal regurgitation in case 2, a patient with Down syndrome, who experienced severe preoperative disturbances.

In four cases, it was not possible to navigate C1 lateral masses and C2 isthmi, owing to targeting the obliquity that does not fit with the neuronavigation optical system, thus misleading the surgeon and strongly suggesting that surgical strategy be changed intraoperatively (occipitocervical with the screwing of the C2 laminar and C3 lateral masses). In another case, it was possible to navigate and perform the screwing of both the C1 lateral masses and the C2 isthmi, resulting in suboptimal screw placements at the immediate postoperative assessment. In this case, the hardware dislodgement occurred 2 months later, requiring the only posterior redo surgery performed in the present series.

No clinical worsening was reported. All the patients significantly improved, according to their Nurick score at the maximum follow-up time.

4 Discussion

4.1 3D 4 K Exoscope

The exoscope (EX) is one of the most interesting technological innovations in neurosurgery: EX has characteristics not inferior to the most modern surgical microscopes, featuring high-definition (HD) magnification, an immersive vision of the operating field, a wide focal distance, and built-in filters that are very useful in the course of oncologic surgical procedures (e.g. 5-ALA and infracyanine).

In addition, 3D technology allows the surgeon to recover and improve the stereopsis that is generally experienced with OM. Moreover, the holding arm allows extreme freedom of movement and the modification of the surgical corridor, enhanced by the possibility of making micromovements and adjustments thanks to a foot pedal controller [9, 10, 12]. In terms of ergonomics and surgical setup, the exoscope is much less bulky and more manageable than the OM and allows surgeons to have more surgical space and a more ergonomically correct position for both the first surgeon and the assistant surgeon [13, 14]. Several papers in the literature present preliminary experiences in the application of EX in microneurosurgery, in studies on animal and cadaveric models and in vivo studies, specifically in the fields of neurooncology, vascular surgery, skull base surgery, and minimally invasive spine surgery [15–23]. Concerning spine surgery, several papers have described the use of EX mainly for non-instrumented or instrumented posterior thoracolumbar approaches; significantly fewer reports have described anterior approaches to the cervical spine [15, 16].

The two surgical exoscopes we used in our procedures were the VITOM exoscope (Karl Storz, Tuttlingen, Germany) and the ORBEYE exoscope (Olympus, Tokyo, Japan). Recent papers have compared the technical characteristics and the advantages and disadvantages of the two exoscopes [12].

In our experience, both instruments have been satisfactory in terms of use, magnification, and 3D definition, although the fixed arm on the VITOM posed a major limit, during the procedures, to needing to frequently mobilize the surgical viewing angle.

4.2 O-Arm Neuronavigation and the Intraoperatory System

In spinal surgery, the introduction of O-arm system has improved the safety of instrumentation procedures, allowing much-more-accurate intraoperative neuronavigation than traditional techniques [10]; moreover, the setting with intraoperative imaging allows a real-time verification of the effectiveness of the procedure, such as in cases of medullary decompression or the correct positioning of arthrodesis systems [24, 25].

In CVJ surgery, O-arm acquisition, compared to fluoroscopy, has the obvious advantage of a better definition with resultantly easier screw insertions; furthermore, it permits an intraoperative direct and indirect assessment of bony and ligamentous CVJ anterior decompression. In two out of six cases, after O-arm acquisition, the craniocaudal decompression was augmented because it proved to be suboptimal in an absolutely reliable and anatomically detailed way. Otherwise, in our previous experience concerning the fluoroscopic monitoring of the TOA, the use of iopamidol, as a contrast filler of the surgical cavity, in a fair way allowed for indirectly evaluating possible residual compression at the CVJ [4, 26]. However, it does not provide a real-time visualization.

Sufficient experience in posterior CVJ complex surgery and confidence with O-arm navigation are needed to safely perform this procedure.

4.3 3D 4 K Exoscope Lights

1. EX allows a better magnification than the OM and an image screen transposition similar to the 4 K endoscopic ones, without the need to handle any specific probes.
2. In such a condition, the role of the surgeon becomes self-sufficient, with better individual surgical freedom than that in endocopic surgery.

4.4 3D 4 K Exoscope Shadows

1. A complex learning curve is necessary in order to avoid wasting time in performing extra surgical maneuvers from frequent camera adjustments.
2. When facing a deep and narrow surgical field, such as transoral surgery, the use of an exoscope may lead to decreased depth perception and a consequently increased operative time.

4.5 O-Arm Neuronavigation System Lights

1. O-arms offer absolutely reliable intraoperative support for more-effective CVJ decompression. In fact, it allows a reliable decompression assessment and an appropriate and reliable real-time neuronavigation compared to preoperative neuroradiological CT and/or MR neuronavigation.
2. O-arms always allow axial, sagittal, and coronal intraoperative reconstructions compared to standard preoperative neuroradiological CT and/or MR neuronavigation, which rarely has a preoperative coexisting navigable axial, sagittal, or coronal image assessment.

4.6 O-Arm Neuronavigation System Shadows

1. O-arms are more time-consuming and much more complex to use than 2D C-arms are or preoperative neuroradiological CT and/or MR assessment neuronavigation is.
2. The planning and the organization of surgery result in more difficulty owing to the need to have the concomitant availability of specialized technical support.

5 Conclusions

Although lights and shadows of such an association have been shown in our experience, the possible advantages of the simultaneous use of a 3D 4 K exoscope and O-arm intraoperative neuronavigation deserve consideration. Future experiences dealing with such simultaneous applications in the CVJ surgical field will provide new knowledge on implementing literature data and proposing more-effective suggestions to overcome actual shadows.

References

1. Visocchi M. Why the Craniovertebral junction? Acta Neurochir Suppl. 2019;125:3–8. https://doi.org/10.1007/978-3-319-62515-7_1.
2. Signorelli F, Stumpo V, Oliva A, Pascali VL, Olivi A, Visocchi M. Mastering craniovertebral junction surgical approaches: the dissection laboratory experience at the Catholic University of Rome. Acta Neurochir Suppl. 2019;125:13–5. https://doi.org/10.1007/978-3-319-62515-7_3.
3. Visocchi M, Iacopino G, Signorelli F, Olivi A, Maugeri R. Walk the line, the surgical hightways to the craniovertebral junction in endoscopic approaches. An historical perspective. World Neurosurg. 2018;110:544–57. https://doi.org/10.1016/j.wneu.2017.06.125.
4. Visocchi M, Signorelli F, Liao C, Rigante M, Paludetti G, Barbagallo G, Olivi A. Transoral versus transnasal approach for craniovertebral junction pathologies: never say never. World Neurosurg. 2018;110:592–603. https://doi.org/10.1016/j.wneu.2017.05.125.
5. Visocchi M, Di Martino A, Maugeri R, González Valcárcel I, Grasso V, Paludetti G. Videoassisted anterior surgical approaches to the craniocervical junction: rationale and clinical results. Eur Spine J. 2015;24:2713.
6. Visocchi M. Transnasal and transoral approach to the clivus and the craniovertebral junction. J Neurosurg Sci. 2019;63(5):498–500. https://doi.org/10.23736/S0390-5616.16.03114-3. Epub 2015 Mar 4.
7. Visocchi M, La Rocca G, Della Pepa GM, Stigliano E, Costantini A, Di Nardo F, Maira G. Anterior video-assisted approach to the craniovertebral junction: transnasal or transoral? A cadaver study. Acta Neurochir (Wien). 2014;156(2):285–92.
8. Visocchi M, Pappalardo G, Pileggi M, Signorelli F, Paludetti G, La Rocca G. Experimental endoscopic angular domains of transnasal and transoral routes to the craniovertebral junction: light and shade. Spine (Phila Pa 1976). 2016;41(8):669–77. https://doi.org/10.1097/BRS.0000000000001288.
9. Ricciardi L, Mattogno PP, Olivi A, Sturiale CL. Exoscope era: next technical and educational step in microneurosurgery. World Neurosurg. 2019;128:371–3. https://doi.org/10.1016/j.wneu.2019.05.162. Epub 2019 May 25.
10. Lauretti L, D'Alessandris QG, Rigante M, Ricciardi L, Mattogno PP, Olivi A. O-arm in Endonasal endoscopic Cranial Base surgery: technical note on initial feasibility. World Neurosurg. 2018;117:103–8. https://doi.org/10.1016/j.wneu.2018.06.015. Epub 2018 Jun 12.

11. Visocchi M, Mattogno PP, Ciappetta P, Barbagallo G, Signorelli F. Combined transoral exoscope and O-arm-assisted approach for craniovertebral junction surgery: light and shadows in single-center experience with improving technologies. J Craniovertebr Junction Spine. 2020;11(4):293–9. https://doi.org/10.4103/jcvjs.JCVJS_176_20. Epub 2020 Nov 26.
12. Langer DJ, White TG, Schulder M, Boockvar JA, Labib M, Lawton MT. Advances in intraoperative optics: a brief review of current exoscope platforms. Oper Neurosurg (Hagerstown). 2019;19:84.
13. Ricciardi L, Chaichana KL, Cardia A, Stifano V, Rossini Z, Olivi A, Sturiale CL. The exoscope in neurosurgery: an innovative "point of view". A systematic review of the technical, surgical and educational aspects. World Neurosurg. 2019;S1878–8750(19):30080–4.
14. Sack J, Steinberg JA, Rennert RC, Hatefi D, Pannell JS, Levy M, Khalessi AA. Initial experience using a high-definition 3-dimensional exoscope system for microneurosurgery. Oper Neurosurg (Hagerstown). 2018;14(4):395–401.
15. Ariffin MHM, Ibrahim K, Baharudin A, Tamil AM. Early experience, setup, learning curve, benefits, and complications associated with exoscope and three-dimensional 4K hybrid digital visualizations in minimally invasive spine surgery. Asian Spine J. 2020;14(1):59–65.
16. Crosetti E, Arrigoni G, Manca A, Caracciolo A, Bertotto I, Succo G. 3D Exoscopic surgery (3Des) for Transoral Oropharyngectomy. Front Oncol. 2020;10:16.
17. Mamelak AN, Drazin D, Shirzadi A, Black KL, Berci G. Infratentorial supracerebellar resection of a pineal tumor using a high definition video exoscope (VITOM [1]). J Clin Neurosci. 2012;19:306–9.
18. Shirzadi A, Mukherjee D, Drazin DG, et al. Use of the video telescope operating monitor (VITOM) as an alternative to the operating microscope in spine surgery. Spine. 2012;37:E1517–23.
19. Bakhsheshian J, Strickland BA, Jackson C, et al. Multicenter investigation of channel-based subcortical trans-sulcal exoscopic resection of metastatic brain tumors: a retrospective case series. Oper Neurosurg (Hagerstown). 2019;16:159–66.
20. Iyer R, Chaichana KL. Minimally invasive resection of deep-seated high-grade gliomas using tubular retractors and exoscopic visualization. J Neurol Surg Part Cent Eur Neurosurg. 2018;79:330–6.
21. Gassie K, Wijesekera O, Chaichana KL. Minimally invasive tubular retractor-assisted biopsy and resection of subcortical intra-axial gliomas and other neoplasms. J Neurosurg Sci. 2018;62:682–9.
22. Oertel JM, Burkhardt BW. VITOM-3D for exoscopic neurosurgery: initial experience in cranial and spinal procedures. World Neurosurg. 2017;105:153–62.
23. Iwata T, Toyota S, Kudo A, Nakagawa K, Shimizu T, Murakami T, Mori K, Taki T, Kishima H. Microsurgery "under the eaves" using ORBEYE: a case of dAVF of the anterior cranial fossa. World Neurosurg. 2020;S1878-8750(20):30467–8.
24. Farah K, Coudert P, Graillon T, Blondel B, Dufour H. Gille 2, Fuentes S prospective comparative study in spine surgery between O-arm and Airo systems: efficacy and radiation exposure. World Neurosurg. 2018;118:e175–84.
25. Knafo S, Mireau E, Bennis S, Baussart B, Aldea S, Gaillard S. Operative and perioperative durations in O-arm vs C-arm fluoroscopy for lumbar instrumentation. Oper Neurosurg (Hagerstown). 2018;14(3):273–8. https://doi.org/10.1093/ons/opx142.
26. Visocchi M, Della Pepa GM, Doglietto F, Esposito G, La Rocca G, Massimi L. Video-assisted microsurgical transoral approach to the craniovertebral junction: personal experience in childhood. Childs Nerv Syst. 2011;27(5):825–31. Epub 2011 Jan 15.

Minimally Invasive Instrumentation of the Cervical Spine: Past, Present, and Future

Sara Lener, Anto Abramovic, Anna Lang, Claudius Thomé, and Sebastian Hartmann

1 Background

The prevalence of degenerative diseases of the cervical spine is increasing because of the demographic development of the population [1]. Surgical treatment needs to be considered when conservative treatment is insufficient and fails to improve the patient's quality of life. An emerging number of patients and related pathologies benefit from posterior cervical spine instrumentation and fusion, either by using a posterior-only approach or as part of a combined antero-posterior strategy. Various techniques and trajectories are known to instrument the cervical spine, including lateral mass screws (LMSs), cervical pedicle screws (CPSs), lamina screws (LSs) and pars interarticularis screws (PISs), each having advantages and disadvantages. Until now, the instrumentation of the cervical spine has been performed almost exclusively with open approaches. Owing to muscular dissection and the long duration of surgery, accompanied by an increased loss of blood, these types of surgeries often lead to unsatisfactory results and peri- and postoperative complications [2]. Any posterior approach to the cervical spine and in particular to the cervicothoracic junction is associated with an increased risk of postoperative wound-related complications, such as infection and deep myofascial dehiscence. In addition, the immobilizing neck pain and functional disability often require revision surgery.

Over the past two decades, minimally invasive surgery (MIS) techniques have gained increasing popularity. MIS could ameliorate the risks of wound-related complications in the posterior cervical spine [3]. Today, MIS is a widely used approach in spine surgery, especially for posterior thoracolumbar instrumentations with similar and/or improved postoperative outcomes compared to open lumbar instrumented procedures in terms of pain relief, loss of blood, return to work and postoperative infections [4–7]. To date, only a few attempts to instrument the cervical spine in a minimally invasive fashion have been reported [8–16]. The indication for the minimally invasive posterior instrumentation of the cervical spine is similar to the open approach, such as in case of spinal trauma, infection, metastatic or degenerative diseases [17]. Segments C2–C6 have been identified as appropriate segments to be fused in an MIS fashion, and their outcomes are favorable [12, 18].

Because of the novelty of this approach in the cervical spine, the aim of this study was to create an overview of the currently available surgical techniques for a posterior minimally invasive cervical spinal instrumentation and to give an outlook on future options.

2 Material and Methods

A detailed review of the currently available literature was performed to identify relevant articles addressing minimally invasive approaches to the posterior instrumentation of the cervical spine. The online databases PubMed and Google Scholar were used to identify appropriate peer-reviewed articles. Specifically, the predefined search string consisted of the following keywords: "minimally invasive cervical instrumentation"; "percutaneous cervical instrumentation"; "MIS cervical"; "minimally invasive cervical spine"; and "minimally invasive cervical fusion." Keyword screening results were used to conduct a more detailed assessment. During the initial screening, full-text articles in German and English were included if the abstracts were suitable for the narrative literature review. Given the limited number of articles for this specific research question, the year of publication was not considered. Articles with full-text availability were included in the review process. Articles without full-text availability and articles that included anterior approaches and the minimally invasive instrumentation of the thoracic or lumbar spine were excluded. After the exclusion of inappro-

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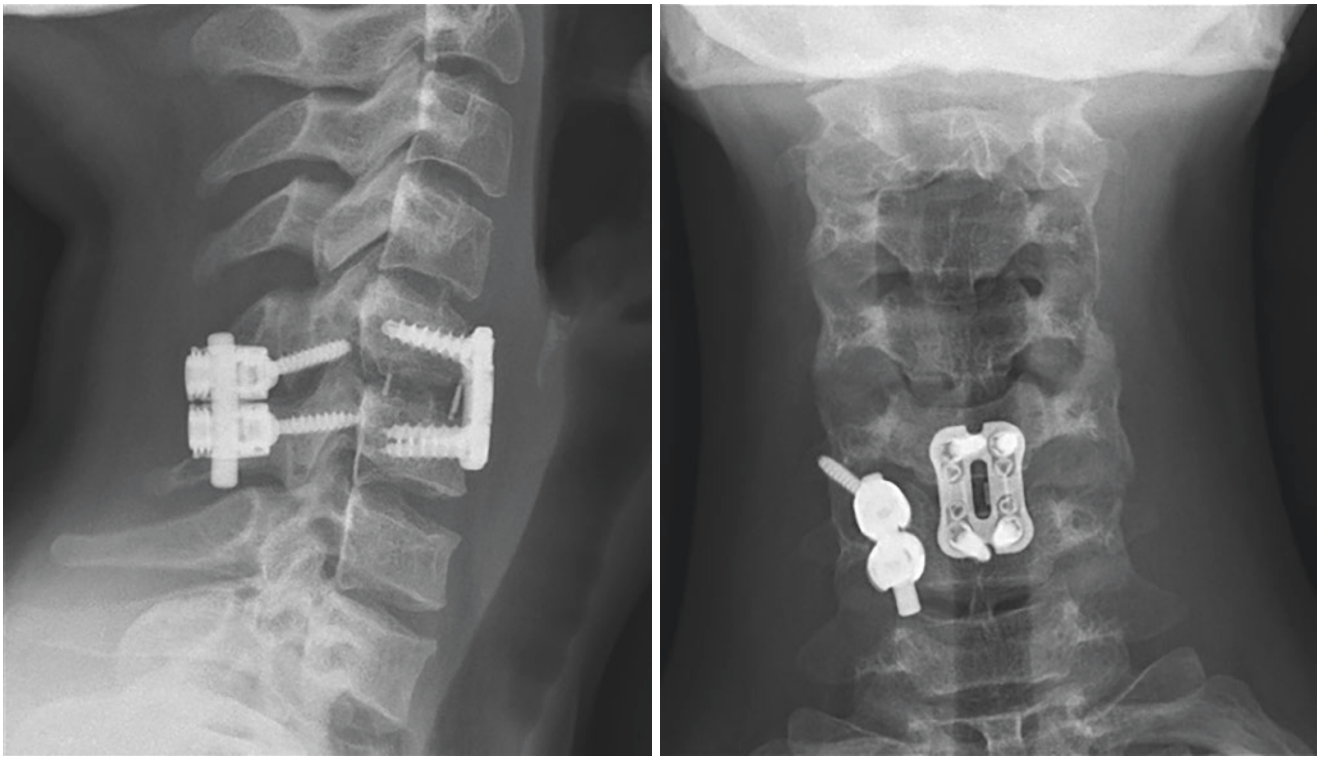


Fig. 1 Type A fracture of C5 and subluxation of the facet joint C5/6 right

priate articles, the full-text articles were copyedited by the authors (SL, AA, and AL). In addition, the references in the selected articles were also screened. Reviews and meta-analyses were excluded (Fig. 1).

3 Past

Minimally invasive or percutaneous screw placement in the lumbar spine was described in the 1980s by Magerl et al. [19]. Nevertheless, it took years until MIS fusion techniques in the lumbar spine were fully developed, accepted and used in a standardized manner [20]. One of the principal reasons for the establishment of MIS was to reduce paraspinal muscle trauma and secondary complications; another was to preserve the dorsal tension band. For anatomical reasons, those factors seem to be even-more present in the cervical than in the lumbar spine. As already mentioned, only a few attempts at MIS in the cervical spine were reported in the past several years; the first two articles were published by Wang et al. in 2003 and 2006 [8, 12]. In the lumbar spine, MIS access is usually gained via a paramedian transmuscular approach with a medial screw angulation similar to that in the open technique. However, in the cervical spine, when using the most common trajectory for LMS, the medial entry point and the traditional trajectories hamper easy access to the entry site. Even with traditional open access to the dorsal cervical spine, the resection of spinous processes or longer skin incisions have to be performed in order to address the corresponding entry points. This represents an anatomical restraint for the establishment of standard MIS approaches to instrumentation procedures for the posterior cervical spine, and it cumbers their uses in daily clinical routines [9, 21].

4 Present

Over the past decades, MIS techniques for spinal pathologies have gained increasing popularity and techniques have improved. To date, segments C2–C6 represent appropriate targets to be fused in an MIS fashion. The implementation and evolution of spinal navigation constituted essential progress in the utilization of MIS. To safely and precisely perform the MIS instrumentation of the cervical spine, different types of navigation techniques, including O-arm navigation, CT-guided navigation and conventional biplanar fluoroscopy, have been described [7, 9–11, 22–28]. So far, cervical MIS fusion is carried out mostly on a similar principle: The typical skin incision line for MIS posterior cervical instrumentation is placed in a paramedian fashion, with a distance of 1.5–2.0 cm to the midline. The incision length depends mainly on the number of segments to be instrumented and has been reported to be 1.5–4.0 cm [10, 17, 18, 29]. In the case of the instrumentation of more than one segment, the skin incision is usually placed one level above the most inferior surgical level [30]. After the successful incision and preparation of the paraspinal musculature, a tubular system is placed under fluoroscopic assistance. Currently, LMS instrumentation forms the standard for posterior MIS fusion, so the lateral mass should be dissected properly. The specific entry point for LMS instrumentation was defined as the midpoint of the lateral mass in the craniocaudal direction and 1 mm medial to the midpoint in the mediolateral axis [30]. Predrilling the insertion hole may lead to a decreased risk of screw misplacement [10, 17, 18, 24, 29]. The Magerl insertion angle has been reported to be accurate in cervical MIS instrumentation [26, 27]. In addition to LMS, several articles reported that CPS instrumentation is an efficient alternative to MIS LMS [10, 17, 18, 24, 28, 29]. In a study conducted by Scheufler et al., the authors were able to provide adequate construct stiffness by using a unilateral approach with transpedicular and translaminar screw placement, separately [18]. Awls and guiding K-wires proved to be efficient tools for increasing screw placement accuracy. Nevertheless, the mediolateral and caudocranial trajectory of LMS marks an important limitation of safe and feasible screw placement in an MIS fashion for anatomical reasons.

Further challenges to MIS approaches to the cervical spine are still outlined by anatomical issues and the complexity in the case of using a navigated approach, due to the higher mobility of the cervical spine. Additionally, technical difficulties in the case of navigated procedures, such as the larger distance between the surgical field and the reference arm affixed on the Mayfield clamp, also have to be considered. Nevertheless, navigation in cervical fusion remains a point of discussion, not only because of the various positions of the navigation array (Mayfield clamp vs. spinous process). Finally, accuracy seems to be comparable in both options [15].

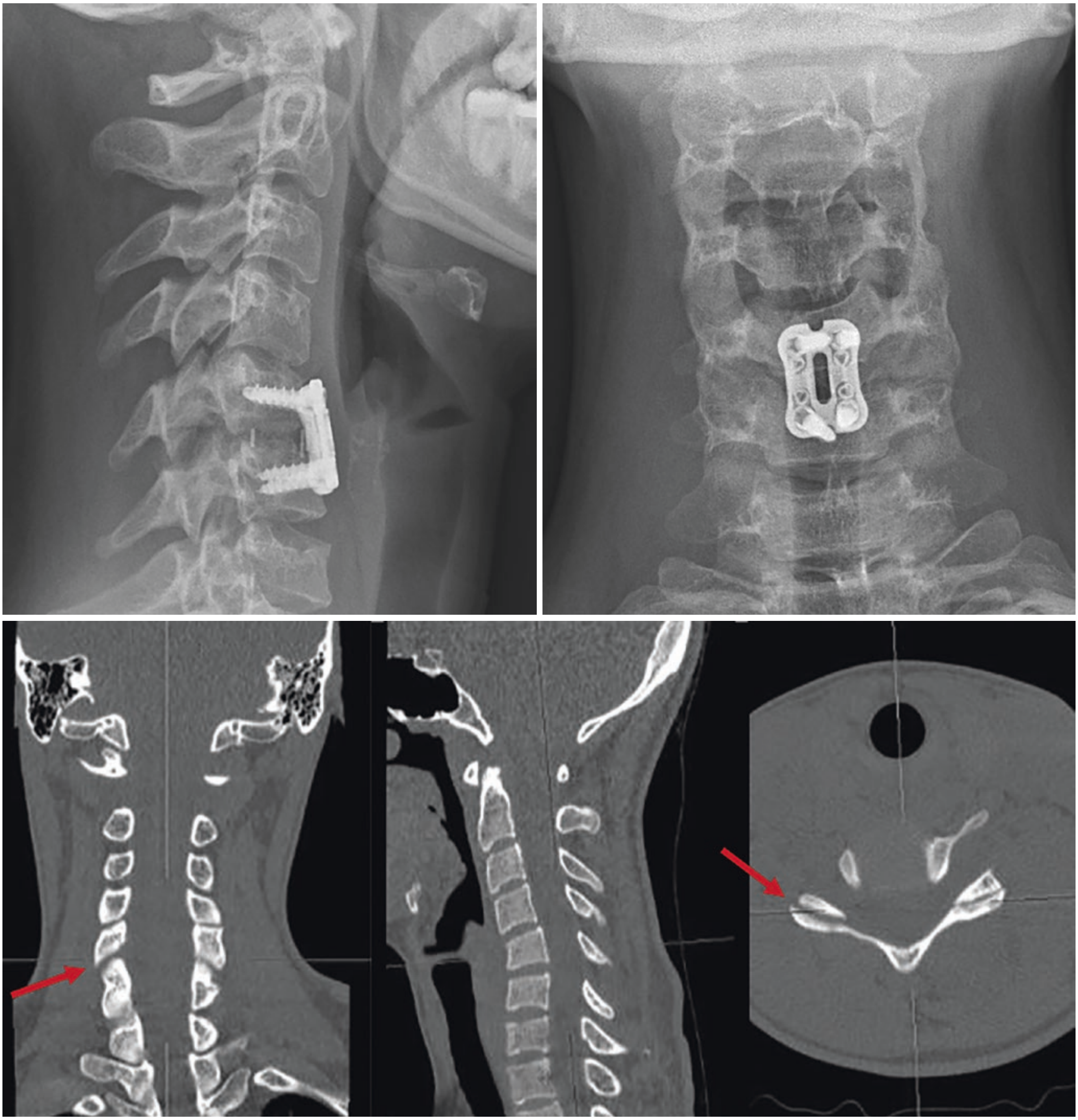
5 Future

Future goals for the establishment of MIS cervical fusion procedures include overcoming some of the aforementioned limitations. For instance, ideas to resolve some of the anatomical issues include novel screw trajectories that might be valuable ways of mitigating LMS fixation as part of MIS procedures. According to the proposed technique of Magerl et al. and to achieve a sufficient mediolateral screw trajectory for an optimal LMS placement within the lateral mass, a resection of the spinous process might occasionally be necessary. In the case of a minimally invasive approach, however, the resection of the spinous process is not possible. With one of the novel trajectories described by the author's research group, screws are inserted at and through the pars interarticularis of the cervical vertebrae in a similar direction as pedicle screws but using approximately the same length and diameter as that for LMS fixation. These pars interarticularis screws (PISs) are already used in the fixation of C2. Prospectively implanted PISs in C3–C6 show their potential to ease the in-line instrumentation of both LMS and CPS and could be options in a salvage strategy for a failed LMS. As a result, PISs might be a reliable alternative. Additionally, outlined methods may have notable advantages in circumferential procedures (e.g. anterior cervical corpectomy and fusion procedures), though they require an additional dorsal instrumentation, as possibilities of MIS screw implantation may lower blood losses and the lengths of operations. The literature provides evidence that two-timed procedures increase morbidity and mortality, as described by Boakye et al., which could therefore be prevented by using advanced MIS procedures [31]. To overcome the limitations and challenges to navigated MIS procedures as stated above, many surgeons have developed alternative strategies, especially for the fixation of the navigation array. Ideas include securement on OR tables close to the operated site, fixation over percutaneously inserted K-wires, mobile options through the fixation of the array on a percutaneously applied rail and many more. To the best of our knowledge, none of the mentioned strategies has yet fully met the demands or has been published in a comprehensive way.

In short, there is still a lot of work to do to fully establish MIS procedures for the dorsal instrumentation of the cervical spine: techniques have to be improved, implants have to be adjusted, supporting mechanisms – such as navigation – have to be refined, experiences have to be shared and, most important, procedures have to be sufficiently indicated.

Case

A 21-year-old professional dancer fell from a 2 m height, headfirst, during training. Imaging showed a type A fracture of C5, plus a discoligamentous injury and a subluxation of the facet joint C5/6 on the right side (Fig. 1). As a first step, a ACDF C5/6 was performed, though the sagittal and coronal alignment could not be restored, and the decision on using an additional dorsal procedure was made. In consideration of the patient's age and profession, a minimally invasive approach was preferred, and the right facet joint C5/6 was reduced and instrumented by using an LMS via a tubular approach (Figs. 2 and 3). Finally, 6 months after the operation, ventral and dorsal fusion was achieved, and the dorsally introduced implants, could be removed upon the patient's request.



Figs. 2 and 3 Postoperative imaging after ACDF C5/6 and dorsal MIS fixation and reduction of C5/6 right

References

1. Oglesby M, Fineberg SJ, Patel AA, Pelton MA, Singh K. Epidemiological trends in cervical spine surgery for degenerative diseases between 2002 and 2009. Spine (Phila Pa 1976). 2013;38(14):1226–32. https://doi.org/10.1097/BRS.0b013e31828be75d.
2. Sebastian A, Huddleston P, Kakar S, Habermann E, Wagie A, Nassr A. Risk factors for surgical site infection after posterior cervical spine surgery: an analysis of 5,441 patients from the ACS NSQIP 2005–2012. Spine J. 2016;16(4):504–9. https://doi.org/10.1016/j.spinee.2015.12.009.
3. Parker SL, Adogwa O, Witham TF, Aaronson OS, Cheng J, McGirt MJ. Post-operative infection after minimally invasive versus open transforaminal lumbar interbody fusion (TLIF): literature review and cost analysis. Minim Invasive Neurosurg. 2011;54(1):33. https://doi.org/10.1055/s-0030-1269904.
4. Vazan M, Gempt J, Meyer B, Buchmann N, Ryang YM. Minimally invasive transforaminal lumbar interbody fusion versus open transforaminal lumbar interbody fusion: a technical description and

review of the literature. Acta Neurochir. 2017;159(6):1137–46. https://doi.org/10.1007/s00701-017-3078-3.
5. Afolabi A, Weir TB, Usmani MF, et al. Comparison of percutaneous minimally invasive versus open posterior spine surgery for fixation of thoracolumbar fractures: a retrospective matched cohort analysis. J Orthop. 2020;18:185–90. https://doi.org/10.1016/j.jor.2019.11.047.
6. Chan AK, Bisson EF, Bydon M, et al. A comparison of minimally invasive and open transforaminal lumbar interbody fusion for grade 1 degenerative lumbar spondylolisthesis: an analysis of the prospective quality outcomes database. Neurosurgery. 2020;87(3):555–62. https://doi.org/10.1093/neuros/nyaa097.
7. Imada A, Huynh TR, Drazin D. Minimally invasive versus open laminectomy/discectomy, Transforaminal lumbar, and posterior lumbar interbody fusions: a systematic review. Cureus. 2017;9(7):e1488. https://doi.org/10.7759/cureus.1488.
8. Wang MY, Prusmack CJ, Green BA, et al. Minimally invasive lateral mass screws in the treatment of cervical facet dislocations: technical note. Neurosurgery. 2003;52:444. https://doi.org/10.1227/01.NEU.0000043814.57539.59.
9. Holly LT, Foley KT. Percutaneous placement of posterior cervical screws using three-dimensional fluoroscopy. Spine (Phila Pa 1976). 2006;31(5):536–40. https://doi.org/10.1097/01.brs.0000201297.83920.a1.
10. Schaefer C, Begemann P, Fuhrhop I, et al. Percutaneous instrumentation of the cervical and cervico-thoracic spine using pedicle screws: preliminary clinical results and analysis of accuracy. Eur Spine J. 2011;20:977. https://doi.org/10.1007/s00586-011-1775-9.
11. Mikhael MM, Celestre PC, Wolf CF, Mroz TE, Wang JC. Minimally invasive cervical spine foraminotomy and lateral mass screw placement. Spine. 2012;37(5):E318. https://doi.org/10.1097/BRS.0b013e31823a43f9.
12. Wang MY, Levi ADO. Minimally invasive lateral mass screw fixation in the cervical spine: initial clinical experience with long-term follow-up. Neurosurgery. 2006;58(5):907–11. https://doi.org/10.1227/01.NEU.0000209929.38213.72.
13. Sehati N, Khoo LT. Minimally invasive posterior cervical arthrodesis and fixation. Neurosurg Clin N Am. 2006;17:429. https://doi.org/10.1016/j.nec.2006.06.009.
14. Buchholz AL, Morgan SL, Robinson LC, Frankel BM. Minimally invasive percutaneous screw fixation of traumatic spondylolisthesis of the axis. J Neurosurg Spine. 2015;22(5):459. https://doi.org/10.3171/2014.10.SPINE131168.
15. Kantelhardt SR, Keric N, Conrad J, Archavlis E, Giese A. Minimally invasive instrumentation of uncomplicated cervical fractures. Eur Spine J. 2016;25:127. https://doi.org/10.1007/s00586-015-4194-5.
16. Lang Z, Tian W, Liu Y, Liu B, Yuan Q, Sun Y. Minimally invasive pedicle screw fixation using intraoperative 3-dimensional fluoroscopy-based navigation (CAMISS technique) for hangman fracture. Spine. 2016;41:39. https://doi.org/10.1097/BRS.0000000000001111.
17. Tokioka T, Oda Y. Minimally invasive cervical pedicle screw fixation (MICEPS) via a posterolateral approach. Clin Spine Surg. 2019;32(7):279–84. https://doi.org/10.1097/BSD.0000000000000832.
18. Scheufler KM, Kirsch E. Percutaneous multilevel decompressive laminectomy, foraminotomy, and instrumented fusion for cervical spondylotic radiculopathy and myelopathy: assessment of feasibility and surgical technique. J Neurosurg Spine. 2007;7(5):514–20. https://doi.org/10.3171/SPI-07/11/514.
19. Magerl F. External skeletal fixation of the lower thoracic and the lumbar spine. In: Current concepts of external fixation of fractures. New York: Springer; 1982. p. 353–66.
20. Foley KT, Holly LT, Schwender JD. Minimally invasive lumbar fusion. Spine. 2003;28(15 SUPPL):S26. https://doi.org/10.1097/01.brs.0000076895.52418.5e.
21. Hussain I, Schmidt FA, Kirnaz S, Wipplinger C, Schwartz TH, Härtl R. MIS approaches in the cervical spine. J Spine Surg. 2019;5:S74. https://doi.org/10.21037/jss.2019.04.21.
22. Yoshida G, Kanemura T, Ishikawa Y. Percutaneous pedicle screw fixation of a hangman's fracture using intraoperative, full rotation, three-dimensional image (O-arm)-based navigation: a technical case report. Asian Spine J. 2012;6(3):194–8. https://doi.org/10.4184/asj.2012.6.3.194.
23. Mayer M, Meier O, Auffarth A, Koller H. Cervical laminectomy and instrumented lateral mass fusion: techniques, pearls and pitfalls. Eur Spine J. 2015;24:168. https://doi.org/10.1007/s00586-013-2838-x.
24. Sugimoto Y, Ito Y, Shimokawa T, Shiozaki Y, Mazaki T. Percutaneous screw fixation for traumatic spondylolisthesis of the axis using iso-c3d fluoroscopy-assisted navigation (case report). Minim Invasive Neurosurg. 2010;53(2):83–5. https://doi.org/10.1055/s-0030-1247503.
25. Koller H, Ames C, Mehdian H, et al. Characteristics of deformity surgery in patients with severe and rigid cervical kyphosis (CK): results of the CSRS-Europe multi-Centre study project. Eur Spine J. 2019;28:324. https://doi.org/10.1007/s00586-018-5835-2.
26. Celestre PC, Pazmiño PR, Mikhael MM, et al. Minimally invasive approaches to the cervical spine. Orthop Clin North Am. 2012;43(1):137–47. https://doi.org/10.1016/j.ocl.2011.08.007.
27. Magerl F, Grob D, Seemann P. Stable dorsal fusion of the cervical spine (C2-Th1) using hook plates. In: Cervical spine I. Vienna: Springer; 1987. p. 217–21. https://doi.org/10.1007/978-3-7091-8882-8_38.
28. Komatsubara T, Tokioka T, Sugimoto Y, Ozaki T. Minimally invasive cervical pedicle screw fixation by a posterolateral approach for acute cervical injury. Clin Spine Surg. 2017;30(10):466–9. https://doi.org/10.1097/BSD.0000000000000421.
29. Holly LT, Foley KT. Percutaneous placement of posterior cervical screws using three-dimensional fluoroscopy. Spine. 2006;31:536. https://doi.org/10.1097/01.brs.0000201297.83920.a1.
30. Mikhael MM, Celestre PC, Wolf CF, Mroz TE, Wang JC. Minimally invasive cervical spine foraminotomy and lateral mass screw placement. Spine. 2012;37:E318. https://doi.org/10.1097/BRS.0b013e31823a43f9.
31. Boakye M, Patil CG, Ho C, Lad SP. Cervical corpectomy: complications and outcomes. Neurosurgery. 2008;63(4 SUPPL):295. https://doi.org/10.1227/01.NEU.0000327028.45886.2E.

Hybrid Implants in Anterior Cervical Spine Surgery: The State of the Art and New Trends for Multilevel Degenerative Disc Disease

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1 Introduction

Anterior cervical discectomy and fusion (ACDF) still represents the first surgical option for cervical degenerative disc disease (DDD) [1, 2]. However, the ensuing fusion may lead to adjacent segment diseases (ASDs) [3, 4]. Other possible complications (e.g., implant migration, bone graft nonunion, subsidence, and bone donor site pain) overall account for a reoperation rate of 10% [5, 6]. In recent years, these concerns have led to the introduction of cervical disc arthroplasty (CDA) as an alternative option conceived in order to prevent adjacent segment degeneration [7, 8]. Although CDA has recently become more popular, it can be burdened by complications such as vertebral body fracture, subsidence, migration, and heterotopic ossification. Therefore, as a matter of fact, a clear predominance over ACDF is still a matter of discussion in terms of clinical outcomes and ASD incidence [2, 9–13].

In order to overcome the limits and drawbacks of both, hybrid surgery (HS) incorporating ACDF and CDA is increasingly performed, with the advantage of avoiding long-level fusion, thus preserving the segmental motion of the cervical spine, thereby preventing further ASD. Herein, we present a retrospective institutional analysis of patients with cervical DDD who underwent the positioning of hybrid implants.

2 Methods

We retrospectively reviewed the clinical, surgical, and outcome data of 85 consecutive patients (M/F, 41/44) who underwent a cervical discectomy on two or more levels using anterior approach between April 2011 and February 2021 at the Department of Neurosurgery of Fondazione Policlinico Gemelli IRCCS, Catholic University, Rome, Italy. All patients provided informed consent for the analysis of their clinical data. All the patients underwent preoperative radiologic and neurophysiologic workups. All the patients were operated on via the anterior approach, with a Caspar distractor with at least one disc prosthesis, along with a cage and plate or an O Profile screwed plate. The indication for cage plating was myelopathy with osteophytes, and the indication for disc prosthesis placement was a soft herniated disc without radiological and clinical signs of myelopathy and osteophytes. Postoperative radiologic follow-up included dynamic cervical X-ray before discharge and after 1 month, a CT scan, and MR at the third postoperative month. Afterward, the patients were examined in an outpatient clinic every 6 months with the help of a dynamic X-ray. Preoperatively and at follow-up, they were clinically evaluated according to a modified Japanese Orthopedic Association (mJOA) scor-

In memory of Professor Pasquale Ciappetta. Uncomparable neurosurgeon, patience master, and unforgettable friend.

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ing system and the Nurick scale to assess the myelopathic status and the visual analog scale to evaluate neck pain intensity. Radiographic assessments included cervical lordosis and the range of motion (ROM) of the cervical spine.

3 Statistical Analysis

Continuous data are presented as mean ± standard deviation and frequency data as counts and percentages. The paired *t*-test was used for continuous variables and the chi-squared test for frequency variables. Analysis of variance (ANOVA) for repeated measures was used to assess time differences in mJOA scores across time points, while the paired *t*-test was used to compare score means between two adjacent time points. Here, *p*-values of <0.05 were considered statistically significant. Quantitative variables at each follow-up time point between the two groups were analyzed by using the Mann–Whitney U test. Data were analyzed by using StatView version 5 software (SAS Institute Inc.).

4 Results

The data of patients are summarized in Table 1.

No statistically significant ($p > 0.05$) relationship between different kinds of prosthesis and their surgical level; the number of cages; and the site of the cages (screwed and/or plated) was found concerning immediate stability, dynamic prosthesis effectiveness, and clinical improvement in all the patients up to the maximum follow-up time. The subgroup analysis among different levels treated and the position of the cage or prosthesis did not reveal a significant difference ($p > 0.05$) in outcomes. All the patients improved postoperatively, and no junctional segmental secondary herniated disc or dislocation were reported at the maximum follow-up time. In particular, both mJOA scores and Nurick grades significantly improved at final follow-up time. The average preoperative Nurick grade was 1.32 ± 0.71, which improved to 1 ± 0.64 at final follow-up time ($p < 0.0095$). Preoperative mJOA score was 9.27 ± 1.57 and improved to 12.88 ± 1.24 at final follow-up ($p < 0.00001$). Subgroup analyses between myelopathic and nonmyelopathic patients revealed statistically significant differences in pre- and postoperative visual analogue scale (VAS), mJOA, and Nurick scores. Only one failure was present in our series, consisting of a displacement of a C5-C6 prosthesis in the patient who underwent a four-level surgery with two cages at levels C3-C4 and C4-C5 and two prostheses at levels C5-C6 and C6-C7 1 month before.

Table 1 Patient's characteristics

	TOT	II Levels	III Levels	IV Levels	Radiculopathy	Myelopathy
No. of Patients	85	57	27	1		
2 (C3-C4) 2 (C4-C5) 2 (C5-C6) 3 (C3-C5) 3 (C4-C6) 4 (C3-C6)		12			8	4
		14			9	5
		31			20	11
			4 (2C + 1P)		3	2
			7 (2C + 1P); 4 (2P + 1C)		9	7
				1 (2C + 2P)	1	1
Operative Time	173.4 ± 36.1 min	155 ± 23.3 min	210 ± 7.7 min	248 min		
Follow-up Months	43.15 ± 29.0	41.3 ± 30.3	33.5 ± 24.9			

C cage; *P* prosthesis

5 Discussion

ACDF is still widely performed for those cervical degenerative disc diseases associated mainly with myelopathy [14–16]. However, current complication rates described in the literature range from 13.2% to 19.3% [17, 18]. Moreover, ACDF can alter the normal biomechanics of the cervical spine, decreasing mobility at the fused segments and overloading the adjacent levels, ultimately accelerating ASD and requiring further surgery in the long term [3, 4, 19]. CDA has recently been introduced to preserve the motion of the treated level and to prevent an overload of the adjacent discs, but it is currently limited by strict indications, the hypermobility of the operative levels, higher medical costs, and a lack of long-term follow-ups [4, 8, 9, 12, 13, 20]. Nevertheless, a progressive development of heterotopic ossification in CDA, with a gradual reduction in range of motion can occur as well [21]. The aim of HS for multilevel cervical DDD [8, 13] is based on the assumption that the most suitable treatment should be utilized at each cervical disc [22], avoiding long-level fusion and preventing further ASD [23, 24]. Current biomechanical evidence indicates that HS preserves the cervical spinal kinematics, intradiscal pressure (IDP) in adjacent segments, and facet joint force [2, 25]. Conversely, two-level fusion largely constrains range of motion (ROM) to operative levels and induces a compensatory increase in motion at adjacent levels that may adversely increase the IDP [25–27].

A recent meta-analysis showed no statistically significant difference in the rate of ASD between CDA and ACDF, so there is still no clear evidence that a lower decrease in motion results in less ASD, which has been attributed by several authors to the fusion-induced increasing IDP [28, 29].

In our series, including both the two and three levels treated and the one case of four levels, neither ASD, cervical instability, nor cage dislocation has occurred at maximum follow-up time, except in one case associated with an overloading of posterior endplate drilling. The dynamic power of the prosthesis remained unchanged at the maximum follow-up time in all the cases. Interestingly, in a previous study conducted at our institution dealing with 99 cases of ACDF at one and two levels with porous tantalum implants, in one patient, the authors observed an adjacent segment disease after 24 months [30]. In Table 2, we report the incidence of ASD with HS versus ACDF in our series and in the literature.

Table 2 Incidence of ASD with HS versus ACDF

Visocchi et al.	Hybrid implants	II-III-IV levels	85 pts	0 ASD (0%)
Papacci et al.	ACDF	I-II levels	99 pts	1 ASD (1%)
Ricciardi et al.	ACDF	III levels	21 pts	3 ASD (14%)

The complication experienced in our series in only one case was secondary to the technical aspects (extensive posterior endplate drilling), and thus, it is possible to prevent it. On the other hand, the absence of adjacent segment disease at maximum follow-up time, compared with the abovementioned series of 99 cases of ACDF, should be the result of a true restoring of the physiological biomechanics of the cervical spine provided by the hybrid implants. Furthermore, our series included patients operated up to three levels (excluding the single patient who underwent four-level hybrid implant surgery); for them, at least in theory, the risk of ASD should be even higher than that at one or two levels, as performed in the previous study. In a further multicentric retrospective study conducted, among others, by our group on 21 patients who underwent three-level contiguous ACDF without plating [31], the fusion rate was 90%, and interestingly, ASD was reported in three cases (14%). Therefore, the absence of ASD observed in our series of long hybrid implants takes on an even-more-significant value (Table 2). In those two papers dealing with ACDF cases, all the patients experienced a statistically significant improvement in all the evaluated scores (VAS and Nurick) at follow-up, as observed in all the patients in our study.

The complication rates of HS differ among the reported series, overall ranging from 0% to 28.6% [12, 23, 24, 32]. In particular, HS shows no higher complication rates according to the comparative studies [12, 24].

6 Conclusions

Although the optimal surgical technique for cervical DDD remains controversial, HS represents a safe and efficacious procedure in select patients with multilevel cervical DDD, as demonstrated by biomechanical and clinical studies and the present series. Further prospective, randomized controlled studies are needed to reach more-reliable conclusions.

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All authors read and approved the final version of the manuscript.

References

1. Fehlings MG, Arvin B. Surgical management of cervical degenerative disease: the evidence related to indications, impact, and outcome. J Neurosurg Spine. 2009;11:97–100.
2. Zechmeister I, Winkler R, Mad P. Artificial total disc replacement versus fusion for the cervical spine: a systematic review. Eur Spine J. 2011;20(2):177–84.
3. Dmitriev AE, Kuklo TR, Lehman RA Jr, Rosner MK. Stabilizing potential of anterior, posterior, and circumferential fixation for multilevel cervical arthrodesis: an in vitro human cadaveric study of the operative and adjacent segment kinematics. Spine. 2007;32(6):E188–96.
4. Matsunaga S, Kabayama S, Yamamoto T, Yone K, Sakou T, Nakanishi K. Strain on intervertebral discs after anterior cervical decompression and fusion. Spine. 1999;24(7):670–5.
5. Pickett GE, Sekhon LH, Sears WR, Duggal N. Complications with cervical arthroplasty. J Neurosurg Spine. 2006;4:98–105.
6. Hacker FM, Babcock RM, Hacker RJ. Very late complications of cervical arthroplasty: results of 2 controlled randomized prospective studies from a single investigator site. Spine. 2013;38:2223–6.
7. Cepoiu-Martin M, Faris P, Lorenzetti D, Prefontaine E, Noseworthy T, Sutherland L. Artificial cervical disc arthroplasty: a systematic review. Spine. 2011;36(25):E1623–33.
8. Cason GW, Herkowitz HN. Cervical intervertebral disc replacement. J Bone Joint Surg Am. 2013;95(3):279–85.
9. Fay LY, Huang WC, Tsai TY, Wu JC, Ko CC, Tu TH, Wu CL, Cheng H. Differences between arthroplasty and anterior cervical fusion in two-level cervical degenerative disc disease. Eur Spine J. 2013;23(3):627–34.
10. Fallah A, Akl EA, Ebrahim S, Ibrahim GM, Mansouri A, Foote CJ, Zhang Y, Fehlings MG. Anterior cervical discectomy with arthroplasty versus arthrodesis for single-level cervical spondylosis: a systematic review and meta-analysis. PLoS One. 2012;7(8):e43407.
11. Jia Z, Mo Z, Ding F, et al. Hybrid surgery for multilevel cervical degenerative disc diseases: a systematic review of biomechanical and clinical evidence. Eur Spine J. 2014;23:1619–32.
12. Shin DA, Yi S, Yoon Do H, Kim KN, Shin HC. Artificial disc replacement combined with fusion versus two-level fusion in cervical two-level disc disease. Spine. 2009;34(11):1153–61.
13. Auerbach JD, Jones KJ, Fras CI, Balderston JR, Rushton SA, Chin KR. The prevalence of indications and contraindications to cervical total disc replacement. Spine J. 2008;8(5):711–6.
14. Spallone A, Izzo C, Galassi S, Visocchi M. Is "mini-invasive" technique for iliac crest harvesting an alternative to cervical cage implant? An overview of a large personal experience. Surg Neurol Int. 2013;4:157.
15. Fontanella MM, Fazio M, Francione A, Bacigaluppi S, Griva F, Visocchi M, Panciani PP, Bergomi R, Spena G. Pre-symptomatic cervical myelopathy: should we operate or should we observe? What is the chance of spinal cord injury from an accident? J Neurosurg Sci. 2014;58(2 Suppl 1):15–22.
16. Visocchi M, Della Pepa GM, Roselli R, La Rocca G, Conforti G, Spallone A, Barbagallo G. Laminoplasty and laminectomy in cervical stenotic myelopathy: allies not enemies. J Neurosurg Sci. 2014;58(2 Suppl 1):101–5.
17. Barbagallo G, Certo F, Albanese V, Visocchi M. The impact of complications following cervical spine surgery: a systematic review. J Neurosurg Sci. 2014;58(2 Suppl 1):55–64.
18. Epstein NE. A review of complication rates for anterior cervical diskectomy and fusion (ACDF). Surg Neurol Int. 2019;10:100.
19. Schwab JS, Diangelo DJ, Foley KT. Motion compensation associated with single-level cervical fusion: where does the lost motion go? Spine. 2006;31(21):2439–48.
20. Kepler CK, Brodt ED, Dettori JR, Albert TJ. Cervical artificial disc replacement versus fusion in the cervical spine: a systematic review comparing multilevel versus single-level surgery. Evid Based Spine Care J. 2012;3(S1):19–30.
21. Barbagallo GM, Certo F, Visocchi M, Sciacca G, Albanese V. Double-level cervical total disc replacement for adjacent segment disease: is it a useful treatment? Description of late onset heterotopic ossification and review of the literature. Eur Rev Med Pharmacol Sci. 2014;18(1 Suppl):15–23.
22. Lee SH, Im YJ, Kim KT, Kim YH, Park WM, Kim K. Comparison of cervical spine biomechanics after fixed- and mobile-core artificial disc replacement: a finite element analysis. Spine (Phila Pa 1976). 2011;36:700–8.
23. Barbagallo GM, Assietti R, Corbino L, Olindo G, Foti PV, Russo V, Albanese V. Early results and review of the literature of a novel hybrid surgical technique combining cervical arthrodesis and disc arthroplasty for treating multilevel degenerative disc disease: opposite or complementary techniques? Eur Spine J. 2009;18(Suppl 1):29–39.
24. Hey HW, Hong CC, Long AS, Hee HT. Is hybrid surgery of the cervical spine a good balance between fusion and arthroplasty? Pilot results from a single surgeon series. Eur Spine J. 2013;22(1):116–22.
25. Barrey C, Campana S, Persohn S, Perrin G, Skalli W. Cervical disc prosthesis versus arthrodesis using one-level, hybrid and two-level constructs: an in vitro investigation. Eur Spine J. 2012;21(3):432–42.
26. Zhao Y, Li Q, Mo Z, Sun Y, Fan Y. Finite element analysis of cervical arthroplasty combined with fusion against 2-level fusion. J Spinal Disord Tech. 2013;26(6):347–50.
27. Cunningham BW, Hu N, Zorn CM, McAfee PC. Biomechanical comparison of single- and two-level cervical arthroplasty versus arthrodesis: effect on adjacent-level spinal kinematics. Spine J. 2010;10(4):341–9.
28. Dmitriev AE, Cunningham BW, Hu N, Sell G, Vigna F, McAfee PC. Adjacent level intradiscal pressure and segmental kinematics following a cervical total disc arthroplasty: an in vitro human cadaveric model. Spine. 2005;30(10):1165–72.
29. Yang B, Li H, Zhang T, He X, Xu S. The incidence of adjacent segment degeneration after cervical disc arthroplasty (CDA): a meta analysis of randomized controlled trials. PLoS One. 2012;7:e3503.
30. Papacci F, Rigante L, Fernandez E, Meglio M, Montano N. Anterior cervical discectomy and interbody fusion with porous tantalum implant. Results in a series with long-term follow-up. J Clin Neurosci. 2016;33:159–62.

31. Ricciardi L, Scerrati A, Bonis P, Miscusi M, Trungu S, Visocchi M, Papacci F, Raco A, Proietti L, Pompucci A, Olivi A, Montano N. Long-term radiologic and clinical outcomes after three-level contiguous anterior cervical diskectomy and fusion without plating: a multicentric retrospective study. J Neurol Surg A Cent Eur Neurosurg. 2021;82(6):556–61.
32. Lee MJ, Dumonski M, Phillips FM, Voronov LI, Renner SM, Carandang G, Havey RM, Patwardhan AG. Disc replacement adjacent to cervical fusion: a biomechanical comparison of hybrid construct versus two-level fusion. Spine. 2011;36(23):1932–9.

The Submandibular Approach: A Descriptive Perspective of the Retropharingeal Corridor to the Craniocervical Junction (Microscopic- vs. Endoscopic-Assisted Dissections)

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1 Introduction

The clival region describes an anatomically complex area forming the initial section of the craniocervical junction. For neurosurgical purposes, this region has traditionally been reachable through transmucosal surgical corridors despite the primary risk of infection and their inherent complexity. Thus, an alternative route through the submandibular approach was described, which provides access to the clivus—amid the anterior rim of the foramen magnum—and to the rostral cervical spine up to C4 [1]. The initial descriptions considered two main variants: (1) an upper cervical spine corridor lateral to carotid sheath (limited at the midline with the vertebral artery lying in the corridor) and (2) a subsequently modified wider midline exposure intending to avoid the previously described vascular structures. This last variant was described as an 11-step approach that kept being a surgical challenge because of the risk of vascular damage, submandibular and hypoglossal nerve lesions, and salivary fistula after salivary gland resection [2]. This approach was simplified; moreover, with the increase in endoscopic knowledge, safeguarding a direct entry to the craniocervical junction [3].

During the following review, we analyze the submandibular approach by overviewing its evolution: a 15 min open surgical corridor to the upper cervical spine, vs. endoscopic surgery, while simultaneously describing the anterior craniocervical junction while aimig the clival region.

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2 Anatomical Description of the Clival Region

The clivus (or Blumenbach's clivus) is the anterior central portion of the floor of the posterior cranial fossa. Its last third assembles the initial portion of the craniocervical junction, which is concomitant with the odontoid process (i.e., C2). The clivus itself is a variably pneumatized bone approximately 4–5.5 cm long and 3 cm wide at its midpoint, with an average angulation of about 116°, while being thicker along the midsection anteriorly and thinner posteriorly. It results from the fusion of the basal portion of the occipital bone (basioccipital) and the body of the sphenoid (basisphenoid) over the spheno-occipital synchondrosis (anterior border, part of the posterior cranial fossa but not of the craniocervical junction), sloping upward and forward from the anterior limit of the foramen magnum (posterior border) to the posterior clinoid processes within a basal subarachnoid space anterior to the brain stem, between the medulla oblongata and the pons, but at the same time separated by the prepontine and perimedullary cisterns [4]. Since the tectorial membrane is an extension of the posterior ligament - and is coming from the posterior surface oft he bodies of C1–C2, the tectorial membrane and the superior longitudinal band of the cruciate ligament will both attach to the posteroinferior surface of the previously described posterior border (anterior limit oft he formen magnum). Laterally, it is flanked by the petro-occipital fissures, in combination with the petro-occipital vein, which connects the cavernous sinus to the internal jugular vein; and it is also related to the CNs (V through XII), the internal jugular veins, and the inferior petrosal sinuses.

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A surgical route to this zone was first explored in 1935 by taking a transoral approach—in dogs—which was later on challenged by Kassam et al. (emulating the work of Alfieri and colleagues [5]). This route is a challenge for neurosurgeons because of its proximity to critical neurovascular structures and cranial nerves [5, 6]. Thus, anterior alternatives were considered, and hence, the submandibular approach described by various authors (e.g., Whitesides and Kelly, Andrade and MacNab, Southwick and Robinson, and McAfee) has highlighted a retropharyngeal prevascular route to the clivus [2, 7].

3 Surgical Methods

In the simplified classic submandibular approach, the head is extended 15° and rotated 30° to the contralateral side of the incision (also consider possible previous instrumentation or instability) and fixed with a Mayfield head clamp holder. The incision follows the axis of the mandible, with a length of approximately 3 cm and two fingers inferior to the mandible margin but extending about 5–6 cm from the midline to the medial margin of the sternocleidomastoid muscle, simultaneously staying caudal to the caudal pole of the submandibular gland (which can be palpated from the beginning). Consequently, the platysma is divided with a flap projection toward the mandible and neck following the dissection of the hyoid bone (superolateral) while identifying—via palpation and exposition—the superolateral surface of the great horn of the hyoid bone. Later, the medialization of the pharyngeal structures and exposure to the retropharyngeal space take place. The dissection and exposure of the prevertebral fascia, with the respective identification of the longus colli muscles, take place at both sides of the vertebral bodies of C1–C4 [2].

Similarly, during the endoscopic-assisted submandibular approach, the head is fixed as in the classical approach—i.e., with a Mayfield head clamp—but slightly extended and the head out and rotated (also consider possible previous instrumentation or instability). Perform an 8 mm incision at C4–C5, followed by a smooth dissection of the platysma and a section of the aponeurosis in between the sternocleidomastoid and pretracheal structures (with a finger), thus further dissecting medial to the trachea and the esophagus and lateral to the carotid and internal jugular vein and to the sternocleidomastoid muscle while reaching the anterior vertebral bodies—subsequently placing the dilator and finally the uniportal endoscope under retraction (e.g., 8 mm diameter endoscope with 165 mm working length through a 9 mm sheath with a view angle of 25° and a working channel diameter of 4.1 mm).

In both cases, the direct visualization of the atlantoaxial joint, thus the anterior arch of the atlas, can be identified and removed by drilling the C1 anterior arch in a cranial to caudal direction. Subsequently release the dens tip from the ligament structures and, finally, drill the base of the dens until it separates from the body of C2. The surgical domain extends from the posterior border of the clival region (also the anterior edge of the foramen magnum) to the inferior endplate of C2, with a lateral exposure amid the contralateral C1–C2 joint and medial two-thirds of the same ipsilateral joint and a final expected decompression and a dural exposure, thus covering a broad range of pathologies (Fig. 1) [8]. More objectively, Salle et al. reported a final mean dural exposure of 19 mm (17–20 mm) in between the C1 lateral masses, which was 18 mm (16–20 mm) at the tip of the clival window and a 57 mm (55–60 mm) distance from the tip of the window within the clivus and C3, thus showing that this is a malleable and flexible approach with a wide surgical window resembling the surgical windows of the transmucosal approaches and other homologues [3].

4 Discussion

The clivus is an important bony structure with complex anatomical variants and pathologies, such as skull-base lesions, tumorous lesions, fixed atlantoaxial subluxations, arthrodesis, and Klippel–Feil syndrome, in between other pathologies that clearly demand a flexible and wide approach. Historically, the transmucosal approaches have fulfilled these previous demands but tolerated the increased risk of infection, complex surgical corridors, and surgery-related comorbidities. Nevertheless, when compared with transmucosal routes, the retropharyngeal corridors have shown lower risks of infection by avoiding the nasopharyngeal and oral flora while diminishing surgery-related comorbidities by avoiding mandibular osteotomy, tongue division, etc. [1], but no comparisons between endoscopic and microscopic perspectives on the submandibular approach have been carried out. Thus, we compared the previous approaches: in Fig. 1, we describe the indications for a submandibular approach (microscopic vs. endoscopic dissections) in which the neoplasms have the highest incidence among the microscopic dissection, contrary to endoscopic access (where no neoplasm has been reported). This observation might be due to the bigger window that microscopic dissection offers, again outlining the flexibility of the submandibular approach, but still showing a lack of data in both cases. By other hand, when Ricciardi et al. compared the transmucosal approaches, they not only claimed a similarity between the submandibular approach and the trans-

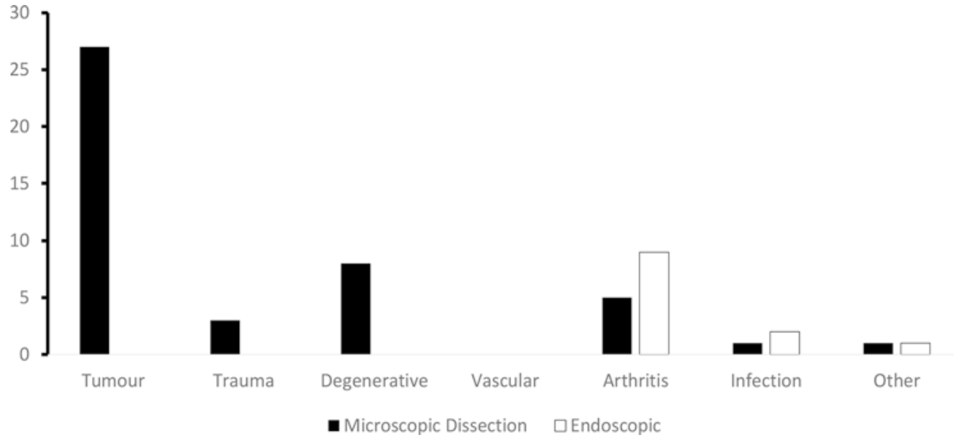

Fig. 1 Comparison of the different indications for a submandibular approach (microscopic vs. endoscopic). When comparing the indications of the submandibular approach through a microscopic dissection vs. an endoscopic one, neoplasms have the highest incidence when performing a microscopic dissection (in the endoscopic approach, no endoscopic neoplasms were reported in the analyzed studies). Interestedly, no vascular indications were reported in either homologous approach. (For additional descriptions, see Appendix, Table 1)

Table 1 Frequency of the different indications for retropharyngeal corridor surgery through microscopic or endoscopic dissection

Author	Technique	Tumour	Trauma	Degenerative	Vascular	Arthritis	Infection	Other	Total
Stevenson et al. 1966	Microscopic dissection	1	0	0	0	0	0	0	**1**
McAffe et al. 1987	Microscopic dissection	11	0	4	0	1	1	0	**17**
Vender et al. 2000	Microscopic dissection	2	2	0	0	2	0	1	**7**
Behari et al. 2001	Microscopic dissection	1	0	4	0	0	0	0	**5**
Yang et al. 2011	Microscopic dissection	11	0	0	0	0	0	0	**11**
Viola et al. 2021	Microscopic dissection	1	1	0	0	2	0	0	**4**
Total		**27**	**3**	**8**	**0**	**5**	**1**	**1**	**45**
London et al. 2018	Endoscopic	0	0	0	0	0	0	1	**1**
Ruetten et al. 2018	Endoscopic	0	0	0	0	6	2	0	**8**
Ohara et al. 2020	Endoscopic	0	0	0	0	3	0		**3**
Total		**0**	**0**	**0**	**0**	**9**	**2**	**1**	**12**

mucosal exposure but also sustained the preservation of vessels and improved the retraction of soft tissue thanks to the submandibular approach [8]. Moreover, the familiarity of the flexible retropharyngeal route offered by the submandibular approach makes it friendly to the neurosurgeon and saves time while allowing the deepest decompression, such as in cases of basilar invagination [9]. Thus, given that the analyzed authors performed an odontoidectomy, it is no surprise that biomechanical consequences are obvious among the highest rates of consequences after a microsurgical dissection through a submandibular approach (Fig. 2). Nevertheless, most authors have agreed to pursue posterior stabilization in any other case, and careful consideration has to be taken when managing obese, barrel-chested, and/or severely

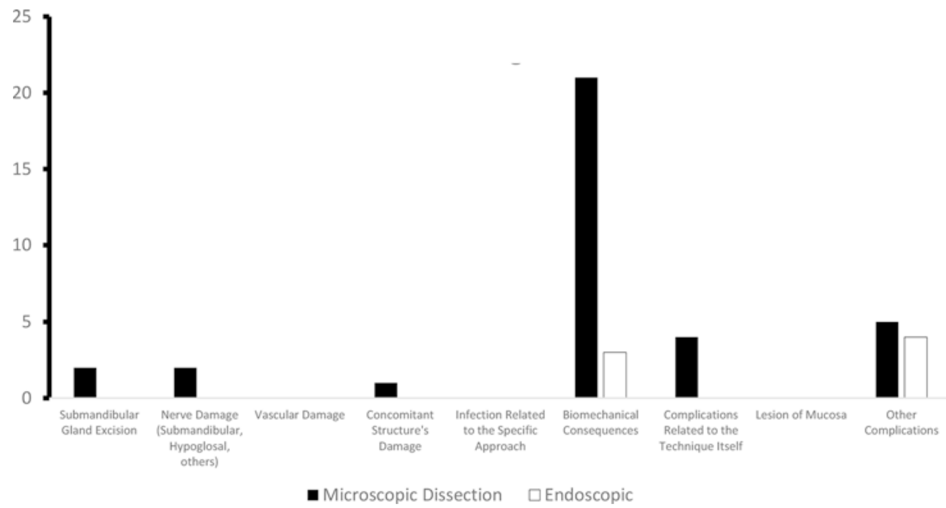

Fig. 2 Documented complications reported by the authors included in Fig. 1. Biomechanical consequences do have the highest incidence. Even though the retropharyngeal corridors goes through a zone where neurovascular damage is a high risk to consider, such complications are not mentioned (i.e. vascular) in the analyzed series. It also highlights the marked predilection of the authors in both approaches to preserve the submandibular excision as also the fact that no infection was reported in any of the series. (For additional description see Appendix, Table 2)

kyphotic patients because of the obvious restriction on the submandibular corridor [9].

Although most authors agree on the potential risk of injury to the recurrent laryngeal nerve, the pharyngeal nerve, and muscular and vascular structures [9], Fig. 2 also shows that both the microdissection and endoscope variants did not have that many neurovascular complications. In any case, this has to be considered because laterally widening the retropharyngeal corridors results in expected increases in risks for vascular lesions; in contrast, when moving toward the midline, blood loss is minimal, even when compared with the transmucosal approaches [10].

Both variants of the submandibular approach (open and endoscopic) offer similar access to the clivus region. Nevertheless, an obvious expansion of the upper cervical spine is offered by the open variant, so it is considered in cases where further instrumentation is needed.

Table 2 Frequency of the different complications reported in Fig. 2

Author	Technique	Submandibular gland excision	Nerve damage (submandibular, hypoglosal, others)	Vascular damage	Concomitant structure's damage	Infection related to the specific approach	Biomechanical consequences	Complications related to the technique itself	Lesion of mucosa	Other complications
Stevenson et al. 1966	Microscopic dissection	0	0	0	0	0	0	0	0	0
McAffe et al. 1987	Microscopic dissection	0	2	0	0	0	13	0	0	1
Vender et al. 2000	Microscopic dissection	0	0	0	0	0	7	0	0	1
Behari et al. 2001	Microscopic dissection	0	0	0	1	0	1	2	0	2
Yang et al. 2011	Microscopic dissection	0	0	0	0	0	0	2	0	1
Viola et al. 2021	Microscopic dissection	0	0	0	0	0	0	0	0	1
Total		**2**	**2**	**0**	**1**	**0**	**21**	**4**	**0**	**5**
London et al. 2018	Endoscopic	0	0	0	0	0	0	0	0	0
Ruetten et al. 2018 [11, 12]	Endoscopic	0	0	0	0	0	0	0	0	4
Ohara et al. 2020	Endoscopic	0	0	0	0	0	3	0	0	0
Total		**0**	**0**	**0**	**0**	**0**	**3**	**0**	**0**	**4**

5 Conclusions

The submandibular approach offers a malleable anterior corridor to the anterior craniocervical junction, with an exposition of the clivus region similar to that of the transmucosal approaches. Its different corridors allow minimally invasive—i.e., endoscopic—surgery toward the same region and different, and wider open variants offer the possibility of further instrumentation in a quick, flexible, low-risk fashion among the upper cervical spine.

Conflicts of Interest No conflicts of interest.

References

1. Alshafai NS, Gunness VRN. The high cervical anterolateral retropharyngeal approach. Acta Neurochir Suppl. 2019;125:147–9. https://doi.org/10.1007/978-3-319-62515-7_21.
2. De Bonis P, Musio A, Mantovani G, Pompucci A, Visani J, Lofrese G, Scerrati A. Simplified four-step retropharyngeal approach for the upper cervical spine: technical note. Eur Spine J. 2020;29(11):2752–7. https://doi.org/10.1007/s00586-020-06521-5.
3. Salle H, de Albuquerque Cavalcanti Mendes G, Gantois C, Lerat J, Aldahak N, Caire F. Endoscopic submandibular retropharyngeal approach to the Craniocervical junction and clivus: An anatomic study. World Neurosurg. 2017;106:266–76. https://doi.org/10.1016/j.wneu.2017.06.162.
4. Rai R, Iwanaga J, Shokouhi G, Loukas M, Mortazavi MM, Oskouian RJ, Tubbs RS. A comprehensive review of the clivus: anatomy, embryology, variants, pathology, and surgical approaches. Childs Nerv Syst. 2018;34(8):1451–8. https://doi.org/10.1007/s00381-018-3875-x.
5. Alfieri A, Jho H-D, Tschabitscher M. Endoscopic endonasal approach to the ventral cranio-cervical junction: anatomical study. Acta Neurochir. 2002;144(3):219–25; discussion 225. https://doi.org/10.1007/s007010200029.
6. Kassam AB, Snyderman C, Gardner P, Carrau R, Spiro R. The expanded endonasal approach: a fully endoscopic transnasal approach and resection of the odontoid process: technical case report. Neurosurgery. 2005;57(1 Suppl):E213; discussion E213. https://doi.org/10.1227/01.neu.0000163687.64774.e4.
7. Park S-A, Lee J-H, Nam Y-S, An X, Han S-H, Ha K-Y. Topographical anatomy of the anterior cervical approach for c2-3 level. Eur Spine J. 2013;22(7):1497–503. https://doi.org/10.1007/s00586-013-2713-9.
8. Ricciardi L, Sturiale CL, Izzo A, Pucci R, Valentini V, Montano N, Polli FM, Visocchi M, Vivas-Buitrago T, Chaichana KL, Quinones-Hinojosa A, Olivi A, Chen S. Submandibular approach for single-stage craniovertebral junction ventral decompression and stabilization: a preliminary cadaveric study of technical feasibility. World Neurosurg. 2019;127:206–12. https://doi.org/10.1016/j.wneu.2019.04.038.
9. Ohara Y, Nakajima Y, Kimura T, Kikuchi N, Sagiuchi T. Full-endoscopic transcervical ventral decompression for pathologies of craniovertebral junction: case series. Neurospine. 2020;17(Suppl 1):S138–44. https://doi.org/10.14245/ns.2040172.086.
10. Viola Á, Kozma I, Süvegh D. Surgery for craniovertebral junction pathologies: minimally invasive anterior submandibular retropharyngeal key-hole approach. BMC Surg. 2021;21(1):199. https://doi.org/10.1186/s12893-021-01198-z.
11. Ruetten S, Hahn P, Oezdemir S, Baraliakos X, Merk H, Godolias G, Komp M. Full-endoscopic uniportal odontoidectomy and decompression of the anterior cervicomedullary junction using the retropharyngeal approach. Spine. 2018a;43(15):E911–8. https://doi.org/10.1097/BRS.0000000000002561.
12. Ruetten S, Hahn P, Oezdemir S, Baraliakos X, Merk H, Godolias G, Komp M. The full-endoscopic uniportal technique for decompression of the anterior craniocervical junction using the retropharyngeal approach: an anatomical feasibility study in human cadavers and review of the literature. J Neurosurg Spine. 2018b;29(6):615–21. https://doi.org/10.3171/2018.4.SPINE171156.

Central Atlantoaxial Dislocation: Presenting Symptoms, Diagnostic Parameters, and Surgical Treatment from Reports on 15 Surgically Treated Patients

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1 Introduction

Atlantoaxial instability is generally associated with neural compression and related symptoms. In 2014, we reported the clinical entity of central or axial atlantoaxial instability (CAAD) wherein there was no radiological evidence of neural compression or of demonstrable instability according to the conventionally adopted radiological parameters [1]. We identified CAAD with chronic or long-standing unstable craniovertebral junction wherein the symptoms were relatively subtle but were relentlessly progressive, and if left untreated, it was ultimately disabling and could be life-threatening [2, 3].

In CAAD, the atlantodental interval is not abnormally affected according to dynamic images, and there is no dural or neural compression due to the odontoid process. The diagnosis of CAAD was essentially established by a "high degree" of suspicion on the basis of telltale radiological and clinical indicators, by analyzing the facetal alignment on lateral profile sagittal imaging, and finally by directly observing instability in the manual manipulation of bones in the atlantoaxial region during surgery. Cases with vertical axial atlantoaxial instability (AAD) [4] and those with partial rotatory AAD [5–7] have been included in the classification of CAAD. We discuss our clinical experience with this hitherto undiagnosed and unknown clinical condition of CAAD. Correct understanding and appropriate treatment can have life-changing repercussions on patients' clinical outcomes.

We identified several musculoskeletal and neural alterations in the face of CAAD. Non-neural and cranial symptoms have been less frequently associated with atlantoaxial instability. However, many symptoms that are not usually recognized in cases with atlantoaxial instability, such as orthostatic refractory syncope and presyncope, lightheadedness, sleeplessness, vertigo, and other autonomic symptoms are frequently associated with CAAD [8]. The management issues and diagnostic characteristics of CAAD are presented. Clinical outcomes following atlantoaxial fixation surgery are analyzed.

2 Material and Methods

During January 2018 to November 2020, 15 patients were diagnosed as having CAAD and were surgically treated in the respective departments of neurosurgery of the authors. This is a retrospective analysis of these patients. Informed consent was provided by all patients. All the clinical tests and surgical procedures were conducted according to principles of the Declaration of Helsinki. Cases having basilar invagination, Chiari formation, "idiopathic" cervicodorsal syringomyelia and syringomyelia associated with Chiari formation, and those having gross cranial and spinal deformities or abnormal bone fusions were not a part of this study. CAAD, in association with cervical spondylosis, ossification of posterior longitudinal ligament, and Hirayama disease were also excluded.

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2.1 Clinical Evaluation

Apart from symptoms that were related to cervicomedullary cord affection at the craniovertebral junction, all the patients presented with a constellation of vague neural and non-neural symptoms that were gradually progressive and that interfered with routine life functions and normal living. The clinical diagnosis was elusive in all the patients, and conservative management failed to treat all of them. The symptoms were divided into musculoskeletal, neurological, orthostatic, cognitive, autonomic, psychiatric, and miscellaneous symptoms. A list of presenting clinical symptoms is summarized in Table 1. The neurological condition was monitored with the use of a specially designed Goel symptom severity index and visual analog scale (VAS) score. As there were symptoms related to craniovertebral junction and multiple other unrelated or nonspecific clinical symptoms, the patients were monitored and evaluated before and after surgery and at follow-up for each of the symptoms.

Table 1 The presenting clinical features

Symptom list	Number of patients
Musculoskeletal symptoms	
Neck pain	15
Restricted range of motion	7
Trauma: Trivial	2
Significant	3
Occipital headache	11
Excessive mobility of skull	7
Shoulder pain	5
Fatigability/chronic fatigue	12
Back pain	8
Jaw pain	5
Pain while swallowing	2
Neurological symptoms	
Weakness in limbs	10
Stiffness	12
Tremors	6
Numbness/tingling	9
Electric-shock-like sensations	3
Decreased sensation	8
Impaired proprioception—missing doorways	6
Giddiness/dizziness/vertigo	14
Impaired balance	10
Tinnitus	6
Impaired gag	3
Dysarthria	6
Voice change	5
Shortness of breath	8
Sleep apnea	12
Orthostatic symptoms	
Tachycardia/palpitations	11
Temperature abnormalities/fever	9
Impaired sweating	5
Presyncope	12
Autonomic symptoms	
Bladder complaints	7
Bowel complaints	2
Sexual dysfunction	3
Cognitive symptoms	
Brain fog	15
Memory abnormalities	15
Concentration issues	15
Blurry vision/focusing issues	7
Miscellaneous symptoms	
Light/sound sensitivity	7
Pressure changes in ears, ear popping	5
Bloating/nausea	9
Hot flashes, hives, rashes	3
Psychiatric symptoms	
Depression	5
Anxiety	2

2.2 Radiological Evaluation

Investigations included dynamic plain radiographs and computed tomography (CT) scans of neck in neutral position, full flexion, and full extension. Magnetic resonance imaging (MRI) in neutral head position was conducted in all cases. Imaging assessed the odontoid process and its relative movements on dynamic imaging, particularly in relationship with the anterior arch of atlas and indicators of neural compression by its tip. It also assessed the relationships and relative movements of facets of atlas and axis. Goel classification was used to classify the atlantoaxial dislocation [1]. For this classification, sagittal images of plain radiographs, CT scans, and MRIs of cuts passing through the facets in neutral head positions were used (Figs. 1 and 2). Type 1 atlantoaxial instability was when the facet of atlas was dislocated anterior to the facet of axis. Patients harboring type 1 atlantoaxial instability were excluded from the analysis because such instability was invariably associated with alterations in atlantodental interval and showed evidence of neural compression due to the odontoid process. Type 2 atlantoaxial instability was when the facet of atlas was dislocated posterior to the facet of axis. Type 2 partial rotatory atlantoaxial instability was when the facet of atlas was dislocated posterior to the facet of axis only on one side, and the contralateral side was in normal alignment. Cases with complete rotatory atlantoaxial dislocation (Fielding types I–IV) were not included. Type 3

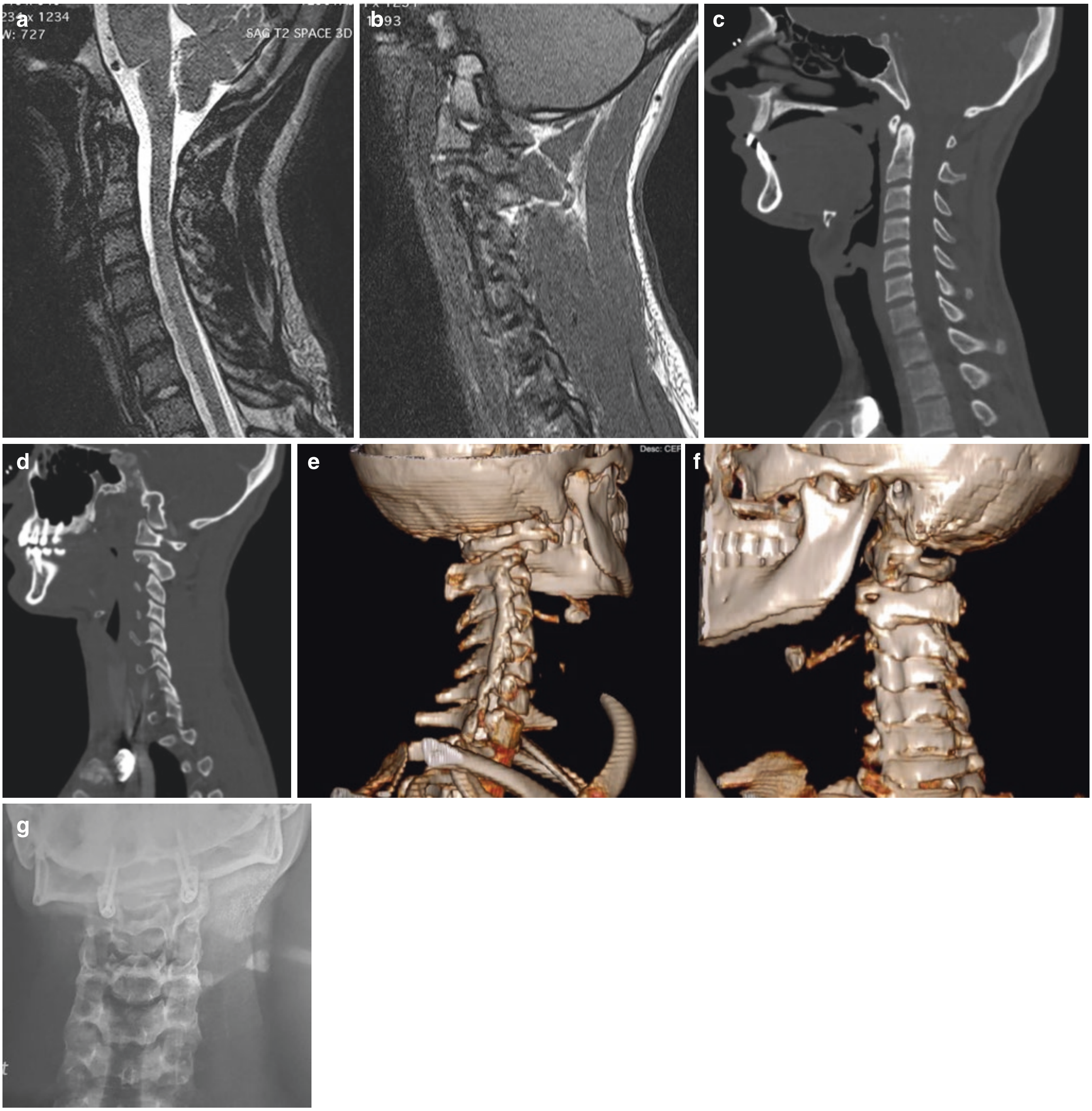

Fig. 1 Images of an 18-year-old male patient. (**a**) T2-weighted MRI showing no evidence of compression at the craniovertebral junction. (**b**) Sagittal cut of MRI through the facets showing type 3 facetal instability. (**c**) Sagittal CT scan showing a normal atlantodental interval. (**d**) Sagittal cut of CT scan passing through the facets showing the type 3 facetal instability. (**e**) 3D reconstructed CT scan showing rotatory atlantoaxial dislocation, where the facet of atlas is in front of the facet of axis. (**f**) 3D reconstructed CT image of the contralateral side, where the facet of atlas is behind the facet of axis. (**g**) Postoperative X-ray showing the atlantoaxial fixation

atlantoaxial instability was when the facets of atlas and axis were in alignment. Alterations of facetal alignments on dynamic imaging were not analyzed. Apart from facetal alignment, instability was diagnosed on the basis of telltale clinical and radiological indicators and was finally confirmed through the direct manipulation of bones during surgery. In both type 2 and type 3, there may be no abnormal alteration of the atlantodental interval on dynamic imaging, and there may be no neural or dural compression due to the odontoid process.

These patients were labeled as having CAAD and are the subject of analysis. The tell tale clinical and radiological

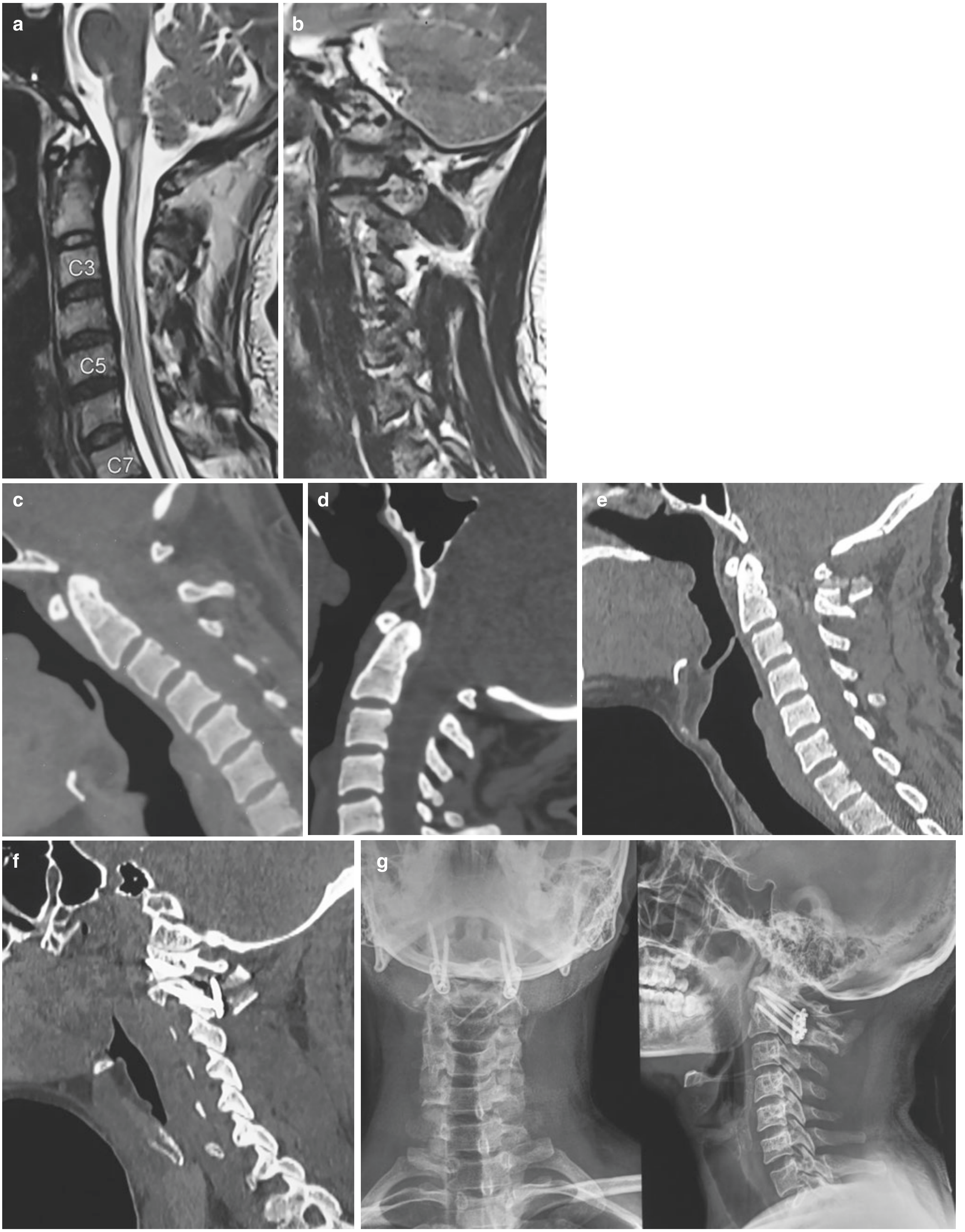

Fig. 2 Images of a 37-year-old male patient. (**a**) T2-weighted MRI of the cervical spine showing hyperintense signal abnormality extending from the craniovertebral junction to the C3-C4 level. (**b**) Sagittal cut of MRI through the facets showing type 2 facetal instability. (**c**) Sagittal CT scan of the craniovertebral junction in flexion showing mild vertical atlantoaxial instability. (**d**) Sagittal CT scan in extension showing the reduction of vertical instability. (**e**) Postoperative CT scan. (**f**) Postoperative CT scan showing the implants. (**g**) Postoperative antero-posterior (AP) and lateral view of X-ray showing the atlantoaxial fixation

Table 2 Table showing the radiological features

Radiological parameter	Number of patients
Goel facetal instability	
Type 1	–
Type 2	9
Type 3	6
Partial rotatory atlantoaxial instability	9
Vertical atlantoaxial instability	2
Lateral atlantoaxial instability	1
External syringomyelia	10

indicators that raised the suspicion of CAAD are detailed in Tables 1 and 2. The vertical dislocation of the odontoid process, wherein the odontoid process moved rostrally upon flexion of the head without abnormally altering the atlanto-dental interval, was identified in two cases. All other possible causes of neural and non-neural symptoms that pointed to nonsurgical treatment were excluded.

Table 3 Table showing the preoperative and postoperative statuses of the patients

Clinical parameter	Preoperative	Postoperative
VAS score	5–9 (Mean - 7.9)	0–3 (Mean - 1.2)
	Preoperative (no. of patients)	Postoperative (no. of patients)
Goel Symptom Severity Index/grade		
Normal functioning	–	12
Occasional symptoms	–	3
Symptoms interfering with normal activity—1 episode/week	3	–
Symptoms interfering with normal activity—2–3 episodes/week	2	–
Symptoms occurring every day	7	–
Unable to function/homebound	3	–

2.3 Surgery

Atlantoaxial fixation was carried out in all patients with the technique described by us earlier, which is summarized here [9, 10]. The patients were placed in a 30° head high position under Gardner–Wells traction. The head high position helped in reducing the venous congestion in the region and provided countertraction. The atlantoaxial joint was exposed after rostrally retracting the C2 ganglion. The articular surfaces of the facets of atlas and axis were denuded of cartilage, bone graft pieces were stuffed in the articular cavity, and then lateral mass plate and screw fixation was carried out. All muscles attached to the C2 spinous process were sharply sectioned. The outer cortical bone of the exposed posterior elements of atlas and axis were drilled to make them suitable hosts for bone grafts. The bone graft was harvested from the iliac crest. The traction was removed after the patient was turned supine after completing the surgery. In one patient, multilevel subaxial cervical spinal fixation was carried out also for cervical kyphosis. Camille's transarticular screw fixation technique was deployed for subaxial spinal stabilization [11].

3 Results

There were six men and nine women. Their ages ranged from 18 to 45 years (mean: 37 years). The duration of symptoms ranged from 8 to 150 months (mean: 86 months). Five patients had a history of trivial or significant trauma prior to the onset of symptoms. All patients had failed a conservative regimen of symptomatic drug treatment and cervical collar and neck exercises. In three patients, the symptoms worsened upon assuming an upright position. In three other patients, the symptoms increased after light exercise or after routine chores. Two patients needed a continuous positive airway pressure (CPAP) machine for their sleep apnea.

Radiological evaluation showed Goel type 2 instability in nine patients and Goel type 3 instability in six patients. Goel type 2 partial rotatory atlantoaxial instability was identified in nine patients. Vertical atlantoaxial instability was seen in two patients.

All patients observed clinical recovery following surgery after they were fully awake and were out of the effects of anesthesia. The clinical improvement was quick, remarkable, and progressive. The follow-up ranged from 6 to 34 months, with an average of 17 months. The clinical status after at least 6 months of surgery is shown in Table 3. Postoperative imaging was carried out after a minimum period of 6 months of surgery. Bone fusion was observed in all patients across the facets and between the treated spinal segments. There were no implant failures. None of the patients worsened after initial clinical recovery or needed any further surgical procedure.

4 Discussion

The atlantoaxial articulation is a highly mobile joint. On the other hand, the occipitoatlantal joint is a highly stable joint. Both stability and mobility are hallmarks of craniovertebral junction. While atlantoaxial instability is relatively common, occipitoatlantal instability is extremely rare. The flat and round articular surfaces that allow circumferential movements for the atlantoaxial joint also make it prone to developing instability. The facets of atlas and axis are placed one above the other in the form of brick-over-brick configuration and participate in forming the human spinal pillar. Our several reviews on the subject have identified that atlantoaxial instability is an underdiagnosed and undertreated clinical entity. All patients in the presented series were severely disabled and troubled and were under clinical evaluation for a prolonged period (average: 86 months).

The only validated radiological parameter that confirms the presence of atlantoaxial instability is the pathological alteration of atlantodental interval on dynamic flexion–extension images. In the flexed head position on lateral profile imaging, an atlantodental interval of more than 3 mm in adults and 5 mm in children is recognized to be indicative or confirmatory evidence of atlantoaxial dislocation. Depending on the mobility of the odontoid process on dynamic imaging, the dislocation is further classified into fixed or irreducible and partially or completely reducible mobile varieties [12]. Direct radiological evidence of neural compression is also an indicator but not confirmatory evidence of an unstable atlantoaxial joint.

In 2014, we identified that there can be atlantoaxial instability even in the absence of an altered atlantodental interval or indicators of neural compression opposite the odontoid process [1]. It was observed that the atlantoaxial joint could be unstable even when the odontoid process was in normal position and when facets were in alignment, and alternative radiological parameters can be used to diagnose atlantoaxial instability [1–3]. We proposed a classification of atlantoaxial instability on the basis of an alignment of facets of atlas and axis on lateral profile imaging with the head in a neutral position, the presence of telltale clinical and radiological indicators, and direct observations of instability through the manual manipulation of bones during surgery [1].

Type 2 partial CAAD includes cases of rotatory AAD wherein on neutral profile imaging, the facet of atlas is displaced posterior to the facet of axis on one side but the facets are in alignment on the contralateral side. All patients with type 2 instability had type 2 partial CAAD. In this series and in our previously reported studies, we have not included cases of Fielding types I–IV of rotatory AAD wherein on lateral profile imaging with the head in a neutral position, the facet of atlas and of axis are in misalignment on both sides, where the facet of atlas is anterior to the facet of axis on one side and posterior to the facet of axis on the contralateral side.

Vertical atlantoaxial instability has specific radiological characteristics [4]. There can be long-standing musculoskeletal and clinical symptoms without any abnormal alterations of atlantodental interval or any kind of compression of the neural tube due to the odontoid process on dynamic imaging. The facets of atlas and axis may or may not be in alignment. Such a type of instability has been listed in the telltale indicators list that is suggestive of CAAD.

In 2015, we first described CAAD in relationship with Chiari formation. Our observation was that tonsillar descent in Chiari formation was secondary to chronic atlantoaxial dislocation and was a natural protective maneuver, and we likened herniated tonsils to the protective air bags of a car that are placed in situ to prevent the compression of neural structures between bones in the event of potential or manifest atlantoaxial instability [13, 14]. The atlantoaxial dislocation in such cases was of the chronic variety and was more often of the central or axial type. We advocated atlantoaxial stabilization for Chiari formation. Accordingly, we preferred the terminology *Chiari formation* rather than *Chiari malformation* [15]. Although this hypothesis has been under discussion and has not yet achieved universal approval, our gratifying clinical experience in more than 400 consecutive cases of Chiari formation treated through atlantoaxial stabilization over a period of more than 10 years gives credence to this hypothesis [16–18].

Essentially, it means that there can be atlantoaxial instability and mild to profound related symptoms even when the facets are in alignment, there is no alteration in atlantodental interval and when there are no indicators of neural compression on radiological assessment. On the basis of our continued experience, apart from Chiari formation, we identified CAAD in cases with retro-odontoid pseudotumor [19], basilar invagination (both groups, A and B) [20–22], "idiopathic" syringomyelia [23], external syringomyelia, bifid arches of atlas and/or axis [24], short neck [25], torticollis, cervical kyphosis [26], dorsal kyphoscoliosis [27–29], bone fusions that include assimilation of atlas, C2–3 vertebral fusion and Klippel–Feil abnormalities and a host of other clinical entities [30, 31]. We observed that there is atlantoaxial instability when each of these musculoskeletal or neural entities is present in a cohort or even when they are present in isolation. More recently, we have identified the presence of CAAD in cases with multilevel cervical spondylosis [32] and in cases where the ossification of the posterior longitudinal ligament leads to myelopathy [33]. It was also observed that CAAD can be a cause of Hirayama disease [34].

Our recent article discussed a number of indicators of atlantoaxial instability. All the indicators mentioned either singly or in cohort can be telltale indicators of atlantoaxial instability or CAAD [35]. We have identified that central or axial atlantoaxial instability can be a cause of severe neurological deficits, including spastic quadriparesis [2]. The clinical symptoms are usually long-standing or chronic. Our observations, which are based on long-term clinical experience, suggest that ignoring atlantoaxial instability in such cases can be a cause of diagnosis failure and deprive the patient of an opportunity to undergo subsequent surgical treatment that can be curative.

In all our patients, there was no systemic or syndromic disorder that could indicate hypermobility of joints in general. Ehlers–Danlos syndrome in particular was ruled out as its related systemic and joint issues have been suspected to result in subtle, potential, or manifest atlantoaxial instability.

Our patients presented with long-standing, slow progressive, and disabling nonspecific cranial and spinal neural and non-neural complex of symptoms that was refractory to medical treatment. Although neural symptoms were present, symptoms generally not associated with the compression of the spinomedullary region dominated. In at least five patients, psychiatric disturbances were identified to be the causes of clinical symptoms. Neck pain was a prominent symptom in all patients. Symptoms such as lightheadedness, vertigo, giddiness, breathlessness on exertion, and sleep disturbances were present in almost all (93.3%) patients. Neural symptoms included gait disturbances, weakness in the hands and fingers, and urinary and bowel affection. In six (40%) patients, there was posterior column neural function affection.

In none of the patients in this series was there evidence of atlantoaxial instability when assessed by validated radiological parameters. CAAD was diagnosed on the basis of a careful analysis of radiological imaging and telltale radiological indicators, as shown in Table 2. A high degree of clinical suspicion is essential to direct the investigations and reach the diagnostic conclusion. There were nine patients who had type 2 and six patients who had type 3 atlantoaxial instability. In all the nine patients with type 2 atlantoaxial instability, the instability was partial or only on one side, an entity that could also be labeled as unilateral rotatory atlantoaxial instability. In 11 patients, the neural structures in the region of the craniovertebral junction were atrophic [36]. The other, more-frequently identified radiological finding was the presence of external syringomyelia in ten patients. External syringomyelia in the region of the craniovertebral junction and in the subaxial cervical spine refers to the presence of more than a normal amount of cerebrospinal fluid (CSF) in the extramedullary space. The quantification of excessive or more than a normal amount of CSF can be assessed on axial images produced by MRI scans. However, the exact parameters of the quantification of external syringomyelia have not yet been identified. Our earlier articles have discussed that cord atrophy and/or external syringomyelia [37] are indicators of atlantoaxial instability.

The clinical entity of CAAD has not yet been universally accepted, and the clinical and radiological diagnostic parameters have not yet been crystalized or validated. In the absence of defining radiological parameters, the diagnosis of atlantoaxial instability is made in such cases on the basis of a high degree of clinical suspicion and on the basis of associated radiological indicators. Given the chronic nature of the symptoms and the presence of nonspecific systemic, cranial, and spinal symptoms, there is a possibility of obtaining the wrong diagnosis and an unnecessarily performed major surgical procedure. On the other hand, correct diagnosis and treatment lay open the possibility of complete recovery from all symptoms. Our 4-decade-long experience and surgical treatment of more than 3000 cases with atlantoaxial fixation using the technique described by us certainly worked in our favor while making the diagnosis and performing the surgery on the basis of otherwise-ignored radiological and clinical guides. Manual manipulation through direct physical handling of bones to assess instability can be performed only after a conclusive and decisive decision has been made on the need for surgical intervention.

The exact cause of neurological and systemic or functional symptoms in the absence of any neural compression cannot be clearly defined and can only be speculated. Rather than neural compression, the nodal point of the generation of symptoms seems to be instability. Intermittent or repeated microinjuries to the cord related to abnormal regional movements might be responsible for initiating a bodily response. Vertebral artery torsion and microischemic consequences could be responsible for clinical symptoms. Following atlantoaxial fixation surgery, all patients had remarkable clinical recovery from all related and unrelated neural and non-neural symptoms. Given that the recovery in symptoms was observed in the immediate postoperative period, ischemia as a cause of symptoms seems unlikely. As neural compression was not observed in either the preoperative or the postoperative images and no decompression by removing bone or soft tissues was conducted, its role in the initiation, persistence, and progression of symptoms needs to be evaluated [38]. The recovery from all major symptoms is clearly demonstrative of the fact that the instability of the joint is the primary source of all neurological, functional, and systemic consequences.

5 Conclusion

The treatment of CAAD can have major therapeutic implications for appropriately and correctly selected patients.

References

1. Goel A. Goel's classification of atlantoaxial "facetal" dislocation. J Craniovertebr Junction Spine. 2014;5:15–9.
2. Goel A. A review of a new clinical entity of "central atlantoaxial instability": expanding horizons of craniovertebral junction surgery. Neurospine. 2019;16(2):186–94.
3. Goel A, Dhar A, Shah A, Jadhav D, Bakale N, Vaja T, Jadhav N. Central or axial atlantoaxial dislocation as a cause of cervical myelopathy: a report of outcome of 5 cases treated by atlantoaxial stabilization. World Neurosurg. 2019;121:e908–16.
4. Goel A, Shah A, Rajan S. Vertical mobile and reducible atlantoaxial dislocation. Clinical article. J Neurosurg Spine. 2009;11(1):9–14.
5. Fielding JW, Hawkins RJ, Hensinger RN, Francis WR. Atlantoaxial rotary deformities. Orthop Clin North Am. 1978;9(4):955–67.

6. Fielding JW, Hawkins RJ. Atlanto-axial rotatory fixation. (fixed rotatory subluxation of the atlanto-axial joint). J Bone Joint Surg Am. 1977;59(1):37–44.
7. Henderson FC Sr, Rosenbaum R, Narayanan M, Koby M, Tuchman K, Rowe PC, Francomano C. Atlanto-axial rotary instability (Fielding type 1): characteristic clinical and radiological findings, and treatment outcomes following alignment, fusion, and stabilization. Neurosurg Rev. 2021;44(3):1553–68.
8. Henderson FC Sr, Rowe PC, Narayanan M, Rosenbaum R, Koby M, Tuchmann K, Francomano CA. Refractory syncope and presyncope associated with atlantoaxial instability: preliminary evidence of improvement following surgical stabilization. World Neurosurg. 2021;149:e854–65.
9. Goel A, Desai K, Muzumdar D. Atlantoaxial fixation using plate and screw method: a report of 160 treated patients. Neurosurgery. 2002;51:1351–7.
10. Goel A, Laheri VK. Plate and screw fixation for atlanto-axial dislocation. (Technical report). Acta Neurochir. 1994;129:47–53.
11. Roy-Camille R, Saillant G, Laville C, Benazet JP. Treatment of lower cervical spinal injuries--C3 to C7. Spine (Phila Pa 1976). 1992;17(10 Suppl):S442–6.
12. Goel A, Kulkarni AG, Sharma P. Reduction of fixed atlanto-axial dislocation in 24 cases: technical note. J Neurosurg Spine. 2005;2(4):505–9.
13. Goel A. Is atlantoaxial instability the cause of Chiari malformation? Outcome analysis of 65 patients treated by atlantoaxial fixation. J Neurosurg Spine. 2015;22:116–27.
14. Goel A. Is Chiari malformation nature's protective "air bag"? Is its presence diagnostic of atlantoaxial instability? J Craniovertebr Junction Spine. 2014;5:107–9.
15. Goel A. Is Chiari a "formation" or a "malformation?". J Craniovertebr Junction Spine. 2017;8(1):1–2.
16. Goel A, Gore S, Shah A, Dharurkar P, Vutha R, Patil A. Atlantoaxial fixation for Chiari 1 formation in pediatric age-group patients: report of treatment in 33 patients. World Neurosurg. 2018;111:e668–77.
17. Goel A, Jadhav D, Shah A, Rai S, Dandpat S, Vutha R, Dhar A, Prasad A. Chiari 1 formation redefined-clinical and radiographic observations in 388 surgically treated patients. World Neurosurg. 2020;141:e921–34.
18. Goel A, Kaswa A, Shah A. Atlantoaxial fixation for treatment of Chiari formation and syringomyelia with no craniovertebral bone anomaly: report of an experience with 57 cases. Acta Neurochir Suppl. 2019;125:101–10.
19. Goel A, Darji H, Shah A, Prasad A, Hawaldar A. Retro-odontoid and retro-C2 body pseudotumor, pannus, and/or cyst. A study based on analysis of 63 cases. World Neurosurg. 2021;151:e170.
20. Goel A, Jain S, Shah A. Radiological evaluation of 510 cases of basilar invagination with evidence of atlantoaxial instability (group a basilar invagination). World Neurosurg. 2018;110:533–43.
21. Goel A, Nadkarni T, Shah A, Sathe P, Patil M. Radiologic evaluation of basilar invagination without obvious atlantoaxial instability (group B basilar invagination): analysis based on a study of 75 patients. World Neurosurg. 2016;95:375–82.
22. Goel A, Sathe P, Shah A. Atlantoaxial fixation for basilar invagination without obvious atlantoaxial instability (group B basilar invagination): outcome analysis of 63 surgically treated cases. World Neurosurg. 2017;99:164–70.
23. Shah A, Sathe P, Patil M, Goel A. Treatment of "idiopathic" syrinx by atlantoaxial fixation: report of an experience with nine cases. J Craniovertebr Junction Spine. 2017;8(1):15–21.
24. Goel A, Nadkarni T, Shah A, Ramdasi R, Patni N. Bifid anterior and posterior arches of atlas: surgical implication and analysis of 70 cases. Neurosurgery. 2015;77(2):296–305; discussion 305–6.
25. Goel A, Shah A. Reversal of longstanding musculoskeletal changes in basilar invagination after surgical decompression and stabilization. J Neurosurg Spine. 2009;10:220–7.
26. Goel A, Kaswa A, Shah A. Role of atlantoaxial and subaxial spinal instability in pathogenesis of spinal "degeneration"-related cervical kyphosis. World Neurosurg. 2017;101:702–9.
27. Goel A, Biswas C, Shah A, Darji H, Bhambere S, Hawaldar A. Atlantoaxial instability as a cause of craniovertebral and cervical spinal alterations and dorsal kyphoscoliosis. World Neurosurg. 2020;144:39–42.
28. Goel A, Vutha R, Shah A, Dharurkar P, Jadhav N, Jadhav D. Spinal kyphoscoliosis associated with Chiari formation and syringomyelia "recovery" following atlantoaxial fixation: a preliminary report and early Results based on experience with 11 surgically treated cases. World Neurosurg. 2019;125:e937–46.
29. Goel A, Vutha R, Shah A, Rai SKR. Rotatory atlantoaxial dislocation presenting as spinal kyphoscoliosis. J Craniovertebr Junction Spine. 2021;12(1):99–101.
30. Shah A, Hawaldar A, Lunawat A, Dandpat S, Goel A. Report of two cases with omovertebral bone and Klippel–Feil syndrome with craniovertebral junction instability. J Craniovertebr Junction Spine. 2021;12(1):95–8.
31. Shah A, Kaswa A, Jain S, Goel A. Atlantoaxial instability associated with pan cervical vertebral fusion: report on management of 4 cases. Neurol India. 2018;66(1):147–50.
32. Goel A. Role of subaxial spinal and atlantoaxial instability in multisegmental cervical Spondylotic myelopathy. Acta Neurochir Suppl. 2019;125:71–8.
33. Goel A, Grasso G, Shah A, Rai S, Dandpat S, Vaja T, Jadhav D, Jadhav N. "Only spinal fixation" as surgical treatment of cervical myelopathy related to ossified posterior longitudinal ligament: review of 52 cases. World Neurosurg. 2020;140:556–63.
34. Goel A, Dhar A, Shah A. Multilevel spinal stabilization as a treatment for Hirayama disease: report of an experience with five cases. World Neurosurg. 2017;99:186–91.
35. Goel A. Indicators of atlantoaxial instability. J Craniovert Junction Spine. 2021;21:103–6.
36. Goel A. Is focal spinal cord "atrophy" evidence of chronic spinal instability? J Craniovertebr Junction Spine. 2017;8(4):295–6.
37. Goel A. External syrinx-introduction of a new term. J Craniovertebr Junction Spine. 2016;7(4):191–2.
38. Goel A. Not neural deformation or compression but instability is the cause of symptoms in degenerative spinal disease. J Craniovertebr Junction Spine. 2014;5(4):141–2.

Atlantoaxial Anterior Transarticular Screw Fixation: Indications and Surgical Technique

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1 Introduction

The atlas and the axis represent a unique anatomic and functional segment of the spine.

The complex anatomy of this joint, thanks to its osseous and ligamentous structures, allows the major part of the rotation of the head [1].

Trauma, tumors, and degenerative diseases may cause atlantoaxial instability by lesioning the integrity of bones (C2 dens, rings, or lateral masses of the atlas) or ligaments (transverses or alars). The closed relationship between eloquent anatomical structures, the spinal cord, and vertebral arteries makes the surgical treatments on this segment challenging for every surgeon.

Among the surgical techniques described to treat atlantoaxial instability, the anterior transarticular screw fixation (ATSF) is probably the least known and performed.

The technique was originally described by Lu on a cadaver [2] (Fig. 1a) and by Reindl on a patient [3]; it has since been modified by Koller in 2006 (Fig. 1b) [4] and later described in multiple cases and technical variations [5–7]. The technical difficulty, the inability to decompress neural structures, and the lack of knowledge among most surgeons are the main reasons for the rare choice of this peculiar technique.

This chapter aims to highlight the advantages and limitations of ATSF, describing technical critical points learned on over a decade of experience with this technique.

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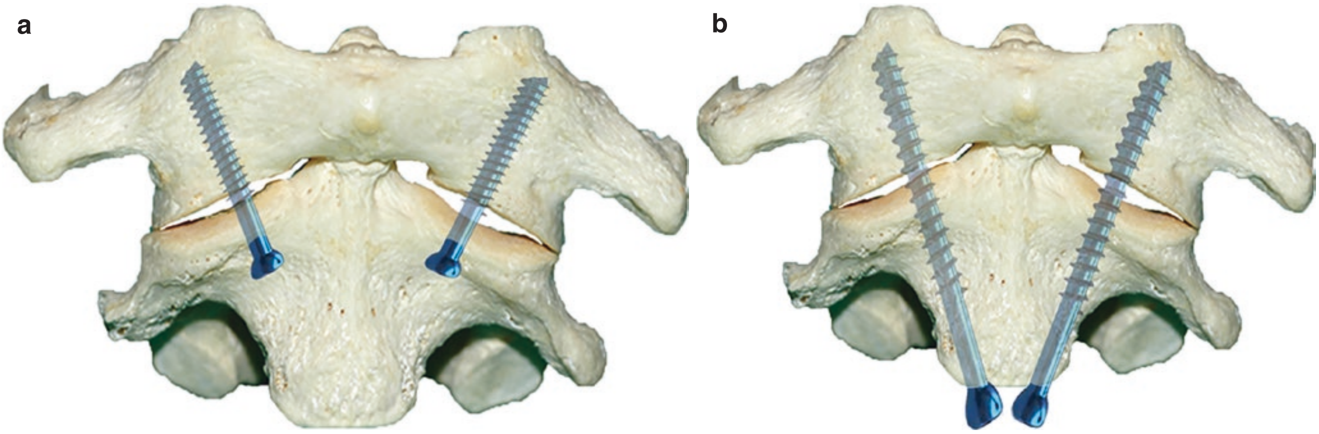

Fig. 1 Antero-posterior view of classical anterior transarticular screw fixation entry points and the screw's direction (partially threaded malleolar screws): (**a**) Lu's entry point, described in vivo by Reindl, at the lateral edge of the medial third of the C2 articular joint lip; (**b**) Koller's technique, with the entry point at the pinafore of the C2 vertebral body

2 Discussion

2.1 Indications

Why should we choose this technique over the well-known posterior Goel–Harms one[8, 9]?

First of all, the supine position is safer. The dens tend to adhere to the anterior ring of the atlas in the case of transverse ligament disruption, reducing the risk of cord compression. It is also safer in patients with multiple fractures and in those with cardiorespiratory pathologies [10–12].

Compared to cervical posterior approaches, ATSF, as all procedures performed by taking a retropharyngeal approach, implicates no muscle trauma, reducing postoperative pain and hospitalization. It also reduces blood loss, avoiding the surgical exposure and management of the C2 periradicular venous plexus, and reduces the risk of delayed kyphosis secondary to C2 posterior scarification.

2.2 Contraindications

Fixed Rotatory C1-C2 Luxation

Because ATSF is a fluoroscopy-guided procedure, proceed only in the case of having a good visualization of C1-C2 bone limits, especially in the Anterior/Posterior (AP) view. A preoperative open-mouth X-ray can help identify patients without having a clear view, such as those with metal alloys used in dental crowns or with limitations in opening their mouths.

In the case of basilar invagination (BI), the technique of choice should be the posterior one. The distance between the skin incision and the working area is excessive, making the surgical field too deep to also comfortably manage retractors and surgical movements. Furthermore, the X-ray open-mouth AP and lateral views in BI may be confusing for the superimposition of the lateral masses of C1 on occipital and mastoid bones.

Performing ATSF in patients with high-riding vertebral arteries in C2 may expose them to serous risk of vascular damage or stroke. However, this is a relative contraindication because in the technique introduced by Koeller (Fig. 1b), the K-wire and the screws follow a trajectory medial to high in comparison to vertebral artery grooves in C2.

Although some authors have described ways to decompress the spinal cord by taking a retropharyngeal approach at the C1-C2 level, patients requiring decompression should undergo the posterior approach.

3 Step-by-Step Technical Description

The patient is placed supine on a radiolucent table. The fluoroscopy AP view keeps the mouth open with specific radiolucent distractors or, thinking out of the box, with anything else could do the job, such as shaped corks or gauzes when the patient is toothless (Fig. 2).

The proper visualization of C1 lateral masses should be checked before fixing the head. Contrary to what we believed necessary at the beginning of our experience with this surgical technique [5], there is no need to fix the head to a radiolucent Mayfield head holder (a very expensive tool not available in every spine center). It is sufficient to tape the head to the table in the desired position.

The procedure is started with a classic Smith–Robinson retropharyngeal approach centered to C4-C5 in order to set up the best trajectory, which is a little divergent from the anterior longitudinal ligament. Once the anterior longitudinal ligament has been exposed, the retropharyngeal space is cranially opened up to the anterior tubercle of C1. The pharynx should be retracted with blunt long retractors by a sec-

Fig. 2 Operating room setting with Medtronic O-Arm2 used as a C-arm fluoroscopy with mechanic automatic rotation; a gauzes's roll was used as a radiolucent open-mouth dilator (no teeth available for the cork); AP and lateral views can be seen on the screen with a good visualization of the C1 lateral masses and their anatomical relationships

ond surgeon in order to reduce postoperative dysphagia. Once the radiological level has been checked, surgery proceeds depending on the technique chosen.

In Lu's technique (Fig. 1a), a progressive scarification of the anterior surface of C2 has to be performed in a medial to lateral direction in order to expose at least the medial third of the C1-C2 joints. At this point, the entry level of the K-wire should be identified both radiologically and macroscopically, consisting of a point on the undersurface of the overhanging lip of the lateral mass of C2, 4–5 mm lateral to the base of the odontoid process[2, 3].

Concerning the trajectory, it could be necessary to partially drill the anterior surface of the C2 promontorium in order to gain the correct inclination with the K-wire guide instrument. We believe that the description of the trajectory with craniocaudal and mediolateral angles is useless or misleading. Because this is not a lab procedure but rather a fluoroscopy-guided technique, the trajectory of the K-wire and the length of the screw should be determined on each side according to the bony structure displayed on the screen. The target areas for the K-wire are the superolateral margin of the C1 lateral mass in the AP view, without passing the lateral or superior cortical rims where the vertebral artery is and C0-C1 articulation trauma can occur, and the posterior third of the C1 lateral mass in the lateral view, aiming to avoid passing beyond the posterior cortical rim, where the ipsilateral vertebral artery usually runs.

In the Koeller technique (Fig. 1b), the K-wire and screw entry point lies underneath the pinafore of C2, increasing the screw purchase in the bone of the C2 promontory and improving the stability of the construct. Therefore, the time-consuming and uncomfortable scarification of C1-C2 joint is not needed if joint scarification for fusion is not mandatory.

In Koller's technique, as well as in dens screwing, the anterior surface of C3 vertebral body and that of the C2-C3 disc need to be drilled away in order to reach the correct angle in the sagittal plane.

Even though ATSF can achieve a solid fixation [13, 14], fusion at this site should be the final target. In the case of traumatic disruption of the C1-C2 articular surfaces or in the case of unilateral degenerative osteoarthritis, fusion can be expected to appear without the need for bone scarification and fusion promotion. In all other cases, the scarification of the articular processes and the injection of bone paste inside the joint could be achieved (not easily) with long curved curettes. ATSF is performed with a standard Smith–Robinson approach, so no blood loss or pain is expected, but mild dysphagia and early discharge are expected. Given the aforementioned bone fusion issue, a temporary cervical collar should be prescribed in the case of high preoperative instability, uncertain bone quality, or screw purchase.

4 Tips and Tricks

- Always preoperatively check the AP visualization of the lateral masses with an open-mouth X-ray.
- An intraoperative fluoroscopic clear view is mandatory for the safety of this procedure. Given that precise AP and lateral positions of the fluoroscopy are needed in each step of the K-wire and then of the screw introduction, our advice is to use two fluoroscopic C-arms, or one C-arm with automatic rotation with displayed degrees (an O-arm, Medtronic, Minneapolis, MN, USA could be used this way; see Fig. 2), or find an expert fluoroscopy technician.
- Use very long and narrow blunt handheld retractors to retract the pharynx.
- A short neck and a prominent chest could limit instrument usability. Therefore, choose a surgical system with an angulated K-wire holder/guide and cardanic screw drivers, keeping available the malleolar screws' system for specific further instruments (e.g., cannulated drill and rescue screws).
- The AP and LL angulations should be well evaluated at the beginning of the K-wire introduction because this procedure often does not allow small variations in direction after the wire is in the bone. Excessive angle variations

Fig. 3 Lateral view of Lu's technique showing the potential cortical bone damage and subsequent failure of the screw whenever a fracture of the C2 articular lip occurs

Fig. 4 Lateral view of Koller's technique showing the potential risk of a in-out-in path of the K-wire and screws, due to the normal narrowness of the C2 vertebral body at this level

during K-wire introduction may result in its breakage inside the bone. In this case, a dedicated cannulated drill bit can be helpful to loosen the wire from the surrounding bone and then pull it out after grabbing its caudal extremity.

- A critical point in Lu's technique is that the K-wire entry point should be at the lateral border of the medial third of the C2 joint, paying attention to being deep enough to leave sufficient bone on the cortical lip of C2 after the screw introduction, to avoid cortical bone damage and screw loosening (Fig. 3).
- A critical point in Koller's technique is that the normal anatomy of the anterior surface of the axis seldomly permits enough space for two divergent screws. The risk is that an in-out-in trajectory may cause the malpositioning of the K-wire or of the screw (Fig. 4). Moreover, once a screw is in place, there is no sufficient bone volume to extract and reposition one or two screws, eventually leading to difficult and extreme surgical solutions (Fig. 5).

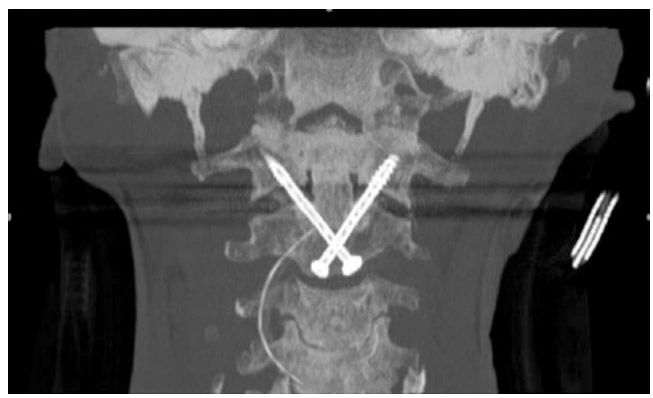

Fig. 5 Multiplanar-reconstructed CT: axial image of a patient submitted to ATSF with Koller's technique, where in this case, the space for the ipsilateral screw was too narrow to be placed side by side with the contralateral, so a modification of the technique was carried out with the two screws crossing inside the C2-body

5 Conclusions

Anterior atlantoaxial screw fixation is a complex surgical technique with a steep learning curve, but it allows for achieving the solid stabilization of this segment with a minimally invasive technique. Every spine surgeon dealing with craniocervical junction instability should have it in their surgical armamentarium, being aware of all the pros and cons of this special technique.

Disclosure of Conflicts of Interest The authors declare no conflicts of interest concerning the materials or methods used in this study or the findings specified in this chapter.

References

1. Steinmetz MP, Mroz TE, Benzel EC. Craniovertebral junction: biomechanical considerations. Neurosurgery. 2010;66(3 Suppl):7–12. https://doi.org/10.1227/01.NEU.0000366109.85796.42. PMID: 20173531.
2. Lu J, Ebraheim NA, Yang H, Heck BE, Yeasting RA. Anatomic considerations of anterior transarticular screw fixation for atlantoaxial instability. Spine. 1998;23:1229–35; discussion 1236.
3. Reindl R, Sen M, Aebi M. Anterior instrumentation for traumatic C1-C2 instability. Spine. 2003;28:E329–33.
4. Koller H, Kammermeier V, Ulbricht D, Assuncao A, Karolus S, van den Berg B, et al. Anterior retropharyngeal fixation C1-2 for stabilization of atlantoaxial instabilities: study of feasibility, technical description and preliminary results. Eur Spine J. 2006;15:1326–38.
5. Polli FM, Miscusi M, Forcato S, Raco A. Atlantoaxial anterior transarticular screw fixation: a case series and reappraisal of the technique. Spine J. 2015;15(1):185–93. https://doi.org/10.1016/j.spinee.2014.09.019. Epub 2014 Sep 26. PMID: 25264177.
6. Ricciardi L, Sturiale CL, Izzo A, Pucci R, Valentini V, Montano N, Polli FM, Visocchi M, Vivas-Buitrago T, Chaichana KL, Quinones-Hinojosa A, Olivi A, Chen S. Submandibular approach for single-stage craniovertebral junction ventral decompression and stabilization: a preliminary cadaveric study of technical feasibility. World Neurosurg. 2019;127:206–12. https://doi.org/10.1016/j.wneu.2019.04.038. Epub 2019 Apr 10. PMID: 30980973.
7. Gembruch O, Ahmadipour Y, Lemonas E, Müller O. The anterior transarticular fixation of C1/C2 in the elderly with dens fractures. Int J Spine Surg. 2020;14(2):162–9. https://doi.org/10.14444/7031. PMID: 32355621; PMCID: PMC7188103.
8. Goel A, Laheri V. Plate and screw fixation for atlanto-axial subluxation. Acta Neurochir (Wien). 1994;129:47–53.
9. Harms J, Melcher RP. Posterior C1-C2 fusion with polyaxial screw and rod fixation. Spine. 2001;26:2467–71.
10. Kaneko K, Milic-Emily J, Dolovich MB, et al. Regional distribution of ventilation and perfusion as a function of body position. J Appl Physiol. 1966;21:767–77.
11. Stone JG, Khambatta HJ. Pulmonary shunts in the prone position. Anaesthesia. 1978;33:512–7.
12. Palmon SC, Kirsch JR, Depper JA, et al. The effect of the prone position on pulmonary mechanics is frame-dependent. Anesth Analg. 1998;87:1175–80.
13. Sen MK, Steffen T, Beckman L, Tsantrizos A, Reindl R, Aebi M. Atlantoaxial fusion using anterior transarticular screw fixation of C1-C2: technical innovation and biomechanical study. Eur Spine J. 2005;14:512–8.
14. Lapsiwala SB, Anderson PA, Oza A, Resnick DK. Biomechanical comparison of four C1 to C2 rigid fixative techniques: anterior transarticular, posterior transarticular, C1 to C2 pedicle, and C1 to C2 intralaminar screws. Neurosurgery. 2006;58:516–21; discussion 516–21.

Neuronavigated Retropharyngeal Anterior Screw Fixation of the Odontoid for the Treatment of C2 Type II Fractures: Case Report

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1 Introduction

Odontoid fractures account for approximately 5–15% of the lesions of the cervical spine and are more frequently seen in elderly patients. The common injury is the fracture of the odontoid base (type II, Anderson–D'Alonzo), which causes atlantoaxial instability. Nonsurgical management with immobilization by the use a rigid tutor or Halo Vest is associated with high morbidity and a significant risk of failure, especially in high-risk populations, such as patients with obesity or other comorbidities. The surgical strategies adopted to date include the anterior fusion approach and the posterior fusion approach [1]. Anterior screw fixation provides stability and significant healing rates and preserves odontoid biomechanics to maintain normal neck mobility. Repeated fluoroscopic checks are required to guide the surgeon toward the correct positioning of the synthesis system. Our experience makes use of the neuronavigation system, by acquiring intraoperative radiological images of the patient in real time, this system reduces the risk of radiation exposure, thus protecting the patient, the surgeon and the operating room staff and improving the accuracy of the instrumentation.

The indications for anterior odontoid screw fixation are as follows: age >50 years, a dislocation of the odontoid >5 mm, reducible type II fracture with the magnetic resonance (MR) integrity of the transverse ligament, or indirectly by calculating the sum of the distances between the lateral masses and C2 (Spence's rule) [2]. Contraindications include the presence of an irreducible fracture, unfavorable anatomical factors such as short neck and barrel chest, a pathological odontoid fracture, or a fracture line with an oblique orientation to the frontal plane (shear forces can stress a misalignment during screw anchoring).

It is technically difficult or impossible to perform in patients with short necks [3], obese patients, patients with limited mobility in the cervical spine and patients with a pronounced kyphosis of the cervical spine [4]. The technique is not indicated in cases of cervical spine stenosis, because of the risk of spinal cord injury associated with hyperextending the neck. This procedure allows the mobility of the structural integrity of the odontoid process (osteosynthesis) without sacrificing normal mobility.

2 Materials and Methods

In this chapter, we present for the first time a case of C2 type II fractures treated at our institute via an anterior retropharyngeal approach [5], guided by a neuronavigated system. The advantages and surgical details of the adopted strategy are highlighted. A 73-year-old woman with a post-traumatic fracture of the odontoid process type II, in the absence of neurological deficits, was treated at our institute in April 2014.

3 Preoperative Evaluation

The patient's clinical status was characterized by having no neck pain (VAS 6), no neurological deficits, and a thin neck. The fracture was evaluated via plain radiography (lateral anteroposterior views), a multislice computed tomography (CT) scan of her cervical spine, and MR of her cervical spine.

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4 Surgical Technique

The surgery was conducted under general anesthesia. Antibiotic prophylaxis was conducted by administering cephalosporin 2 g intravenous. The patient was positioned supine with the Mayfield-Keiss head holder in extension in order to reduce the fracture and to facilitate the insertion of the screw. Fluoroscopy was used to identify the odontoid apophysis in anteroposterior and lateral projection. The skin incision site was determined along the natural folds of the neck at the level of C5-C6, and the dissection was carried out in the retropharyngeal space by a tunnel up to the body of C2. The self-locking retraction system was then positioned. With the aid of the Neuronavigation System (Medtronic StealthStation S7 Minnesota, USA), the trajectory for screw placement was identified (with the reference fixed on the Mayfield headboard) (Fig. 1). The Kirschner wire was inserted from the entry point in the midline to go through the C2 body and the fracture site to reach the posterior tip of the odontoid. Tapping was carried out by using a cannulated tap inserted on top of the K-wire. Finally, we inserted a single cannulated lag screw (3.5 mm diameter) (Fig. 2 and 3). At the end of the procedure, the integrity of the transverse ligament was confirmed through the careful flexion of the neck under lateral fluoroscopic vision. The procedure lasted for 50 min; no blood loss was observed.

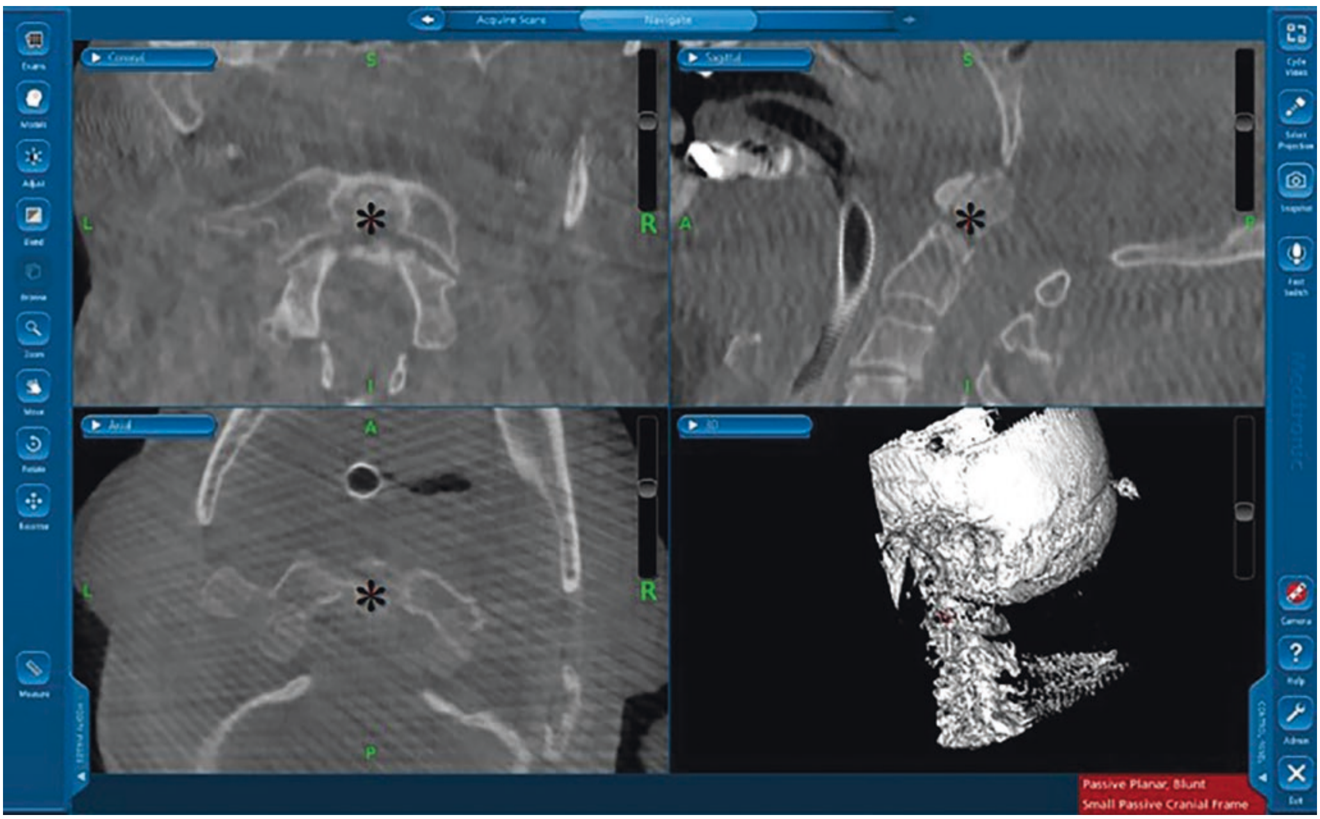

Fig. 1 Verification of the position on the neuronavigation system

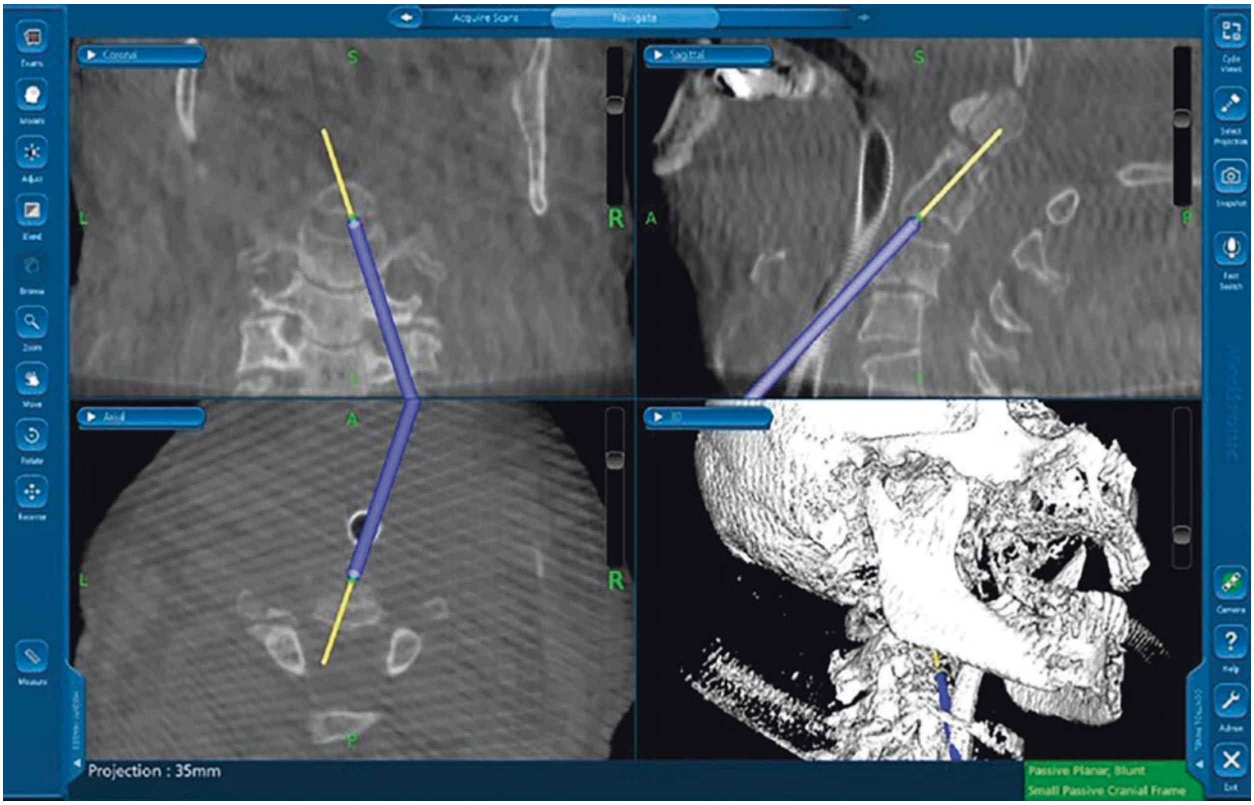

Fig. 2 Titanium screw length calculation

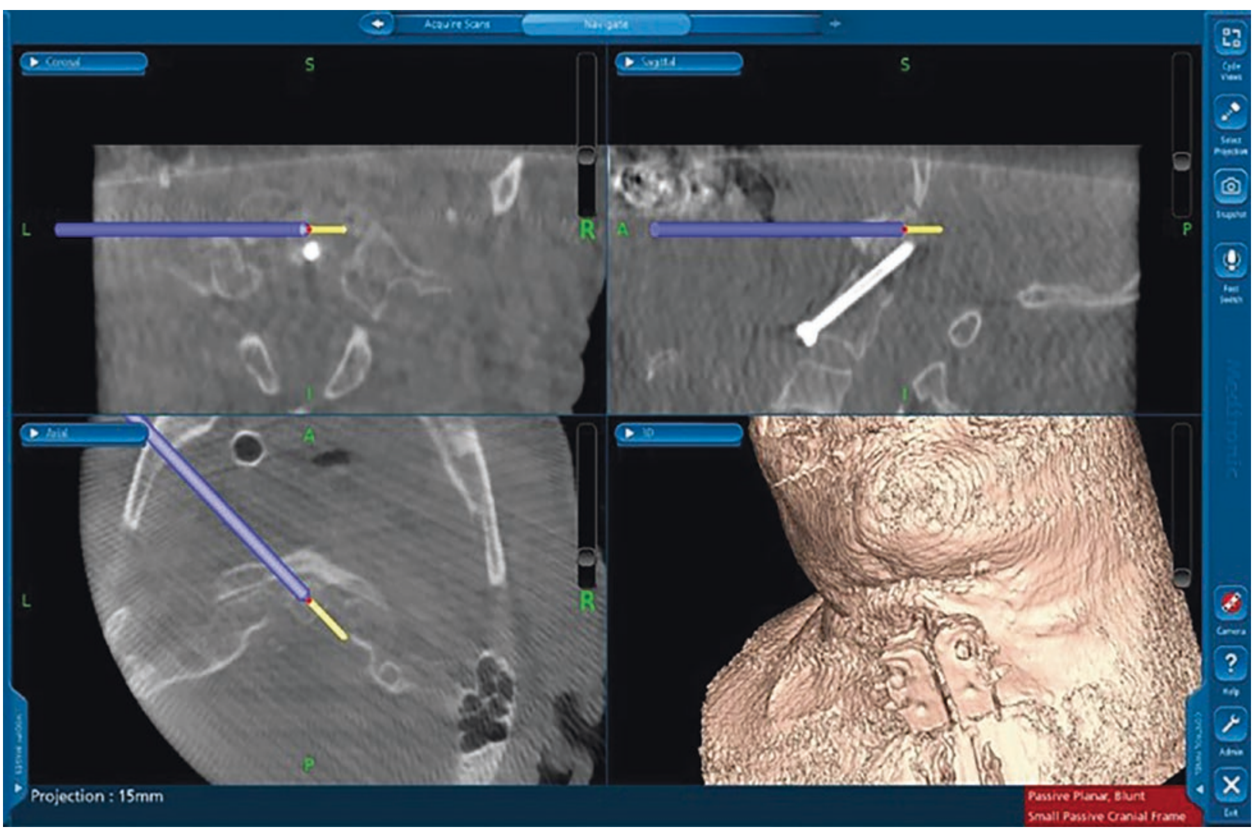

Fig. 3 Correctly seated titanium screw

5 Results

The patient had an uneventful postoperative period, with the exception of dysphagia (a complication most commonly found in the postoperative period) [6] that spontaneously disappeared in a few hours. Antibiotic prophylaxis was continued for 2 days, with a total of 12 g of cephalosporin. The patient was mobilized early during the first postoperative day, without a collar, she was discharged on the third postoperative day. Her neck pain had subsided (VAS 0). Bone fusion was checked after 40 days by taking a CT scan, which demonstrated trabeculation across the fracture site and the anatomical alignment of the fracture fragment without a gap in the fracture site. The patient was transferred to a rehabilitation center, where she remained for 3 weeks.

6 Discussion

In this chapter, we presented for the first time a case of C2 type II fractures treated at our institute with a neuronavigated retropharyngeal approach. Anterior odontoid fixation is the surgical strategy employed in the treatment of type 2 axis tooth registrations, according to Anderson–D'Alonzo. When compared to posterior instrumentation, anterior odontoid screw fixation is technically simple, less morbid, and retains biomechanical cervical movement. The main surgical indications include age >50 years, the integrity of the transverse ligament of the atlas, and newly emerged conditions.

The use of intraoperative neuronavigation has recently revolutionized surgery by providing real-time data feedback, ensuring precision and accuracy and greatly reducing surgical time and radiation exposure. Neuronavigation avoids the risks of malpositioning of the screw, which is one of the main complications. The cornerstones of excellent odontoid screw placement include preoperative imaging information, appropriate patient positioning, rigorous dissection, complete anatomical understanding, and a few other surgical nuances. This type of treatment allows, as can be seen from the illustrated case, the immediate stabilization of the fractured site, the early mobilization of the patient (especially in elderly patients), and the preservation of C2 function in terms of head rotation. It is associated with high fusion rates and a low incidence of complications [7, 8]. Careful attention to the technical aspect of the procedure and patient selection are the keys to a successful surgery and a good outcome.

Conflicts of Interest The authors report no conflicts of interest with respect to the materials or methods used in this study or the results specified in this document.

References

1. Joaquim AF, Patel AA. Surgical treatment of Type II odontoid fractures: anterior odontoid screw fixation or posterior cervical instrumented fusion? Neurosurg Focus. 2015;38(4):E11.
2. Fielding JW, G van B Cochran, Lawsing JF, Hohl M. Tears of the transverse ligament of the atlas. A clinical and biomechanical study. J Bone Joint Surg Am. 1974;56(8):1683–91.
3. Aebi M. Surgical treatment of upper, middle and lower cervical injuries and non-unions by anterior procedures. Eur Spine J. 2010;19(Suppl 1):33–9.
4. Denaro V, Papalia R, Di Martino A, Denaro L, Maffulli N. The best surgical treatment for type II fractures of the dens is still controversial. Clin Orthop Relat Res. 2011;469(3):742–50.
5. Geisler FH, Cheng C, Poka A, Brumback RJ. Anterior screw fixation of posteriorly displaced type II odontoid fractures. Neurosurgery. 1989;25(1):30–7; discussion 37–8.
6. Mazur MD, Mumert ML, Bisson EF, Schmidt MH. Avoiding pitfalls in anterior screw fixation for type II odontoid fractures. Neurosurg Focus. 2011;31(4):E7.
7. Apfelbaum RI, Lonser RR, Veres R, Casey A. Direct anterior screw fixation for recent and remote odontoid fractures. J Neurosurg. 2000;93(2 Suppl):227–36.
8. Böhler J. Anterior stabilization for acute fractures and non-unions of the dens. J Bone Joint Surg Am. 1982;64(1):18–27.

New Trend in Craniovertebral Junction Surgical Strategy: Technical Note for the Treatment of Hangman's Fractures Through a Minimally Invasive Approach

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1 Introduction

The traumatic spondylolisthesis of the axis—defined also as hangman's fracture, first by Schneider [1] for its similar fracture pattern to those associated with hangmen—is a relatively common injury caused by the bilateral fracture of the C2 pars interarticularis with a variable displacement of the C2 body on C3. It accounts for 4–7% of all cervical spine fractures and 20–22% of all C2 fractures [2, 3], and it most commonly occurs during road traffic accidents and falls; thus, this is associated with an important age distribution peak in young people, and hangman's fractures are often a component of combined atlantoaxial injuries [4, 5]. Although the hangman's fracture has a relatively common incidence, evidence-based treatment algorithms and the consequent best treatment choice remain controversial. Several classification systems have been developed for guiding treatment decisions; the Levine–Edwards classification system modified the original proposed by Effendi [6], and it is currently the most used. It classifies fractures according to the injury mechanism, fracture morphology on the radiologic appearance, and consequent stability into four types, where type I fractures result from a hyperextension-axial loading force, type II from a combined hyperextension-axial loading force with an additional anterior flexion and compression force, and type IIA and III from a primary flexion force. In types II and III, extension forces have been implicated in the disruption of the anterior longitudinal ligament, posterior longitudinal ligament, and/or C2–3 disk. While type I injuries are considered stable with minimal C2-C3 angulation and translation (<2 mm) and can be treated nonsurgically with either a hard collar or rigid immobilization, types II, IIA, and III are considered unstable, with C2-C3 angulation and translation from >2 mm to severe grade, and they may benefit from surgical treatment [2, 3]. The goals of surgery for unstable hangman's fracture are the anatomical reduction of the spondylolisthesis, the stabilization of the cervical segments, the osteosynthesis/healing rate, and the maintenance of alignment [7]. The choice of the surgical strategy could also be conditioned by other aspects, such as vertebral anatomy, age, comorbidities and other patient factors, and surgeon experience [8]. Herein, we report our experience in treating the case of an unstable hangman's fracture through an anterior stabilization of C2-C3 alone through a minimally invasive approach.

2 Methods

We report the case of a 44-year-old woman who was admitted to our neurosurgical department after she was involved in a polytrauma road traffic collision. A total body computed tomography (CT) scan was performed, and an unstable hangman's fracture (type II according to the Levine–Edwards classification), multiple rib fractures, a severe hemothorax, and a displaced clavicle fracture were found. Upon admission, her neurological examination was negative. The specific

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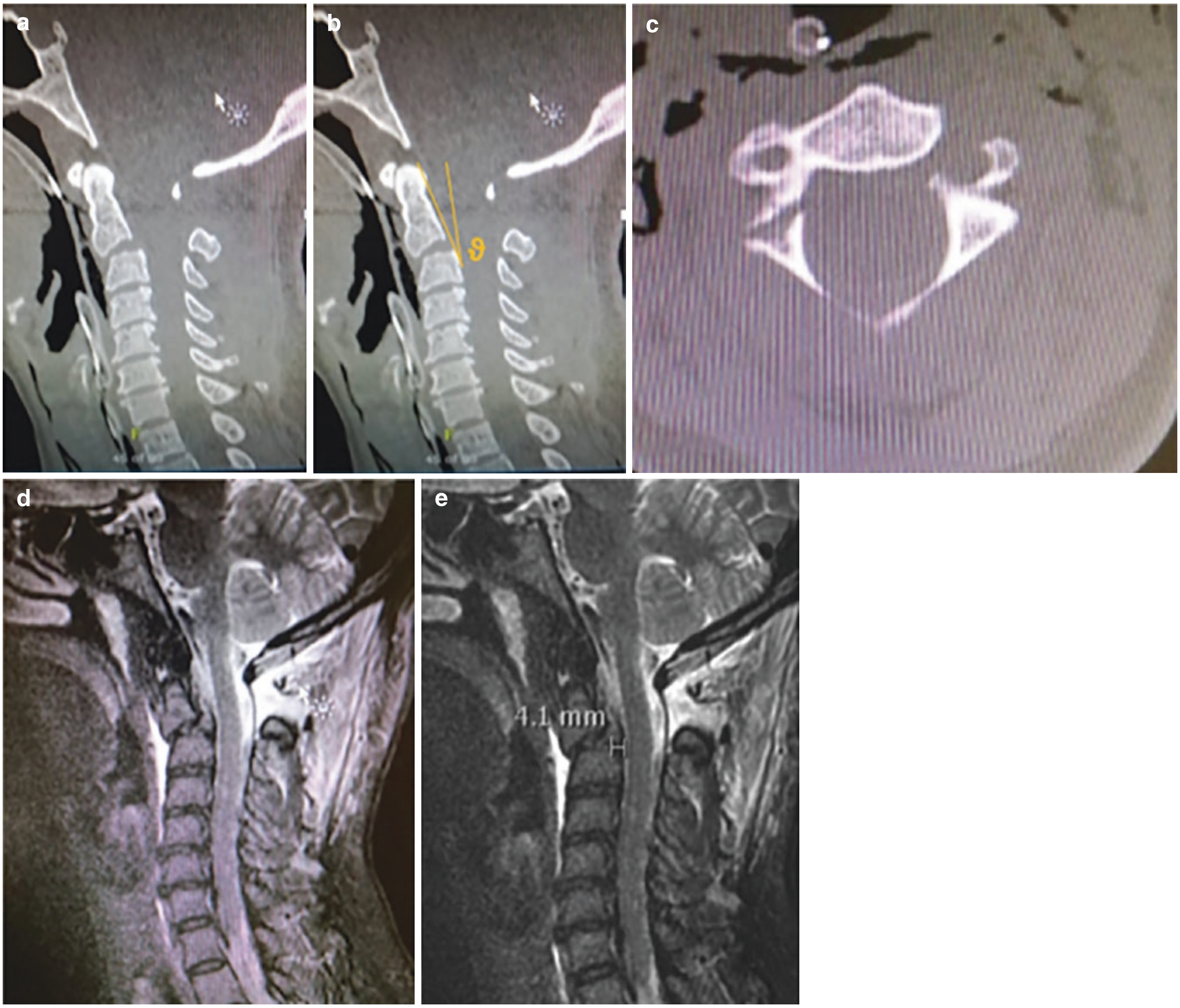

Fig. 1 (**a**) Preoperative sagittal CT cervical spine shows a type II hangman's fracture with severe angulation ($\vartheta > 11°$ as shown in **b**) and (**b**) the displacement of C2 on C3; (**c**) axial CT scan clearly shows a C2 pars interarticularis fracture; (**d** and **e**) the preoperative sagittal T2-weighted MRI shows C2-C3 disk herniation and traumatic posterior extrusion with no impact on the spinal cord; (**e**) the rate of displacement of C2 on C3 is an indirect sign of an unstable fracture (>4 mm)

radiological features of the fracture were C2-C3 subluxation with angulation (ϑ) > 11°, the displacement of C2-C3 >3 mm, the rupture of the C2-C3 disk, and <4 mm wide C2 pedicles (Fig. 1). The case evaluation centered on a collegial choice conditioned by the type of fracture, the vertebral anatomy, and the severe chest trauma; a cervical posterior approach with pedicle screw implants was judged to be not executable. Moreover, because of the patient's young age, one of the goals of the treatment was to preserve the range of cervical motion. Thus, an anterior cervical approach was preferred.

3 Surgical Technical Description

General tracheal anesthesia assisted by fiberoptic bronchoscopy was performed in order to prevent spinal cord injury risk during intubation, as per protocol. The patient was placed in the supine position on a radiolucent table. The intraoperative reduction of the listhesis was obtained with fracture alignment dislocation, confirmed by C-arm fluoroscopic control (Fig. 2a). A small anterior incision on the right side was performed by using a standard anterior cervical approach to the C5-C6 level with blunt dissection performed

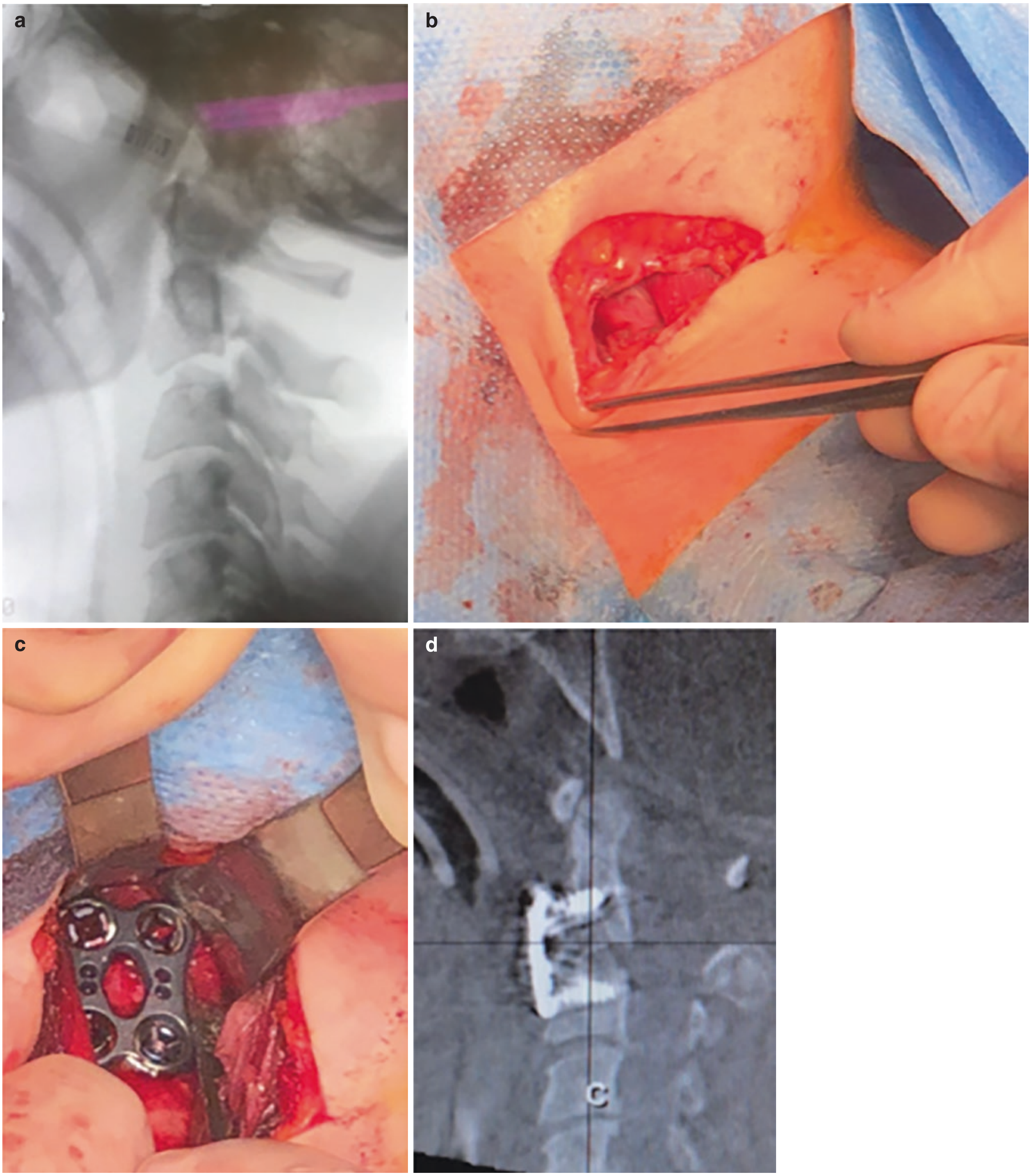

Fig. 2 (**a**) Intraoperative C-arm film after the C2-C3 listhesis reduction maneuver; (**b**) small cervical anterior incision on the right side; (**c**) cervical anterior plate placement fixed by using four screws without performing a discectomy; (**d**) intraoperative 3D C-arm scan after place the plate and screws

cranially up to the C1 region (Fig. 2b). The cervical spine target was reached through a bloodless plane dissection; specifically, the C3 body and C2 were exposed with the help of radiolucent hand spatulas. The surgical working angle was not exactly perpendicular to the target, but it was possible to position the plate with four holes to fix C2-C3 without

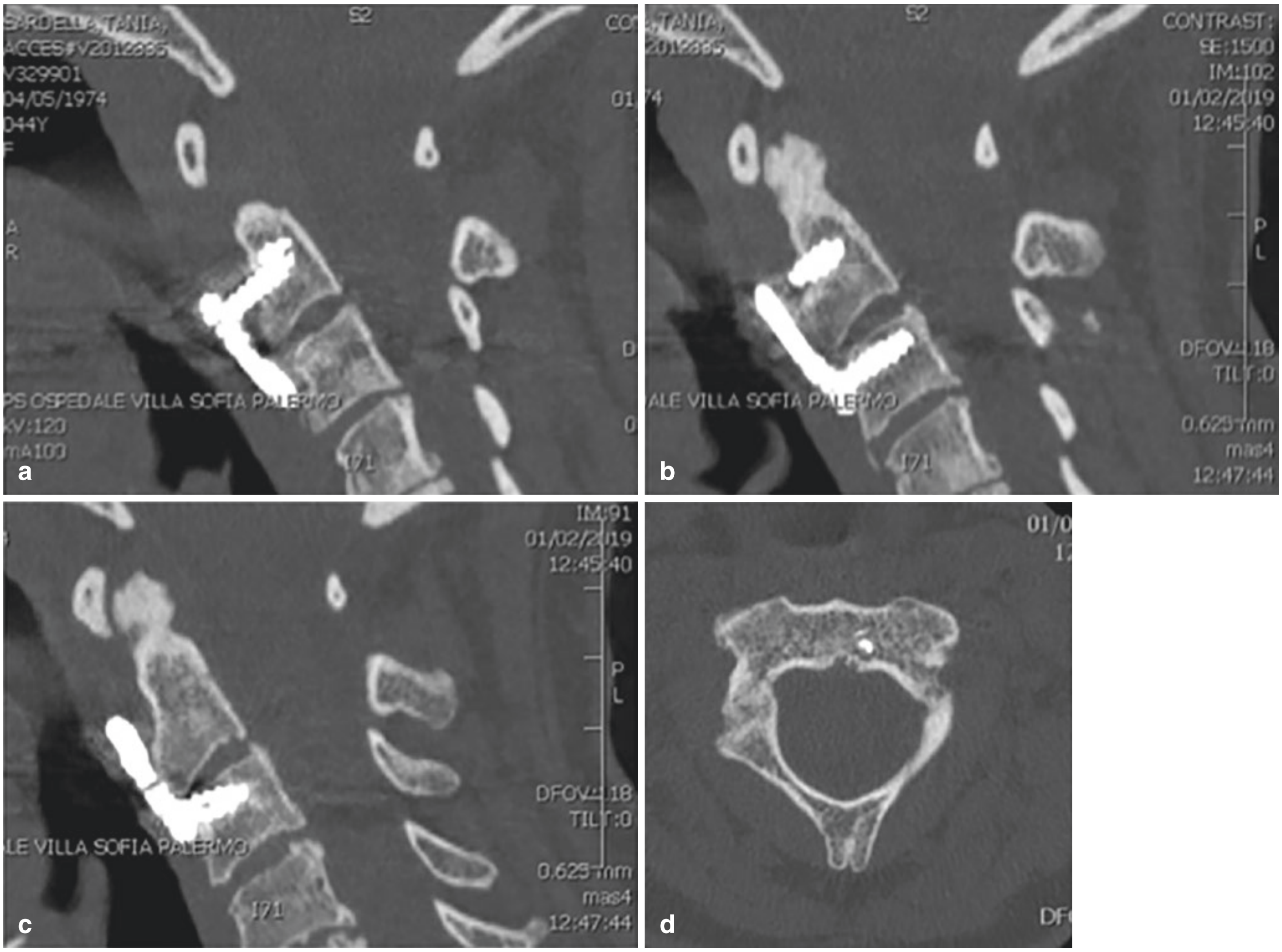

Fig. 3 Several 6-month postoperative CT scans: (**a–c**) sagittal scan document with satisfactory C2-C3 alignment and anterior plate fixation without complications; (**d**) a postoperative axial scan documenting bone healing in the C2 pars interarticularis compared to a preoperative scan (as shown in Fig. 1c)

performing discectomy and body fusion. The postoperative course was uneventful. The patient used a rigid cervical collar for 6 weeks and was discharged without leaving neurological sequelae. A 6-month postoperative CT scan was performed, and it showed that the cervical alignment was achieved without complications. Bone healing in the pars interarticularis of C2 was documented (Fig. 3).

4 Discussion

Before the development of segmental posterior cervical fixation, multiple studies documented the efficacy of nonoperative treatment and stratified the results according to fracture type [7]. Conservative treatment achieves a healing rate approaching 100% in type I stable injuries, and this assessment has not changed in reviewing meta-analyses over time [7]. Conversely, the healing rate has been documented to be progressively reduced for type III (40%) compared to that for type II (60%), causing potential angulation and C2/3 kyphosis, anterior dislocation, or pseudarthrosis [7, 8]. As a rule, nonoperative treatment is used if the fracture is stable and surgery if it is unstable. A recent review [3] showed that the surgical treatment of unstable hangman's fractures increases the rate of osteosynthesis/fusion by ninefold. The surgical treatment of hangman's fractures remains poorly standardized. None of the available clinical studies has shown significant differences in outcomes or complication rates between the various types of anterior and/or posterior fusion, the choice of the fixation segment, or the choice of screw type [4, 9]. Anterior cervical discectomy and fusion (ACDF), posterior fixation and fusion (C2 transpedicular screws, C2-C3 fixation, arthrodesis from C1 to C3, and occipitocervical fusion), or combined anterior–posterior fusion [10–12] were surgical experiences collected and treatment options still considered. No statistically significant differences in fusion rates, complications, mortality, or treatment failure were documented among the surgical choices [3, 10]. Because of this, the contemporary literature still claims that the surgical approach should be determined on a case-by-case basis, and neither the posterior approach nor the anterior approach seems to be superior. An anterior approach has the advantage of a relatively less-traumatic procedure and a short fusion construct involving a C2-C3 discectomy with interbody fusion and plating [11, 13]. Published data indicate that the anterior approach provides better dynamic stabilization and also prevents delayed neurological compromise related to post-traumatic disk herniation [4]. Other advantages include a lower risk of intraoperative vertebral artery injury and the preservation both of C1-C2 mobility and, therefore, of most of the movements at the cervical spine. This approach, however, cannot address the detached posterior arch of C2 [13, 14], and the high risks of the anterior approach were mainly embodied in injuries to vital structures, especially in the facial and hypoglossal nerves, the branches of the external carotid artery, the contents of the carotid sheath, and the superior laryngeal nerve [13]. In skilled hands, the anterior approach offers patients high primary stability, a high union rate in almost 100% of patients, anatomical reduction with the reconstruction of cervical lordosis, favorable clinical outcomes, and the option to avoid secondary salvage fusions after the primary conservative treatment has failed [15]. The posterior approach was associated with a lower complication risk rate for visceral structures during exposure, even if the main risk is represented by the vertebral artery [3]. Several posterior fixation techniques have been reported and are currently used. Directly repairing the C2 pars fracture with a transpedicular screw across the fracture line, described first by Leconte [16], is the most popular technique, and it is widely recognized as a "physiologic operation" because it has the advantage of preserving motion in all the cervical spine segments [4, 13]. However, direct pars repair does not address instability at the disk, and it can be used only in cases with no—or at least minimal—C2-C3 disk injury [14]. Other posterior technique options include C1-C3 pedicle screw fixation and C1-C3 wiring techniques, but they block the C1-C2 joint, restricting range of motion particularly in rotation, and they need a more extensive approach in that postop halo-thoracic immobilization is needed for wiring techniques; thus, this type of posterior fixation is by far in the minority [4, 14]. Both the ACDF and posterior screw fixation will lose mobility in the fused segment [13]. The treatment goals for a hangman's fracture are not only to achieve and maintain cervical spine alignment, preserving all vascular and neural structures, but also to maintain the patient's ability to have an active life. For each of these procedures, technical variations or tips and tricks for overcoming difficulties and guiding treatment choice were published in the literature. Some authors [3] suggested, for example, that if the position of a pedicle screw is possible, a bilateral C2 pedicle construct or a C2-C3 posterior cervical fusion could be performed to lay back the C2 vertebral body; if the fracture is severe and it is not possible to insert the C2 pedicle screws, then in a young patient, a C2-C3 ACDF could be performed, whereas in an elderly patient, a C1-C3 posterior cervical fusion should be performed [17]. On the basis of the clinical observation that most of the C2 vertebral is free of fractures, Wang et al. [9] designed a transoral bucking bar and combined it with a posterior C2 semithreaded lag screw and a C3 pedicle screw to help with the reduction, under fluoroscopy and with appropriate pressure in front of the posterior pharyngeal wall and in front of the anterior vertebral body, all to overcome the potential failed functional recovery (worse fracture, false joints, C2/C3 dislocation, and angling) of the conventional pedicle screw, thus preserving atlantoaxial rotation and reducing the risk of injury to the vertebral artery and spinal cord. Percutaneous screw fixation techniques navigated by using 3D intraoperative imaging were also developed with potential implications for decreasing the risk of screw malposition while diminishing the complication rate, thanks to the smaller incision and muscle detachment [4, 18–21]. With the same goal, other surgeons have used a tubular retractor system in minimally invasive transpedicular C2-C3 screw fixation [18]. Table 1 shows technical variations

Table 1 Technical variations about surgical treatment of Hangman's Fractures: case reported in the last 5-years literature research

References	Technical description	Type of article
Lang, 2016 [23]	Minimally invasive surgical (MIS) techniques for C2-C3 fixation vs. open surgical techniques using intraoperative 3D fluoroscopy-based navigation (ITFN)	Comparative case series (20 patients: 6 MIS, 14 open techniques)
Ould-Slimane, 2018 [19]	Percutaneous C1-C2 Harms fusion navigated using 3D intraoperative O-arm imaging	Case series (11 patients)
Kyu, 2019 [18]	Minimally invasive transpedicular screw fixation using the tubular retractor system	Case series (7 patients)
Soliman, 2019 [20]	Unilateral transfixation with minimally invasive percutaneous screw placement, using 3D neuronavigation and bidirectional intraoperative fluoroscopy	Case reports (2 patients)
Zhu, 2019 [21]	Anterior odontoid screw fixation and posterior C2 percutaneous screw fixation using intraoperative O-arm navigation	Case report (1)
Wang, 2019 [9]	Posterior C2–3 pedicle screw fixation combined with pharyngeal bucking bar technique	Case series (32 patients)
Authors, 2021	C2-C3 plating with four holes without discectomy and body fusion for unstable hangman's fracture type II	Case report (1)

on the surgical treatment of hangman's fractures over the past 5 years of research in the literature.

Surgical decisions between an anterior, a posterior, and a combined anterior/posterior approach rest on the assessment of fracture displacement and of concomitant damage to the disks and ligaments [4]. In managing our case, the anterior approach via C2-C3 plating was the more feasible surgical strategy. The patient was a polytraumatized young woman with concomitant hemothorax, and she presented prohibitive anatomical and radiological features such as <4 mm wide bilateral C2 pedicles, disk and anterior and posterior ligament ruptures with >3 mm C2-C3 disruptions, consequent >11-degree angulation (type II according to the Levine–Edwards classification), and prohibitive conditions for prone positioning. The high anterior surgical exposure of the upper cervical spine provides direct exposure for a C2 hangman's fracture, but it has always been considered difficult and dangerous because of the anatomical properties of the region of interest; thus, some controversy remains about the best approach. In several cases, the anterior high retropharyngeal approach was used because it involves blunt dissection through soft tissues to reach the spine; although rare, it shows that there are several intra- and postoperative risks of injury to tissues, such as the hypoglossal and superior laryngeal nerves, the marginal mandibular branch of the facial nerve, and the submandibular gland [22]. In performing our case, a small horizontal incision was made, and it allows a sufficient working angle for easily and quickly positioning the plate, after the manual preoperative reduction of the listhesis under general anesthesia. Using the anterior approach via primary plate fixation alone, without discectomy or cage implant, solid fusion and healing were achieved with no complications.

5 Conclusions

Unstable hangman's fractures can be managed with both anterior approaches and posterior approaches with comparable clinical and radiological outcomes. The anterior approach usually involves cervical discectomy and fusion, and it is considered a less invasive and earlier pain-free procedure than the posterior ones. The authors of this chapter describe a feasible, safe, and effective alternative operative technique to treat hangman's fractures. In some selected and prohibitive cases and in cases where external immobilization has a high risk of nonunion, unstable hangman's fractures can be treated with just the anterior plating of C2-C3, along with taking a minimally invasive approach with fewer intraoperative risks.

Disclosure of Interest The authors declare that they have no known personal financial or institutional interest in any of the drugs, materials, or devices described in this chapter.

Conflicts of Interest The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this chapter. All the coauthors have reviewed and approved the final version of the manuscript. All the coauthors had full access to all the data in the study and take responsibility for the integrity of the accuracy of data presentation.

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References

1. Schneider RC, Livingston KE, Cave AJ, et al. "HANGMAN'S fracture" of the cervical spine. J Neurosurg. 1965;22:141–54.
2. LeFever D, Whipple SG, Menger RP. Hangman's fractures. In: StatPearls [Internet]. Treasure Island: StatPearls Publishing; 2021. PMID: 30137780.
3. Murphy H, Schroeder GD, Shi WJ, Kepler CK, Kurd MF, Fleischman AN, Kandziora F, Chapman JR, Benneker LM, Vaccaro AR. Management of Hangman's fractures: a systematic review. J Orthop Trauma. 2017;31(Suppl 4):S90–5.
4. Prost S, Barrey C, Blondel B, Fuentes S, Barresi L, Nicot B, Challier V, Lleu M, Godard J, Kouyoumdjian P, Lonjon N, Marinho P, Freitas E, Schuller S, Allia J, Berthiller J, Charles YP, French Society for Spine Surgery (SFCR). Hangman's fracture: management strategy and healing rate in a prospective multi-centre observational study of 34 patients. Orthop Traumatol Surg Res. 2019;105(4):703–7. https://doi.org/10.1016/j.otsr.2019.03.009. Epub 2019 Apr 17. PMID: 31005699.
5. Stulik J, Vyskocil T, Sebesta P, Kryl J. Combined atlantoaxial fractures. Acta ChirOrthop Traumatol Cech. 2005;72:105–10.
6. Levine A, Edwards C, Maryland B. The management of traumatic spondylolisthesis of the axis. J Bone Joint Surg Am. 1985;67:217–26.
7. Li XF, Dai LY, Lu H, Chen XD. A systematic review of the management of hangman's fractures. Eur Spine J. 2006;15(3):257–69. https://doi.org/10.1007/s00586-005-0918-2. Epub 2005 Oct 19. PMID: 16235100; PMCID: PMC3489291.
8. Pommier B, Ollier E, Pelletier JB, Castel X, Vassal F, Tetard MC. Conservative versus surgical treatment for odontoid fracture: is the surgical treatment harmful? Systematic Review and Meta-Analysis. World Neurosurg. 2020;141:490–499.e2. https://doi.org/10.1016/j.wneu.2020.02.169. Epub 2020 Mar 7. PMID: 32151771.
9. Wang G, Jiang D, Wang Q, Xu S, Yang J, Yang C. A novel technique using a pedicle screw and bucking bar for the treatment of hangman's fracture. Orthop Traumatol Surg Res. 2019;105(4):709–11. https://doi.org/10.1016/j.otsr.2019.03.005. Epub 2019 Apr 19. PMID: 31010738.
10. Hur H, Lee JK, Jang JW, Kim TS, Kim SH. Is it feasible to treat unstable hangman's fracture via the primary standard anterior retropharyngeal approach? Eur Spine J. 2014;23(8):1641–7. https://doi.org/10.1007/s00586-014-3311-1. Epub 2014 Apr 23. PMID: 24756893.
11. Patel JYK, Kundnani VG, Kuriya S, Raut S, Meena M. Unstable Hangman's fracture: anterior or posterior surgery? J Craniovertebr Junction Spine. 2019;10(4):210–5. https://doi.org/10.4103/jcvjs.JCVJS_112_19. Epub 2020 Jan 23. PMID: 32089613; PMCID: PMC7008659.
12. Xie N, Khoo LT, Yuan W, Ye XJ, Chen DY, Xiao JR, Ni B. Combined anterior C2-C3 fusion and C2 pedicle screw fixation for the treatment of unstable hangman's fracture: a contrast to anterior approach only. Spine (Phila Pa 1976). 2010;35(6):613–9. https://doi.org/10.1097/BRS.0b013e3181ba3368. PMID: 20150833.
13. Liu Y, Zhu Y, Li X, Chen J, Yang S, Yang H, Jiang W. A new transpedicular lag screw fixation for treatment of unstable hangman's

fracture: a minimum 2-year follow-up study. J Orthop Surg Res. 2020;15(1):372. https://doi.org/10.1186/s13018-020-01911-3. PMID: 32873313; PMCID: PMC7466811.

14. Ma W, Xu R, Liu J, Sun S, Zhao L, Hu Y, Jiang W, Liu G, Gu Y. Posterior short-segment fixation and fusion in unstable hangman's fractures. Spine (Phila Pa 1976). 2011;36(7):529–33. https://doi.org/10.1097/BRS.0b013e3181d60067. PMID: 21079544.
15. Xu H, Zhao J, Yuan J, Wang C. Anterior discectomy and fusion with internal fixation for unstable hangman's fracture. Int Orthop. 2010;34(1):85–8. https://doi.org/10.1007/s00264-008-0658-0. Epub 2008 Oct 14. PMID: 18853157; PMCID: PMC2899270.
16. Leconte P. Fracture et luxation des deux premières vertèbres cervicales. In: Judet R, editor. Luxation Congenénitale de la Hanche: Fractures du Cou-de-pied Rachis Cervical. Actualités de Chirurgie Orthopédique de l'Hö pital Raymond-Poincaré. Paris: Masson et Cie; 1964. p. 147–66.
17. Robinson AL, Olerud C, Robinson Y. Surgical treatment improves survival of elderly with axis fracture-a national population-based multiregistry cohort study. Spine J. 2018;18(10):1853–60. https://doi.org/10.1016/j.spinee.2018.03.021. Epub 2018 Apr 9. PMID: 29649609.
18. Man Kyu C, Youngseok K, Ki Hong K, Dae-Hyun K. Direct trans-pedicular screw fixation for atypical hangman's fracture: a minimally invasive technique using the tubular retractor system. J Clin Neurosci. 2019;70:146–50. https://doi.org/10.1016/j.jocn.2019.08.046. Epub 2019 Aug 17. PMID: 31431401.
19. Ould-Slimane M, Ferracci F-X, Le Pape S, Perez A, Michelin P, Gauthé R. Posterior C1C2 harms fusion with 3D surgical navigation. Orthop Traumatol Surg Res. 2018;104:585–8.
20. Soliman MAR, Kwan BYM, Jhawar BS. Minimally invasive unilateral percutaneous transfracture fixation of a Hangman's fracture using neuronavigation and intraoperative fluoroscopy. World Neurosurg. 2019;122:90–5. https://doi.org/10.1016/j.wneu.2018.10.140. Epub 2018 Nov 1. PMID: 30391610.
21. Zhu XC, Liu YJ, Li XF, Yan H, Zhang G, Jiang WM, Sun HY, Yang HL. Min-invasive surgical treatment for multiple axis fractures: a case report. World J Clin Cases. 2019;7(7):898–902. https://doi.org/10.12998/wjcc.v7.i7.898. PMID: 31024962; PMCID: PMC6473124.
22. Park SH, Sung JK, Lee SH, Park J, Hwang JH, Hwang SK. High anterior cervical approach to the upper cervical spine. Surg Neurol. 2007;68(5):519–24; discussion 524. https://doi.org/10.1016/j.surneu.2006.11.070. Epub 2007 Sep 6. PMID: 17825365.
23. Lang Z, Tian W, Liu Y, Liu B, Yuan Q, Sun Y. Minimally invasive pedicle screw fixation using intraoperative 3-dimensional fluoroscopy-based navigation (CAMISS technique) for hangman fracture. Spine (Phila Pa 1976). 2016;41(1):39–45. https://doi.org/10.1097/BRS.0000000000001111. PMID: 26267827.

Direct Transpedicular C2 Fixation for the Surgical Management of Hangman's Fractures: A "Second Youth" for the Judet Approach

Francesco Certo, Roberto Altieri, Marco Garozzo, Massimiliano Visocchi, and Giuseppe M. V. Barbagallo

1 Introduction

Traumatic spondylolisthesis of the epistropheus (or axis), also known as hangman's fracture, represents the second most common fracture of the axis following those involving the odontoid process [1, 2]. It consists of a bilateral fracture of the C2 pars interarticularis (or isthmus), with separation of the posterior neural arch from the vertebral body of the axis, leading to vertebral instability [2].

The term *hangman's fracture* was originally coined by Wood Jones in 1913 to describe a peculiar type of C2 fracture occurring in victims of judicial hanging [3, 4]. Nowadays, such injury typically affects patients after motor vehicle or sport accidents which entail a hyperextension (less commonly hyperflexion) and axial loading or distraction mechanism of the head and upper cervical structures, causing a breakthrough in the inter-articular portion of the C2 neural arch [4, 5]. Several authors have classified fractures of the C2 interarticular motion segment, and the most widely used classification system based on lateral view radiographic findings, according to Effendi first [1] and to Levine and Edward afterwards [6], is grouped in three types: in type I there is an isolated hairline fractures of the axis ring, with minimal dislocation of the vertebral body (<3 mm) and intact C2-C3 disc space; in type II there is angulation (>11°) and translation (>3 mm) between C2 and C3 vertebral bodies (in type IIA translation is absent); in type III there are also uni- or bilateral dislocated and locked facet joints [5]. In cases of C2 vertebral body's posterior wall involvement in association to neural arch, fractures are grouped as "atypical," with a greater risk of spinal injuries. Atypical hangman's fractures are not included in any classification system and only few case series are reported in the literature [7]. They include bilateral C2 pedicle fractures extending also to the posterior part of the vertebral body. The peculiar features of these fractures make them at high risk for neural damage [7].

Usually, traumatic spondylolisthesis produces acute decompression of the neural canal by fracture of the pedicles, and neural damage is relatively uncommon (6–10%) [8]. Although hangman's fractures can be diagnosed by lateral X-ray, computed tomography (CT) adds essential information to detect and better evaluate fracture lines, particularly in cases of asymmetric atypical fractures including the vertebral body. Magnetic resonance (MR) is useful to demonstrate soft tissue involvement [9, 10]. This allows to evaluate the stability of the fracture and to manage accordingly the appropriate conservative or surgical treatment. CT scan is also useful to identify fracture lines across the transverse foramen and related risk of vertebral artery injury (VAI) [11].

There is not general consensus on algorithms for conservative or surgical treatment in hangman's fractures yet, also because definitions of stability vary in the literature. In the most recent review on the management of typical and atypical hangman's fracture by Al-Mahfoudh et al., more than three quarters (92.4%) of all fractures (type I, II and IIa) were treated conservatively, with rigid collar for 6–12 weeks or halo fixation and immobilization, that should be reserved only when surgical treatment is not feasible for patients' impaired general status [12]. However, halo vest produces lower stabilization effect than internal fixation. Surgical management should be reserved for "unstable" type III fractures, while type I fractures are usually considered stable; for type II and IIA, there is no consensus on their stability [8–10, 13]. Instability of a type II fracture is based on the presence of soft tissue damage (disk or ligaments) [13].

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Different surgical approaches have been described for the management of hangman's fractures, including anterior, posterior or combined procedures [14].

For unstable traumatic spondylolisthesis of the axis anterior C2-C3 interbody fusion with plating has been proposed as the most appropriate surgical option. A C2-C3 anterior fusion is always possible by a trans-oral or retropharyngeal approach, but these procedures are not routinely performed, because of their high complication rate [8–10, 14]. Stating that the C2-C3 instability also involves posterior element of C2-C3 joints, a posterior C2-C3 stabilization is often indicated [14]. However, the number of included instrumented levels varies according to the individual fracture morphology. In some cases, the procedure includes a temporary C1 instrumentation associated to C2-C3, followed by early screws removal at the same level, with restoration of range of motion; however, this approach is still controversial [14].

In 1964, Leconte first described the direct transpedicular screw osteosynthesis of C2 pars interarticularis fractures [15]; next, Judet, in 1970, described a new technique using cancellous lag screws, also known as "Judet screws" [16]. This procedure is only effective and useful in type I fracture, stable and without any soft tissue damage, and in few cases of atypical hangman's fractures.

We reviewed the literature on direct transpedicular fixation using Judet lag screws, underlying its indications, tips, tricks and pitfalls with two illustrative cases.

2 Technical Case Reports

2.1 Case Illustration 1

A 37-year-old man presented with severe neck tenderness and restricted range of motion (ROM) following a swimming injury with hyperextension of the head. He was admitted to emergency department, fully conscious and without neurological deficits. Multiplanar reconstructed computed tomography (CT) of craniovertebral junction showed a traumatic C2 spondylolisthesis extending to the posterior wall of the vertebral body and lateral masses. He was referred to our department and the fracture was classified as atypical type I hangman's fracture (Fig. 2). Radiological assessment was completed by magnetic resonance imaging (MRI) of craniovertebral junction and cervical spine to rule out any associated soft tissue or ligamentous damage to the cervical spine (Fig. 1). Direct transpedicular fixation of C2 was performed using 30 mm lag screws. Visualization of the medial border of C2 pedicles as well as lateral view fluoroscopy assisted the screws' insertion maneuvers. No intra- and/or post-operative complications were observed. Postoperative CT scan showed complete reduction of the fracture lines (Fig. 2). Patient experienced complete recovery of neck pain and optimal ROM was restored, as documented by his last clinical follow-up.

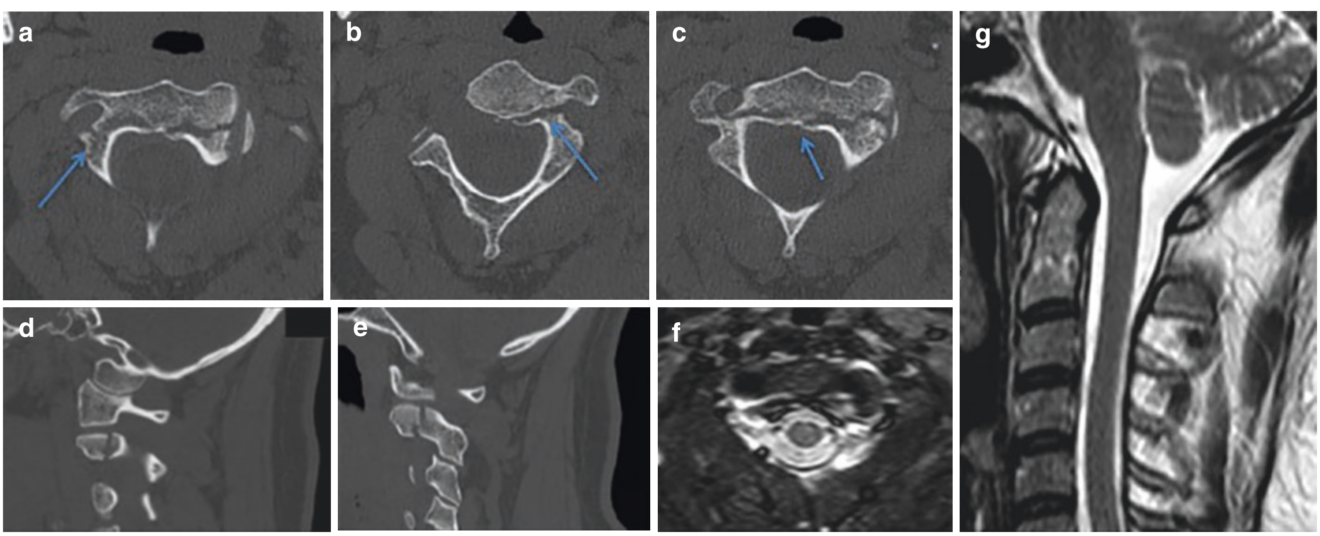

Fig. 1 Illustrative case 1: preoperative multiplanar reconstructed CT scan of the craniovertebral junction documented the fracture of right (**a**, blue arrow) and left (**b**, blue arrow) C2 pedicles, also involving the posterior wall of C2 vertebral body (**c**, blue arrow); sagittal reconstructed images depicted the fracture of right (**d**) and left (**e**) pedicles; axial (**f**) and sagittal (**g**) T2-weighted MR of craniovertebral junction and cervical spine ruled out soft tissue or ligamentous injuries

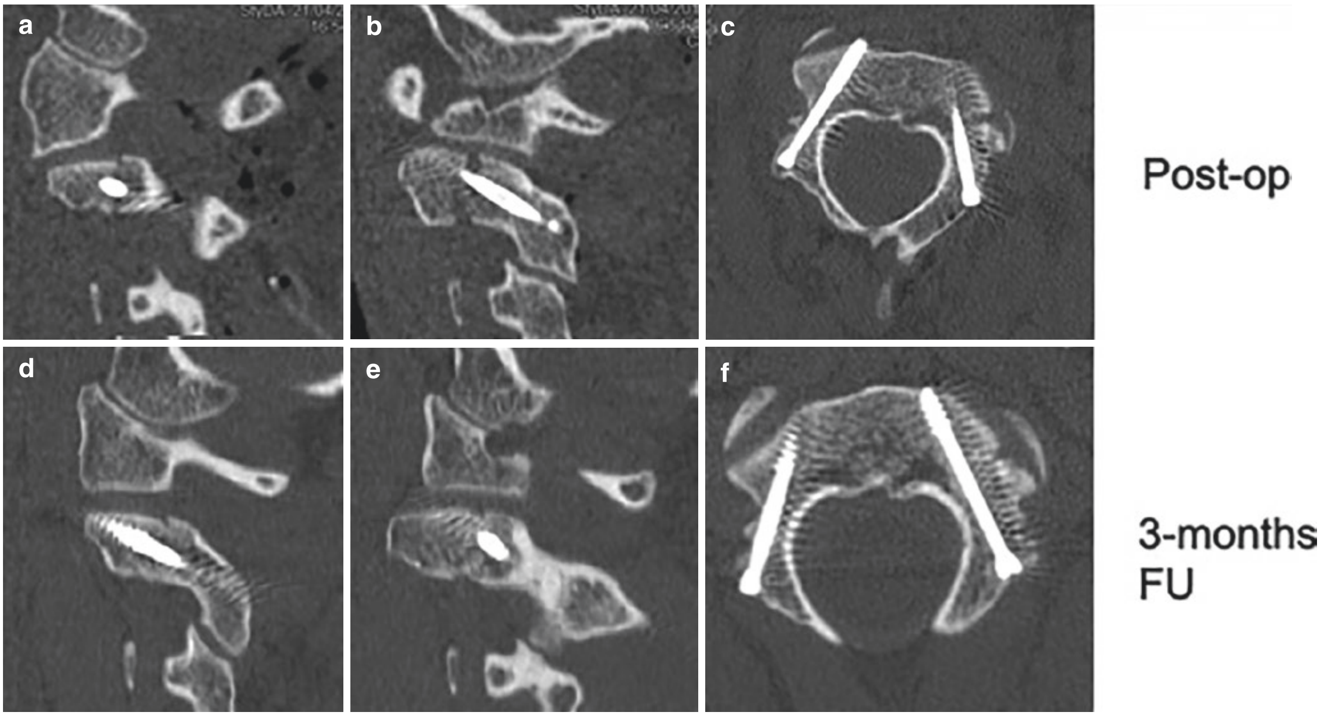

Fig. 2 Postoperative CT-scan showing a satisfactory screw's positioning also documenting the reduction of fracture, immediately after surgery (**a–c**) and at 3-months (**d–f**); a solid osseous fusion of both pedicle is documented by sagittal views (**d**, **e**) 3 months after surgery

2.2 Case Illustration 2

A 42-year-old man presented with severe neck pain, acute flaccid paraplegia, hypoesthesia down to the mammillary line, multiple costal fractures and pneumothorax, after a high-energy trauma due to car accident. Emergency CT scan showed a type IIa hangman's fracture, a Th7 Margerl type A3 and a Th8 type A2 vertebral fractures. Cervical spine MRI ruled out any disco-ligamentous injury at cranio-vertebral junction, and documented a post-traumatic C5-C6 herniated disk, likely due to cervical spine hyperflexion and axial load mechanism. Because of neurological impairment, the patient underwent emergency thoracic fractures treatment: Th7-Th8 mini-invasive laminectomy and Th5-Th10 pedicle screw fixation was performed. While in prone position, direct C2 transpedicular fixation with Judet approach was also performed (Fig. 3). A further surgical procedure was performed for C5-C6 anterior discectomy and fusion with an interbody, standalone, carbon fiber cage. Preservation of rotational head motion was documented at last follow-up, as well as the healing of C2 fractures.

2.3 Surgical Technique

The patient is positioned prone and the head is fixed with Mayfield clamp. Fluoroscopic assistance during head positioning maneuvers may help the C2 lysthesis reduction and allows realignment of the spine. Reduction is obtained by head traction and extension. Further adjustments of the skull clamp position could be required throughout the surgical procedure; therefore, patient's draping should allow to move the articulated arm fixating the clamp to the surgical table.

A posterior midline skin incision from the inion to C4 spinous process is performed. The paraspinal muscle are detached from the midline and a careful subperiosteal dissection of C1-C2 posterior elements is started from the midline. The use of microscope provides adequate visualization of the anatomy and enhances surgical safety.

Subperiosteal dissection of C2 laminae reduces the chances to violate the venous plexus surrounding vertebral arteries. Careful dissection of C2 laminae allows to reach the upper and medial surface of C2 pedicles. The C2 pedicles

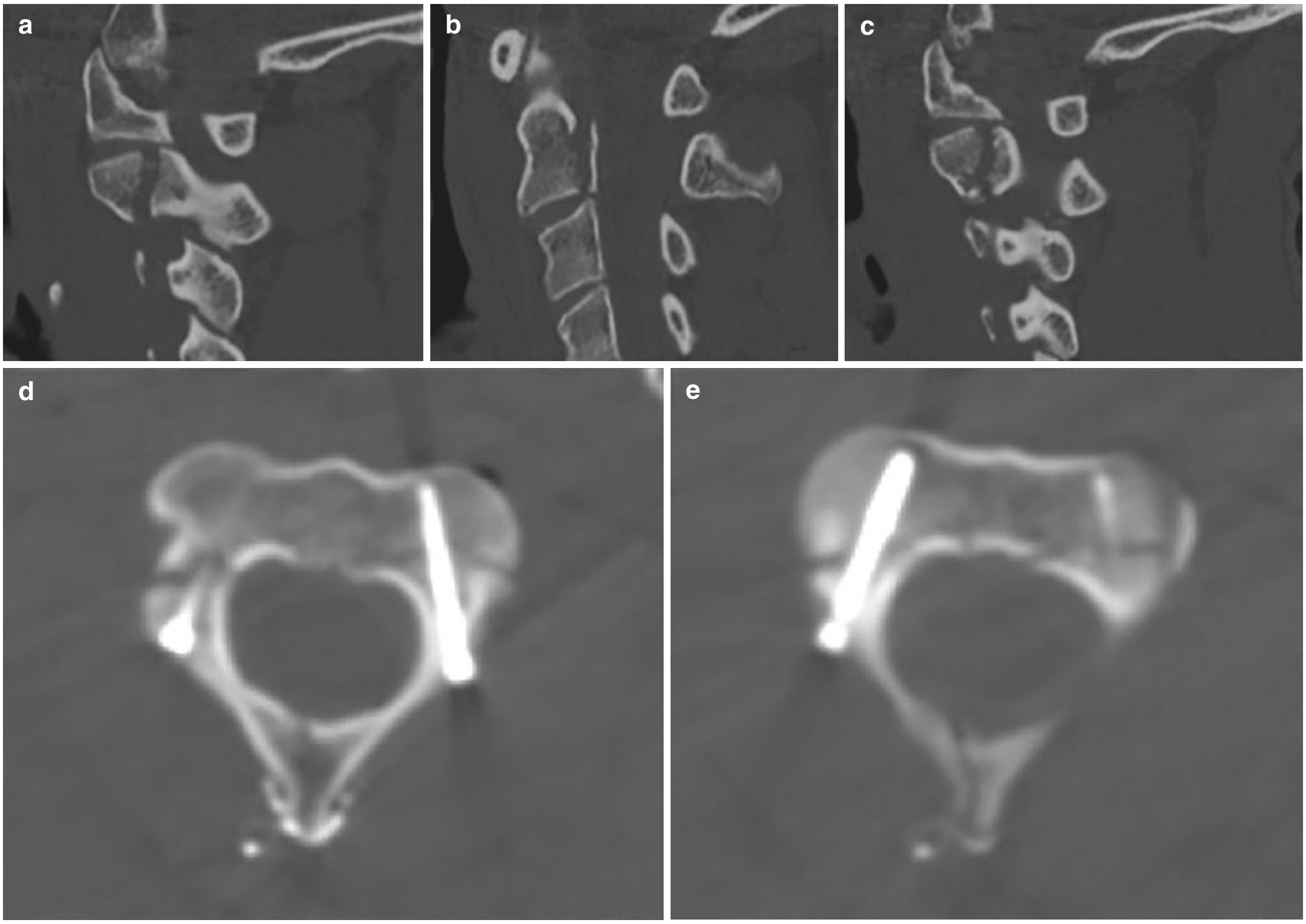

Fig. 3 Illustrative case 2: pre-operative sagittal views of reconstructed CT-scan of cranio-vertebral junction depcted a hangman's type IIa fracture (**a–c**); post-operative CT-scan documented the direct C2 pedicle reconstruction with Judet screws on left (**d**) and right (**e**) sides

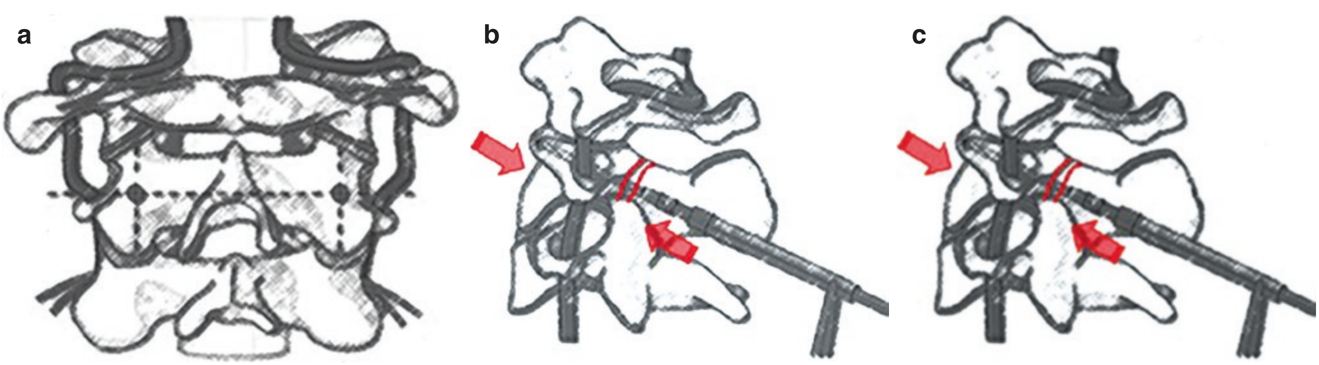

Fig. 4 A schematic drawing depicts the entry point (**a**), and screw's trajectory (**b**, **c**) of Judet's technique

anatomy and orientation can be appreciated with a smooth dissector, also to confirm proper landmarks for screw positioning.

During this step, complete detachment of the atlantoaxial membrane is helpful to guarantee direct visualization of all C2 posterior anatomy and landmarks identification for screw insertion. The dura must be identified and, if required, gently pushed medially in order to clearly visualize the medial surface of C2 pedicles.

Exposure of screw entry points can be performed after identifying the C2-C3 articular process. The entry point is identified in the upper medial quadrant of the posterior aspect of C2 articular process. After breaking the entry point cortical bone, a 2 mm hand drill is used to create the screw trajectory (Fig. 4). The drill must be gently rotated and pushed into the pedicle through the fracture line. It should be oriented 15–20° medially and 15–20° cranially. The medial edge of C2 pedicle should be directly visualized to change the trajectory in case of inadvertent pedicle's medial wall breach causing screw penetration into the spinal canal. During this step, it is important to gently but constantly push and rotate the drill. This helps to clearly feel the fracture line. Indeed, the bony resistance stops at the first fracture line (i.e., starting from posterior when the drill reaches the fracture site), then a second resistance is perceived when the drill penetrates the anterior fracture fragment. Finally, the lag screws are inserted in the track created by drill. After the screw-head reaches the bony entry-point and the tip is into the C2 body beyond the fracture line, a fluoroscopically-assisted over-screwing maneuver allows bilateral reduction of the fracture. The pedicles lag is essential to reduce time for fracture healing. A final antero-posterior and lateral fluoroscopic check is performed before wound closure.

Postoperatively, a Philadelphia collar is advised for 3 months.

3 Literature Review

A systematic review of the literature on surgical treatment of hangman's fractures with C2 pars-pedicle screws was performed. The Medline database was queried through the PubMed website. The research was focused on papers published in the English-language literature, between 1970 (year of publication of the paper by Judet) and 2020. Only clinical studies focusing on the surgical treatment of hangman's fractures were selected for review. The following keywords were used: "pedicle screws hangman's fractures," "pedicle screws ring axis fractures," "pars screws hangman's fractures," "pars screws ring axis fractures," "Judet screws hangman's fractures," "Judet screws ring axis fractures." The PRISMA checklist was used to guide the review process (Fig. 5).

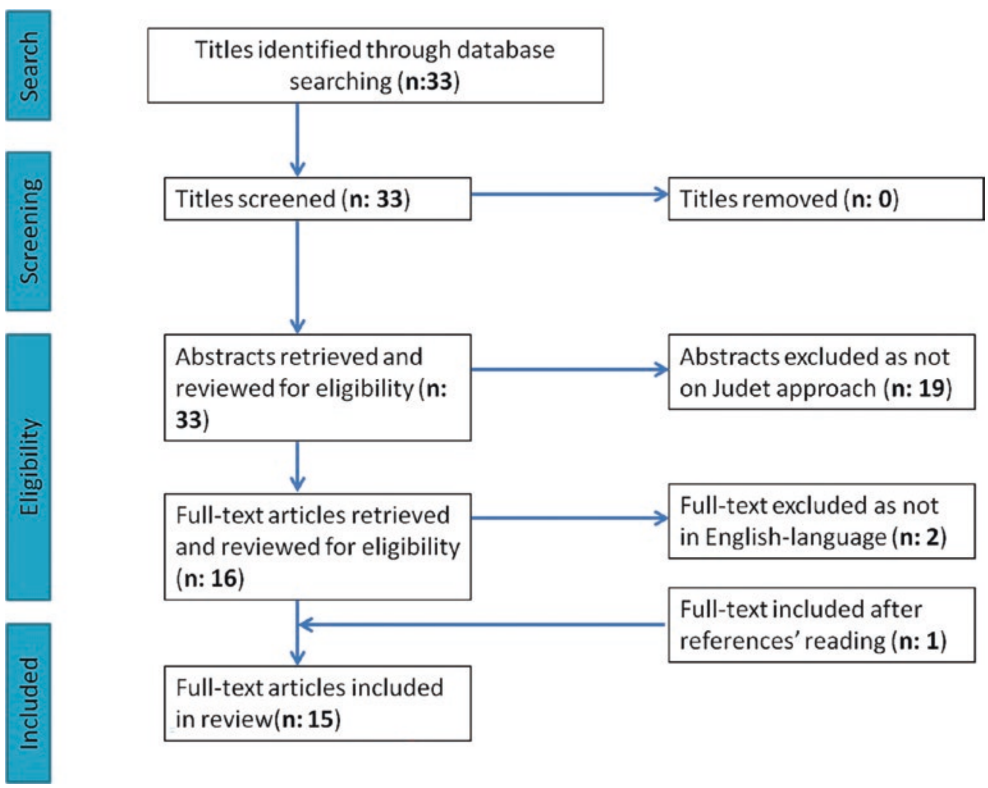

Fig. 5 Flowchart schematizing the review process and paper selection

Table 1 Review of the English-language literature on Judet approach for hangman's fractures

Authors/Years	N. of patients	Fracture type (according to Levine-Edwards)	Screw type	Pre-operative evaluation	Post-operative evaluation
Borne et al./1984 [26]	12	NA	Transpedicular	NA	NA
Verheggen and Jansen/1998 [23]	16	II: 5 IIa: 8 III: 3	Transpedicular	X-ray, CT	X-ray
Taller et al./2000 [5]	10	NA	Transpedicular	X-ray, CT (intraoperative)	X-ray
Muller et al./2000 [34]	4	II	Transpedicular	X-ray, CT (not routinely)	NA
Arand et al./2001 [27]	2	NA	Navigated Transpedicular	X-ray, CT	X-ray, CT
Moon et al./2001–2002 [35]	4	II	Transpedicular	X-ray	X-ray
Boullosa et al./2004 [28]	8	I: 2 II: 6	Transpedicular	X-ray, CT	X-ray
Bristol et al./2005 [37]	1	II	Trans-pars	X-ray, CT	X-ray
Hakało and Wroński/2008 [31]	8	II	Trans-pars	X-ray, CT	X-ray
Dalbayrak et al./2009 [38]	2	II	Trans-pars	X-ray, CT, MR	X-ray
El Miligui et al./2010 [32]	15	II	Transpedicular	X-ray, CT, MR (not routinely)	X-ray, CT
Sugimoto et al./2010 [29]	1	II	Navigated percutaneous transpedicular	X-ray, CT	X-ray
Wu et al./2013 [30]	10	I: 3 II: 5 IIa:2	Percutaneous transpedicular	X-ray, CT	X-ray, CT
Elliot and Kirkpatrick/2014 [36]	1	IIa	Transpedicular	X-ray, CT, MR	X-ray
Salunke et al./2016 [33]	9	II	Transpedicular	X-ray, CT, MR (not routinely)	X-ray, CT

4 Results

In total, 33 papers matched the search criteria. The abstracts of all these papers were reviewed. After abstract reading, 16 papers were deemed suitable for inclusion in the present review. These papers were obtained and carefully reviewed. One more paper was found after reading the reference list of previously reviewed papers and two manuscripts were excluded as they were not in English. In the end, 15 papers were identified and included in this review. Figure 5 shows the different steps of the review process. A total number of 103 patients were included in these 15 studies. The Judet approach was used in: 5 cases (4.85%) of type I fractures, 60 cases (58.25%) of type II fractures, 11 cases (10.68%) of type IIA fractures, 3 cases (2.91%) of type III fractures; in the remaining 24 cases (23.31%) the type of fracture was not reported. Two different surgical approaches were used in the reported papers: trans-pedicular screws were used in 92 cases (89.32%) and trans-pars screws in 11 cases (10.68%).

Table 1 summarizes the main findings of these 15 papers on hangman's fractures treated with the Judet technique.

5 Discussion

Despite several authors have discussed the management of traumatic fractures of the axis [14], the best treatment option for Hangman's fractures remains controversial. As pointed out by Ryken in 2013, only class III medical evidences appeared in literature on the management of Hangman's fractures [17]. The reported clinical series are retrospective and include a small number of patients [14]. The classification systems of hangman's fractures proposed by Effendi [1] and modified by Levine and Edwards [6] have the potential advantages to address the preferable management options as summarized by Li et al. in 2006 [14]. In their literature review, the authors suggested that for Levine–Edwards type I and II fractures non-rigid external fixation led to union in all reported cases; Levine–Edwards type II fractures should be treated by traction followed by external immobilization (rigid or not rigid); Levine–Edwards type IIA and III fractures require rigid immobilization with halo brace or surgical fixation. The rationale of this scheme is based on appropriate evaluation of the fracture's stability for a correct classification, but a thorough analysis of papers included in the review by Li et al. revealed that in most of papers, patients' evaluation had been based on X-rays and CT scan, according to the extent of bone translation [14].

Selection of the correct surgical approach (i.e., anterior vs. posterior) for Hangman's fractures deemed suitable for surgical treatment, should be based on a pre-operative radiological assessment, which also includes MRI of the craniovertebral junction for evaluation of soft-tissues, as well as disc and ligamentous complex involvement. As noted by Li et al., posterior approaches have been used more frequently than other approaches, as they allow direct control of C2-C3 facets in cases of type III Levine–Edwards fractures, and they can correct local kyphosis and prevent flexion deformities [14]. Different posterior approaches have been proposed over the years fort type IIa and III fractures including C0-C3 or C0-C2 [18], C1-C3 [19], C2-C3 [20], using screws or wires [21, 22], with satisfactory results in terms of fracture healing and stability but with severe motion limitation. Anterior C2-C3 discectomy and fusion has been advocated to reinforce posterior construction in type III fractures with severe dislocation, albeit the surgical approach is challenging and anterior anatomy of C2 often does not provide adequate surface for plating [23]. C2-C3 anterior approach with grafting only has been advocated as good alternative to posterior fixation, allowing rotation motion preservation [5]. However, only few patients treated with this technique have been reported in published clinical series and strong data on their outcome are not available [24, 25].

Among non-surgical options, the application of rigid external fixation with Halo-vest has been considered as a valid alternative to surgery also in type IIA and type III fractures; however, placement of Halo vest is associated with a complication rate similar to surgery with regard to infections and non-union [26, 27].

The use of pars-pedicle C2 screws for "direct" fixation of hangman's type IIA fractures is another motion preserving approach, which has gained appeal in recent years despite the first report of this technique is not recent [16]. Indeed, Judet et al. described the technique for direct fixation of C2 hangman's fractures in 1970. They introduced the use of lag screws to facilitate the intraoperative reduction and fixation of C2 fractures, not achievable with head traction during patient positioning [16]. This technique, albeit effective in motion preservation of the cranio-vertebral junction, has been poorly applied in clinical practice, as demonstrated by the limited number of reports published on this technique over the following decades. Indeed, the Judet approach was considered surgically challenging because of the increased risk of neural and vascular damages [11, 14].

In recent years, the Judet approach was re-considered as a surgical option in selected cases of Hangman's fractures [14]. The renewed interest on this surgical procedure may be explained by the introduction and diffusion of Goel–Harm's technique for the treatment of several craniovertebral junction traumatic and degenerative conditions, that encouraged many spinal surgeons to approach more confidently C2 pedicles for screws placement [28, 29].

Borne et al., in 1984, published a clinical series of patients treated for "pedicular fractures of the axis." They used the approach described by Judet in 12 out of 18 reported cases, hypothesizing the superiority of pedicle screw fixation to C1-C3 or C2-C3 wiring in terms of outcome and stability [30].

In 1998 Verheggen and Jansen used the Judet technique in 16 cases of Levine–Edwards type II, IIA, and III fractures, emphasizing the advantages of a real reconstruction of the C2 anatomical condition, which maintains the atlantoaxial rotational mobility [24]. Interestingly, they also included in their series patients with type II hangman's fractures, pointing out the benefits related to early mobilization and short hospitalization. Moreover, in type IIA and III fractures, they did not observe post-operative worsening of chin-breastbone distance or hypomobility of C2-C3 joints [24].

Intraoperative image guidance for C2 Judet screws placement has been proposed to increase the safety and accuracy of such procedure: in 2000, Taller et al. described a CT-guided technique for placement of C2 pars-pedicle screws according to Judet approach [25]; 1 year later, Arand et al. reported their positive experience with Judet screws implanted under navigation guidance in two patients [31].

The Judet technique has also been proposed as second line option to manage patients suffering from pseudoarthrosis after conservative treatment or with contraindications to the halo vest, like skull fractures or large scalp lacerations [32].

The application of minimally invasive techniques to the Judet approach for Hangman's fractures has been proposed by Sugimoto et al., in 2010, who reported a case of percutaneous insertion of C2 pedicle screws under 3D fluoroscopic-based navigation [33]. Similarly, in 2013, Wu et al. described a series of 10 patients treated by percutaneous transpedicular screw fixation performed under fluoroscopic assistance [34].

In 2008, Hakalo compared the direct C2 pedicle reconstruction technique with anterior C2-C3 cage and plate fixation [35]. They concluded that anterior plate-cage stabilization is indicated for type II fracture with extension displacement, whereas posterior Judet approach may be used for flexion displacement [35].

El Miligui et al. published the only prospective clinical series on Judet approach [36]. They included 15 patients and focused on the importance of adequate pre-operative radiological assessment including X-rays, CT, and MRI. These Authors also emphasized the role of follow-up CT scan to assess fractures solid bony fusion and provided some relevant surgical tips to increase safety and accuracy of screw placement [36]. Detachment of the atlantoaxial ligament is an essential step for correct identification of the C2 pedicle [36]. Not surprisingly, the clinical and neuroradiological outcome reported by El Miligui et al. is favorable in all cases, suggesting that proper surgical plan and correct patients' selection are crucial to determine the success of Judet approach [36].

Recently, Salunke et al. reported their experience with C2 pars-pedicle screws for type II hangman's fractures; they analyzed the results of their clinical and radiological follow-up on 11 patients, focusing on the correlation between fractures' radiological features and outcome [37]. They observed that the Judet technique might not be the optimal surgical option for fractures with more than 4.5 mm of translation [37]. Moreover, they debated the real rotational motion preservation after this approach, as they observed the spontaneous tendency to C2-C3 somatic and/or facet fusion over the clinical and radiological follow-up period.

Our literature review suggests that all included papers are based on small case-series; hence an evidence-based approach to address the best application of the Judet approach to hangman's fractures is still not applicable. Nevertheless, some consideration may be formulated after a thorough analysis of the reported clinical series. According to our institutional experience and to the existing literature, Levine-Edwards type IIA hangman's fractures are probably the best indication for C2-pedicle lag screws insertion with the Judet technique [14, 36, 38–40]. However, we believe that this technique could also be considered for the surgical management of atypical type I or type II fractures in selected patients, who require early mobilization (i.e., polytrauma) and short hospitalization, as in the second case that we report. The importance of early bony healing in hangman's fractures is proportional to the high risk of non-union and late-onset of post-traumatic deformity. Indeed, the direct and immediate synthesis of fractured fragments, achieved with the Judet technique, could reduce the risks of non-union, avoiding further and more complex surgical approaches [41–44]. The correct patient selection needs a thorough pre-operative radiological evaluation including MRI, to assess the ligamentous and disc involvement, and angio-CT, to study the course of vertebral arteries in relation to C2 pedicles [36].

Two of the reviewed papers reported the use of pars screws for direct repair of the fracture, but the literature lacks of consistent data supporting the use of pars screws rather than pedicle screws [45, 46]. We believe that, stating the proven biomechanical superiority of pedicle screws compared to pars screws, the formers should be preferred for direct Hangman's fracture osteosynthesis.

6 Conclusion

Traumatic lesions of the cranio-vertebral junction are associated with severe clinical pictures and may dramatically affect patients' quality of life. The right approach to these lesions implies a proper classification and a correct surgical indication, based on scientific evidences but still tailored on the individual patient [47–49]. In this scenario, the Judet approach represents an effective surgical option to treat Hangman's fractures. Correct diagnostic assessment and careful patient selection are the most important factors affecting the outcome as well as the long-term motion preservation of cranio-vertebral and C2-C3 junctions.

This approach, in expert hands, allows achieving solid fusion while respecting anatomical conditions and avoiding vascular as well as neural damages. Its application to atypical type I Hangman's fractures, as in one of the cases here reported, should be considered for future investigation. Multicentric studies with larger number of patients are encouraged to better understand risks and benefits associated with this surgical option.

References

1. Effendi B, Roy D, Cornish B, Dussault RG, Laurin CA. Fractures of the ring of the axis. A classification based on the analysis of 131 cases. J Bone Joint Surg Br. 1981;63-B(3):319–27.
2. Ferro FP, Borgo GD, Letaif OB, Cristante AF, Marcon RM, Lutaka AS. Traumatic spondylolisthesis of the axis: epidemiology, management and outcome. Acta Ortop Bras. 2012;20(2):84–7.
3. Wood-Jones F. The ideal lesion produced by judicial hanging. Lancet. 1913;181(4662):53.
4. Schneider RC, Livingston KE, Cave AJ, Hamilton G. "Hangman's fracture" of the cervical spine. J Neurosurg. 1965;22:141–54.
5. Francis WR, Fielding JW, Hawkins RJ, Pepin J, Hensinger R. Traumatic spondylolisthesis of the axis. J Bone Joint Surg Br. 1981;63-B(3):313–8.
6. Levine AM, Edwards CC. The management of traumatic spondylolisthesis of the axis. J Bone Joint Surg Am. 1985;67(2):217–26.
7. Starr JK, Eismont FJ. Atypical hangman's fractures. Spine. (Phila Pa 1976). 1993;18(14):1954–7.
8. Greene KA, Dickman CA, Marciano FF, Drabier JB, Hadley MN, Sonntag VK. Acute axis fractures. Analysis of management and outcome in 340 consecutive cases. Spine (Phila Pa 1976). 1997;22(16):1843–52.
9. Hadley MN, Browner C, Sonntag VK. Axis fractures: a comprehensive review of management and treatment in 107 cases. Neurosurgery. 1985;17(2):281–90.
10. Hadley MN, Dickman CA, Browner CM, Sonntag VK. Acute axis fractures: a review of 229 cases. J Neurosurg. 1989;71(5 Pt 1):642–7.
11. Ding T, Maltenfort M, Yang H, et al. Correlation of C2 fractures and vertebral artery injury. Spine (Phila Pa 1976). 2010;35(12):E520–4.

12. Al-Mahfoudh R, Beagrie C, Woolley E, Zakaria R, Radon M, Clark S, Pillay R, Wilby M. Management of typical and atypical Hangman's fractures. Global Spine J. 2016;6(3):248–56.
13. Shin JJ, Kim SH, Cho YE, Cheshier SH, Park J. Primary surgical management by reduction and fixation of unstable hangman's fractures with discoligamentous instability or combined fractures: clinical article. J Neurosurg Spine. 2013;19(5):569–75.
14. Li X-F, Dai L-Y, Lu H, Chen X-D. A systematic review of the management of hangman's fractures. Eur Spine J. 2006;15(3):257–69.
15. Leconte P. Fracture et luxation des deux premieres vertebres cervicales. In: Judet R, editor. Luxation Congenitale De La Hanche. Fractures Du Cou-De-Pied Rachis Cervical. Actualites De Chirurgie Orthopedique De l'Hopital Raymond-Poincare, vol. 3. Paris: Masson et Cie; 1964. p. 147–66.
16. Judet R, Roy-Camille R, Saillant G. Actualités de chirurgie orthopédique de l'Hospital Raymond-Poin caré. VIII. Fractures du rachis cervical. Paris: Masson; 1970. p. 174–95.
17. Ryken TC, Hadley MN, Aarabi B, Dhall SS, Gelb DE, Hurlbert RJ, Rozzelle CJ, Theodore N, Walters BC. Management of isolated fractures of the axis in adults. Neurosurgery. 2013;72(Suppl 2):132–50.
18. Cosan TE, Tel E, Arslantas A, Vural M, Guner AI. Indications of Philadelphia collar in the treatment of upper cervical injuries. Eur J Emerg Med. 2001;8(1):33–7.
19. Choi WG, Vishteh AG, Baskin JJ, Marciano FF, Dickman CA. Completely dislocated hangman's fracture with a locked C2-3 facet. Case report. J Neurosurg. 1997;87(5):757–60.
20. Jeong DH, You NK, Lee CK, Cho KH, Kim SH. Posterior C2-C3 fixation for unstable hangman's fracture. Korean J Spine. 2013;10(3):165–9.
21. Visocchi M, Fernandez EM, Ciampini A, Di Rocco C. Reducible and irreducible os odontoideum treated with posterior wiring, instrumentation and fusion. Past or present? Acta Neuroch (Wien). 2009;151(10):1265–74.
22. Visocchi M, Pietrini D, Tufo T, Fernandez E, Di Rocco C. Preoperative irreducible C1- C2 dislocations: intraoperative reduction and posterior fixation. The "always posterior strategy". Acta Neuroch (Wien). 2009;151(5):551–9.
23. Dussault RG, Effendi B, Roy D, Cornish B, Laurin CA. Locked facets with fracture of the neural arch of the axis. Spine (Phila Pa 1976). 1983;8(4):365–7.
24. Verheggen R, Jansen J. Hangman's fracture: arguments in favor of surgical therapy for type II and III according to Edwards and Levine. Surg Neurol. 1998;49:253–61; discussion 261–2.
25. Taller S, Suchomel P, Lukas R, Beran J. CT-guided internal fixation of a hangman's fracture. Eur Spine J. 2000;9:393–7.
26. Talamonti G, Debernardi A, Visocchi M, Villa F, D'Aliberti G. Complications of halo placement. Acta Neurochir Suppl. 2019;125:355–61.
27. Visocchi M, Mattogno PP, Signorelli F, Zhong J, Iacopino G, Barbagallo G. Complications in craniovertebral junction instrumentation: hardware removal can be associated with long-lasting stability. Personal experience. Acta Neurochir Suppl. 2017;124:187–94.
28. Goel A, Laheri V. Plate and screw fixation for atlanto-axial subluxation. Acta Neurochir. 1994;129(1–2):47–53.
29. Harms J, Melcher RP. Posterior C1-C2 fusion with polyaxial screw and rod fixation. Spine (Phila Pa 1976). 2001;26(22):2467–71.
30. Borne GM, Bedou GL, Pinaudeau M. Treatment of pedicular fractures of the axis. A clinical study and screw fixation technique. J Neurosurg. 1984;60(1):88–93.
31. Arand M, Hartwig E, Kinzl L, Gebhard F. Spinal navigation in cervical fractures - a preliminary clinical study on Judet-osteosynthesis of the axis. Comput Aided Surg. 2001;6(3):170–5.
32. Boullosa JL, Colli BO, Carlotti CG Jr, Tanaka K, dos Santos MB. Surgical management of axis' traumatic spondylolisthesis (Hangman's fracture). Arq Neuropsiquiatr. 2004;62(3B):821–6.
33. Sugimoto Y, Ito Y, Shimokawa T, Shiozaki Y, Mazaki T. Percutaneous screw fixation for traumatic spondylolisthesis of the axis using iso-C3D fluoroscopy-assisted navigation (case report). Minim Invasive Neurosurg. 2010;53:83–5.
34. Wu Y-S, Lin Y, Zhang X-L, et al. Management of hangman's fracture with percutaneous transpedicular screw fixation. Eur Spine J. 2013;22(1):79–86.
35. Hakało J, Wroński J. Operative treatment of hangman's fractures of C2. Posterior direct pars screw repair or anterior plate-cage stabilization? Neurol Neurochir Pol. 2008;42(1):28–36.
36. ElMiligui Y, Koptan W, Emran I. Transpedicular screw fixation for type II Hangman's fracture: a motion preserving procedure. Eur Spine J. 2010;19(8):1299–305.
37. Salunke P, Sahoo SK, Krishnan P, Chaterjee D, Sodhi HB. Are C2 pars-pedicle screws alone for type II Hangman's fracture overrated? Clin Neurol Neurosurg. 2016;141:7–12.
38. Müller EJ, Wick M, Muhr G. Traumatic spondylolisthesis of the axis: treatment rationale based on the stability of the different fracture types. Eur Spine J. 2000;9(2):123–8.
39. Moon MS, Moon JL, Moon YW, Sun DH, Choi WT. Traumatic spondylolisthesis of the axis: 42 cases. Bull Hosp Jt Dis. 2001–2002;60(2):61–6.
40. Elliott MR, Kirkpatrick JS. Type IIa Hangman's fracture with pure distraction: not your typical type IIa fracture. Spine J. 2014;14(7):1360–1.
41. Visocchi M, Della Pepa GM, Doglietto F, Esposito G, La Rocca G, Massimi L. Video-assisted microsurgical transoral approach to the craniovertebral junction: personal experience in childhood. Childs Nerv Syst. 2011;27(5):825–31.
42. Visocchi M, Doglietto F, Della Pepa GM, Esposito G, La Rocca G, Di Rocco C, Maira G, Fernandez E. Endoscope-assisted microsurgical transoral approach to the anterior craniovertebral junction compressive pathologies. Eur Spine J. 2011;20:1518–25.
43. Visocchi M, Di Martino A, Maugeri R, González Valcárcel I, Grasso V, Paludetti G. Videoassisted anterior surgical approaches to the craniocervical junction: rationale and clinical results. Eur Spine J. 2015;24(12):2713–23.
44. Tosi F, Genovese O, Jovanovic T, Visocchi M. Management of anaesthesia in CVJ surgery. Acta Neurochir Suppl. 2019;125:381–6.
45. Bristol R, Henn JS, Dickman CA. Pars screw fixation of a hangman's fracture: technical case report. Neurosurgery. 2005;56(1 Suppl):E204; discussion E204.
46. Dalbayrak S, Yilmaz M, Firidin M, Naderi S. Traumatic spondylolisthesis of the axis treated with direct C2 pars screw. Turk Neurosurg. 2009;19(2):163–7.
47. Ciappetta P, Alsagheir M, Signorelli F, Visocchi M. The decision-making process in traumatic lesions of the craniovertebral junction: an evidence-based approach? Part I. Acta Neurochir Suppl. 2019;125:309–11.
48. Ciappetta P, Alsagheir M, Signorelli F, Visocchi M. Posttraumatic anatomical injuries of the craniovertebral junction and treatment implications: part I. Acta Neurochir Suppl. 2019;125:297–302.
49. Ciappetta P, Alsagheir M, Signorelli F, Visocchi M. Posttraumatic anatomical injuries of the craniovertebral junction and treatment implications: part II. Acta Neurochir Suppl. 2019;125:303–7.

Computerized Three-Dimensional Analysis: A Novel Method to Assess the Effect of Open-Door Laminoplasty

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1 Introduction

Three-dimensional printing (3DP) is one of the latest tools in the armamentarium of today's spine surgeon [1–3]. The printing of the models is based on the elaboration of the data obtained from computed tomography (CT) and magnetic resonance imaging (MRI) scans, and its aim is to highlight the anatomical regions of interest: a process known as "segmentation." Segmentation yields masks corresponding to the analyzed anatomical regions, which are the precursors of three-dimensional models. Finally, the models are obtained through a variety of mathematical algorithms, including marching cubes and ray casting [4, 5].

Virtual models are tessellated geometrical entities made of triangles, which together define a mesh, namely a folded surface that accurately fits the anatomical representation. Three-dimensional data are stored in a standard tessellation language (STL) file. Virtual geometrical models provide great advantages for surgical planning and anatomical study, allowing for a rich understanding of the anatomy through a three-dimensional perspective, regardless of soft tissues and blood. Moreover, STL files can be easily handled in engineering software packages, enabling the user to perform accurate calculations on them and perform operations such as geometry refinement, alignment, and object characterization.

Here, we introduce a novel method to visualize the enlargement of the vertebral canal space after open-door laminoplasty and to measure its magnitude. Through the observation of three-dimensional virtual models, our purpose is to assess the effectiveness of the surgical procedure by comparing the volume of the spinal canal before and after a cervical laminoplasty.

2 Materials and Methods

The study was conducted by using the technologies available in the virtual surgical planning and 3D printing laboratory and data from the anonymized patients treated in the Spine and Spinal Cord Surgery Unit.

2.1 Surgical Technique and Clinical Data

Patients with cervical myelopathy caused by a multilevel degenerative spinal canal stenosis were treated by using classic Hirabayashi open-door laminoplasty [6]. After exposing the laminae, a longitudinal gutter was made on one side with a high-speed drill at the junction of the laminae and facet joints, leaving the inner cortex intact. Next, a similar groove was made at the opposite side, cutting the inner cortex. The flava ligaments at the open side were resected by using a Kerrison rongeur. The opened laminae were lifted, and the spinous processes were pushed toward the hinge side and fixed down to the deep layer of the muscles with a nonabsorbable thread.

The neurologic status was assessed by using the modified Japanese Orthopedic Association (mJOA) scoring system for cervical myelopathy. All the patients underwent a cervical MRI and CT scan before surgery and at their respective 3-month follow-ups.

2.2 Acquisition Protocol and Image Processing

Both before and after surgery, all patients underwent a cervical spine CT scan so that a digital reconstruction of the bone

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anatomy could be performed. Parameters were as follows: multidetector 64-row CT with slice thickness 0.625 mm and acquisition matrix of at least 512 × 512 px or, preferably, 768 × 768 px. Moreover, all patients underwent a preoperative volumetric MR acquired in the T1 Weighted (T1W), T2 Weighted (T2W), and Short Tau Inversion Recovery (STIR) sequences, with similar spatial parameters, namely a slice thickness of 1 mm and a matrix of 512 × 512 px. The position of the head was standardized as much as possible in order to acquire similar spine morphologies between the various patients and to make preoperative imaging comparable with postoperative counterparts.

Digital Imaging and Communication in Medicine (DICOM) data were extracted from preoperative imaging and imported into the software program Materialise Mimics version 24 (Materialise, Leuven, BE), where a CT scan and multiple MR sequences were coregistered to share the same spatial coordinate system by using an automatic overlapping algorithm. By using a basic thresholding technique, bone structures were segmented and a mask representing the cervical spine was obtained and checked for optimal correspondence with the MR, especially across the limits of the vertebral canal. MR was then processed, and the dural sac was used as a reference to define the limits of the spinal cord and subarachnoid space, a space that was then filled to yield another segmentation mask defining the intradural space within the vertebral canal.

Postoperative imaging was processed accordingly, but the rotated laminae were isolated by using a split mask function and subsequently hidden to uncover the underlying window caused by the open-door laminoplasty through which the intradural contents could expand. Similarly, the structures defined by the boundaries of the dural sac were reconstructed in a DICOM mask from the volumetric MR data. Masks were then converted into parts consisting of tessellated STL geometries and were imported into the anatomical computer-aided design (CAD) package (Materialise 3-Matic v16, Materialise, Leuven, BE).

2.3 Virtual Model Analysis

Models of the cervical spine and the intradural contents were merged into a composite geometry to be moved together while keeping the correct reciprocal relationships. This yielded two pairs of models: (1) the combination of the preoperative spine and the stenotic intradural space (Fig. 1) and (2) the postoperative spine and the widened intradural space (Fig. 2). Given that the preoperative entity was "fixed" and the postoperative entity was "mobile," a rough alignment was initially performed by using a point-to-point registration that used anatomical landmarks. Next, the registration of the models was refined by using a global alignment function that was based on the iterative closest point algorithm, aiming to nullify all Euclidean distances between the vertices of both entities. Once the optimal superimposition had been assessed, Euclidean distances were mathematically computed by using a surface deviation analysis and graphically represented by using a red–green color scale; divergences across the preoperative stenotic and postoperative, dilated intradural space were emphasized in red (Fig. 3). Moreover, the magnitude of divergence was quantified by using the root-mean-square error (RMSE) parameter—that is, the root square of the averaged quadratic distances.

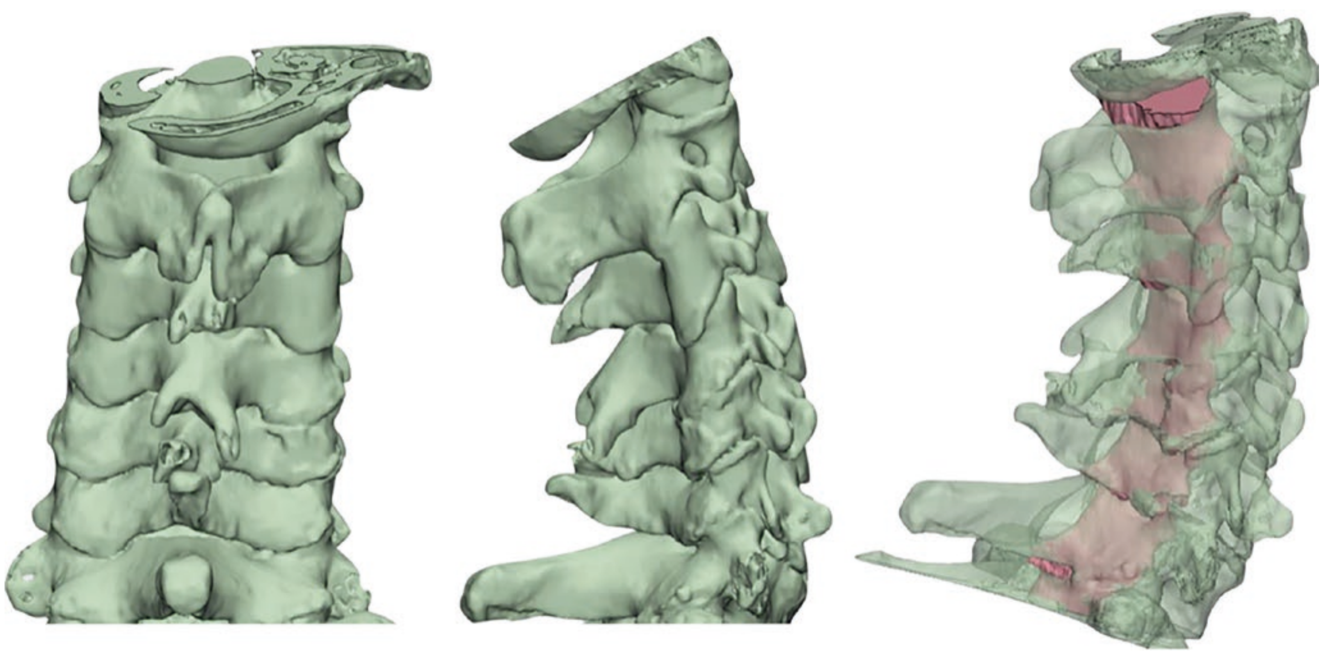

Fig. 1 Preoperative models consisting of the cervical spine and the stenotic intradural space

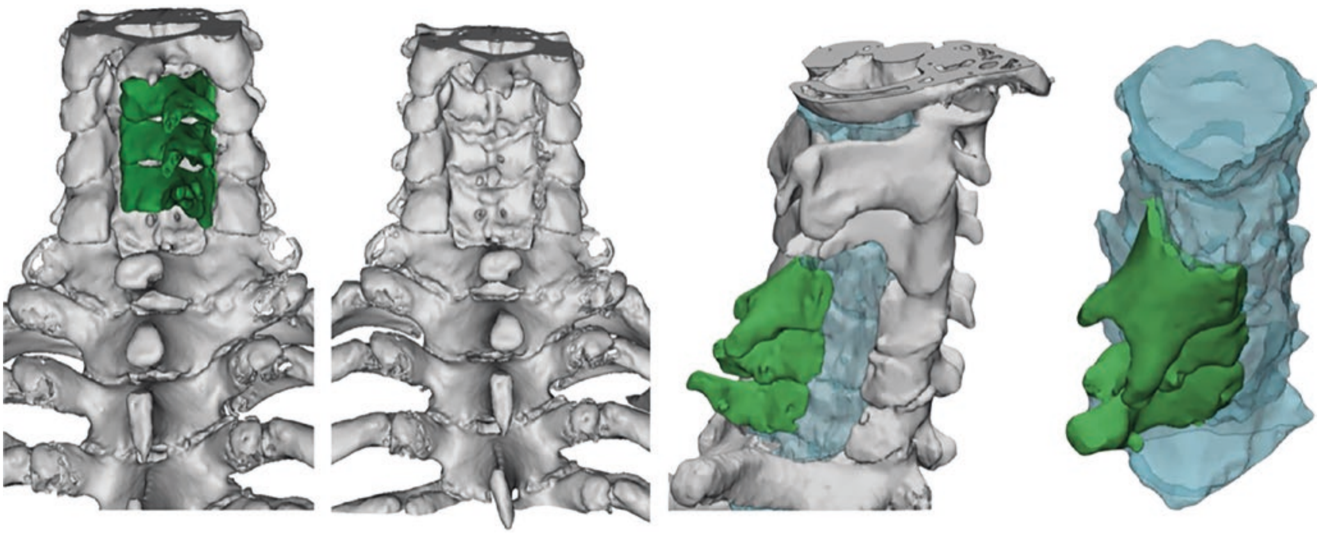

Fig. 2 Anatomical models after open-door laminoplasty from postoperative CT; isolation and removal of rotated laminae is shown in green; laminae are then hidden to uncover the expanded intradural space, reconstructed in blue

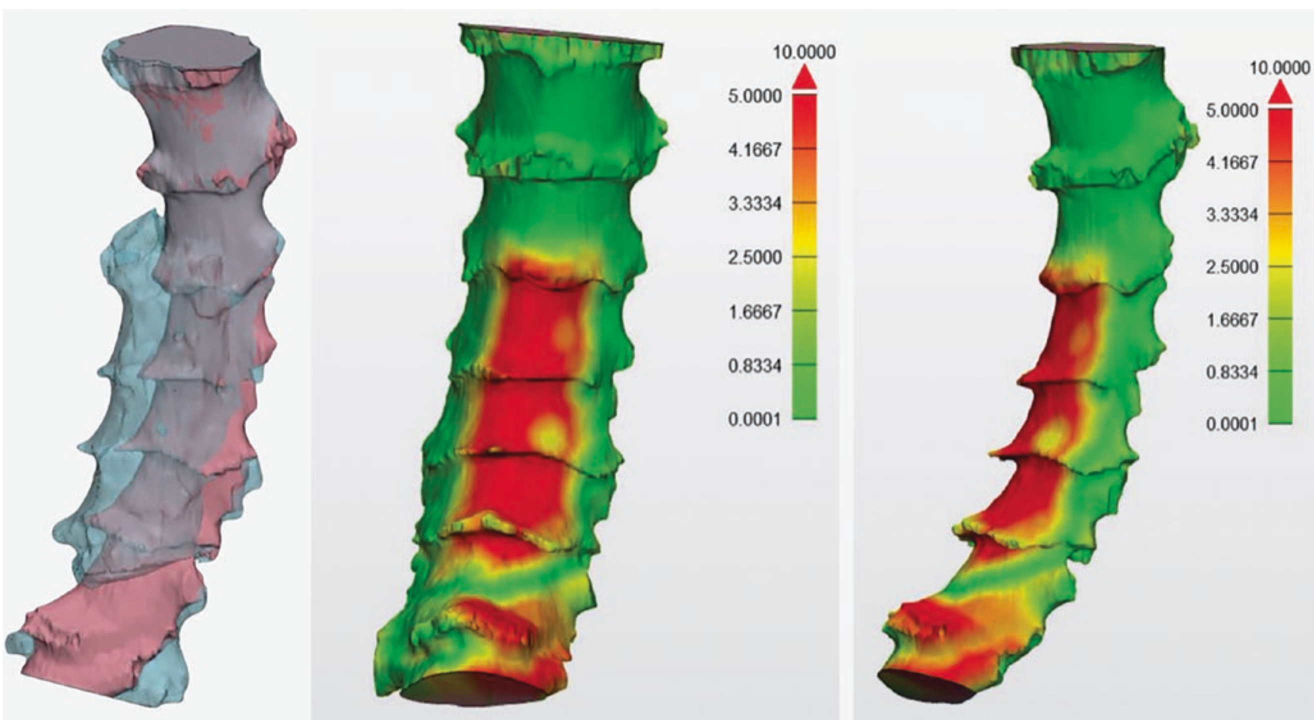

Fig. 3 Left panel features superimposition of preoperative (red) and postoperative (blue) intradural space, where enlargement is visible across the opening of laminae; central and right panels feature surface deviation analysis—where red indicates the maximum displacement, while green indicates neutrality

3 Results

The new method was applied to four patients to test the feasibility of this protocol. Patients' details are reported in Table 1. The results of surface deviation analysis revealed the wide representation of green across unvaried bone anatomy for all cases, signifying that alignment was correctly performed, and the red over the intradural space segment corresponded to the dilation following the laminoplasty. A threshold of 5 mm was used to highlight in red the difference between the preoperative stenotic intradural space and the postoperative dilated intradural space. The mean RMSE was

Table 1 Patient characteristics

Patient	Sex	Age	Preoperative mJOA score	Postoperative mJOA score	Percentage of increase in intradural space (%)
Case #1	M	62	11	13	46.6
Case #2	F	75	11	14	35.4
Case #3	M	72	15	16	33.3
Case #4	M	58	15	17	49.5

2.3 mm (SD: ±1.72 mm). The maximum average displacement, calculated by sampling ten points with equal distribution over the red area, was 5.86 mm (SD: ±2.34 mm). The average increase in intradural space after surgical expansion was 41.2%.

4 Discussion

Cervical spondylotic myelopathy (CSM) is most commonly seen in elderly patients (typically >60 year) who experience a gradual, stepwise deterioration with limited potential for spontaneous resolution. Therefore, surgical treatment is often recommended [7, 8]. The term *laminoplasty* denotes several operative procedures in which the vertebral lamina is reconstructed after opening the spinal canal. It most commonly means creating hinge(s) on which the lamina is lifted but not removed [6, 9]. We use the Hirabayashi technique, a single-door open laminoplasty [6].

Spinal canal expansion is one of the critical factors affecting clinical results after cervical laminoplasty. Especially as concerns spinal canal expansion, there is a positive correlation between the likelihood of functional spinal cord recovery and the degree of spinal cord decompression.

Several studies have reported the dimension of the spinal canal as the average transverse area in mm^2 or as the average of the sagittal diameters in mm. The minimal extent to which the spinal canal must be widened to obtain good results remains unclear, although the relationship between the degree of spinal canal expansion and clinical outcomes after laminoplasty has been investigated. Itoh and Tsuji reported that satisfactory surgical results are related to an enlargement of the canal to 4.1 mm on average in the anteroposterior diameter on the postoperative computed tomograms [10]. This is consistent with researchers who proposed that the optimal postoperative sagittal canal diameter increment be 4–5 mm [6, 11].

Hamburger et al. [12] reported that patients with a postoperative cross-sectional area of 160 mm^2 achieved better outcomes, and these authors recommended forming an operation plan to reach this target area. Kohno et al. [13] also showed that widening by 95 mm^2 in the canal area was associated with good recovery and suggested that the stenotic cervical canal be enlarged to over 200 mm^2 for residual canal area. Dong et al. measured the volume-occupying rate of a cervical spinal canal in a neutral position, calculated by using the MATLAB bony canal area and the fibrous canal area in each cross section, and the sagittal diameters of the cervical spinal canal and the cervical spinal body were measured. The cervical spinal canal ratio and the effective cervical spinal canal ratio were calculated. With this method, the authors found that the volume-occupying rate of the cervical spinal canal was significantly higher in CSM patients than in subjects without CSM [14]. Recently, Wang et al. presented a new surgical technique, defined as lift-open laminoplasty, that avoids damaging paraspinal muscles. The increase in the spinal canal area before and after open-door and lift-open laminoplasty was measured on CT images. They demonstrated the adequacy of the expansion of the spinal canal obtained with the new technique by calculating the increase in the spinal canal area by using the Pythagorean theorem, expressed in mm^2 [15].

Although numerous studies have investigated the range of optimal spinal canal expansion, aiming to increase the sagittal diameter, a bidimensional parameter, few studies have focused their attentions on the increase in the volume of the spinal canal after laminoplasty. The lack of any volumetric calculations on the spinal canal led us to develop a novel method by busing the mathematical-geometric knowledge of recent three-dimensional studies. The spinal cord is contained in a dural "cylinder," making it more appropriate to calculate the space in terms of volume, a three-dimensional parameter.

In the past, attempts have been made to calculate the volume with, for example, the use of three-dimensional (spiral) CT [16]. Hernandez-Duran et al. compared the volumetric results in terms of spinal canal enlargement between laminoplasty and a novel technique of bilateral osteoligamentous decompression (OLD) via hemilaminectomy. They concluded that OLD can yield a comparable volume extent of decompression to laminoplasty in cervical spondylotic myelopathy [17].

We wanted to test the potential of 3D technology in cervical spondylotic myelopathy [18]. Because of the complex anatomy of the spine, as well as the delicate nature of the surrounding structures, computer-guided surgery and a three-dimensional analysis can consistently improve patient outcomes [19]. In 1999, D'Urso et al. [20] first used 3DP technology in spinal surgery. Various authors have published their experiences with these anatomical models for complex spine surgery.

A further development of 3D technology in cervical spondylotic myelopathy is the use of virtual models in surgical planning, simulating the anatomy by using templates. The simulation better identifies the levels to be decompressed and improves the precision of surgery. For example, Zhang et al. [21] used patient-specific vertebral models for a preoperative expansive open-door laminoplasty surgery (ELOP) simulation and a navigation template for navigating high-speed drilling during actual ELOP. The depth of drilling is important, inasmuch as too-deep drilling will lead to hinge fractures and possibly severe neurovascular damage, whereas too-shallow drilling will lead to excessive bone remaining, affecting laminar elevation. In addition, although some attempts have been made in the computerized surgical planning for open-door laminoplasty [22], there is a lack of knowledge on how such technologies might allow us to assess the effectiveness of the surgical result.

The adoption of 3D technologies opens up new perspectives and can be of help in evaluating the results obtained by a specific surgical technique. Such technologies employ geometric models to elucidate the difference in volume of the spinal canal before and after surgery. The surface deviation analysis provides a three-dimensional representation of the amount of the enlargement of the vertebral canal. Instead of selecting single points on two-dimension images, it is possible to quantify the difference between preoperative and postoperative vertebral space across each point of the two paired meshes. Moreover, the segmentation and reconstruction of the postoperative CT and the possibility to isolate and selectively manipulate separated laminae contribute to enhancing the evaluation of surgical outcomes, including the shapes of the osteotomies and the rotational angles. Laminoplasty does not directly remove the pathological structures that compress the spinal cord but rather allows for extensive decompression. In a study performed by Baba et al., the neurological improvement of patients undergoing laminoplasty for CSM was correlated with the postoperative dorsal migration of the spinal cord and the volumetric gain of the bony spinal canal [23]. The analysis method based on virtual models could allow us to assert that in its traditional form, laminoplasty is still an effective treatment today, as we found an increase in the volume of the spinal canal consistent with results already described in literature. Although our preliminary results do not yet justify the use of model parameters to drive decisions during surgery, which necessarily need further studies with a more extensive patient recruitment, the present study can shed light on how three-dimensional computerized analysis is nowadays an indispensable method to refine the evaluation of postoperative outcomes, at the same time providing unprecedented insight into each surgical procedure. A further step will be to correlate the results of the computerized analysis with the clinical outcomes and define the possible metrological parameters that might reasonably drive the preoperative planning toward the best clinical result.

5 Conclusions

The originality of our method is that it studies the spinal canal by using a fully computerized three-dimensional method. The spinal cord is contained in an irregular dural cylinder, and therefore, the estimation of the volume through geometrical models allows us to compare, the pre- and postoperative values. The ultimate goal is to correlate the mathematical results to clinical outcomes in order to define the possible parameters that can help in the preoperative planning toward the best clinical result.

References

1. Izatt MT, Thorpe PL, Thompson RG, D'Urso PS, Adam CJ, Earwaker JW, Labrom RD, Askin GN. The use of physical biomodelling in complex spinal surgery. Eur Spine J. 2007;16(9):1507.
2. Paiva WS, Amorim R, Bezerra DA, Masini M. Aplication of the stereolithography technique in complex spine surgery. Arq Neuropsiquiatr. 2007;65(2b):443–5.
3. Yamazaki M, Okawa A, Akazawa T, Koda M. Usefulness of 3-dimensional full-scale modeling for preoperative simulation of surgery in a patient with old unilateral cervical fracture-dislocation. Spine. 2007;32(18):E532–6.
4. Dietrich CA, Scheidegger CE, Schreiner J, Comba JL, Nedel LP, Silva CT. Edge trans- formations for improving mesh quality of marching cubes. IEEE Trans Vis Comput Graph. 2009;15(1):150–9.
5. Tolhuisen ML, de Jong GA, van Damme RJM, van der Heijden F, Delye HHK. Cranial shape comparison for automated objective 3D craniosynostosis surgery planning. Sci Rep. 2018;8(1):3349.
6. Hirabayashi K, Watanabe K, Wakano K, et al. Expansive open-door laminoplasty for cervical spinal stenotic myelopathy. Spine. 1983;8:693–9.
7. Badhiwala JH, Wilson JR. The natural history of degenerative cervical myelopathy. Neurosurg Clin N Am. 2018;29:21–32.
8. Fehlings MG, Tetreault LA, Riew KD, Middleton JW, Wang JC. A clinical practice guideline for the management of degenerative cervical myelopathy: introduction, rationale, and scope. Global Spine J. 2017;7(3_Suppl):21S–7S.
9. Cho SK, Kim JS, Overley SC, Merrill RK. Cervical laminoplasty: indications, surgical considerations, and clinical outcomes. J Am Acad Orthop Surg. 2018;26(7):e142–52.
10. Itoh T, Tsuji H. Technical improvements and results of laminoplasty for compressive myelopathy in the cervical spine. Spine. 1985;10:729–36.
11. Gu Z, Zhang A, Shen Y. Relationship between the laminoplasty opening size and the laminoplasty opening angle, increased sagittal canal diameter and the prediction of spinal canal expansion following open-door cervical laminoplasty. Eur Spine J. 2015;24:1613–20.
12. Hamburger C, Buttner A, Uhl E. The cross-sectional area of the cervical spinal canal in patients with cervical spondylotic myelopathy: correlation of preoperative and postoperative area with clinical symptoms. Spine. 1997;22:1990–4.

13. Kohno K, Kumon Y, Oka Y, Matsui S, Ohue S, Sakaki S. Evaluation of prognostic factors following expansive laminoplasty for cervical spinal stenotic myelopathy. Surg Neurol. 1997;48(3):237–45.
14. Dong F, Shen C, Jiang S. Measurement of volume-occupying rate of cervical spinal canal and its role in cervical spondylotic myelopathy. Eur Spine J. 2013;22:1152–7.
15. Wang H, Zhang L. Expansion of spinal canal with lift-open Laminoplasty: a new method for compression cervical myelopathy. Orthop Surg. 2021;13(5):1673–81.
16. Baba H, Uchida K, Maezawa Y, Furusawa N, Wada M, Imura S. Three-dimensional computed tomography for evaluation of cervical spinal canal enlargement after en bloc open-door laminoplasty. Spinal Cord. 1997;35(10):674–9.
17. Hernández-Durán S, Zafar N, Behme D, et al. Volumetric analysis of bilateral spinal canal decompression via hemilaminectomy versus laminoplasty in cervical spondylotic myelopathy. Acta Neurochir. 2020;162:2069–74.
18. Burnard JL, Parr WC, Choy WJ, Walsh WR, Mobbs RJ. 3D-printed spine surgery implants: a systematic review of the efficacy and clinical safety profile of patient-specific and off-the-shelf devices. Eur Spine J. 2020;29(6):1248–60.
19. Garg B, Mehta N. Current status of 3D printing in spine surgery. J Clin Orthop Trauma. 2018;9(3):218–25.
20. D'Urso PS, Askin G, Earwaker JS. Spinal biomodeling. Spine. 1999;24(12):1247.
21. Zhang C, Feng Y, Yan X, Yang T, Shao C, Shang L, Zhao X. 3D printed guiding device assisted bilateral crossing cervical microendoscopic laminoplasty for cervical spondylotic myelopathy: a study protocol for a randomized controlled trial. PREPRINT (Version 1) available at Research Square; 2019. https://doi.org/10.21203/rs.2.12206/v1.
22. Ling Q, He E, Ouyang H, Guo J, Yin Z, Huang W. Design of mulitlevel OLF approach ("V"-shaped decompressive laminoplasty) based on 3D printing technology. Eur Spine J. 2018;27(Suppl 3):323–9.
23. Baba H, Uchida K, Maezawa Y, Furusawa N, Azuchi M, Imura S. Lordotic alignment and posterior migration of the spinal cord following en bloc open-door laminoplasty for cervical myelopathy: a magnetic resonance imaging study. J Neurol. 1996;243:626–63.

Nuance in Craniovertebral Junction Surgical Approach for Posterior C1-C2 Harms Stabilization: "Window Transposition" of the External Vertebral Venous Plexus for Bloodless C1 Lateral Mass Screw Insertion: Anatomical Aspects and Technical Notes

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1 Introduction

Atlantoaxial instrumentation is required when spine instability occurs at the craniocervical junction. It can be due to several pathologies, such as traumatic, neoplastic, congenital/developmental, degenerative, or inflammatory-infectious disorders [1, 2]. The main aim of fixation is to stabilize the segment, correct or reduce eventual deformity, and prevent neurological deterioration until bony fusion has been achieved. The introduction of screw-based posterior segmental instrumentation revolutionized the treatment of atlantoaxial instability (AAI). It is considered to be technically demanding because of the anatomy of the C1-C2 vertebral complex and its proximity to neural and vascular structures [3]. The first posterior screw-based approach was the transarticular C1-C2 screw technique, described by Magerl in 1979. Biomechanically, this technique offers a significantly better biomechanical profile, greater resistance to lateral bending and axial rotation than any posterior wiring or clamping technique, and higher stability in both flexion/extension (compared with the posterior wiring techniques) [4]. The reported fusion rates of C1-C2 transarticular fixation are relevant. Despite its enormously high efficacy, this technique is still considered a challenging procedure: It has several drawbacks, mostly the transarticular screw trajectory relate to superomedial orientation of C2 pedicles and the risk of vertebral artery injury during screw insertion, ranging from 1.3 to 4.1% [3, 5, 6]. Additionally, the anatomical alignment of C1 relative to C2 is mandatory; therefore, transarticular fixation is not feasible in patients with irreducible anterior, posterior, or rotatory subluxations [7, 8]. The advent of the C1-C2 screw–rod construct (C1 lateral mass and C2 pedicle polyaxial screws, respectively) in the Harms technique has revolutionized the treatment of atlantoaxial instability. It has proved to be biomechanically equivalent [9–11] or superior [12], and it is thus a reasonable option for C1-C2 transarticular fixation because of its high-quality fusion rate and the good reproducibility of correct screw positioning, as reported in literature [4]. According to the Harms technique [2], C1 lateral mass screw insertion requires the careful subperiosteal dissection of the posterior elements of C1, the identification of the screw entry point by the downward distraction of C2 nerve root, and the cautious sparing of the overlying posterior external vertebral venous plexus (peVVP), whose bleeding, obstructing the surgical field, is usually controlled by hemostatic agents and swabbing. Sometimes, venous bleeding may be persistent and hard to control, even for experienced neurosurgeons, which hinders screw placement and causes significant blood volume loss and prolonged operative time; in some cases, the stopping of the surgical procedure has also been reported [13].

The aim of this study is to describe in detail the anatomical features and surgical technique for the bloodless anatomical exposition of the posterior surface of the C1 lateral mass and the C2 pars interarticularis via the microsurgical trans-

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position of the C1-C2 interposed posterior external vertebral venous plexus as part of posterior C1-C2 Harms stabilization.

2 Methods

We report the case of a 68-year-old woman with a history of rheumatoid arthritis who experienced 2 years of paresthesia, weakness and motor disability in the left side of her body, gradual worsening in the contralateral one, and the deterioration of her quality of life. Computed tomography (CT) and MRI studies showed a retro-odontoid degenerative pseudotumor (retro-odontoid pannus), causing spinal cord compression and myelopathy (Fig. 1a–d). Upon admission, a neurological examination documented right hemiparesis, hypoesthesia in both upper limbs, the bilateral weakening of prehensile function, and hyperreflexia. Preoperative CT angiography (CTA) was performed to assess vertebral arteries' course and patency. In light of the progressive neurological symptoms and the related radiological findings, surgery was planned via a posterior cervical approach. C1-C2 fusion was performed according to the Harms technique. The postoperative course was uneventful (Fig. 1e, f).

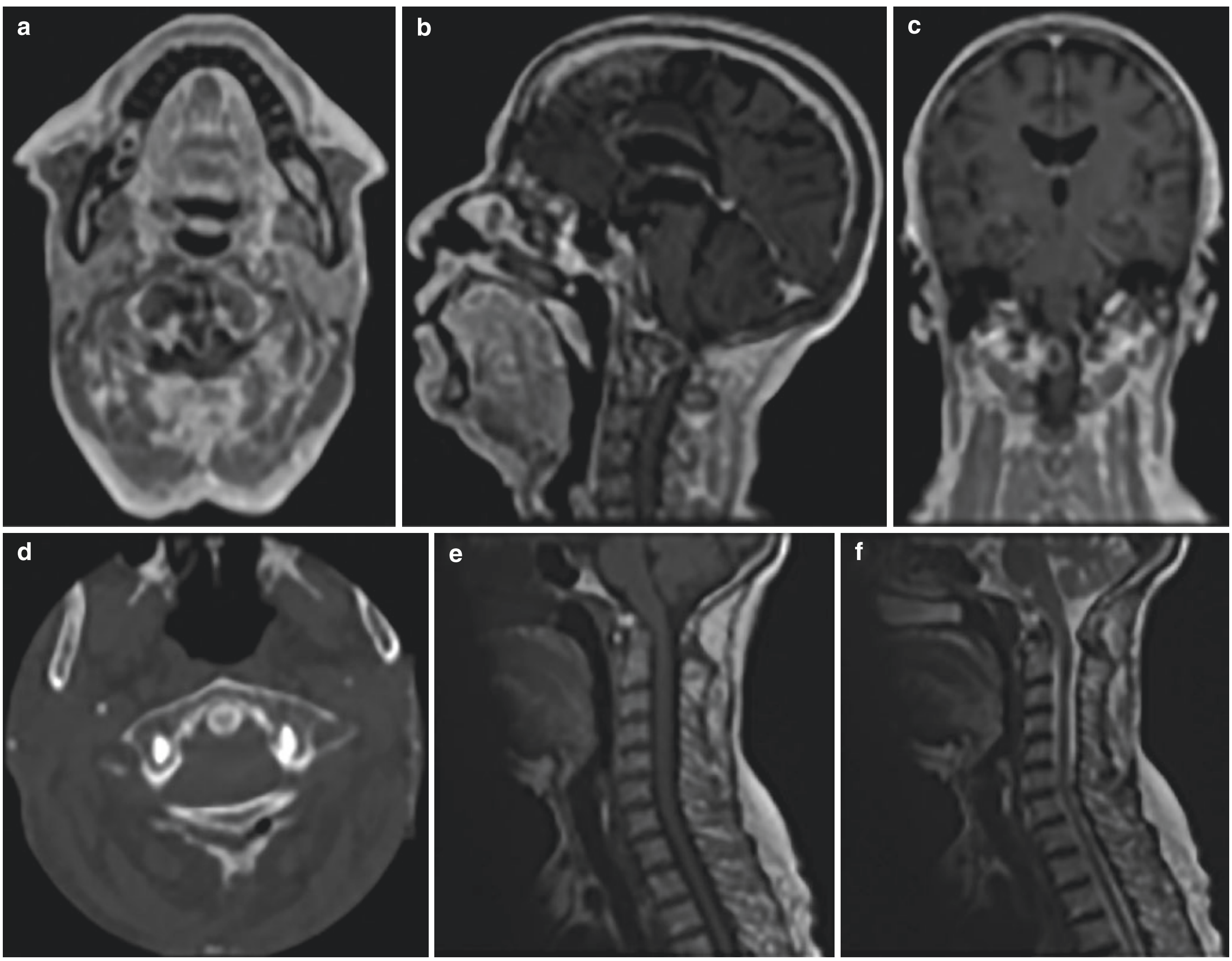

Fig. 1 Post-contrast T1 axial (**a**), sagittal (**b**), and coronal (**c**) MRI images showing a retro-odontoid degenerative pseudotumor (retro-odontoid pannus) causing spinal cord compression; (**d**) postoperative axial bone-window CT images; (**e**, **f**) 1-year postoperative T1- and T2-weighted MRI images

3 Results

3.1 Surgical Technique Description

The patient is positioned prone while the head is fixed by the Mayfield clamp in slight flexion in order to improve posterior C0-C1-C2 exposure. The midline skin incision is performed from the inion to C3. While median muscle craniocaudal dissection proceeds, the first prominent C2 spinous process comes into view, followed progressively by the exposition of the occiput, the C1 posterior tubercle, and the C3 spinous process. Subperiosteal dissection proceeds in mediolateral fashion, detaching respectively the rectus capitis major and obliquus capitis inferior from the spinous process of C2, and the rectus capitis minor from the C1 posterior tubercle. Occipitocervical muscles are progressively released from the occiput and from the posterior elements of atlas, axis, and C3, while close attention is paid to avoid atlantooccipital and atlantoaxial interlaminar space violations, vertebral artery injuries, and dural lesions. C1 lateral mass screw insertion requires, at this stage, the careful subperiosteal dissection of the inferior surface of the laminae of C1, followed by the identification of the screw entry point—which is, according to Goel et al. [7, 14], in the middle of the junction of the C1 posterior arch and the midpoint of the posterior inferior part of the C1 lateral mass. C1 screw entry point exposition requires the downward distraction of the C2 nerve root and the cautious sparing of the overlying external venous plexus, whose bleeding, obstructing the surgical field, is usually challenging and controlled by hemostatic agents and swabbing. At this point, rather than directly manipulating the C2 nerve root and the overlining venous plexus, the longitudinal median incision of the atlantoaxial membrane is performed, taking care to preserve the underlying dura mater. The atlantoaxial membrane, not vascularized at this median point, mediolaterally splits into a superficial layer and a deep layer, among which the posterior external vertebral venous plexus is confined (Fig. 2). These two layers merge before joining the periosteum of the inferior border of C1 and the superior border of C2 laminae. The longitudinal median avascular incision of the atlantoaxial membrane is followed by its mediolateral microsurgical section, respectively at the inferior border of the C1 laminae and at the superior border of the C2 laminae: This procedure allows, as a "window opening," the symmetrical mediolateral transposition of the posterior external vertebral venous plexus, which sometimes can be temporarily secured by a 5-0 suture for lateral suspension (Fig. 3). The above procedure provides a faster and cleaner mobilization of the C2 nerve root and a simpler anatomical exposition of the posterior surface of C1 lateral mass

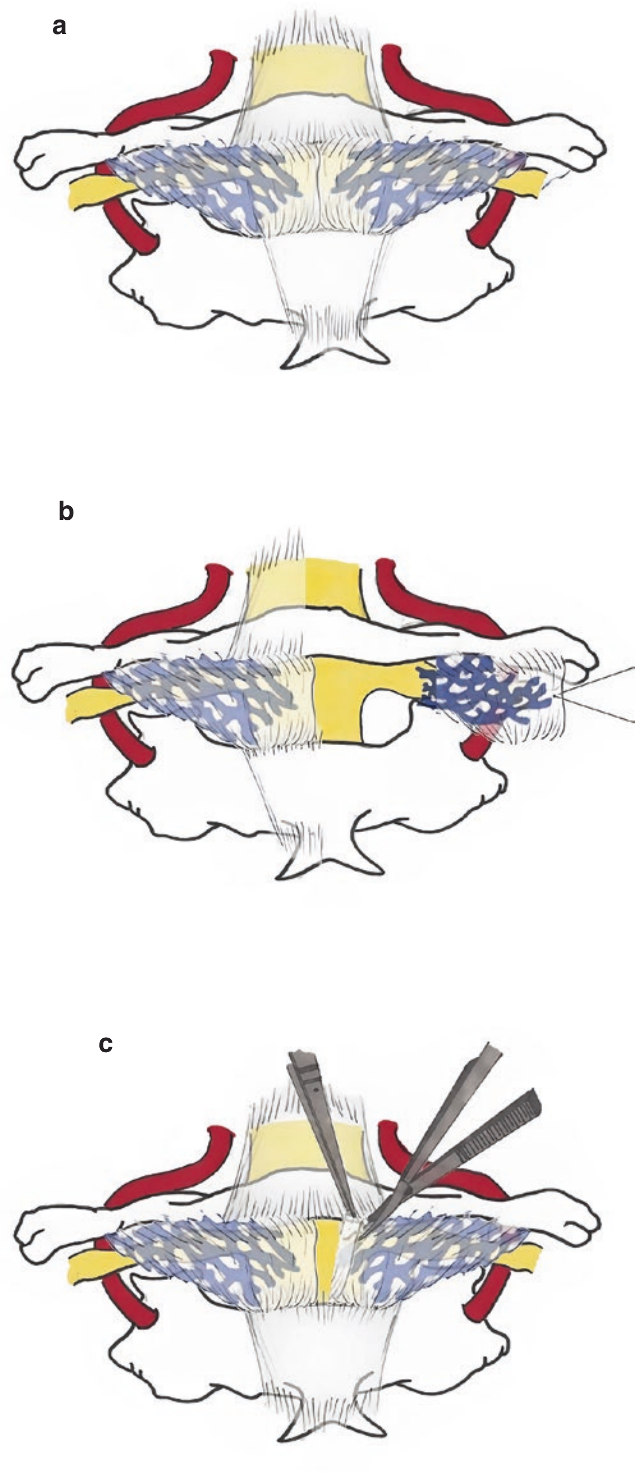

Fig. 2 Drawing anatomy of C1-C2 peVVP (**a**); longitudinal median incision and medio-lateral microsurgical section of the atlantoaxial membrane (**b**); window opening for mediolateral transposition of the peVVP (**c**)

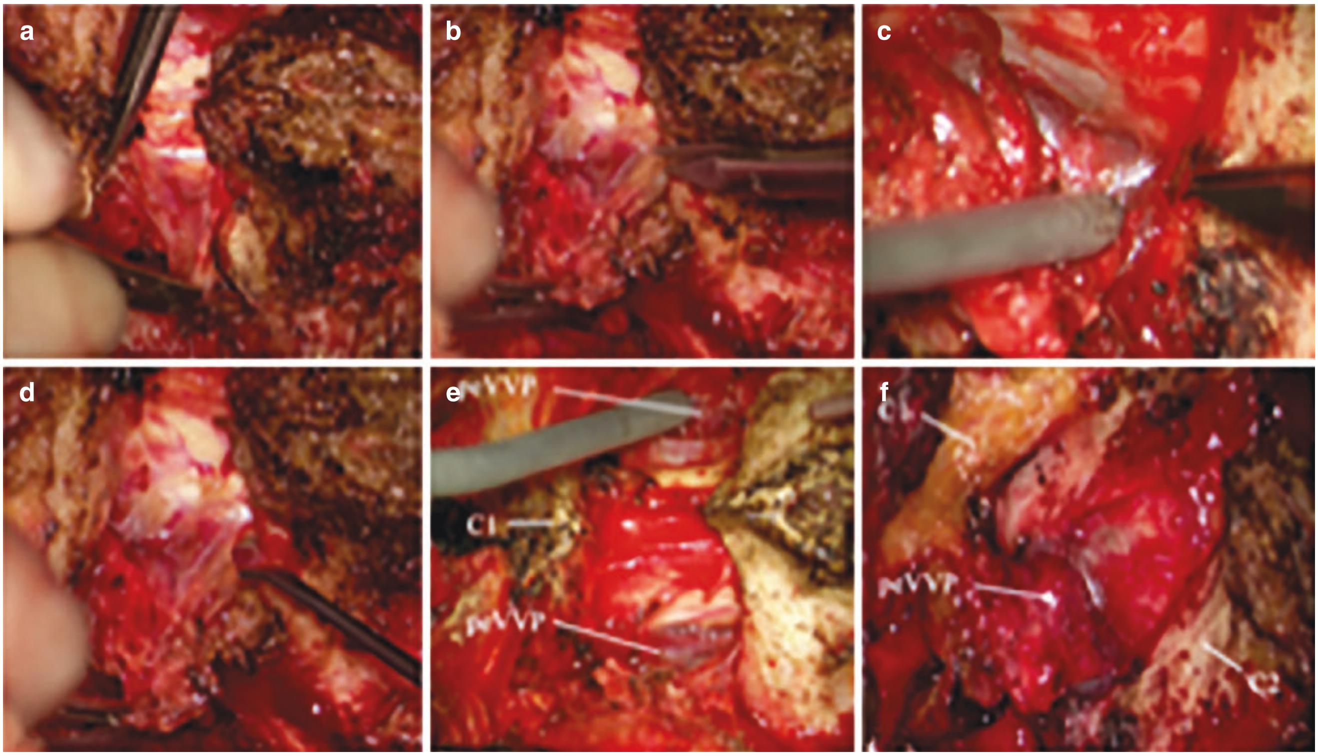

Fig. 3 Window transposition of the external vertebral venous plexus: mediolateral microsurgical section of the atlantoaxial membrane respectively at the inferior border of the C1 laminae (**a**) and at the superior border of the C2 laminae (**b–d**); in (**e**, **f**), the symmetrical mediolateral transposition of the peVVP, called the window opening; the peVVP is visualized between the superficial layer and the deep layer of the membrane

and of the C2 isthmus, preventing troublesome intraoperative venous bleeding that hinders C1 lateral mass screw insertion. Furthermore, the anatomical exposition of the C2 pars interarticularis allows the identification of the lateromedial trajectory for C2 pedicle screw insertion and decreases the risk of vertebral artery injuries. A C1 lateral mass screw and a C2 pedicle screw are then inserted according to the Harms and Melcher [2] technique. At the end, the cautious hemostasis of the surgical field is assured, and if necessary, minor bleedings are easily controlled with hemostatic agents.

4 Discussion

4.1 Harms Surgical Technique

Since its introduction, the Harms technique for atlantoaxial stabilization has represented an innovative way to avoid the risks and difficulties related to other C1-C2 fusion techniques, minimizing, for instance, the risk of injuring vertebral arteries [12]. Harms et al. modified the technique of atlantoaxial fusion, originally described by Goel in 1994 [7, 14], by introducing the polyaxial screw–rod construct [2]. As derived from the original description of the technique, the main technical difficulties faced in the Harms surgical approach concern two maneuvers: first, a typical venous bleeding arises during the aforementioned subperiosteal dissection that exposes the posterior surface of the C1 lateral mass, and second, the caudal retraction of the dorsal root ganglion of C2 exposes the entry point for the C1 lateral mass screw, which could lead to severe occipital postoperative neuralgia and the worsening of the intraoperative venous bleeding [2, 4]. Partially threaded screws have been utilized to minimize the risk of C2 root irritation, although there is no high-quality evidence of its effectiveness [2]. It has been reported in the literature that venous bleeding from nearby venous plexuses may be controlled with a combination of bipolar electrocautery, hemostatic agents, and cotton pledgets [2]. Some authors have described that these plexuses should be carefully distracted downward, preventively during exposure, by using spatulas and hemostatic agents [4]; others have suggested C2 bilateral root ligature and its sacrifice to promote hemostasis, but with obvious clinical impact (the hypoesthesia of the gonion and retroauricolar region and the risk of persistent neuralgia) [4, 13]. However, if unsuccessful bleeding control occurs, the intentional sacrifice of the C2 nerve roots remains controversial [13]. Sometimes, during the exposition of the C1 lateral mass entry point, venous bleeding may be persistent and hard to control, even for experienced neurosurgeons, causing the obscuration of the surgical field, the hindering of screw placement, significant blood volume loss, and a prolonged operative time; in some cases, the stopping of the surgical procedure has also been reported [13]. A recently published study of 50 elderly patients who underwent Harms fusion surgery for traumatic odontoid fractures reported significant intraoperative blood loss that required blood transfusion in 36% of cases [13, 15].

4.2 Vertebral Venous Plexuses in the Craniocervical Junction (CCJ) Region

The operative management of the C1-C2 region demands a deep knowledge of the microsurgical anatomy of the aforementioned vascular and neural structures, all of which are cushioned in a complex venous compartment and embedded in ligaments and membranes. Traditionally, the vertebral venous plexuses longitudinally extend from the coccyx to the skull base and have been described as segmentally consisting of four components: anterior external and anterior internal (outside and inside the spinal canal, respectively) plus posterior external and posterior internal (epidural) [16–18]. The posterior external vertebral venous plexus (peVVP) ramifies over the posterior parts of the spinous process, laminae, transverse processes, and articular facets to connect them to the posterior internal vertebral venous plexus (piVVP). First Breschet [19] in 1819 and then Batson [20] over a century later gave detailed descriptions of the vertebral venous plexus (VVP) and its functional importance. Relatively recently, the connections between the intracranial venous sinuses and the vertebral venous plexuses have received more attention, focusing on interesting similarities to the dural venous sinuses, particularly their anatomies; patterns of flow, typically bidirectional and influenced by postural, anatomical and pathological variation; and functions (the thermoregulation of the spinal cord) [18]. Radiological improvements, including angiography, have enhanced knowledge about this complex venous system. An enlightening study published by Arnautović et al. [21] has described a strikingly anatomical resemblance between this venous complex and the cavernous sinus, hence calling it the suboccipital cavernous sinus. This similarity was noticed first in 1964 by Zolnai [22] and then in 1969 by Yasargil [23]: The internal carotid artery (ICA) enters the bony petrous carotid canal accompanied by two veins and continues into the cavernous sinus, whose veins communicate with the surrounding venous structures, and the vertebral artery is surrounded by a venous plexus that communicates with the posterior VVP. This venous plexus, enveloping the vertebral artery, is composed of the venous compartment cushioning the horizontal part of the third segment of the vertebral artery (V_3h), which continues below the transverse foramen of the atlas—gradually becoming the vertebral artery venous plexus (VAVP)—that surrounds the vertical part of the third segment of the vertebral artery (V_3v). The VAVP is the inferior continuation of the aforementioned suboccipital cavernous sinus, which is between the intermediate and deep muscular layers, below the transverse foramen of the atlas, and which also proximally communicates with the transverse sigmoid sinus via the mastoid emissary and occipital veins. The VVP was also called by Batson the vertebral venous system (VVS) or Beatson's plexus because it acts as a bypass system to the canal system [18]. The piVVP lies within the spinal canal and is contained within the dural leaflets at the occipitoatlantal interspace, representing an inferior continuation of the occipital and marginal dural sinuses and the basilar venous plexus. The peVVP is at the atlantoaxial interspace, predominantly around the axis and continuing farther below it, and it connects the two contralateral venous compartments around the V_3h at the occipitoatlantal interspace and the two contralateral VAVPs at the atlantoaxial interspace. At every vertebral interspace, the internal VVP and the external VVP are connected by intervertebral veins.

4.3 Bleeding Control in C1-C2 Fixation: Literature Review

The peVVP is the main source of bleeding during the subperiosteal dissection of the C1 lateral mass entry point. Several technical modifications of the Harms technique have been attempted to reduce this venous bleeding; several alternative methods have been attempted to limit the extensive exposure of the C1-C2 facet joint; and the nerve roots have been described [24–26]. Recently, Ishak et al. [13] published a series of 63 patients surgically treated by using a modified high entry point at the junction between the C1 posterior arch and the superior-posterior C1 lateral mass, exposing only up to the medial part of the C1-C2 facet joint, while Paterson et al. [27] have proposed the use of a threaded K-wire for the insertion of a C1 lateral mass screw, which aims to avoid the extensive dissection of the C2 nerve root and to reduce the risk of significant hemorrhage from the epidural venous plexus.

So far, apart from technical variations in screw placement surgical tricks, no alternative or modified techniques have been described in the Harms technique to prevent—rather than to control—bleeding from peVVP. This is even more important given that some investigators have found that the vertebral venous plexus could represent the main intracranial venous outflow in the upright position and a secondary pathway of intracranial egress during Valsalva maneuvers or in the case of compromised internal jugular veins [18]. Venous plexus bleeding control may be sometimes challenging as it derives from large veins with concomitant significant blood flow [21]. Furthermore, in the majority of cases, the source of bleeding from a venous plexus cannot be easily identified. A variety of techniques have been used to stop venous bleeding from the peVVP, including packing it with Gelfoam, Surgicel, and/or fibrillar collagen; applying suction over the cottonoids; and bipolar cautery [28]. The injection of fibrin glue, with extreme caution for the potential reflux into the cerebral/cerebellar/brainstem veins or into major venous sinuses, was also described [28].

4.4 Authors' Technical Notes and Considerations

The aim of this study is not to demonstrate the superiority of one technique over another but rather to describe and promote a microsurgical nuance, from our lesson-learned experience, that has proved to be useful to prevent, instead of simply using tamponade, the bleeding of the vertebral venous plexus during C1-C2 exposure. The advantages of this technique, over other commonly performed hemostatic techniques, are several. First, it allows for isolating the embedded peVVP in an atraumatic way without violating it, so a careful dissection with microinstruments should be required. Furthermore, the operative field is not obstructed, contrary to what happens with the most common application of hemostatic agents during active bleeding. Probably, the dissection technique could take longer, but surely, it could balance the time that the surgeon should spend in controlling bleeding in the traditional way. The proposed technique could therefore be considered as a promising alternative to the previously reported tips and tricks suggested for C1-C2 exposure required for performing the Harms technique. Further prospective comparative studies are needed to support our findings.

5 Conclusions

Bleeding from the posterior external vertebral venous plexus during C1-C2 exposure for Harms technique fixation could be difficult to control and could result in significant blood loss. The authors describe a feasible, safe, and effective alternative operative technique to prevent and control venous bleeding, resulting in significant reductions in blood loss and operative time and allowing easier intraoperative management in the C1-C2 Harms surgical approach.

Disclosure of Interest The authors declare that they have no known personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Conflicts of Interest The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. All the coauthors have reviewed and approved the final version of the manuscript. All the coauthors had full access to all the data in the study and take responsibility for the integrity and accuracy of how the data were presented.

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References

1. Fried LC. Atlanto-axial fracture–dislocations. Failure of posterior C1 to C2 fusion. J Bone Joint Surg Br. 1973;55:490–49.
2. Harms J, Melcher RP. Posterior C1-C2 fusion with polyaxial screw and rod fixation. Spine (Phila Pa 1976). 2001;26(22):2467–71. https://doi.org/10.1097/00007632-200111150-00014.
3. Fiorenza V, Ascanio F. Safety and efficacy of posterior atlanto-axial stabilization using intraoperative navigation system with preoperative computed tomographic scan. World Neurosurg. 2019;129:110–9. https://doi.org/10.1016/j.wneu.2019.05.242.
4. Bourdillon P, Perrin G, Lucas F, Debarge R, Barrey C. C1-C2 stabilization by Harms arthrodesis: indications, technique, complications and outcomes in a prospective 26-case series. Orthop Traumatol Surg Res. 2014;100(2):221–7. https://doi.org/10.1016/j.otsr.2013.09.019.
5. Lall R, Patel NJ, Resnick DK. A review of complications associated with craniocervical fusion surgery. Neurosurgery. 2010;67:1396–402.
6. Naderi S, Crawford NR, Song GS, Sonntag VK, Dickman CA. Biomechanical comparison of C1–C2 posterior fixations, cable, graft, and screw combinations. Spine. 1998;23:1946–55, discussion 1955–6.
7. Goel A, Laheri V. Plate and screw fixation for atlanto-axial subluxation. Acta Neurochir. 1994;129:45–53.
8. Goel A, Pareikh S, Sharma P. Atlantoaxial joint distraction for treatment of basilar invagination secondary to rheumatoid arthritis. Neurol India. 2005;53:238–40.
9. Claybrooks R, Kayania M, Milks R, benzel E. Atlantoaxial fusion: a biomechanical analysis of two C1-C2 fusion techniques. Spine J. 2007;7(6):682–8.
10. Hott JS, Lynch JJ, Chamberlain RH, Sonntag VKH, Crawford NR. Biomechanical comparison of C1-C2 posterior fixation techniques. J Neurosurg Spine. 2005;2:175–81.
11. Kuroki H, Rengachary SS, Goel VK, Holekamp SA, Pitkanen V, Ebraheim NA. Biomechanical comparison of two stabilization techniques of the atlantoaxial joints: transarticular screw fixation versus screw and rod fixation. Neurosurgery. 2005;56:151–9; discussion 151–9.
12. Oda I, Abumi K, Sell LC, Haggerty CJ, Cunningham BW, McAfee PC. Biomechanical evaluation of five different occipito-atlanto-axial fixation techniques. Spine. 1999;24:2377–82.
13. Ishak B, Schneider T, Tubbs RS, Gimmy V, Younsi A, Unterberg AW, Kiening KL. Modified posterior C1 lateral mass screw insertion for type II odontoid process fractures using intraoperative computed tomography-based spinal navigation to minimize postoperative occipital neuralgia. World Neurosurg. 2017;107:194–201. https://doi.org/10.1016/j.wneu.2017.07.159.

14. Goel A, Desai KI, Muzumdar DP. Atlantoaxial fixation using plate and screw method: a report of 160 trated patients. Neurosurgery. 2002;51:1351–6;discussion 1356–7.
15. Ryang YM, Torok E, Janssen I, et al. Early morbidity and mortality in 50 very elderly patients after posterior atlantoaxial fusion for traumatic odontoid fractures. World Neurosurg. 2016;87:381–91.
16. Carpenter K, Decater T, Iwanaga J, Maulucci CM, Bui CJ, Dumont AS, Tubbs RS. Revisiting the vertebral venous plexus-a comprehensive review of the literature. World Neurosurg. 2021;145:381–95. https://doi.org/10.1016/j.wneu.2020.10.004.
17. Griessenauer CJ, Raborn J, Foreman P, Shoja MM, Loukas M, Tubbs RS. Venous drainage of the spine and spinal cord: a comprehensive review of its history, embryology, anatomy, physiology, and pathology. Clin Anat. 2015;28(1):75–87.
18. Tubbs RS, Demerdash A, Loukas M, Curé J, Oskouian RJ, Ansari S, Cohen-Gadol AA. Intracranial connections of the vertebral venous plexus: anatomical study with application to neurosurgical and endovascular procedures at the craniocervical junction. Oper Neurosurg (Hagerstown). 2018;14(1):51–7. https://doi.org/10.1093/ons/opx080.
19. Nathoo N, Caris EC, Wiener JA, Mendel E. History of the vertebral venous plexus and the significant contributions of Breschet and Batson. Neurosurgery. 2011;69(5):1007–14; discussion 1014.
20. Batson OV. The function of the vertebral veins and their role in the spread of metastases. Clin Orthop Relat Res. 1940;1995(312):4–9.
21. Arnautović KI, al-Mefty O, Pait TG, Krisht AF, Husain MM. The suboccipital cavernous sinus. J Neurosurg. 1997;86(2):252–62.
22. Zolnai B. Die zwischen der arteria vertebralis und den vertebralen und zerbralen venen bestehende verbindung am atlantookzipitalen abschnitt beim menschen. Anat Anz Bd. 1964;114:400–7.
23. Yasargil MG. Microsurgery. Applied to neurosurgery. New York: Thieme; 1969. p. 82–8.
24. Hitti FL, Hudgins ED, Chen HI, Malhotra NR, Zager EL, Schuster JM. Intraoperative navigation is associated with reduced blood loss during C1-C2 posterior cervical fixation. World Neurosurg. 2017;107:574–8.
25. Lee SH, Kim ES, Eoh W. Modified C1 lateral mass screw insertion using a high entry point to avoid postoperative occipital neuralgia. J Clin Neurosci. 2013;20(1):162–7.
26. Moisis M, Fisahn C, Tkachenko L, Jeyamohan S, Reinties S, Grunert P, et al. Posterior arch C1 screw technique: a cadaveric comparison study. J Neurosurg Spine. 2017;26(6):679–83.
27. Paterson A, Byrne S, Hansen M, Kuru R. Modified C1 lateral mass screw insertion using a threaded K-wire. A technical note. J Clin Neurosci. 2020;79:95–9. https://doi.org/10.1016/j.jocn.2020.07.036.
28. Sekhar LN, Natarajan SK, Manning T, Bhagawati D. The use of fibrin glue to stop venous bleeding in the epidural space, vertebral venous plexus, and anterior cavernous sinus: technical note. Neurosurgery. 2007;61(3 Suppl):E51;discussion E51

Emergency Treatment of Cervical Vertebromedullary Trauma: 10 Years of Experience and Outcome Evaluation

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1 Introduction

Traumatic cervical spine fractures are rare but often result in significant morbidity and death.

Cervical spine injury occurs in 3% of blunt trauma victims, but the results of spinal cord injuries can be devastating. The subaxial spine runs from C3 to C7 and is one of the most common sites of cervical spine injuries. In adults, approximately 63% of spinal cord injuries involve the cervical spine, of which 75% occur in the C3–C7 region; of those injuries, 50% occur between C5 and C7 [1, 2].

The most prevalent mechanisms of injury described in the literature are typically motor vehicle accidents (MVAs) and/or falls [1, 3]. Most often, these are highly unstable dislocated fractures involving the anterior column and the posterior tension band. These injuries are often responsible for causing secondary damage to the spinal cord.

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There is currently no gold standard of treatment. Surgically treated patients have been reported to have lower mortalities than nonsurgically treated patients [4].

In recent years, many clinical trials and cohort studies have compared the efficacies of early and late surgical decompression types, which together provide a suitable basis for conducting a meta-analysis on human studies. But none of these studies has been able to determine which is the best surgical approach for dislocated fractures. In the literature, studies on the correct surgical treatment for cervical fractures/dislocations with high levels of evidence are few. Furthermore, there is currently no consensus on what classification systems should be used to make the treatment acceptable [5].

2 Materials and Methods

The present investigation consists of a retrospective study. All the patients affected by cervical spine injuries (SCIs) who were treated at the Policlinico Gemelli Emergency Room (ER) from January 2010 to January 2020 were analyzed.

Inclusion criteria was the presence of traumatic subaxial cervical spine fracture/dislocation. Data were obtained from the study on patient imaging, mostly computed tomography (CT) scans; magnetic resonance imaging (MRI) scans were requested to demonstrate ligament or disk lesions, in the event of doubts after the analysis of the CT scan. X-rays were used only during follow-up. We used the American Spinal Injury Association (ASIA) system for clinic evaluation upon arrival and at the final follow-up. The patients were divided into three groups: patients who had surgery within 12 h, from 12 to 24 h, and after 24 h from their arrival in the ER.

The timing of follow-up was at 3, 6, and 12 months after the accident and then every year thereafter. We used both imaging and clinical criteria: cervical spine CT scans, X-rays in antero-posterior and lateral projections, and the Italian version of the Neck Disability Index were used to evaluate

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residual deficits and disabilities in everyday activities. This questionnaire was self-administered in order to avoid acquiescence bias.

We have also analyzed short- and medium-term complications, the application of the Nascis III protocol, the 5-year mortality rate, comorbidities, and other lesions upon arrival at the ER.

We analyzed the ASIA scores before and after surgery with the anterior approach or the posterior approach by using changes in chi-squared tests and ASIA scores among the different groups according to the results from paired sample of Student *t*-tests.

3 Results

In total, 80 patients responded to the criteria: a one- or two-level cervical spine injury with or without medullary involvement. The median age was 45.1 (15–88 years). The study included 64 men and 16 women (M:F = 5:1). Among these, 15 patients had spondylopathy histories, and 15 were polytrauma patients. The causes of trauma were car accidents in 30 patients, downfalls in 42, and other causes in the remaining eight patients.

The highest prevalence was in the C6-C7 involvement (37%, 30 patients), followed by that in C5-C6 (22.5%, 18), C3-C4 (12.5%, 10 patients), C4-C5 (18.75%, 15 patients), C7-T1 (6.25%, 5 patients), and C2-C3 (2.5%, 2 patients)—as shown in Table 1.

In total, 50 patients underwent the posterior approach, and 24 patients underwent the anterior approach. Both approaches were performed in six patients: one-stage surgery in two cases, and the two-stage surgeries were deferred by 6 days in four cases—11 days in one case and 52 days in the last case. Moreover, 22 patients underwent surgery with posterior cervical decompression and fusion within 12 h; 20 patients between 12 and 24 h (12 one-stage anterior approach and eight posterior); and the remaining 38 patients after 24 h from their arrival. Specifically, 13 underwent the anterior approach, 19 the posterior approach, and six the combined one.

The ASIA scores are shown in Table 2, describing patients' neurological statuses upon arrival and at their final follow-up.

Despite early intervention (within 24 h of arrival at the ER), we observed in less than 50% patients a statistically significant improvement in their ASIA scores, and there were no statistically significant differences between the various surgical approaches. The average follow-up time was 4.2 years (1–8.5 years).

The most common complication was tracheostomy, in 12 patients (11 of them were treated with only the posterior approach and the other with the combined one). In those patients, the levels of fractures were C3-C4 (two cases), C4-C5 (four cases), and C7-T1 (two cases).

The values calculated according to the Student *t*-test for determining changes in the ASIA scores were $p = 0.0000007$ in the group of anterior approaches and $p = 0.0000000014$ in the group of posterior approaches. The unpaired data for the preoperative ASIA group was 0.33 and for postoperative ASIA group was 0.34. They were not statistically significant. Table 3 presents the differences among ASIA scores between the anterior approach and the posterior approach, which are not statistically significant ($p < 0.05$)

Further complications were soft tissue infections in three patients, each of whom required a wound revision; dural tears in five patients (three who underwent the posterior approach and two the anterior approach); anterolisthesis needing corpectomy in two patients 15 months after surgery;

Table 1 The prevalence of level involvement

Level	Prevalence
C6-C7	30 (37%)
C5-C6	18 (23.07%)
C3-C4	10 (18.5%)
C4-C5	15 (18.75%)
C7-T1	5 (6.25%)
C2-C3	2 (2.5%

Table 2 ASIA score changes from arrival to follow-up

ASIA score	ASIA change
A-A	13
A-B	12
B-C	9
B-B	4
C-C	2

Table 3 ASIA score prevalence in different surgical approaches upon arrival and at final follow-up

Arrival	A	B	C	D	E
ant	36%	40%	16%	8%	0
post	31%	52%	17%	0	0
both	50%	50%	0	0	0
p-value (ant-post)	0.9289756057	0.8705046383	0.9761496987	–	–
p-value (ant-both)	0.8430529669	0.887537084	–	–	–
p-value (post-both)	0.7885354328	0.9805471143	–	–	–

Table 3 (continued)

Follow-up	A	B	C	D	E
ant	16%	28%	12%	20%	24%
post	17%	17%	14%	28%	24%
doppio	25%	0	50%	25%	0
p-value (ant-post)	0.9761496987	0.7955566211	0.9614924657	0.8851553412	0.9977599822
p-value (post-both)	0.8766853954	–	0.6086210265	0.9587485037	–

and the loosening of fixation devices in two patients (one anterior approach and one posterior approach).

The overall survival at 5 years was 46%. Surgery-related mortality was 3.8%, and 2-year mortality was 16%. The average of disability registered at follow-up was 43.4% (26–100%), calculated by using the Italian version of the NDI.

4 Discussion

Despite the overall low incidence of severe subaxial cervical fractures/dislocations, there is still a great debate in the literature on the classifications and their respective abilities to offer easy and reliable systems for use both in emergencies to establish the severity of injuries and after emergencies to assist spinal surgeons in planning appropriate treatments (conservative and/or surgical). Many researchers believe that treatment decisions are likely to be affected by the neurological status of the patient, the interpretation of a disk herniation, and the classification of the injury as a unilateral or bilateral injury [4, 6–8].

In our study, there were no statistically significant changes in ASIA scores, using either the anterior approach or the posterior approach, probably due to the low number of cases. The ASIA changes in patients treated with different surgical approaches were not statistically significant, proving that there was no reason to prefer one of them.

Good clinical outcomes have been reported with the use of a posterior approach; in support of this, many biomechanical studies have demonstrated the superiority of the posterior stabilization method to resist flexion-extension injuries over anterior arthrodesis [9, 10].

The authors supporting the anterior approach have stated that one of the advantages of this approach is the direct decompression of the spinal cord, especially when there are disk injuries and any ejected disk fragments. Among the positive factors of the anterior approach, there are also lower traumatic surgical access and usually shorter-level fusions. However, especially in the case of the dislocation and subluxation of the facet joints, a failure to reduce them with the anterior approach implies that a second posterior approach for reduction is required [11]. Radcliff and coworkers reported a 61.5% incidence of dysphagia after anterior cervicotomy [12].

Other described complications that can occur include respiratory crisis, which in some case studies such as that of Visocchi et al. is zero as both a transient and permanent complication [8]. Moreover, the work of Della Pepa et Al. also reports an almost zero incidence of the complication respiratory crisis [13].

According to several authors, the posterior cervical approach is disadvantageous compared to the anterior one because it comes with greater blood loss, longer surgical times, and longer hospital stays than the anterior approach group does. On the other hand, the dislocated or subdislocated joint facets can be reduced under direct visualization with the posterior approach, avoiding traction maneuvers and their associated consequences. This method is more advantageous if the dislocation is unilateral [14–16].

The distraction that is exerted on the ligament structures results in a loss of integrity in the posterior ligament complex. These structures are fundamental to maintaining the cervical axis, and they act as stabilizers in the flexion movements of the spine. Consequently, in planning the treatment of these traumas, it should be considered in restoring their relationships. This is much easier when performing posterior approach surgery via fixation. Furthermore, in combined approaches, this facilitates anterior cervical instrumentation [6]. However, hardware failure and/or delayed cervical deformity after the single anterior approach is a non-negligible complication, which has been observed in previous studies [15, 17–19].

The posterior lateral mass screw fixation clinically provides excellent correction for fractured vertebra and a high fusion rate. Consequently, several authors have agreed that with these techniques, it is possible to save the stabilized segments in separation fractures or fractures with mild comminution, on the basis of an evaluation of the adjacent disk and ligament. However, severely comminuted lateral mass fractures with coronal plane malalignment required more-level posterior fixation. Furthermore, exclusive posterior stabilization with a cervical pedicle screw system provides short fusion and a normal spinal alignment, even in lateral mass fractures with severe spinal instability.

Cervical pedicle screws yield the best results in single-stage posterior fusion for various pathologies of the subaxial cervical vertebrae. The mini-laminotomy technique is the treatment of choice among experienced surgeons because it poses a negligible risk of neurovascular injury during transpedicular screw fixation, without morbidity or mortality [20, 21].

Biomechanical work has shown that the extraction force of screws in different positions is greater when they are positioned at the level of the pedicle, with an 88% increase in extraction force compared to screws positioned in the lateral mass [22, 23].

The unstable type fractures or the split type and the comminution type injuries with coronal malalignment can be treated with exclusive two-level posterior stabilization, demonstrating excellent clinical outcomes without pseudoarthrosis [24]. Even in our experience, there were only two cases of implant failure from using the posterior approach that needed subsequent revision.

Special attention should be paid to similar spondylolytic patients. At our institute over the years, several patients have been treated for spondylopathies. Most of them also underwent an MRI before the surgery. MRI in these patients is useful for diagnosing the presence of epidural hematomas, which may be the main cause of medullary compression [17].

Some authors believe that even in cases of trauma, corpectomy may be a treatment option to be considered [25].

As far as surgical timing is concerned, it is universally accepted that surgery must be performed in the shortest possible amount of time. But this does not change the final result of recovery from neurological damage, because the inflammatory biomolecular cascade that is triggered following a spinal cord injury is only the secondary cause of neurological failure [19].

The situations in which it is mandated to intervene surgically quickly is when one is faced with mechanical instability, which is often clinically not very significant but can worsen rapidly. Because rapid and effective surgery can prevent neurolgic damage before it sets in [26].

Despite being a retrospective study, even in our case, we have not recorded any significant changes in the ASIA scores in cases treated early, within 12 h of the trauma, or significant differences between the group treated within 24 h and the group treated beyond 24 h.

5 Conclusion

The evidence from our study shows that choosing the anterior rather than the posterior route did not yield clear advantages in terms neurological recovery. Thus, although the type of approach remains a matter of fervent debate, the prevalence of one type over the other is also dictated by the manual dexterity and confidence that individual surgeons have in the surgical technique, conditioned secondarily by their wealth of experience. Opting for rapid surgery certainly gives the patient a better chance of recovery and a lower perioperative mortality rate.

References

1. Wang H, Xiang Q, Li C, Zhou Y. Epidemiology of traumatic cervical spinal fractures and risk factors for traumatic cervical spinal cord injury in China. J Spinal Disord Tech. 2013;26:E306–13.
2. Woodworth RS, Molinari WJ, Brandenstein D, Gruhn W, Molinari RW. Anterior cervical discectomy and fusion with structural allograft and plates for the treatment of unstable posterior cervical spine injuries. J Neurosurg Spine. 2009;10(2):93–101. https://doi.org/10.3171/2008.11.SPI08615. PMID: 19278321.
3. Morganti C, Sweeney CA, Albanese SA, Burak C, Hosea T, Connolly PJ. Return to play after cervical spine injury. Spine (Phila Pa 1976). 2001;26:1131–6.
4. Pearson AM, Martin BI, Lindsey M, Mirza SK. C2 vertebral fractures in the Medicare population: incidence, outcomes, and costs. J Bone Joint Surg Am. 2016;98:449–56.
5. Sribnick EA, Hoh DJ, Dhall SS. Traumatic high-grade cervical dislocation: treatment strategies and outcomes. World Neurosurg. 2014;82(6):1374–9. https://doi.org/10.1016/j.wneu.2014.02.008. Epub 2014 Feb 14. PMID: 24530458.
6. Brodke DS, et al. Comparison of anterior and posterior approaches in cervical spinal cord injuries. J. Spinal Disord Tech. 2003;16(3):229–35.
7. Nassr A, Lee JY, Dvorak MF. Variations in surgical treatment of cervical facet dislocations. Spine. 2008;33(7):E188–93.
8. Visocchi M, Iacopino G, Germanò A, Barbagallo G. Focus on functional delayed central sleep apnea following cervical laminectomy. an example of respiratory dysfunction in restorative neurosurgical procedures. Acta Neurochir Suppl. 2017;124:219–20. https://doi.org/10.1007/978-3-319-39546-3_33. PMID: 28120077.
9. Panczykowski DM, Tomycz ND, Okonkwo DO. Comparative effectiveness of using computed tomography alone to exclude cervical spine injuries in obtunded or intubated patients: meta-analysis of 14,327 patients with blunt trauma. J Neurosurg. 2011;115:541–9.
10. Pizones J, Sanchez-Mariscal F, Zuniga L, et al. Prospective analysis of magnetic resonance imaging accuracy in diagnosing traumatic injuries of the posterior ligamentous complex of the thoracolumbar spine. Spine. 2013;38:745–51.
11. Eismont FJ, Arena MJ, Green BA. Extrusion of an intervertebral disc associated with traumatic subluxation or dislocation of cervical facets. Case report. J Bone Joint Surg Am. 1991;73:1555–60.
12. Radcliff KE. What is the incidence of dysphagia after posterior cervical surgery? Spine. 2013;38(13):1082–8.
13. Della Pepa GM, La Rocca G, Barbagallo G, Spallone A, Visocchi M. Transient breathing disorders after posterior cervical surgery for degenerative diseases: pathophysiological interpretation. Eur Rev Med Pharmacol Sci. 2014;18(1 Suppl):89–92. PMID: 24825050.
14. Quarrington RD, et al. Traumatic subaxial cervical facet subluxation and dislocation: epidemiology, radiographic analyses, and risk factors for spinal cord injury. Spine J. 2018;18(3):387–98.
15. Reindl R, et al. Anterior reduction for cervical spine dislocation. Spine (Phila Pa 1976). 2006;31:648–52.
16. Theodotou CB, Ghobrial GM, Middleton AL, Wang MY, Levi AD. Anterior reduction and fusion of cervical facet dislocations. Neurosurgery. 2019;84(2):388–95. https://doi.org/10.1093/neuros/nyy032. PMID: 29547951.
17. Tamburrelli FC, Meluzio MC, Masci G, Perna A, Burrofato A, Proietti L. Etiopathogenesis of traumatic spinal epidural hematoma. Neurospine. 2018;15(1):101–7. https://doi.org/10.14245/

ns.1834938.469. Epub 2018 Mar 28. PMID: 29656630; PMCID: PMC5944636.
18. Torretti JA, Sengupta DK. Cervical spine trauma. Indian J Orthop. 2007;41:255–67.
19. Yan L, Luo Z, He B, et al. Posterior pedicle screw fixation to treat lower cervical fractures associated with ankylosing spondylitis: a retrospective study of 35 cases. BMC Musculoskelet Disord. 2017;18(1):81.
20. Celikoglu E, Borekci A, Ramazanoglu AF, Cecen DA, Karakoc A, Bektasoglu PK. Posterior transpedicular screw fixation of subaxial vertebrae: accuracy rates and safety of mini-laminotomy technique. Asian J Neurosurg. 2019;14(1):58–62. https://doi.org/10.4103/ajns.AJNS_178_17. PMID: 30937009; PMCID: PMC6417301.
21. Nakashima H, Yukawa Y, Ito K, et al. Posterior approach for cervical fracture-dislocations with traumatic disc herniation. Eur Spine J. 2011;20:387–94.
22. Caron T, Bransford R, Nguyen Q, et al. Spine fractures in patients with ankylosing spinal disorders. Spine (Phila Pa 1976). 2010;35:E458–64.
23. Mountney J, Murphy AJ, Fowler JL. Lessons learned from cervical pseudoarthrosis in ankylosing spondylitis. Eur Spine J. 2005;14:689–93.
24. Kotani Y, Abumi K, Ito M, Minami A. Cervical spine injuries associated with lateral mass and facet joint fractures: new classification and surgical treatment with pedicle screw fixation. Eur Spine J. 2005;14(1):69–77. https://doi.org/10.1007/s00586-004-0793-2. Epub 2004 Nov 3. PMID: 15723250; PMCID: PMC3476686.
25. Pescatori L, Tropeano MP, Visocchi M, Grasso G, Ciappetta P. Cervical spondylotic myelopathy: when and why the cervical corpectomy? World Neurosurg. 2020;140:548–55. https://doi.org/10.1016/j.wneu.2020.03.100. PMID: 32797986.
26. Visocchi M, Di Rocco F, Meglio M. Subacute clinical onset of postraumatic myelopathy. Acta Neurochir (Wien). 2003;145(9):799–804; discussion 804. https://doi.org/10.1007/s00701-003-0082-6. PMID: 14505109.

Long-Term Clinical and Radiographic Outcomes After Bryan Cervical Disk Arthroplasty: A Systematic Literature Review

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1 Introduction

Cervical disk arthroplasty (CDA) is a potential alternative procedure to anterior cervical decompression and fusion (ACDF) that represents the gold-standard treatment for cervical disk disease [1]. ACDF is a valid, reliable, and repeatable procedure for the treatment of radiculopathy and/or myelopathy [2], but several potential limitations specific to ACDF, including adjacent segment disease (ASD), perioperative immobilization, pseudarthrosis, and bone graft site morbidity, have been identified [3]. These well-documented potential complications, above all the ASD, have led to a search for motion-preserving alternatives that will slow down the adjacent segment degeneration [4–8]. Many studies reported in literature have concluded that the use of Bryan cervical disk arthroplasty (BCDA) had acceptable to good clinical and functional outcomes in the short term [9, 10] and mid term [11, 12]. A recent long-term (18-year) follow-up retrospective study revealed the acceptable survival of the adjacent segment (AS) and good clinical results with the optimal resolution of the symptoms over time [13]. However, another recent prospective comparative study found that adjacent level degeneration occurs in a similar manner in both the ACDF group and the total disk arthroplasty group [14]. The aim of the study was to perform a systematic literature review on long-term clinical and radiological outcomes after the implantation of a BCDA.

2 Material and Methods

2.1 Study Setting and Search Strategy

In the present study, a systematic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). Medline via PubMed and Embase, Scopus, and the Cochrane Library database were searched while using the keywords "Bryan prosthesis", "cervical disk arthroplasty", "outcomes", and "long-term follow-up" and their MeSH terms in any possible combinations using the logical operators "AND" and "OR." The reference lists of relevant studies were forward screened to identify other studies of interest. The search was reiterated until April 10, 2021.

2.2 Inclusion and Exclusion Criteria

In this review, the full-text articles describing the long-term outcomes (at least 10 years of follow-up), after Bryan cervi-

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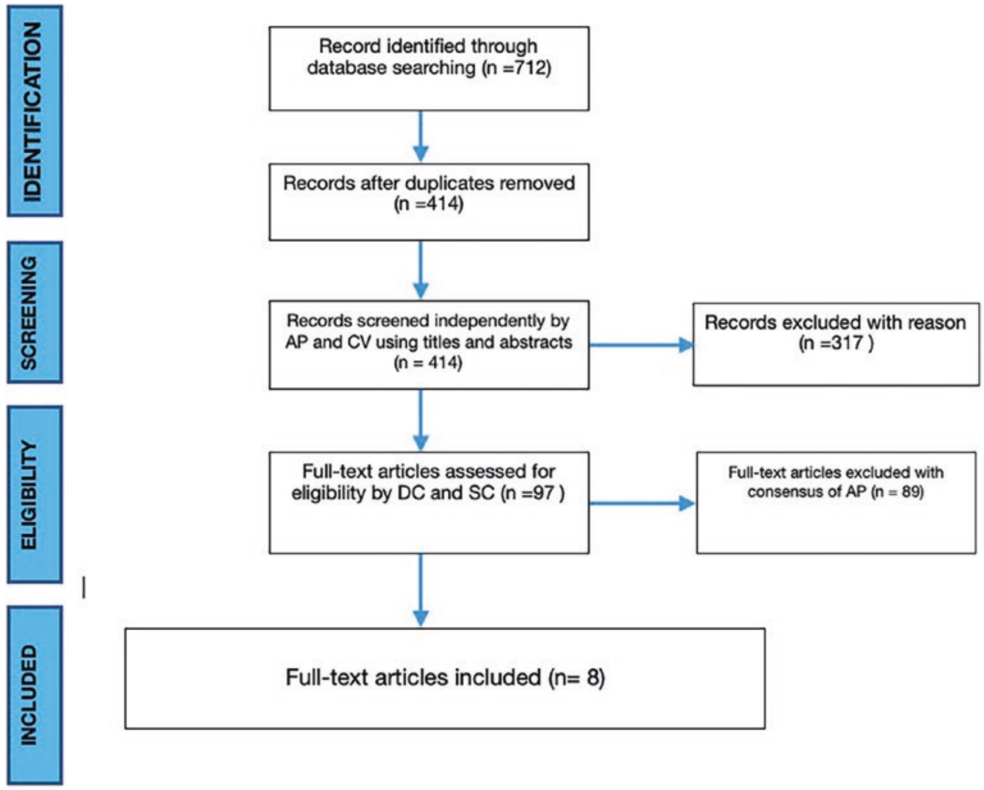

Fig. 1 PRISMA flowchart

cal disk arthroplasty for cervical degenerative diseases were considered eligible. Only articles written in English were included. No date limits were set on publication. Expert opinions, studies on animals, unpublished reports, in vitro investigations, case reports, letters to the editor, abstracts from scientific meetings, and book chapters were excluded from this review.

2.3 Data Extraction and Analysis

Two independent authors (A.P. and C.V.) searched and collected data from the included studies. Any discordances were solved by consensus with a third author (A.S). The following data were extracted: demographic features, diagnosis, the presence of periprosthetic ossification, range of motion of the treated segment, sagittal alignment, segmental and global lordosis, possible complications, clinical outcomes and follow-up. Risk of bias and quality assessments of included studies was checked using Cochrane risk of bias tool (Fig. 2). Numbers software (Apple Inc., Cupertino, CA) was used to tabulate the obtained data. Categorical variables are presented as frequency and percentages. Continuous variables are presented as means and standard deviation. Only one decimal digit was reported and was rounded up.

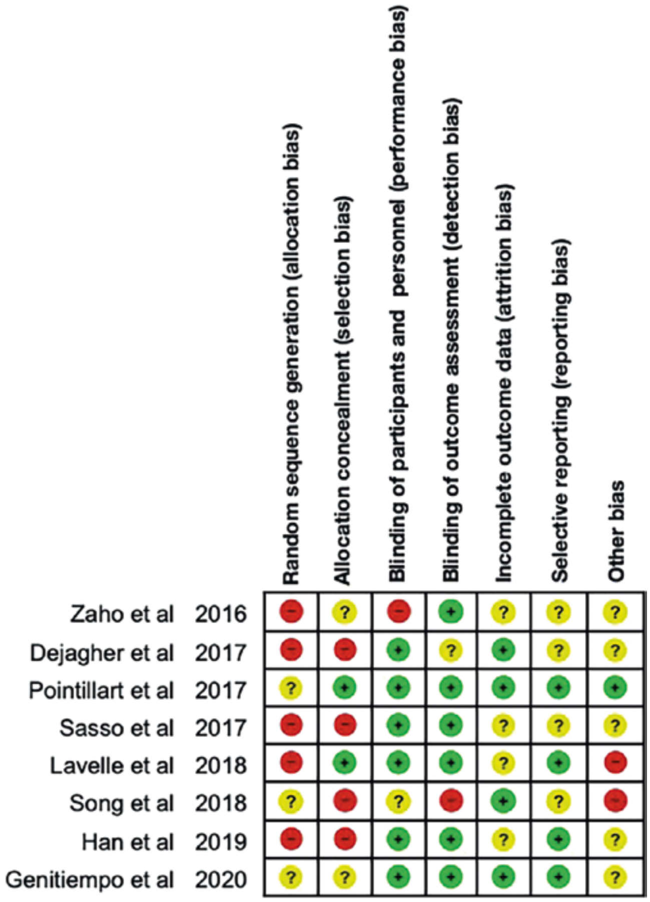

Fig. 2 Cochrane risk of bias tool for bias and quality assessments of included studies

3 Results

3.1 Study Selection

After electronic research of the literature 414 articles were retrieved and reviewed by title and abstract after duplicate removal. Ninety-seven articles were included for full text revision. Only eight articles with at least 10 years of follow up were considered for eligibility [11–13, 15–19]. Therefore, full text papers were downloaded, carefully reviewed and clinical, surgical and radiological data were collected as described below. All studies included in the review are Level of Evidence (LoE) IV.

3.2 Patient Characteristics

A total of 481 patients were enrolled in the studies. Among the reported results, the M:F ratio was 1.09:1 (241 M, 221 F) and the mean age was 41.61 years. Sasso et al. [18] did not describe any demographic data among the 19 patients included in their study. Other demographic data are summarized in Table 1.

3.3 Diagnosis

Clinical data were reported from all eight studies included in the review. The 481 patients included were affected by spondylotic myelopathy or cervical radiculopathy or cervical disk herniation or degenerative cervical canal stenosis. *Lavelle* et al. included in their study only patients who were not responding to at least 6 weeks of nonoperative management [16]. *Han* et al., divided instead the patients who underwent surgery in two groups according to the pathology presented: radiculopathy and myelopathy [11]. Patients included in the study of *Dejaegher* et al. had either radiculopathy or myelopathy caused by spondylosis and/or disk herniation that did not respond to conservative treatment [15]. *Pontillart* et al., included patients with cervical disk herniation or spondylosis with radiculopathy that had not responded to conservative treatment for at least 6 weeks [17]. *Sasso* et al. included in their study patients with single-level cervical degenerative disk disease with 6 weeks of failed non-operative treatment for either cervical radiculopathy or myelopathy [18]. In the prospective study of *Song* et al., the patients included underwent cervical disk arthroplasty for single-level cervical disk herniation or degenerative cervical canal stenosis between C3/4 and C6/7 levels with no response to conservative treatment for at least 12 weeks [12]. Other data were summarized in Tables 2 and 3.

3.4 Surgical Technique

In all included studies the same surgical technique was reported. All procedures were performed in general anesthesia and supine position through a standard anterior approach according to Smith–Robinson. A complete discectomy was performed and after the preparation and milling of the vertebral endplates, the disk was replaced by a Bryan Prosthesis. Due to multiple levels treatment in some of the 481 patients, a total of 588 arthroplasty were performed, divided as follows: 12 C3/4 cervical disk arthroplasty (2.01%), 63 C4/5 (10.71%), 325 C5/6 (55.27%), 188 C6/7 (31.97%).

3.5 Sagittal Alignment

Among the included articles, two of them described the preoperative and the last follow up cervical lordosis (CL) [12, 13]. A total of 128 patients were assessed for cervical sagittal alignment (C2-C7). Measurements were conducted on standing radiographs with the Cobb method. The mean preoperative cervical lordosis was 13.6 ± 9.3° whereas the last follow up value was 12.8 ± 8.7°. Both articles reported a mild decrease of the CL but no further statistical analysis is possible due to the small number of included papers. Segmental cervical lordosis was also evaluated and a similar decrease was described as shown in Table 1.

Table 1 Demographic and surgical data of patients

Authors	Year	N° of patients	Male/female	Mean age	Diagnosis	Treated level	
Zaho et al.	2016	33	19/14	44.8	Spondylotic myelopathy or cervical radiculopathy	**42**	
						3	C3/C4
						7	C4/C5
						26	C5/C6
						6	C6/C7
Dejagher et al.	2017	89	38/51	43.2 ± 9.0	Spondylotic myelopathy or cervical radiculopathy	**89**	
						1	C3/C4
						2	C4/C5
						34	C5/C6
						52	C6/C7
Pointillart et al.	2017	18	10/8	46.2	Spondylotic myelopathy or cervical radiculopathy	**22**	
						2	C4/C5
						11	C5/C6
						9	C6/C7
Sasso et al.	2017	19	–	–	Spondylotic myelopathy or cervical radiculopathy	–	
Lavelle et al.	2018	128	58/70	44.4	Radiculopathy or Myelopathy from single-level cervical disk disease that had failed at least 6 weeks of nonoperative management	**242**	
						3	C3/C4
						12	C4/C5
						140	C5/C6
						87	C6/C7
Song et al.	2018	71	44/27	55.69 years	Myeloradiculopathy, cervical disk herniation, degenerative cervical canal stenosis	**70**	
						2	C3/C4
						14	C4/C5
						45	C5/C6
						9	C6/C7
Han et al.	2019	66	41/25	55.9 ± 7.9 years	Spondylotic myelopathy or cervical radiculopathy	**66**	
						2	C3/C4
						13	C4/C5
						43	C5/C6
						8	C6/C7
Genitiempo et al.	2020	57	31/26	42.7 (±12.7) years	Spondylotic myelopathy or cervical radiculopathy	**57**	
						1	C3/C4
						13	C4/C5
						26	C5/C6
						17	C6/C7
Total	–	481	241/221	41.61 years	–	**588**	
						12	C3/C4
						63	C4/C5
						325	C5/C6
						188	C6/C7

The bold is the total of patient treated in the examined study

Table 2 Clinical and radiographic data of patients before surgery

Preoperative								
Authors	Cervical lordosis	Disk angle	Cervical spine ROM	Discal ROM	VAS	NDI	SF-36	mJOA
Zaho et al.	–	–	–	7.8 ± 2.7°	6.5	28.4	–	11.8 ± 1.7
Dejagher et al.	–	–	–	8.79°	–	40.7	35.2	–
Pointillart et al.	–	–	–	6.5 ± 4.1°	Neck 5.5	40.6	–	–
					Arm 5.8			
Sasso et al.	–	–	–	–	Neck 7.18	50.45	–	–
					Arm 7.77			
Lavelle et al.	–	–	–	6.5°	Neck 75.4	51.4	32.6	–
					Arm 71.2			
Song et al.	12.3 ± 10.6°	2.1 ± 1.3°	45.9 ± 15.2°	9.7 ± 4.5°	–	27.6 ± 8.8	–	13.0 ± 2.7
Han et al.	–	–	45.5 ± 15.1°	–	–	28.0	–	12.0/15.0
			45.8 ± 15.7°			26.0		
Genitiempo et al.	15.1 ± 7.6°	3.1 ± 1.2°	48.2 ± 12.7°	10.1 ± 3.1°	7.2 ± 1.4	28.2 ± 10.6	35.3 ± 8.2	–

mJOA Modified Japanese Orthopedic Association, *NDI* Neck Disability Index, *ROM* range of motion, *SF-36* short-form-36, *VAS* visual analog scale

Table 3 Clinical and radiographic data of the patients after surgery at last follow up and complications of CDA reported by authors

Postoperative												
Authors	Cervical lordosis	Disk angle	Cervical spine ROM	Discal ROM	VAS	NDI	SF-36	mJOA	PO	Adiacent segments	Complications	Follow-up
Zaho et al.	–	–	–	4.7 ± 4.2°	0.9	11.3	–	15.9 ± 0.9	69.0%	47.6%	2 uncoforaminal stenosis	120.5 months
Dejagher et al.	–	–	–	8.6°	–	20.9	45.9	–	–	3 second Bryan prosthesis 2 fusion in adjacent levels	7 second surgeries 2 removed prosthesis	120 months
Pointillart et al.	–	–	–	8.4 ± 5.8°	Neck 2.6 Arm 1.8	14.9	–	–	54.5%	64.7% (upper), 43.7% (inferior)	2 removed prosthesis	186 months
Sasso et al.	–	–	–	–	Neck 1.26 Arm 0.84	8.05	–	–	–	–	–	120 months
Lavelle et al.	–	–	–	8.7°	–	38.3	–	–	–	9.7%	1 implant loosening 1 mal-positioned implant 1 excessive neck/arm pain 5 spinal events	120 months
Song et al.	11.1 ± 9.4°	1.2 ± 1.9°	46.3 ± 13.0°	8.6 ± 5.3°	–	15.6 ± 10.6	–	15.8 ± 1.4	93.0%	46.5% 25.4% cranial 43.7% caudal	60.6% of degenerative cervical canal stenosis	10 years
Han et al.	–	–	45.6 ± 13.1 48.8 ± 11.0°	9.0°	–	14.0 12.0	–	15.5 17.0	28.9% 32.1%	–	–	10 years
Genitiempo et al.	14.9 ± 8.2°	2.3 ± 1.4°	47.1 ± 14.3°	6.1 ± 1.5°	1.8 ± 1.6	14.2 ± 10.2	47.5 ± 5.7	–	89.3%	DROM **ACrL**: 9.3 ± 2.3 to 7.9 ± 2.1 DROM **ACdL** 9.8 ± 2.7° to 7.1 ± 1.8	–	18 years

CDA cervical disk arthroplasty, *ROM* range of motion, *VAS* visual analog scale, *NDI* Neck Disability Index, *SF-36* short-form-36, *mJOA* modified Japanese Orthopedic Association scale, *DROM ACrL* discal range of motion of adjacent cranial level, *DROM ACdL* discal range of motion of adjacent caudal level

3.6 Residual Motion of the Bryan Prosthesis and Cervical Range of Motion (ROM)

Six of the included studies reported the preoperative and postoperative discal range of motion of the treated segment [12, 13, 15–17, 19] whereas only three articles described cervical (C2-C7) ROM [11–13]. One of the articles described the postoperative discal range of motion only [11]. There are many available techniques to assess cervical and segment ROM, both clinically and radiologically. Among the included cases, residual cervical motion was assessed radiologically analyzing flexo-extension radiographs. Only two articles specified the rate of mobile devices at the last follow-up. In particular, Genitiempo et al. and Dejaegher et al. reported similar rates of mobile devices, respectively 85.7% and 81% at 10 years follow-up [13, 15]. The mean pre op segmental ROM was 8.2 ± 3.6° among 396 investigated levels. In the last follow-up, the mean value was 8.2 ± 3.3° among 588 investigated levels. A total of 193 segments were assessed for pre and postoperative cervical ROM which was respectively 46.4 ± 14.4 and 46.3 ± 13.4, demonstrating almost unvaried motility conditions.

3.7 Periprosthetic Ossification (PO)

The importance of evaluating PO is due to the effects on the clinical outcome that several studies reported in terms of alteration of cervical ROM of the adjacent segment [20]. *Mcafee* et al. firstly classified PO as five grades: grade zero represented no ossification [21]. Grade I was described as ossification not invasive into intervertebral space that does not influence the ROM of the vertebral motion segment. Grade II presented ossification invasive into intervertebral space which possibly affected the ROM. In Grade III the ossification formed bridging bone between adjacent vertebral bodies, and the ROM of index level was affected due to postoperative osteophytes evident on flexion-extension or lateral bending radiographs; Grade IV finally, was described as the complete fusion with bridging trabecular bone continuous between adjacent endplates and a ROM of index level less than 3°. *Han* et al. reported in their study an incidence of PO in the group of patients affected by radiculopathy, 28.9%, respectively, and 32.1% in the group of patients affected by myelopathy [11]. *Zaho* et al. reported an incidence of PO in 69% of treated patients [19]. *Pointillart* et al. described 54.5% of PO [17] whereas *Song* et al. 93% of PO [12]. Finally, *Genitiempo* et al. identified PO in 89.3% of treated patients [13]. The incidence of PO increases according to years of follow up as shown in Table 1. However, the incidence of postoperative PO is correlated not only with patients who had more than 10 years follow-up, but also with the amount of degeneration in the target level before surgery [22].

3.8 The Fate of the Adjacent Segments

It is well-known that vertebral segment fusion determines biomechanical changes in the spinal motion segment which may lead to the degeneration of intervertebral disks and osteoarthritis of the facet joints [23]. This condition is the so-called ASD. The Literature reported that the degeneration of AS is described in about half of the treated patients after 10 years of follow-up. In particular, *Zhao* et al., reported an Adjacent Segment Degeneration Rate (ASDR) of 47.6% (30 patients) [19]. *Dejaegher* et al. among the 89 patients treated reported two fusion in adjacent levels [15]. *Pointillart* et al. instead described at 186 months follow-up upper adjacent segment degeneration in 64.7% of patients, whereas 43.7% developed inferior adjacent segment degeneration [17]. *Han* et al. reported an ASDR of 46.5% at 10-year follow-up [11] while *Sasso* et al. did not reported ASDR but reported the 9% reoperation rate in patients who underwent arthroplasty at 10 years while patients requiring reoperation were higher in number in the arthrodesis cohort (32%) [18]. Similar results were also evaluated by *Lavelle* et al.*,* CDA group had numerically lower rates of second surgeries at adjacent levels (9.7% vs. 15.8%) [16] with respect to ACDF group. This is suggestive of a preservation of the adjacent levels by CDA to a degree not provided by arthrodesis in the same vertebral level.

Finally, *Genitiempo* et al. demonstrated an overall ASDR of 77.1% after 18 years of follow-up [13].

3.9 Clinical and Functional Outcomes

In all included studies the clinical and functional outcome was assessed with the Neck Disability Index (NDI). In particular, five studies [13, 16–19] included the Visual Analogue Scale (VAS), three studies [13, 15, 16] also evaluated the Short Form (SF)—36, and three studies [11, 12, 19] used the Modified Japanese Orthopedic Association scale (mJOA) (all data are summarized in Table 1).

3.10 Complications

Surgical procedures were not free by perioperative and postoperative complications such as dysphonia or superficial wound infection. Five articles reported long-term postoperative complication including symptomatic osteophytosis, unco-foraminal stenosis and degenerative cervical canal stenosis [12, 15–17, 19] (Table 1). PO and AS degeneration were analyzed separately. Among the 269 patients from the previously mentioned articles, 22 cases demanded for second surgery. A single case of implant loosening was described by Lavelle et al. [16]. Further analysis was not possible because data were presented as aggregated.

4 Discussion

CDA primary indication is in patients with radiculopathy [9], however more and more studies recently reported that the principal indication for cervical disk arthroplasty seems to be healthy young patients with disk degeneration who may need revision surgery during their lifetime [24]. Cervical spinal alignment gained more and more interest over the past decades because of its possible clinical implications. Until now, there is no consensus on the physiological cervical lordosis (CL) as there are up to 35% of asymptomatic kyphosis [25]. However, the overall reported CL is approximately 16° [25]. As concerns measurements, many methods are already available, but the Cobb angle still represents a gold standard. Furthermore, many studies tried to assess if there is a relation between cervical sagittal imbalance and clinical outcomes. This association has been largely described for adult spinal deformities, both for sagittal and coronal alignment [26]. However, up to now, the correlation between cervical sagittal alignment, QoL and adjacent segment disease remains controversial. In the light of our results, we can say that patients who undergo CDA do not significantly worsen their cervical lordosis, despite its implication on QoL.

Many studies already demonstrated that segmental and cervical range of motion are in relationship with neck pain. Therefore, their long-term measures are useful to understand how much CDA avoids neck impairment. Up to now, there is no consensus as concerns the definition of a mobile device. Genitiempo et al. [13] considered a segment mobile if there were at least 3° of discal ROM whereas Dejaegher et al. [15] considered a threshold ROM of 2°. None of the other studies describe when a device was considered mobile. Our review of the literature demonstrates almost unvaried segmental residual mobility and cervical ROM at the last follow up, encouraging the hypothesis that CDAs preserves native cervical spine biomechanics.

Periprosthetic ossification is an almost inevitable complication of CDA described as a formation of heterotopic ossification and osteophytes in and around a disk replacement probably due to biomechanical environment alteration after surgery [27]. Recently, several studies showed that the PO is linked not so much to a loosening of the prosthesis rather than a dynamic phenomenon related to predisposing and influencing factors such as genetic factors, tissue trauma during surgery, surgical technique (including the removal of bone dust) [28]. The pre-existing spondylotic osteophytes seem to increase the incidence of PO at last follow-up [27].

Since the development of AS degeneration following vertebral fusion is a major cause of revision surgery [29], some studies tried to demonstrate if this condition is due to disease progression or only a fusion-associated phenomenon [30]. For this reason, since the Bryan prosthesis is totally unconstrained and preserves the ROM, the possibility of avoiding AS degeneration should be considered among the advantages. However, in the light of our results, although cervical disk arthroplasty is an effective method to manage degenerative cervical disease, it leads to excessive loading and additional motion in the adjacent segments, which causes AS degeneration.

4.1 Limitations

The main limitation of the review depends on the low level of evidence (LoE) of the papers included in the study. In particular there is a lack of Randomized Clinical Trials (RCTs) aimed to determine the incidence of complications among the adjacent segments after CDAs compared to ACDFs. Moreover, many data were described as aggregated because single level results were not always available from included papers.

5 Conclusion

Unconstrained cervical disk arthroplasty is a valid alternative for the treatment of cervical spine degenerative pathologies in young patients. In fact, the systematic analysis of the literature revealed a good long-term device survival and motility. Moreover, CDA does not seem to affect sagittal alignment which remains stable on long-term follow-up. Clinical outcomes are good regardless of adjacent segment degeneration and periprosthetic ossification. However, some complications are still present with uncommon need for reoperation. Future high evidence studies are needed to better define the best treatment between CDA and ACDF.

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Compliance with Ethical Standards All procedures performed were in accordance with the 1964 Helsinki declaration. This research has been approved by the IRB of the authors' affiliated institutions.

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Conflicts of Interest The authors declare that they have no conflicts of interest.

References

1. Hou Y, Liu Y, Yuan W, Wang X, Chen H, Yang L, Zhang Y. Cervical kinematics and radiological changes after discovery of artificial disc replacement versus fusion. Spine J. 2014;14:867–77. https://doi.org/10.1016/j.spinee.2013.07.432.
2. Bohlman HH, Emery SE, Goodfellow DB, Jones PK. Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients. J Bone Joint Surg Am. 1993;75:1298–307. https://doi.org/10.2106/00004623-199309000-00005.
3. Anderson PA, Sasso RC, Rouleau JP, Carlson CS, Goffin J. The Bryan Cervical Disc: wear properties and early clinical results. Spine J. 2004;4:303s–9s. https://doi.org/10.1016/j.spinee.2004.07.026.
4. Boden SD, Balderston RA, Heller JG, Hanley EN Jr, Zigler JE. An AOA critical issue. Disc replacements: this time will we really cure low-back and neck pain? J Bone Joint Surg Am. 2004;86:411–22.
5. Goffin J, van Loon J, Van Calenbergh F, Plets C. Long-term results after anterior cervical fusion and osteosynthetic stabilization for fractures and/or dislocations of the cervical spine. J Spinal Disord. 1995;8:500–8; discussion 499.
6. Ishihara H, Kanamori M, Kawaguchi Y, Nakamura H, Kimura T. Adjacent segment disease after anterior cervical interbody fusion. Spine J. 2004;4:624–8. https://doi.org/10.1016/j.spinee.2004.04.011.
7. Matgé G. Cervical cage fusion with 5 different implants: 250 cases. Acta Neurochir. 2002;144:539–49; discussion 550. https://doi.org/10.1007/s00701-002-0939-0.
8. Matgé G. Approaches to cervical spine. In: Sindou M, editor. Practical handbook of neurosurgery: from leading neurosurgeons. Vienna: Springer; 2009. p. 1141–60. https://doi.org/10.1007/978-3-211-84820-3_68.
9. Goffin J, Casey A, Kehr P, Liebig K, Lind B, Logroscino C, Pointillart V, Van Calenbergh F, van Loon J. Preliminary clinical experience with the bryan cervical disc prosthesis. Neurosurgery. 2002;51:840–5; discussion 845–7. https://doi.org/10.1227/00006123-200209000-00048.
10. Goffin J, Van Calenbergh F, van Loon J, Casey A, Kehr P, Liebig K, Lind B, Logroscino C, Sgrambiglia R, Pointillart V. Intermediate follow-up after treatment of degenerative disc disease with the Bryan cervical disc prosthesis: Single-level and bi-level. Spine (Phila Pa 1976). 2003;28:2673–8. https://doi.org/10.1097/01.Brs.0000099392.90849.Aa.
11. Han X, He D, Zhang N, Song Q, Wang J, Tian W. Comparison of 10-year outcomes of Bryan cervical disc arthroplasty for myelopathy and radiculopathy. Orthop Surg. 2019;11:1127–34. https://doi.org/10.1111/os.12565.
12. Song Q, He D, Han X, Zhang N, Wang J, Tian W. Clinical and radiological outcomes of cervical disc arthroplasty: ten year follow-up study. Int Orthop. 2018;42:2389–96. https://doi.org/10.1007/s00264-018-3947-2.
13. Genitiempo M, Perna A, Santagada DA, Meluzio MC, Proietti L, Bocchi MB, Logroscino CA, Tamburrelli FC. Single-level Bryan cervical disc arthroplasty: evaluation of radiological and clinical outcomes after 18 years of follow-up. Eur Spine J. 2020;29:2823–30. https://doi.org/10.1007/s00586-020-06486-5.
14. Miller J, Sasso R, Anderson P, Riew KD, McPhilamy A, Gianaris T. Adjacent level degeneration: Bryan total disc arthroplasty versus anterior cervical discectomy and fusion. Clin Spine Surg. 2018;31:E98–e101. https://doi.org/10.1097/bsd.0000000000000598.
15. Dejaegher J, Walraevens J, van Loon J, Van Calenbergh F, Demaerel P, Goffin J. 10-Year follow-up after implantation of the Bryan cervical disc prosthesis. Eur Spine J. 2017;26:1191–8. https://doi.org/10.1007/s00586-016-4897-2.
16. Lavelle WF, Riew KD, Levi AD, Florman JE. Ten-year outcomes of cervical disc replacement with the Bryan cervical disc: results from a prospective, randomized, controlled clinical trial. Spine (Phila Pa 1976). 2019;44:601–8. https://doi.org/10.1097/brs.0000000000002907.
17. Pointillart V, Castelain JE, Coudert P, Cawley DT, Gille O, Vital JM. Outcomes of the Bryan cervical disc replacement: fifteen year follow-up. Int Orthop. 2018;42:851–7. https://doi.org/10.1007/s00264-017-3745-2.
18. Sasso WR, Smucker JD, Sasso MP, Sasso RC. Long-term clinical outcomes of cervical disc arthroplasty: a prospective, randomized, controlled trial. Spine (Phila Pa 1976). 2017;42:209–16. https://doi.org/10.1097/brs.0000000000001746.
19. Zhao Y, Zhang Y, Sun Y, Pan S, Zhou F, Liu Z. Application of cervical arthroplasty with Bryan cervical disc: 10-year follow-up results in China. Spine (Phila Pa 1976). 2016;41:111–5. https://doi.org/10.1097/brs.0000000000001145.
20. Srinivasan S, Kumar SD, Shruthi R, Jebaseelan DD, Yoganandan N, Rajasekaran S. Effect of heterotopic ossification after Bryan-cervical disc arthroplasty on adjacent level range of motion: a finite element study. J Clin Orthop Trauma. 2021;15:99–103. https://doi.org/10.1016/j.jcot.2020.10.027.
21. McAfee PC, Cunningham BW, Devine J, Williams E, Yu-Yahiro J. Classification of heterotopic ossification (HO) in artificial disk replacement. J Spinal Disord Tech. 2003;16:384–9. https://doi.org/10.1097/00024720-200308000-00010.
22. Zhou FF, Li SY, Zhao YB, Zhang FS, Pan SF, Sun Y. [Quantitative analysis of the degeneration of cervical spine and the correlation to the heterotopic ossification after artificial cervical disc replacement]. Zhonghua Yi Xue Za Zhi. 2021;101:945–9. https://doi.org/10.3760/cma.j.cn112137-20200814-02377.
23. Proietti L, Perna A, Ricciardi L, Fumo C, Santagada DA, Giannelli I, Tamburrelli FC, Leone A. Radiological evaluation of fusion patterns after lateral lumbar interbody fusion: institutional case series. Radiol Med. 2021;126:250–7. https://doi.org/10.1007/s11547-020-01252-5.
24. Cao JM, Zhang YZ, Shen Y, Ding WY. Complications of Bryan cervical disc replacement. Orthop Surg. 2010;2:86–93. https://doi.org/10.1111/j.1757-7861.2010.00069.x.
25. Guo G-M, Li J, Diao Q-X, Zhu T-H, Song Z-X, Guo Y-Y, Gao Y-Z. Cervical lordosis in asymptomatic individuals: a meta-analysis. J Orthop Surg Res. 2018;13:147. https://doi.org/10.1186/s13018-018-0854-6.
26. Proietti L, Perna A, Velluto C, Smakaj A, Bocchi MB, Fumo C, Fresta L, Tamburrelli FC. Correction of a severe coronal malalignment in adult spinal deformity using the "kickstand rod" technique as primary surgery. J Orthop. 2021;25:252–8. https://doi.org/10.1016/j.jor.2021.05.028.
27. Tian W, Han X, Liu B, He D, Lv Y, Yue J. Generation and development of paravertebral ossification in cervical artificial disk replacement: a detailed analytic report using coronal reconstruction CT. Clin Spine Surg. 2017;30:E179–e188. https://doi.org/10.1097/bsd.0000000000000044.
28. Yi S, Oh J, Choi G, Kim TY, Shin HC, Kim KN, Kim KS, Yoon DH. The fate of heterotopic ossification associated with cervical artificial disc replacement. Spine (Phila Pa 1976). 2014;39:2078–83. https://doi.org/10.1097/brs.0000000000000640.
29. Zhang C, Berven SH, Fortin M, Weber MH. Adjacent segment degeneration versus disease after lumbar spine fusion for degenerative pathology: a systematic review with meta-analysis of the literature. Clin Spine Surg. 2016;29:21–9. https://doi.org/10.1097/bsd.0000000000000328.
30. Song KJ, Choi BW, Jeon TS, Lee KB, Chang H. Adjacent segment degenerative disease: is it due to disease progression or a fusion-associated phenomenon? Comparison between segments adjacent to the fused and non-fused segments. Eur Spine J. 2011;20:1940–5. https://doi.org/10.1007/s00586-011-1864-9.

Multilevel Corpectomy for Subaxial Cervical Spondylodiscitis: Literature Review and Role of Navigation, Intraoperative Imaging and Augmented Reality

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1 Introduction

Subaxial cervical spine spondylodiscitis represents a real challenge in spine surgery. The infection usually starts at the level of the vertebral body and subsequently involves the intervertebral disc and the extradural compartment [1]. In later stages, multiple vertebrae can be involved because of a pathological infection, and the alteration of the spinal stability can lead to spinal deformity. Because of the cervical spine's close relation to neural structures, including the spinal cord, brainstem, and posterior fossa, the infection of the cervical spine may cause—in addiction to direct spinal cord compression and related myelopathy—sepsis, meningitis, and even death if untreated [2]. The treatment strategy usually requires combined anterior and posterior approaches in order to relieve spinal cord compression and restore cervical alignment and balance, thus regaining spinal stability. The intraoperative samples used to isolate the pathogens offer useful information for targeted antibiotic therapy. There is scant literature on subaxial cervical spondylodiscitis management, but especially on multilevel cervical corpectomy (≥three levels) [1–8]. The authors present an emblematic case of a patient treated with circumferential cervical fixation and four-level cervicothoracic corpectomy, performed by merging augmented reality, neuronavigation, and intraoperative imaging, and theyconducted a systematic review on this topic.

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2 Materials and Methods

A comprehensive literature review was performed by using the combined MeSH terms *(multilevel) AND (sub axial spine OR cervical spine) AND (spine osteomyelitis OR spinal osteomyelitis)*, to search in the PubMed and Scopus databases. This search was limited to studies published in English. Eligibility criteria were limited by the nature of the existing literature on multilevel corpectomy with ≥three corpectomy levels due to spondylodiscitis, which consists only of case series and case reports. The reference lists of all the articles discovered during these searches were examined for possible additional papers. We excluded papers with patients affected by tumors or trauma and those that lacked detailed descriptions of the surgical treatment and outcome.

We present a representative case of a four-level anterior corpectomy without sternotomy and posterior fusion. Intraoperative imaging (Ziehm RFD, Ziehm Imaging, Reggio Emilia, Italy), neuronavigation (BrainLab, Munich, Germany), and augmented reality (apoQlar GmbH, Hamburg, Germany) were merged during both the planning stage and the surgical procedure.

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2.1 Data Extraction

All the included studies were meticulously reviewed and scrutinized for their study design, methodology, and patient characteristics. Patients' data were recorded when available, including age, sex, coexisting comorbidities, the number of corpectomy levels, the type of treatment (anterior, posterior, or combined), the technology used, and outcomes (Table 1). Our case was included in this literature review. From our literature search, we selected 13 papers; eight were excluded because they did not match our inclusion criteria (the involvement of only one or two levels, discectomy, and no cervical spine localization). Two more papers were included after a manual search.

2.2 Case Illustration

We present a 71-year-old patient in poor general clinical status. She was treated for right-sided frontal low-grade glioma 2 years before at another institution. She developed a bone flap infection, which required revision surgery with bone flap

Table 1 Literature review on anterior cervical corpectomy for a minimum of three levels

Author and year	Age/sex	No. of patients	Corpectomy levels	Approach	Complications	Outcome	Technology	Follow-up
Lu et al. (2009) [6]	44/F	4	4 (C3–C6)	Anterior and posterior	Pneumonia, wound infection, death, UTI, retained drain	Recovery	X-ray, postoperative CT scan, MRI	39 months
	52/M		4 (C4–C7)	Anterior and posterior		Recovery		36 months
	59/M		3 (C5–C7)	Anterior and posterior		Improve		28 months
	54/M		3 (C6–T1)	Anterior and posterior		Recovery		16 months
Theologis et al. (2016) [2]	NR specifically	6	5 pt, 3 levels	Anterior and posterior	Revision surgery, pneumonia, epidural hematoma	Improvement	X-ray, postoperative CT scan, MRI	25 months
			1 patient 4 levels (C3–C6) which was extended to 6 levels (C2–C7) due to cage migration					
Auguste et al. (2006) [4]	59/M	1	3	Anterior only	Subsidence (5 mm)	Improvement	X-ray, postoperative CT scan, MRI	22 months
Acosta et al. (2008) [3]	68/F	4	3 (C4–C6)	anterior and posterior	Transient dysphagia, soft tissue swelling	Improvement	X-ray, postoperative CT scan, MRI	53 months
	50/F		6 (C4–T2)	Sternotomy, corpectomy, posterior				35 months
	44/F		4 (C3–C6)	Anterior and posterior				29 months
	57/F		3 (C4–C6)	Anterior and posterior				18 months
Strowitzki et al. (2011) [7]	68/M	1	3 expandible cages: 2 levels (C2–C4) + 3 levels (C5–T1) + 1 level (C4–C5 interspace)	Anterior and posterior; tracheostomy	None	Improvement	X-ray, postoperative CT scan, MRI	8 months
Wadhwa et al. (2014) [8]	NR specifically	11	>3 (not reported in detail)	Anterior and posterior	8% wound hematoma	Improvement	NR	20 months
Kunert et al. (2016) [5]	44/F	1	3 (C5–C6–C7)	Oblique corpectomy	NR	Recovery	X-ray, postoperative CT scan, MRI	110 months
Present case	72/F	1	4 (C5–T1)	Anterior and posterior	Dural tear	Partial recovery	CT, MRI, AR, intraoperative imaging, navigation	8 months

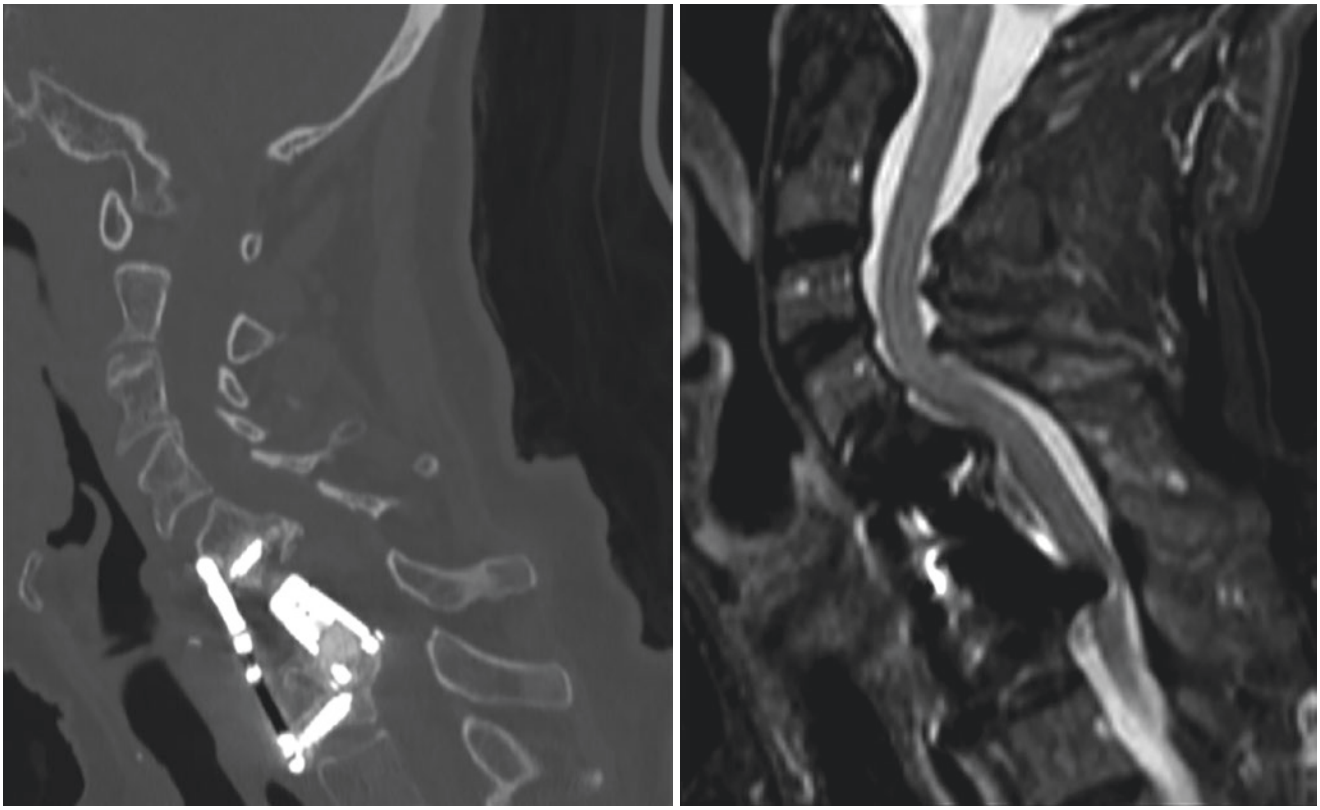

Fig. 1 Sagittal cervical CT scan (left) and MRI scan (right) documenting C6-C7 intersomatic cage displacement

removal and proper antibiotic therapy. During follow-up, the patient developed tetraparesis and underwent cervical MRI examination, which revealed C6-C7 spondylodiscitis. A C6-C7 corpectomy with an expandable cage and anterior C5-T1 plating was performed. After a 6-month follow-up, cervical spine imaging documented the cage's displacement (Fig. 1). The patient was then referred to our department, and a clinical examination revealed cachexia (BMI 20), mental confusion, and tetraparesis british medical research council ((BMRC) scale 1\5 left, 2\5 right limbs). We removed the displaced cage and extended the corpectomy to T1 with the positioning of an expandable cage, larger than the previous one, with somatic screws but without plating (MediExpand, Medicon, Tuttlingen, Germany) (Fig. 2). We planned a posterior fixation, which was staged because of intraoperative difficulties, including bradycardia and hypotension, related to the poor general conditions of the patient. The surgical time was 8.15 h, and blood loss amounted to 150 cc. The intraoperative dural defect was documented and repaired with duroplasty (Dura-guard, Synovis Life Technologies Inc., St. Paul, MN, USA), TachoSil, and fibrin glue. The postoperative period was uneventful: the wound did not show any signs of cerebrospinal fluid (CSF) leakage, and the motor strength in the right limbs improved (MRC 2\5), while it remained stable in the left. On postoperative day 5, a computed tomography (CT) scan documented a new, asymptom-

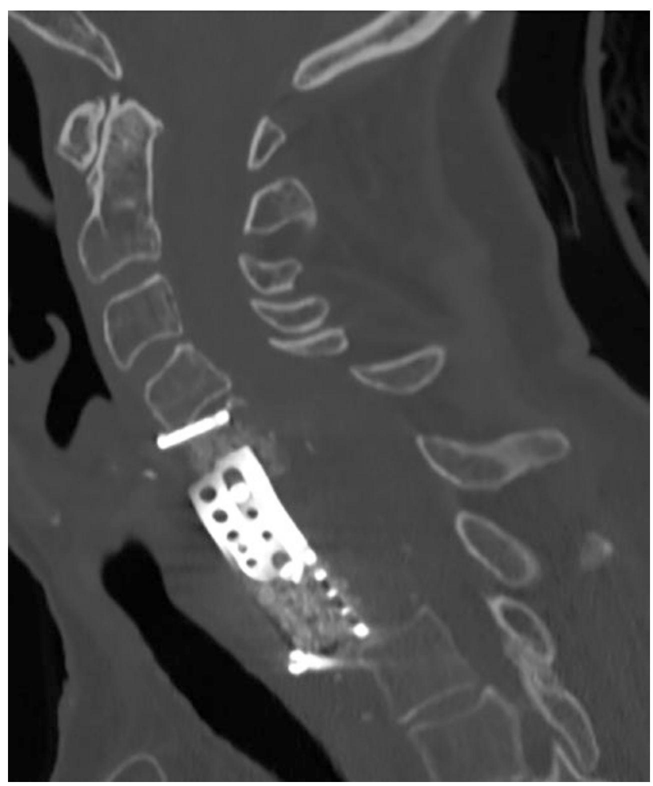

Fig. 2 Sagittal cervical CT scan documenting further expandable cage (without anterior plating) displacement

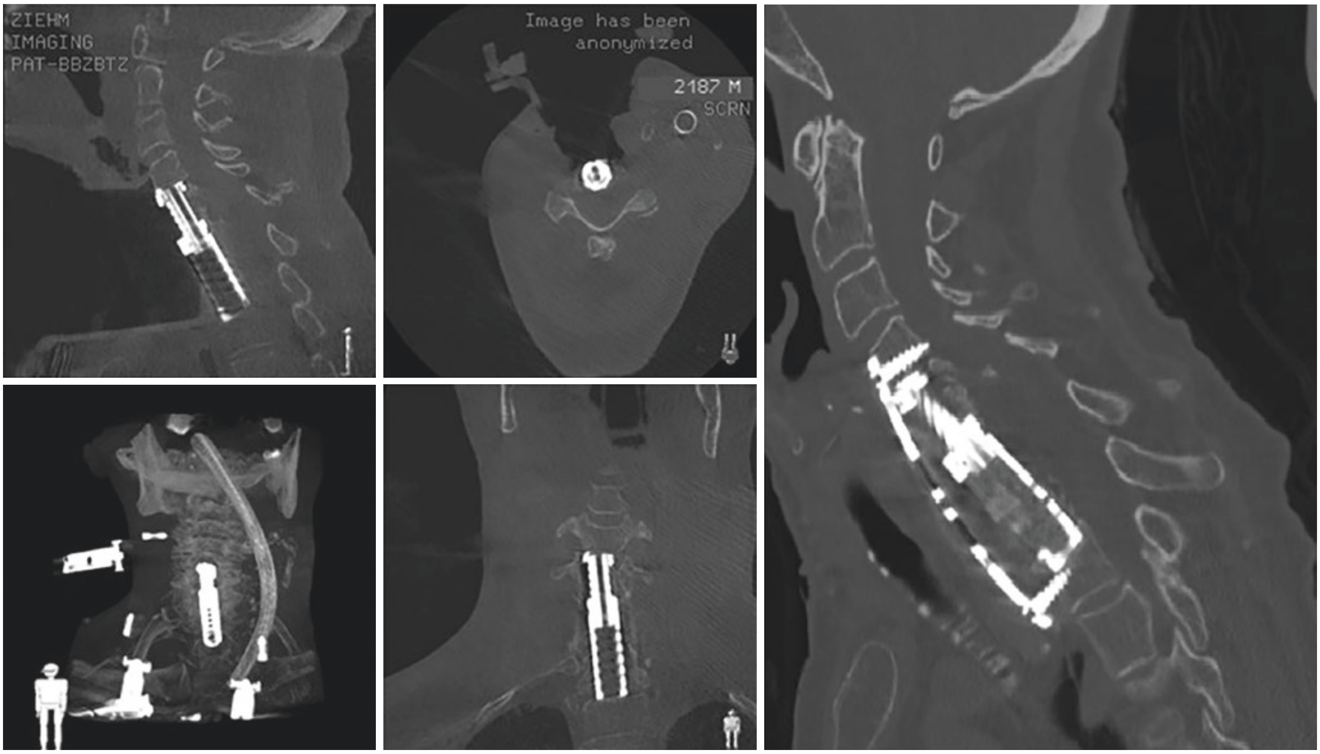

Fig. 3 Intraoperative imaging with Ziehm (left) and postoperative CT scan (right) showing a four-level corpectomy (C5, C6, C7, and T1) and plating with an expandable C5-T1 cage

atic cage displacement. The cage implant was removed again, and we performed a four-level corpectomy (C5, C6, C7, T1) and plating with an expandable C5-T1 cage. C4-T2 plating was performed with a standard anterior cervical Smith–Robinson approach, without sternotomy (Fig. 3). The surgical time was 2 hours. No new neurological deficits were documented, and the BMRC remained stable on the right (2\5). Intraoperative imaging was used to assess the correct positioning of the plating's somatic screws at T2. The posterior fixation was again staged to reduce the operating time, keeping in mind the patient's fragility. The postoperative period was regular: The patient did not show hoarseness or new neurological deficits. In the planning stage of the posterior approach, we used augmented reality (AR) for cervical spinal fixation planning and cervicothoracic implant reconstruction to better examine the cervical kyphotic deformity, increase our familiarity with the patient's spine deformity, and explain the pathology to the patient and her family in a friendlier and more understandable way (Fig. 4).

In the posterior fixation step, screws were applied into the C3/C7 lateral masses and T2-T3 pedicles. We used 3D spinal navigation and intraoperative imaging acquisition with multiplanar reconstruction (Ziehm RFD) to overcome the limitations in visualizing the T2-T3 pedicles (Fig. 5). The intraoperative dural tearing of the posterior aspect of the dural sac was documented at the level of C2-C3 and repaired with TachoSil and fibrin glue. The surgical time was 4 h, and blood loss amounted to 190 cc. The postoperative CT scan documented satisfactory implant positioning with the partial restoration of the sagittal alignment and the coronal alignment. The wounds healed well, and the patient showed stable improvement in the motor deficit to the right upper and lower extremities. The patient was transferred to a rehabilitation center on postoperative day 16 and continued follow-up for the low-grade glioma. Because of the patient's fragility, we decided to postpone the cranioplasty procedure. All the procedures were performed with intraoperative neurophysiological monitoring (NIM Eclipse E4 system).

Fig. 4 Surgical planning using the augmented reality (AR) for posterior cervical spinal fixation and for a better study on the cervical kyphotic deformity

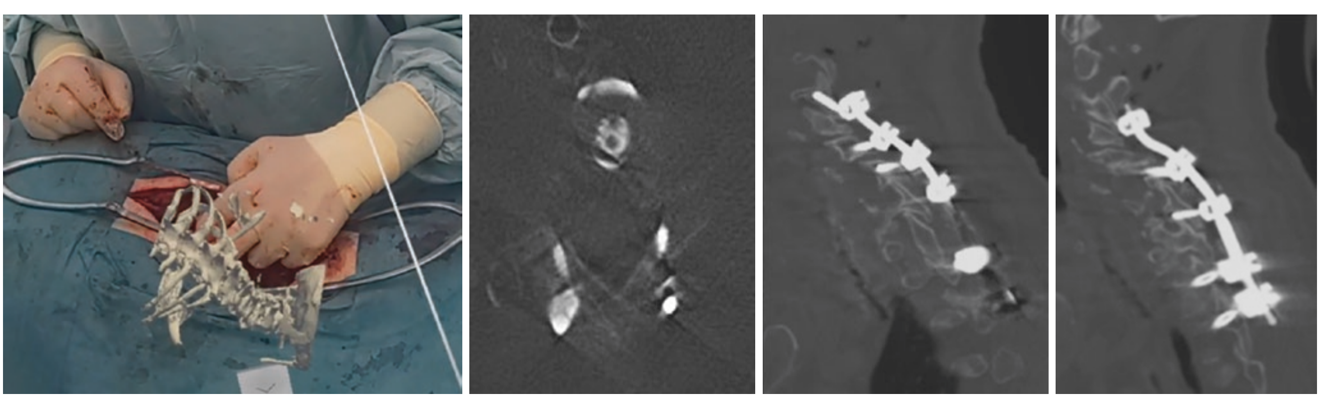

Fig. 5 Intraoperative use of AR for posterior cervical spine fixation (C3/C7 lateral masses and T2-T3 pedicles)

3 Results

This systematic review included 28 patients treated with ≥ three-level corpectomy (11 patients with three-level corpectomy, 15 patients with four-level corpectomy, and 2 patients with six-level corpectomy), 6 women, 5 men, and 17 not reported specifically, with a mean age of 55.9 years (range: 44–72 years). A combined anterior and posterior approach was performed in all but one case, which was treated with the anterior approach only. In one case of a six-level cervicothoracic corpectomy, sternotomy was necessary. All the reported patients recovered after surgery. No major intraoperative complications were reported. Usual postoperative complications include wound hematoma, pneumonia, subsidence, epidural hematoma, dural leakage, dysphagia, soft tissue swelling, and death. The technology used for pre-, intra-, and postoperative imaging included standard C-arms, X-rays, CT scans, and MRI scans. The mean follow-up time was 31.9 months (range: 8–110 months). In our case, the combined use of intraoperative imaging, neuronavigation, and augmented reality was instrumental to overcoming the technical limitations from the difficulty of properly visualizing, with a standard intraoperative C-arm, the vertebral pedicles at the level of T1-T2 and the vertebral body of T2, where somatic screws were applied after that anterior plating had been positioned.

4 Discussion

Cervical spine osteomyelitis (CSO) accounts for 1–7% of bone infections [9], with an incidence of one per 100,000 people per year [10]. The most common pathogen is *Staphylococcus aureus*, followed by *Enterococcus* spp., *Streptococcus* spp., gram-negative bacteria, *M. tuberculosis*, *Candida* spp., polymicrobial, and sterile [2, 11–14]. CSO represents a dangerous pathology that must be promptly suspected and documented in order to try to prevent spinal deformity, neurological deficits, and even death. The introduction of antibiotics dramatically reduced the mortality of the patients, which ranged from 40% to 70% [15]. After identifying the pathogen obtained from a microbial culture, intravenous and then oral antibiotic therapy alone is indicated in the absence of neurological deficits [12]. External orthosis and seriated imaging are required to assess the efficacy of the therapy.

Surgery is needed in patients in whom antibiotic therapy alone does not provide the expected results or with instability/compression in the neurological structure [6]. Surgery can obtain tissue for cultures, relieve neurological structures from compression, improve spinal alignment, and fix spinal instability [15]. Anterior decompression through corpectomy with a cage and anterior plating is recommended in association with posterior fixation, especially if more than three levels are involved [16–19]. The use of titanium or PEEK implants, without reinfection, has been reported in the literature [20, 21]. Spinal osteomyelitis presents a remarkable complication rate (33%), with a mortality rate of up to 33%, according to several authors [13, 17, 22–24]. Such high mortality and high morbidity rates are due to the frequent presence of general fragilities, such as immunodeficiency, drug abuse, and sepsis.

CSO is rarer than osteomyelitis in other spinal metamers [20]. In this study, we presented the first literature review dedicated to CSO treated with at least three corpectomy levels, along with an emblematic case of a four-level corpectomy, in which multimodal navigation and multiplanar imaging were used. We presented a series of 28 patients treated with ≥three corpectomy levels, reporting the technology used, outcome, levels affected, and approach. To the best of our knowledge, this is the first study on this topic, aiming to provide specific indications for particularly challenging cases and better assess the therapeutic perspectives and risk stratification. All the reported cases implanted titanium cages and anterior plating; no reinfection was reported at medium- and long-term follow-ups. The number of levels fused did not affect the clinical outcome, which was reported as improved after surgery. In all cases, CT scans, MRI scans, and X-rays were assessed.

None of the reported cases mentioned the use of neuronavigation, intraoperative imaging, or augmented reality, probably owing to the rarity of this pathology and the relatively recent introduction of such methods [25–32]. In our patient, the use of augmented reality in the planning stage offered the opportunity to better explain the complex clinical situation to the patient's family, and it improved our familiarity with the pathological anatomy. AR was also used during surgery to compare its accuracy with that of standard navigation. According to our preliminary experience with AR-based navigation, AR is a promising tool that allows the visualization of the neuroimaging dataset directly in the operating field, without the need to look at the navigator's monitor. Nonetheless, it is still a new technology, with several limitations: the overlapping of the hologram with the patient's anatomy is operator dependent; thus, the accuracy cannot be standardized, and there are several risks of mispositioning the hologram. The software should be improved to overcome this limitation and automatically match the hologram of the patient. Moreover, the hologram can be appropriately visualized only by switching off the surgical lights, which is customary also in other intraoperative methods, such as 5-ALA and ICG, but it still represents a limitation, and further attention is recommended. If these improvements were made, AR could represent a better navigation tool than the standard navigation and offer the information and surgical feeling of the open procedure also for percutaneous techniques. Intraoperative imaging has proven to be of utmost importance in cases where the proper visualization of the radiological anatomy is complex, such as the cervicothoracic junction. The mean blood loss reported in literature for the CSO procedure was 363.8 mL[13], and our results were in line with such data.

The strength of our study is represented by the first and largest literature search on multilevel cervical spine osteomyelitis surgery reported to date and by the presentation of the utility of merged technologies (AR, intraoperative imaging, and navigation), which have never been reported before for this complex patient population. The limitation of the study is the overall small sample size and the low strength of evidence for the related data, from case reports and case series, which made it impossible to accomplish a systematic literature search.

5 Conclusion

According to our literature search, multilevel corpectomies for CSO are safe and effective surgical procedures, even in procedures involving up to six levels and those in the cervicothoracic junction. The use of multimodal navigation, merging intraoperative imaging acquisition, navigation, and augmented reality may provide helpful information during implant positioning in complex and altered anatomy and for assessing the best final result.

References

1. Frederickson B, Yuan H, Olans R. Management and outcome of pyogenic vertebral osteomyelitis. Clin Orthop Relat Res. 1976;131:160–7.
2. Theologis AA, Lansdown D, McClellan RT, Chou D, Pekmezci M. Multilevel corpectomy with anterior column reconstruction and plating for subaxial cervical osteomyelitis. Spine. 2016;41:1088–95.
3. Acosta FL Jr, Aryan HE, Chou D, Ames CP. Long-term biomechanical stability and clinical improvement after extended multilevel corpectomy and circumferential reconstruction of the cervical spine using titanium mesh cages. J Spinal Disord Tech. 2000;21:165–74.
4. Auguste KI, Chin C, Acosta FL, Ames CP. Expandable cylindrical cages in the cervical spine: a review of 22 cases. J Neurosurg Spine. 2006;4:285–91.
5. Kunert P, Prokopienko M, Nowak A, Czernicki T, Marchel A. Oblique corpectomy for treatment of cervical spine epidural abscesses: report on four cases. Neurol Neurochir. 2016;50:491–6.
6. Lu DC, Wang V, Chou D. The use of allograft or autograft and expandable titanium cages for the treatment of vertebral osteomyelitis. Neurosurgery. 2009;64:122–30.
7. Strowitzki M, Vastmans J, Vogel M, Jaksche H. Complex 360°-reconstruction and stabilization of the cervical spine due to osteomyelitis. Eur Spine J. 2010;20:248–52.
8. Wadhwa R, Mummaneni PV, Lau D, Le H, Chou D, Dhall SS. Perioperative morbidity and mortality comparison in circumferential cervical fusion for osteomyelitis versus cervical spondylotic myelopathy. Neurosurg Focus. 2014;37:7.
9. Schimmer RC, Jeanneret C, Nunley PD, Jeanneret B. Osteomyelitis of the cervical spine: a potentially dramatic disease. J Spinal Disord Tech. 2002;15:110–7.
10. Dimar JR, Carreon LY, Glassman SD, Campbell MJ, Hartman MJ, Johnson JR. Treatment of pyogenic vertebral osteomyelitis with anterior debridement and fusion followed by delayed posterior spinal fusion. Spine. 2004;29:326–32.
11. Fiori R, Coco I, Nezzo M, Kabunda G, Umana GE, Fraioli MF, Simonetti G. Spinal hydatidosis relapse: a case report. Case Rep Orthop. 2014;2014:207643.
12. Hadjipavlou AG, Mader JT, Necessary JT, Muffoletto AJ. Hematogenous pyogenic spinal infections and their surgical management. Spine. 2000;25:1668–79.
13. Hee HT, Majd ME, Holt RT, Pienkowski D. Better treatment of vertebral osteomyelitis using posterior stabilization and titanium mesh cages. J Spinal Disord Tech. 2002;15:149–56.
14. Jensen AG, Espersen F, Skinhøj P, Rosdahl VT, Frimodt- Møller N. Increasing frequency of vertebral osteomyelitis following Staphylococcus aureus bacteraemia in Denmark 1980-1990. J Infect. 1997;34:113–8.
15. Shields LB, Raque GH, Glassman SD, Campbell M, Vitaz T, Harpring J. Adverse effects associated with high-dose recombinant human bone morphogenetic protein-2 use in anterior cervical spine fusion. Spine. 2006;31:542–7.
16. Mummaneni PV, Dhall SS, Rodts GE, Haid RW. Circumferential fusion for cervical kyphotic deformity. Clinical article. J Neurosurg Spine. 2008;9:515–21.
17. Ogden AT, Kaiser MG. Single-stage debridement and instrumentation for pyogenic spinal infections. Neurosurg Focus. 2004;17:5.
18. Ponzo G, Umana GE, Giuffrida M, Furnari M, Nicoletti GF, Scalia G. Intramedullary craniovertebral junction metastasis leading to the diagnosis of underlying renal cell carcinoma. Surg Neurol Int. 2020;11:152.
19. Visocchi M, Conforti G, Roselli R, La Rocca G, Spallone A. From less to maximally invasiveness in cervical spine surgery: a "nightmare" case who deserve consideration. Int J Surg Case Rep. 2015;9:85–8. https://doi.org/10.1016/j.ijscr.2015.01.050. Epub 2015 Feb 17. PMID: 25734320; PMCID: PMC4392186.
20. Mondorf Y, Gaab MR, Oertel JMK. PEEK cage cervical ventral fusion in spondylodiscitis. Acta Neurochir. 2009;151:1537–41.
21. Ruf M, Stoltze D, Merk HR, Ames M, Harms J. Treatment of vertebral osteomyelitis by radical debridement and stabilization using titanium mesh cages. Spine. 2007;32:275–80.
22. Rath SA, Neff U, Schneider O, Richter HP. Neurosurgical management of thoracic and lumbar vertebral osteomyelitis and discitis in adults: a review of 43 consecutive surgically treated patients. Neurosurgery. 1996;38:926–33.
23. Redfern RM, Miles J, Banks AJ, Dervin E. Stabilisation of the infected spine. J Neurol Neurosurg Psychiatry. 1988;51:803–7.
24. Rezai AR, Woo HH, Errico TJ, Cooper PR. Contemporary management of spinal osteomyelitis. Neurosurgery. 1999;44:1018–26.
25. Nicoletti GF, Umana GE, Chaurasia B, Ponzo G, Giuffrida G, Vasta G, Tomasi SO, Graziano F, Cicero S, Scalia G. Navigation-assisted extraforaminal lumbar disc microdiscectomy: technical note. J Craniovertebr Junct. 2020;11:316–20.
26. Umana GE, Passanisi M, Fricia M, Chiriatti S, Fagone S, Cicero S, Nicoletti GF, Scalia G. Letter to the Editor Regarding "Accuracy of pedicle screw insertion among 3 image-guided navigation systems: a systematic review and meta-analysis". World Neurosurg. 2020;138:595–7.

27. Umana GE, Passanisi M, Fricia M, Cicero S, Narducci A, Nicoletti GF, Scalia G. Letter to the Editor Regarding "Minimally invasive thoracolumbar corpectomy and stabilization for unstable burst fractures using intraoperative computed tomography and computer-assisted spinal navigation". World Neurosurg. 2020;139:692–3.
28. Umana GE, Passanisi M, Fricia M, Distefano G, Cicero S, Nicoletti GF, Scalia G. Letter to the Editor Regarding "Radiolucent carbon fiber-reinforced pedicle screws for the treatment of spinal tumors: advantages for radiation planning and follow-up imaging". World Neurosurg. 2020;139:674–5.
29. Umana GE, Scalia G, Perrone C, Garaci F, Pagano A, De Luna A, et al. Safety and efficacy of navigated trocarless pedicle screw placement: technical note. Interdiscip Neurosurg. 2020;21:100771.
30. Umana GE, Passanisi M, Fricia M, et al. Letter to the Editor Regarding "Minimally invasive thoracolumbar corpectomy and stabilization for unstable burst fractures using intraoperative computed tomography and computer-assisted spinal navigation". World Neurosurg. 2020;139:692–3.
31. Massimiliano V, Giulio M. Six level cervico-thoracic circumferential reconstruction: report of the second case of the literature. Acta Neurochir Suppl. 2011;108:187–90. https://doi.org/10.1007/978-3-211-99370-5_28. PMID: 21107957.
32. Visocchi M, La Rocca G, Signorelli F, Roselli R, Jun Z, Spallone A. 10 Levels thoracic no-intrumented laminectomy for huge spontaneous spinal subdural hematoma removal. Report of the first case and literature review. Int J Surg Case Rep. 2015;15:57–62. https://doi.org/10.1016/j.ijscr.2015.06.032. Epub 2015 Jul 9. PMID: 26318128; PMCID: PMC4601942.

Lateral Approach to the Cervical Spine to Manage Degenerative Cervical Myelopathy and Radiculopathy

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1 Introduction

Many pathological conditions affecting the cervical spine can result in a symptomatic compression of the spinal cord, nerve roots, or vertebral artery. The spectrum of those pathological conditions is broad and includes congenital or acquired cervical stenosis, disk herniations, synovial cysts, and enthesopathies, such as the ossification of the longitudinal ligament, diffuse idiopathic skeletal hyperostosis, ankylosing spondylitis (with or without a lack of spinal alignment and stability [1]), and tumoral and vascular pathologies [2–6]. The most common clinical presentation is either a cervical myelopathy or a cervical radiculopathy, which is a selective nerve root compression with the sparing of the intramedullary long tracts [7, 8]. Anterior and posterior open surgical options for those conditions include single or multilevel discectomies [9, 10], corpectomy [11], laminectomy [6, 12–16], and laminoplasty [17–22]. To date, the superiority of the anterior approaches over the posterior approaches, or vice versa, is still matter of debate [23], and only a few clinical trials have tried to answer this research question [24]. It is much less known that open lateral techniques using multiple oblique vertebrectomies (MOVs) and/or foraminotomies [6, 25–31] have also been proposed as valid and safe alternatives for the management of degenerative cervical myelopathies (DCMs) and radiculopathies. The supporters of such a lateral route claim that MOV can provide very good clinical results and the long-term preservation of spinal alignment without needing bone grafting and/or instrumentation [32]. The main goal of this narrative review is to illustrate the rationale, advantages, disadvantages, complications, and pitfalls of this elegant technique and to highlight areas for future development.

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2 Materials and Methods

To investigate the origin, evolution, and current diffusion of MOV, a search was carried out by using the Medline via PubMed database. The search strategy used both keywords, namely "cervical oblique corpectomy," "multilevel oblique corpectomy and foraminotomy," and "lateral vertebrectomy," and MeSH terms, which were combined with the appropriate Boolean connectors. The search covered the period from 1 January 1991, up to 31 December 2021. Biomechanical cadaveric studies were included to define the historical context within which such a technique was initially conceived, and case reports and surgical series on the application of MOV for various cervical spine pathologies were also considered to estimate its diffusion. Letters and commentaries were excluded from this search strategy. To ensure the quality assessment of this review, its design and reporting have been conceived and conducted in agreement with the SANRA guidelines for narrative review articles [33].

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3 Results

The literature on MOV is very heterogeneous, indicating that the initial development of lateral approaches to the subaxial spine dates back to cadaveric studies that were conducted in Europe in the early 1990s and that afterwards quickly spread across the globe. The articles triaged during this search also suggest that the use of such a technique has faded over time, with only a handful of anatomical studies published over the past few years.

In the end, 29 clinical studies met all the inclusion criteria and were retained for data analysis; the latter clinical records matching our search criteria demonstrated that up to 2021, a cohort of 1200 patients underwent such an approach for the management of DCMs or radiculopathies. Those clinical syndromes were caused by cervical stenosis, degenerative disk disease and spondylosis, or a mix of them, in over 88% of cases. On the other hand, the ossification of the posterior longitudinal ligament was rarely found (4.3%), and other pathologies, such as synovial cysts and intradural extramedullary lesions, were only anecdotal.

The clinical course was reported as favorable in 78% of cases, out of which 14% of patients experienced complete recovery at the latest follow-up. The literature demonstrates that the most frequent complications were transient and permanent Horner syndrome in 13.6% and 9.2% of cases, respectively. Other complications included cerebrospinal fluid (CSF) leakage (0.4%) and postoperative hematoma (0.3%); in contrast, MOV-associated mortality appears to be 0.08%. In terms of long-term stability, 97% of patients undergoing MOV did not require additional stabilization.

4 Discussion

This narrative review followed a precise chronological scheme aimed at illustrating the past, present, and future of MOV by accurately synthesizing the data acquired through the aforementioned study design.

Historical Sketch The rationale for considering MOV is based on the evidence that the anterolateral compression of the cervical spine and the nerve roots may be best managed via an anterolateral approach providing direct exposure of the abnormal area without compromising spinal stability. Such a route represents a variation on the Verbiest technique [34, 35], and a thorough description of its various steps has been previously reported elsewhere [6, 26–28, 32, 36–38]. The first reports on MOV began in 1989 and were spurred from anatomical studies on various front-of-neck approaches on cadaver specimens [39].

From this literature review, it emerges that the initial employment of anterolateral approaches in a clinical setting was related to the treatment of degenerative spinal cord and nerve root compression, where the first clinical series was published in the early 1990s [6, 38]; however, MOV rapidly expanded beyond the management of degenerative pathologies, and it has also been used to treat other pathological conditions, including spinal intradural tumors [40].

Indications for MOV On the basis of an analysis of the clinical series identified by this review, the best indications for the anterolateral decompression of the cervical spine can be summarized: the presence of a predominant anterior spinal canal or anterolateral foraminal compression and a straight or kyphotic cervical alignment without needing significant instability. On the contrary, the exclusion criteria for MOV include the following: a preoperative lack of spinal alignment; signs of microinstability, such as segmental listhesis >2 mm or a disk height >2 mm; or the presence of a single-level soft disk disease (see also Table 1) [27, 28, 41].

Surgical Pearls on Patient Positioning and Anterolateral Dissection [27, 28, 41] Generally speaking, the anterolateral approach to the cervical spine should be attempted from the most symptomatic side, but if the symptoms are bilateral, a few anatomical considerations should be taken into account. The first is that drilling is easier and safer from the side with the larger osteophytes, disk herniation, or narrowest lateral foramina because the operating surgeon has direct control on the tip of the surgical instruments and can identify a cleavage plane with the dura mater. The second is that a careful understanding of the anatomical characteristics of the vertebral artery (VA) should guide the surgeon to approach the C3–C6 segments of the cervical spine from the side of the smaller VA because such a choice increases the overall safety of the procedure.

Table 1 Indications for MOV in patients with DCM or radiculopathy

(a) Clinical evidence of cervical myelopathy and/or radiculopathy
(b) Cervical CT-MRI scan with evidence of single/multiple-level nerve roots and/or spinal cord compression, mainly anterolateral and/or myelopathy
(c) Evidence of neutral or kyphotic cervical alignment in a plain lateral cervical X-ray as well as the absence of significant instability[a] documented by a dynamic cervical X-ray
Exclusion criteria for MOV
(a) Soft disk herniation documented on MRI within 6 months (only for MOV)
(b) The presence of preoperative anterolisthesis >2 mm between any two contiguous vertebral bodies

[a] Spinal instability defined as segmental listhesis >2 mm or a disk height >2 mm

Patients undergoing MOV are usually in supine positions, with their respective heads slightly extended and rotated to the contralateral side. A longitudinal skin incision is made along the medial border of the sternocleidomastoid (SCM) muscle at the level of the vertebral body (VB) to be exposed. The incision may extend to the mastoid tip to expose C2–C3 and to the sternal notch to expose C7–T1. The subcutaneous tissue and the platysma muscle are incised along with the skin incision. The natural space between the SCM muscle and the internal jugular vein is opened via sharp dissection. The SCM muscle is laterally retracted, while the great vessels, trachea, and esophagus are medially kept undissected and protected by a blunt retractor. There is always a variable amount of fat in the depth of this space. This fatty sheath surrounds the accessory nerve, which must be identified when the C2–C3 and the C3–C4 levels need to be exposed. At that point, the transverse processes, which are covered by the prevertebral muscles, can be easily palpated and then visually identified. Under the aponeurosis of the longus colli muscle, the sympathetic chain must be recognized to prevent iatrogenic damage. The aponeurosis is longitudinally divided medial to the sympathetic chain; both the aponeurosis and the sympathetic chain are then carefully retracted laterally. The longus colli muscle may be resected between the transverse processes and vertebral bodies of the index levels. Care must be taken to ensure that the VA is not entering the transverse foramen at an abnormally high level (C5, C4, or even C3 instead of C6); in this case, the artery may be running in front of the transverse processes and be injured during longus colli muscle division. At that point, the transverse processes and the lateral aspect of the vertebral bodies are clearly exposed.

Foraminotomy and Vertebrectomy [41] The fluoroscopic confirmation of the correct level is generally obtained through laterolateral (LL) views. After the subperiosteal dissection of the vertebral artery, the intervertebral foramen is opened by removing the anterior part of the transverse foramen with a Kerrison rongeur: this maneuver helps with additional lateral VA mobilization by creating a plane between the lateral aspect of the uncovertebral joint and the medial border of the VA. Once both structures have been separated, the hypertrophied uncovertebral joint can be safely removed with a drill and/or rongeurs. In this way, the cervical nerve root can be completely decompressed from its dural origin up to the VA lateral border. The VA must be identified before beginning the oblique drilling of the vertebral body because it may present medial loops. Attention should therefore be paid when resecting the anterior part of the transverse foramen; it is important to preserve the periosteal sheath surrounding the VA and containing its venous plexus. Notably, intraoperative ultrasound can prove very helpful in increasing the safety of such a step and avoiding vascular injury [42]. Drilling is then started with a cutting drill on the vertebral bodies on both sides of the disk and proceeds vertically down into the bodies until the cortical bone of the posterior aspect of the bodies has been reached, which is then removed with a Kerrison rongeur. The drilling is extended obliquely toward the opposite side: it is crucial to start with a vertical trench just medial to the VA and to then move obliquely so as to reduce as much as possible the extent of the anterior bone resection. In fact, the decompression is achieved through limited bone resection (<50% of the VB), creating a convex posterior aspect with significant sparing for the anterior aspect of the VB and the anterior longitudinal ligament. There are no anatomical landmarks to identify where the horizontal drilling should end. For this reason, we determine the contralateral point on computed tomography (CT) scans. The contralateral point frequently corresponds to the maximum extension of osteophytes at the junction between the body and the contralateral pedicle. Good surgical planning requires calculating the distance between the contralateral point and the medial border of the ipsilateral VA on a preoperative CT scan. Such a distance can also be intraoperatively checked to confirm adequate decompression in the horizontal plane; and in the majority of cases, its length ranges between 22 and 28 mm. If available, an intraoperative CT scan may be of considerable help.

Key Advantages of MOV The various advantages of MOV include the wide anterolateral decompression of the spinal canal and foramen at single or multiple levels (including the upper cervical spine, which might be difficult to reach via a standard anterior approach). Notably, the loss of cervical lordosis and even proper kyphotic changes do not represent absolute contraindications as long as spinal stability is preserved. Furthermore, because the route is so different from conventional anterior surgery, MOV can represent a valuable alternative in the case of recurrent stenosis, adjacent disk disease, or the failure of a prior anterior approach [43]. Because this approach preserves spinal stability and avoids the need for bone grafting and/or instrumentation, it is more suitable not only for patients with poor bone quality who would carry a high risk of implant failure but also for those neuro-oncological patients requiring adjuvant radiotherapy and serial MRI follow-up [44].

Complications and Their Management MOV is a quite demanding procedure with a steep learning curve; its most frequent complication is transient or permanent Horner syndrome in approximately one patient out of ten undergoing the anterolateral approach at the C3–C7 levels. Postoperative Horner syndrome is characterized by an ipsilateral myosis, ptosis, enophthalmos, and facial anhidrosis, and it is due to the stretching, compression, or disruption of any part of the ipsilateral cervical sympathetic trunk, also called the third-order neuron lesion, to distinguish it from the central (first-order neuron) and preganglionic (second-order neuron) causes of Horner syndrome. Additionally, a traction injury to the XI cranial nerve is possible when approaching the C2–C3 levels. With regard to those iatrogenic nerve damages, surgeons must be aware that besides traction and transection, heat injury induced by monopolar diathermy, ultrasonic aspirator, and scalpels can cause transient nerve damage during the dissection of the adipose tissue of the cervical sheath. Those risks can be reduced only by gaining a deep understanding of neck anatomy and careful preoperative planning similar to that described earlier on the possible variation in the VA course. The management of perioperative iatrogenic injuries requires prompt recognition; the timely assistance of other specialists, including vascular surgeons, endovascular radiologists, and ophthalmologists; and transparent communication with patients and relatives.

The Role of MOV in the Future of Spine Surgery Recently, the Spine Committee of the World Federation of Neurosurgical Societies recommended that additional research on cost–benefit analyses on various surgical approaches for DCM be carried out and their efficacy values with long-term outcomes be compared. Unfortunately, some authors have suggested that it is highly probable that MOV will not be included in cost–benefit investigations, because of its currently infrequent application by spine surgeons [45]. One trend should be highlighted, whereas surgical skills for open anterolateral approaches should be cherished, as this route may prove valuable in challenging degenerative and tumoral scenarios. Over time, the management of DCM via anterolateral corridors has also expanded thanks to the progresses in endoscopic spine surgery [46]. The latter may actually represent the wise conjunction between older and newer thinking in spine surgery.

5 Conclusion

Although MOV remains a demanding technique with a steep learning curve, this narrative review indicates that it yields satisfactory clinical outcomes and could be considered as a valid alternative for the management of DCM that is caused by multisegmental cervical spondylosis. Anatomical dissection in cadaver labs and good knowledge of the VA variations are essential for spine surgeons interested in developing such skills. A careful analysis of preoperative scans and the use of intraoperative imaging are recommended to increase the safety of MOV. This review also indicates that MOV favors early patient mobilization without postoperative bracing. In fact, this technique does not compromise stability as much as other anterior and posterior approaches do. Hence, we suggest that it would provide an advantage for patients with a low fusion rate, such as elderly, diabetic, and/or heavy-smoking patients. As is always the case in neurosurgery, optimal results rely on scrupulous patient selection and the continuous analysis of surgical results in international forums. For all the above, we advocate the inclusion of MOV in cost–benefit investigations related to DCM and radiculopathies.

Conflict of Interest The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this chapter.

References

1. Chibbaro S, Gubian A, Zaed I, et al. Cervical myelopathy caused by ventrally located atlanto-axial synovial cysts: an open quest for the safest and most effective surgical management. Case series and systematic review of the literature. Neurochirurgie. 2020;66(6):447–54.
2. Chibbaro S, Mirone G, Yasuda M, Marsella M, Di Emidio P, George B. Vertebral artery loop–a cause of cervical radiculopathy. World Neurosurg. 2012;78(3–4):375.
3. Cornelius JF, George B, N'dri Oka D, Spiriev T, Steiger HJ, Hänggi D. Bow-Hunter's syndrome caused by dynamic vertebral artery stenosis at the cranio-cervical junction–a management algorithm based on a systematic review and a clinical series. Neurosurg Rev. 2012;35(1):127–35; discussion 135.
4. Cornelius JF, Pop R, Fricia M, George B, Chibbaro S. Compression syndromes of the vertebral artery at the craniocervical junction. Acta Neurochir Suppl. 2019;125:151–8.
5. Cornelius JF, Slotty PJ, Tortora A, Petridis AK, Steiger HJ, George B. Bow Hunter's syndrome caused by compression of the subaxial vertebral artery: surgical technique of anterolateral decompression (video). World Neurosurg. 2018;119:358–61.
6. George B, Zerah M, Lot G, Hurth M. Oblique transcorporeal approach to anteriorly located lesions in the cervical spinal canal. Acta Neurochir. 1993;121(3-4):187–90.
7. Martin AR, Jentzsch T, Wilson JRF, et al. Inter-rater reliability of the modified Japanese orthopedic association score in degenerative cervical myelopathy: a cross-sectional study. Spine. 2021;46(16):1063–9.
8. Tetreault L, Palubiski LM, Kryshtalskyj M, Idler RK, Martin AR, Ganau M, Wilson JR, Kotter M, Fehlings MG. Significant predictors of outcome following surgery for the treatment of degenerative cervical myelopathy: a systematic review of the literature. Neurosurg Clin N Am. 2018;29(1):115–27.
9. Adams CB, Logue V. Studies in cervical spondylotic myelopathy. II. The movement and contour of the spine in relation to the neural complications of cervical spondylosis. Brain. J Neurol. 1971;94(3):568–86.
10. Kawaguchi Y, Kanamori M, Ishihara H, Ohmori K, Nakamura H, Kimura T. Minimum 10-year followup after en bloc cervical laminoplasty. Clin Orthop. 2003;411:129–39.
11. Hukuda S, Mochizuki T, Ogata M, Shichikawa K, Shimomura Y. Operations for cervical spondylotic myelopathy. A comparison of the results of anterior and posterior procedures. J Bone Joint Surg Br. 1985;67(4):609–15.
12. Edwards CC, Heller JG, Silcox DH. T-Saw laminoplasty for the management of cervical spondylotic myelopathy: clinical and radiographic outcome. Spine. 2000;25(14):1788–94.

13. Goel VK, Clark CR, Harris KG, Schulte KR. Kinematics of the cervical spine: effects of multiple total laminectomy and facet wiring. J Orthop Res. 1988;6(4):611–9.
14. Graham AW, Swank ML, Kinard RE, Lowery GL, Dials BE. Posterior cervical arthrodesis and stabilization with a lateral mass plate. Clinical and computed tomographic evaluation of lateral mass screw placement and associated complications. Spine. 1996;21(3):323–8; discussion 329.
15. Hirabayashi K, Watanabe K, Wakano K, Suzuki N, Satomi K, Ishii Y. Expansive open-door laminoplasty for cervical spinal stenotic myelopathy. Spine. 1983;8(7):693–9.
16. Iwasaki M, Kawaguchi Y, Kimura T, Yonenobu K. Long-term results of expansive laminoplasty for ossification of the posterior longitudinal ligament of the cervical spine: more than 10 years' follow-up. J Neurosurg. 2002;96(2):180–9.
17. Cantore GP, Ciapetta P, Delfini R, Raco A. Fibular graft in anterior surgery of cervical spondyloarthrosis myelopathy. Zentralbl Neurochir. 1986;47(2):111–5.
18. Graham JJ. Complications of cervical spine surgery. A five-year report on a survey of the membership of the Cervical Spine Research Society by the Morbidity and Mortality Committee. Spine. 1989;14(10):1046–50.
19. Heller JG, Edwards CC, Murakami H, Rodts GE. Laminoplasty versus laminectomy and fusion for multilevel cervical myelopathy: an independent matched cohort analysis. Spine. 2001;26(12):1330–6.
20. Jeffreys RV. The surgical treatment of cervical myelopathy due to spondylosis and disc degeneration. J Neurol Neurosurg Psychiatry. 1986;49(4):353–61.
21. Kaptain GJ, Simmons NE, Replogle RE, Pobereskin L. Incidence and outcome of kyphotic deformity following laminectomy for cervical spondylotic myelopathy. J Neurosurg. 2000;93(2):199–204.
22. Orabi M, Chibbaro S, Makiese O, Cornelius JF, George B. Double-door laminoplasty in managing multilevel myelopathy: technique description and literature review. Neurosurg Rev. 2008;31(1):101–10.
23. Kato S, Ganau M, Fehlings MG. Surgical decision-making in degenerative cervical myelopathy - anterior versus posterior approach. J Clin Neurosci. 2018;58:7–12.
24. Fehlings MG, Barry S, Kopjar B, et al. Anterior versus posterior surgical approaches to treat cervical spondylotic myelopathy: outcomes of the prospective multicenter AOSpine North America CSM study in 264 patients. Spine. 2013;38(26):2247–52.
25. Aebi M, Zuber K, Marchesi D. Treatment of cervical spine injuries with anterior plating. Indications, techniques, and results. Spine. 1991;16(3):38–45.
26. Bruneau M, Cornelius JF, George B. Multilevel oblique corpectomies: surgical indications and technique. Neurosurgery. 2007;61(3):106–12; discussion 112.
27. Chibbaro S, Mirone G, Bresson D, George B. Cervical spine lateral approach for myeloradiculopathy: technique and pitfalls. Surg Neurol. 2009;72(4):318–24; discussion 324.
28. Chibbaro S, Mirone G, Makiese O, George B. Multilevel oblique corpectomy without fusion in managing cervical myelopathy: long-term outcome and stability evaluation in 268 patients. J Neurosurg Spine. 2009;10(5):458–65.
29. Emery SE, Bohlman HH, Bolesta MJ, Jones PK. Anterior cervical decompression and arthrodesis for the treatment of cervical spondylotic myelopathy. Two to seventeen-year follow-up. J Bone Joint Surg Am. 1998;80(7):941–51.
30. Fehlings MG, Cooper PR, Errico TJ. Posterior plates in the management of cervical instability: long-term results in 44 patients. J Neurosurg. 1994;81(3):341–9.
31. Kumar VG, Rea GL, Mervis LJ, McGregor JM. Cervical spondylotic myelopathy: functional and radiographic long-term outcome after laminectomy and posterior fusion. Neurosurgery. 1999;44(4):771–7; discussion 777-778.
32. Bruneau M, Cornelius JF, George B. Microsurgical cervical nerve root decompression by anterolateral approach. Neurosurgery. 2006;58(1):108–13; discussion ONS108-113.
33. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. Res Integr Peer Rev. 2019;4(1):5.
34. Verbiest H. The lateral approach to the cervical spine. Clin Neurosurg. 1973;20:295–305.
35. Verbiest H, Paz Geuse HD. Anterolateral surgery for cervical spondylosis in cases of myelopathy or nerve-root compression. J Neurosurg. 1966;25(6):611–22.
36. Cagli S, Chamberlain RH, Sonntag VKH, Crawford NR. The biomechanical effects of cervical multilevel oblique corpectomy. Spine. 2004;29(13):1420–7.
37. George B. Extracranial vertebral artery anatomy and surgery. Adv Tech Stand Neurosurg. 2002;27:179–216.
38. George B, Gauthier N, Lot G. Multisegmental cervical spondylotic myelopathy and radiculopathy treated by multilevel oblique corpectomies without fusion. Neurosurgery. 1999;44(1):81–90.
39. George B, Cornelius JF. Vertebral artery: surgical anatomy. J Oper Tech Neurosurg. 2001;4:168–81.
40. Yasuda M, Bresson D, Cornelius JF, George B. Anterolateral approach without fixation for resection of an intradural schwannoma of the cervical spinal canal: technical note. Neurosurgery. 2009;65(6):1178–81; discussion 1181.
41. Bruneau M, Cornelius JF, George B. Anterolateral approach to the V2 segment of the vertebral artery. Neurosurgery. 2005;57(4):262–7; discussion 262–267.
42. Ganau M, Ligarotti GK, Apostolopoulos V. Real-time intraoperative ultrasound in brain surgery: neuronavigation and use of contrast-enhanced image fusion. Quant Imaging Med Surg. 2019;9(3):350–8.
43. Cornelius JF, George B. Cervical nerve root decompression by lateral approach as salvage operation after failed anterior transdiscal surgery: technical case report. Eur Spine J. 2009;18(2):272–5.
44. Nicácio JM, Rodrigues JC, Galles MHL, Faquini IV, de Brito Pereira CA, Ganau M. Cervical intramedullary schwannoma: a case report and review of the literature. Rare Tumors. 2009;1(2):e44.
45. Balak N, Baran O, Denli Yalvac ES, Esen Aydin A, Kumbasar A, Tanriover N. Cervical oblique corpectomy: revitalizing the underused surgical approach with step-by-step simulation in cadavers. J Craniofac Surg. 2022;33(1):337–43.
46. Ganau M, Holly LT, Mizuno J, Fehlings MG. Future directions and new technologies for the management of degenerative cervical myelopathy. Neurosurg Clin N Am. 2018;29(1):185–93.

Comparison Between Sagittal Balance Outcomes After Corpectomy, Laminectomy, and Fusion for Cervical Spondylotic Myelopathy: A Matched Cohort Study

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1 Introduction

Cervical spondylotic myelopathy (CSM) is a progressive degenerative disease [1] and constitutes the leading cause of spinal cord dysfunction in individuals above 50 years of age [2]. For patients with documented disease progression, or risk factors for poor outcomes, such as radiculopathy or instability, surgery is indicated [3]. When considering surgery for spinal cord compression behind the vertebral bodies, two options—anterior cervical corpectomy and fusion (ACCF) and laminectomy and posterior fusion (LMF)—provide efficient spinal cord and nerve root decompression and provide short-term neurological improvement [4]. Each of these procedures comes with specific complications, namely the risk of pseudarthrosis and hardware failure for multilevel ACCF [5], which is incremental with the number of operated levels [6], whereas LMF may be complicated by surgical site infection, screw misplacement with neurological or vascular damage, and C5 palsy [7].

The choice of approach is traditionally based on the location or the predominant spinal cord compression—anterior or posterior—and the number of cervical spine levels affected [8]. Moreover, the choice of the procedure is also largely based on the preoperative sagittal balance, as lordotic spines tend to be approached posteriorly and straight and kyphotic ones anteriorly. However, in the case of multilevel ACCF (more than two levels), it can be technically demanding to reconstruct cervical lordosis with the currently available straight-design devices. Consequently, all the comparative studies between the two techniques published so far on postoperative sagittal balance outcomes reaffirm conclusions that are poisoned by this patient selection bias, according to their preoperative sagittal alignments. We aimed to eliminate this bias by studying a matched cohort of patients for their preoperative cervical sagittal balance. The goal of our study was to compare the impact of ACCF and LMF on global and segmental cervical alignment in order to include these parameters in the decision-making process when choosing the ideal approach for an individual patient.

2 Material and Methods

Between 2012 and 2020, patients with multilevel cervical compression behind the vertebral body were treated with either ACCF or LMF, without taking into account their preoperative sagittal alignments when determining a specific approach. All patients involved had myelopathy or a combination of myelopathy and radiculopathy and showed evidence of cervical spine cord compression on MRI scans. Clinical data were collected on their epidemiological characteristics (gender, age at time of surgery, topography and the number of levels operated on, and the duration of follow-up). Patients were excluded if their clinical data were incomplete. In total, 34 patients were included: 17 in the ACCF arm and 17 in the LMF arm. We performed retrospective data collection from pre- and postoperative neutral-position cervical spine X-rays, including parameters such as C0-2, C2-3, C3-7, index angles, the T1 slope, and SVA by using SECTRA (Sectra AB, Linkoping, Sweden) imaging software. The statistical analysis was performed with SPSS v. 23 (IBM Corp,

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USA), using descriptive statistics and a Pearson correlation test. We expressed kyphosis as negative values and lordosis as positive values.

3 Results

In total, 34 patients were enrolled, equally divided between both surgical arm groups (ACCF and LMF). The mean preoperative C3-7 Cobb angle was similar in both groups, with a mean angle of 11.58 ± 16.00° (range −19.9 to 35.9°) for ACCF versus 13.36 ± 12.21° (range: −15.1 to 33.5°) for LMF (Fig. 1). Variations in sagittal balance parameters are displayed in Table 1. Both techniques are associated with a similar trend toward the loss of global C3-7 lordosis (Δ of −2.68 ± 13.8°, p = 0.0.43 for ACCF vs. −2.94 ± 11.5°, p = 0.31 for LMF). At the index level, both procedures lost lordosis, with a more pronounced effect seen in ACCF (Δ of

Table 1 Postoperative variations in sagittal balance parameters after LMF and after ACCF

Sagittal balance parameters				
	LMF		ACCF	
C3-7	−2.68 ± 3.8	↓	−2.94 ± 1.5	↓
Index levels	−3.1 ± 11.6	↓	−3.8 ± 12.1	↓
cSVA	2.2 ± 8.6	↑	7.1 ± 11.9	↑
T1 slope	−4.4 ± 11.6	↓	−2.1 ± 7.3	↓
C0-2	3.5 ± 15.4	↑	−0.9 ± 8.0	↓
C2-3	3.1 ± 7.7	↑	0.7 ± 9.5	↑

LMF laminectomy and fusion, *ACCF* anterior cervical corpectomy and fusion, *cSVA* cervical sagittal vertical axis

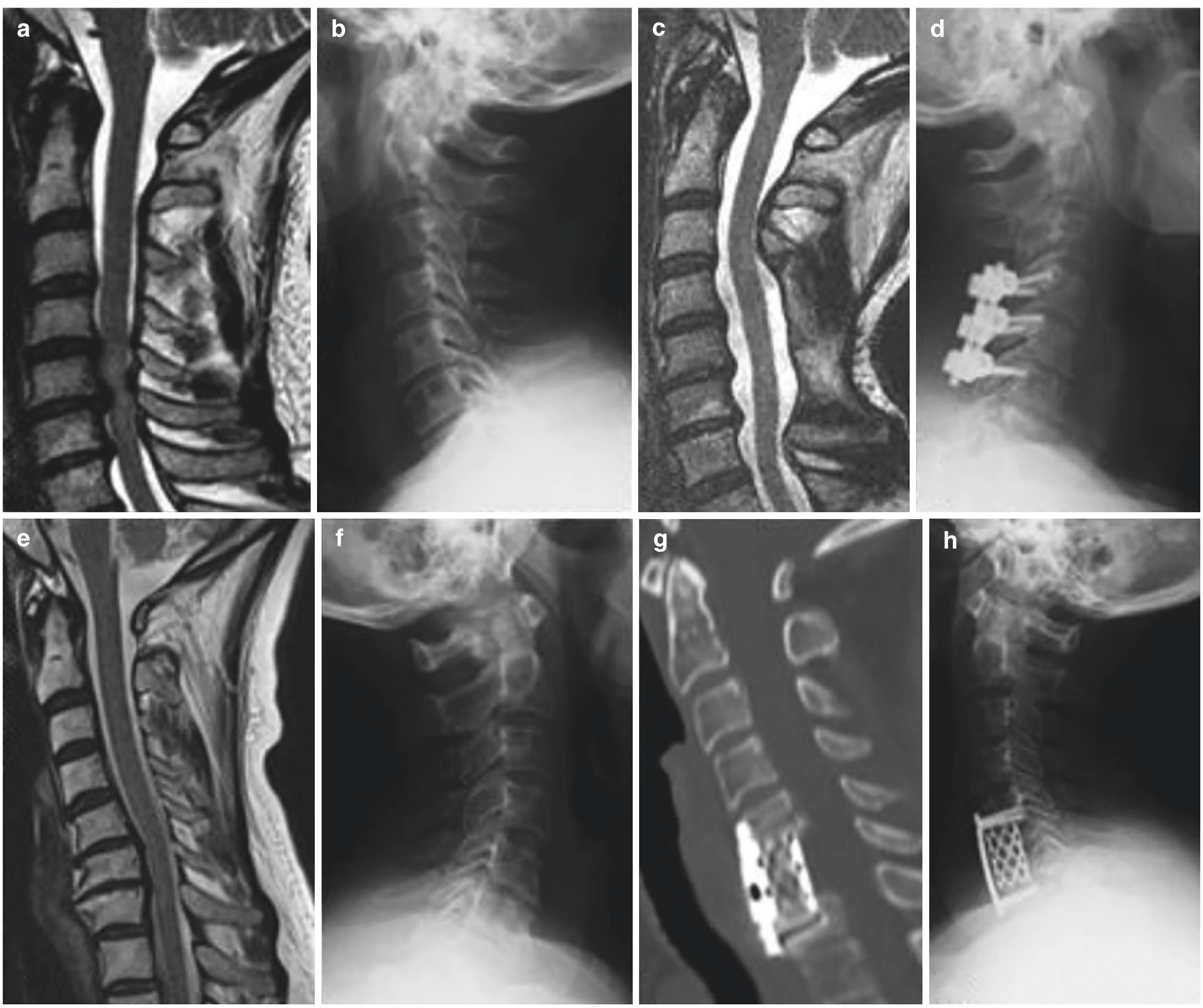
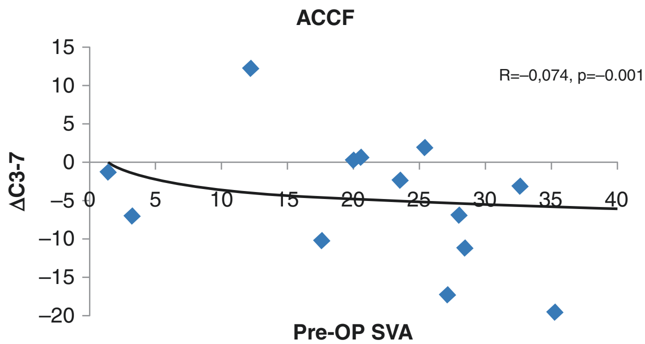


Fig. 1 (**a**–**d**) C4-6 laminectomy and fusion in a 58-year-old man with myelopathy, where the patient lost 1° in global lordosis while increasing 18.3° in the C0-2 functional unit, maintaining approximately the same SVA (Δ −0.6 mm) and C2-3 slope (Δ −0.1°); (**e**–**h**) C6 corpectomy and reconstruction with mesh and anterior plate in a 65-year-old woman with myeloradiculopathy, where the patient lost 7.4° in global lordosis, increased SVA by 9.7 mm, and lost 5.8° at C0-2 m while gaining 4.4° with the C2-3 slope



Graph 1 Linear regression plot showing correlation between the preoperative cSVA and the loss of lordosis in ACCF. *ACCF* anterior cervical corpectomy and fusion, *cSVA* cervical sagittal vertical axis

−3.8 ± 12.1°, $p = 0.22$) when compared to that in LMF (−3.1 ± 11.6°, $p = 0.23$), but with a fairly even distribution of values for ACCF. Both techniques reduced the T1 slope, especially in LMF (−4.4 ± 11.6°, $p = 0.142$) when compared to that in ACCF (−2.1 ± 7.3°, $p = 0.252$), but without any statistically significant difference. At the C0-2 level, there was a contrasting trend toward an increase in the mean angle after LMP (Δ 3.5 ± 15.4°, $p = 0.357$), whereas ACCF caused a decrease in the angle at this functional unit (Δ −0.9 ± 8.0°, $p = 0.709$). At the C2-3 angle, ACCF barely had an effect (Δ of 0.7 ± 9.5°, $p = 0.801$), whereas LMF displayed a more consistent trend toward an increase (3.1 ± 7.7°, $p = 0.122$). Significantly, ACCF led to an important mean increase in SVA (7.1 ± 11.9 mm, $p = 0.002$) when compared with an increase of only 2.0 ± 8.6 mm ($p = 0.306$) with LMF. Using the Pearson correlation, a data analysis showed a strong negative correlation between preoperative SVA and the loss of global lordosis in ACCF ($R = −0.074$, $p = −0.001$; see Graph 1). A similar trend was also seen in LMF, but it was not significant ($R = 0.014$, $p = −0.32$). Only in LMF was the preoperative C0-2 angle also statistically correlated with a loss of lordosis at the index level ($R = 0.003$, $p = 0.009$) and an increase in SVA ($p = 0.001$).

4 Discussion

To the best of our knowledge, this is the first study to match preoperative sagittal alignment between two cohorts of patients treated with one of two techniques in order to better assess the factual approach's effect on the final alignment parameters. Several studies have separately analyzed the effects of ACCF and LMF on sagittal balance: Ikeda et al. [9], in their study of 31 patients after ACCF had been performed, found a significant decrease of 5.0 ± 7.7° ($p < 0.01$) in lordosis, while Oni et al. [6] described anterior approaches, both anterior cervical discectomy and fusion (ACDF) and ACCF, as effective at restoring lordosis. However, an intrinsic effect of ACCF could not be perceived, because these patients were pooled together with ACDF patients. By comparing ACCF patients and LMF patients but departing from different preoperative sagittal parameters, in a cohort of 48 patients, Hitchon et al. [10] found anterior approaches to be superior to posterior laminectomy and fusion in lordosis restoration. However, they also described a greater loss of correction in the long term and higher rates of hardware failure with ACCF. Liu et al. [11] and Aghayev et al. [12] described that the same loss of anterior column support could lead to a reduction in lordosis in ACCF in the long term. On the other hand, Lee et al. [13], in their comparison of radiological outcomes of cervical posterior fusion with either a pedicle or lateral mass screws, found that lordosis, SVA, and the T1 slope tended to return to preoperative levels, though with a loss of correction. These and other studies supported the assumption that preoperative kyphotic- or straight-aligned patients should be approached anteriorly. However, by departing from patients with strictly similar preoperative sagittal indexes in long-term outcomes, we found equivalence with both techniques, with a tendency toward greater losses of lordosis in ACCF compared to LMF, at either an index level or a global level. This trend is in contrast with the published literature, which tends to report an advantage for anterior approaches, ACCF included. The ACCF kyphotic effect is a direct consequence of the straight-design limitations of the currently available corpectomy implants and of the long-term subsidence of reconstructive corpectomy implants. In both techniques, there seems to be a follow-up-dependent phenomenon, which could be related to the progression of the degenerative process.

Myiasaki et al. [14] reported significant positive correlations between the T1 slope and cervical lordosis—where a high T1 slope was associated with greater cervical lordosis. In the current study, the trend toward a decrease in the mean T1 slope seen in both techniques may reflect the loss of lordosis that both groups of patients experienced. Yang et al. [15] described that a critically low T1 slope (odds ratio of 5.63, $p = 0.005$) may accelerate cervical degeneration, especially at the C6-7 level. According to our results, any patient with a low T1 slope baseline should avoid LMF because it is the technique that most negatively influences the T1 slope.

Regarding SVA, Hitchon et al. [10] described that both anterior and posterior approaches led to a significant increase in SVA. Ikeda et al. [9] described a significant increase in SVA (1.9 ± 5.3 mm, $p = 0.04$) after ACCF. A postoperative increase in SVA inversely correlates with mJOA scores and directly correlates with disability and instability [16]. Although several studies have described good outcomes for posterior fusions for the treatment of cervical deformity [17], the literature has sparse evidence on the effect of LMF on SVA in nondeformity cases. The greater negative impact of ACCF on SVA, in comparison to LMF, is one of the major findings of our study. In addition, we found a strong negative correlation ($p = -0.001$) between preoperative SVA and postoperative lordosis in ACCF patients, a correlation that was absent in LMF cases. Thus, not only baseline lordosis but also initial SVA should guide the decision on whether to solve myelopathy compression via the anterior approach or the posterior approach. According to our study, it is clear that patients with high preoperative SVA values should be preferentially managed by LMF instead of ACCF in order to achieve better outcomes and stop progressive cervical spine degeneration.

Ikeda et al. [9] described in their study an inverse relation between cervical lordosis and the C0-2 angle. The loss of lordosis after ACCF led to a compensatory increase in the C02 angle, which maintained the horizontal gaze. In our study, both cohorts lost lordosis, but only LMF showed a compensatory increase in the C0-2 angle. We also found a correlation between the preoperative C0-2 angle on one hand and the loss of lordosis at the index level ($p = 0.009$) and an increase in SVA ($p = 0.001$) in LMF on the other. Despite the posterior muscle weakness induced by dissection and retraction during LMF, the preservation of C2 muscles attachment from using our technique may allow the C0-2 compensation mechanism to come into play. Conversely, the anterior implants were unable to provide long-term anterior column support because of subsidence, as demonstrated by the loss of lordosis and the significant increase in SVA. These may have obliterated the compensatory mechanisms expected to occur at C0-2.

The role of the C2-3 disk as a transition zone between C0-2 and the subaxial cervical spine is still unknown. Lee et al. [18] found an association between a high C2-3 disk angle (above 32.3° ± 17.2°) and adverse outcomes after 171 procedures of laminectomy and instrumented fusion. They postulated that higher C2-3 angles were associated with increased burdens on the C1-2 unit, which maintains the horizontal gaze. Both cohorts in our study increased C2-3 angles after the procedures, especially LMF, though the result was not statistically significant.

In terms of limitations to our study, we acknowledge the small number of patients, although this is seen in a significant number of published and cited studies on this topic, and the lack of clinical data that were out of the scope of this purely radiological study.

5 Conclusions

When departing from patients with identical preoperative sagittal alignment, both procedures result in the loss of lordosis at the index and global levels, which is related to the loss of anterior column support (after ACCF) and posterior muscle weakness (after LMF). This effect is more pronounced for ACCF than for LMF. The subsidence seen with ACCF is not reversible, whereas a muscle-strengthening program may mitigate the effect after LMF in the long term. A higher preoperative SVA value is more adequately managed with LMF, whereas a higher baseline T1 slope justifies an ACCF—according to the different effects of both techniques on these parameters. Both procedures affect the C0-2 functional unit and C2-3 disk, with a trend toward kyphosis for ACCF and lordosis with LMF. For multilevel CSM, the preoperative C0-2 angle, the SVA value, and the T1 slope should be strongly weighted in the surgical decision algorithm, as have been so far the conventional criteria related to the location of compression, the number of affected levels, and cervical lordosis.

Contributions RR performed the data collection and analysis and wrote the chapter. DK and LP contributed to the data collection and statistical work. OLA elaborated on the intellectual concept of the article, designed the study, and wrote the chapter. All authors have reviewed the manuscript.

Ethics Statement The authors are accountable for all aspects of the work, including ensuring that questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

References

1. Kalsi-Ryan S, Karadimas SK, Fehlings MG. Cervical spondylotic myelopathy: the clinical phenomenon and the current pathobiology of an increasingly prevalent and devastating disorder. Neuroscientist. 2013;19:409–21.
2. Fehlings MG, Tetreault LA, Riew KD, Middleton JW, Wang JC. A clinical practice guideline for the management of degenerative cervical myelopathy: introduction, rationale, and scope. Global Spine J. 2017;7(3):21–7.
3. Fehlings MG, Tetreault LA, Riew KD, Middleton JW, Aarabi B, Arnold PM, Brodke DS, Burns AS, Carette S, Chen R, Chiba K, Dettori JR. A clinical practice guideline for the management of patients with degenerative cervical myelopathy: recommendations for patients with mild, moderate, and severe disease and nonmyelopathic patients with evidence of cord compression. Global Spine J. 2017;7(3 Suppl):70S–83S.
4. Lawrence BD, Jacobs WB, Norvell DC, Hermsmeyer JT, Chapman JR, Brodke DS. Anterior versus posterior approach for treatment of cervical spondylotic myelopathy: a systematic review. Spine. 2013;38(22 Suppl 1):173–82.
5. Jain V, Madan A, Thakur M, Thakur A. Functional outcomes of subaxial spine injuries managed with 2-level anterior cervical corpectomy and fusion: a prospective study. Neurospine. 2018;15(4):368.
6. Oni P, Schultheiß R, Scheufler KM, Roberg J, Harati A. Radiological and clinical outcome after multilevel anterior cervical discectomy and/or corpectomy and fixation. J Clin Med. 2018;7(12):E469.
7. Bajamal AH, Kim SH, et al. Posterior surgical techniques for cervical spondylotic myelopathy: WFNS Spine Committee Recommendations. Neurospine. 2019;16(3):421–34.
8. Deora H, Kim SH, Behari S, Behari S, Rudrappa S, Rajshekhar V, Zileli M, Parthiban JKBC. Anterior surgical techniques for

cervical spondylotic myelopathy: WFNS Spine Committee Recommendations. Neurospine. 2019;16(3):408–20.
9. Ikeda N, Odate S, Shikata J. Compensatory mechanisms for kyphotic change in the cervical spine according to alignment analysis of the cases after anterior cervical corpectomy and fusion. World Neurosurg. 2020;133:e233–40.
10. Hitchon PW, Woodroffe RW, Noeller JA, Helland L, Hramakova N, Nourski KV. Anterior and posterior approaches for cervical myelopathy: clinical and radiographic outcomes. Spine. 2019;44(9):615–23.
11. Liu Y, Hou Y, Yang L, Chen H, Wang X, Wu X, Gao R, Wang C, Yuan W. Comparison of 3 reconstructive techniques in the surgical management of multilevel cervical spondylotic myelopathy. Spine. 2012;37:E1450–8.
12. Aghayev K, Doulgeris JJ, Gonzalez-Blohm SA, Eleraky M, Lee WE, Vrionis FD. Biomechanical comparison of a two-level anterior discectomy and a one-level corpectomy, combined with fusion and anterior plate reconstruction in the cervical spine. Clin Biomech. 2014;29:21–5.
13. Lee S, Cho DC, Roh SW, Jeon SR, Moon EJ, Lee JJ, Park JH. Cervical alignment following posterior cervical fusion surgery: cervical pedicle screw versus lateral mass screw fixation. Spine. 2018;46(10):E576–83.
14. Miyazaki M, Ishihara T, Notani N, Kanezaki S, Tsumura H. Relationship of T1 slope with loss of lordosis and surgical outcomes after laminoplasty for cervical ossification of the posterior longitudinal ligament. Clin Neurol Neurosurg. 2018;164:19–24.
15. Yang BS, Lee SK, Song KS, Yoon SP, Jang G, Lee CC, Moon SH, Lee HM, Lee SH. The Use of T1 sagittal angle in predicting cervical disc degeneration. Asian Spine J. 2018;9(5):757–61.
16. Ames CP, Blondel B, Scheer JK, Schwab FJ, Huec JL, Massicotte EM, Patel AA, Traynelis VC, Kim HJ, Shaffrey CI, Smith JS, Lafage V. Cervical radiographical alignment: comprehensive assessment techniques and potential importance in cervical myelopathy. Spine. 2013;38(22 Suppl 1):149–60.
17. Abumi K, Shono Y, Taneichi T, Ito M, Kaneda K. Correction of cervical kyphosis using pedicle screw fixation systems. Spine. 1999;24(22):2389–96.
18. Lee BS, Walsh KM, Lubelski D, Knusel KD, Steinmetz MP, Mroz TE, Schlenk RP, Kalfas IH, Benzel EC. The effect of C2-3 disc angle on postoperative adverse events in cervical spondylotic myelopathy. J Neurosurg Spine. 2018;30(1):38–45.

Minimally Invasive Posterior Cervical Fusion: A Handsome Option

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1 Introduction

Cervical spondylosis is the leading cause of age-related cervical degeneration. It may present with one of three main symptom combinations, including neck pain, cervical radiculopathy, or cervical myelopathy. When disabling symptoms are combined with disease progression, surgery is indicated. The choice of the surgical approach is generally based on the location of the predominant neural compression, the number of affected levels, the cervical sagittal alignment, and the surgeon's experience. Open posterior approaches eliminate the risk for dysphagia, esophageal injury, and recurrent laryngeal nerve palsy when compared to a standard anterior cervical surgery [1]. However, they are linked to a significant increase in postoperative pain and analgesic intake, blood loss, C5 nerve palsy, incidental durotomy, length of hospital stay, and a substantial risk of wound infection and dehiscence [2]. When instrumentation is added to posterior surgery, lateral mass and pedicle screws are associated with increased risks of nerve root and vertebral artery injuries, along with hardware failures. The most common long-term complications include junctional kyphosis, ASD, and pseudoarthrosis [2, 3]. Over all, the complication rates of traditional open posterior cervical decompression and fusion are estimated to range from about 15% to 25% [3].

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Tissue-sparing minimally invasive spine surgery (MISS) is supported by a strong body of literature in that it leads to improved outcomes and lower complications rates. Although cervical MISS is popularly used on the lumbar spine [4], relatively fewer reports have addressed cervical MISS. Nevertheless, PCF through percutaneous facet joint cages has emerged as a reliable alternative in cases of cervical radiculopathy secondary to foraminal stenosis (Fig. 1) because it provides indirect foraminal decompression and may apply to many other clinical conditions whenever a solid fusion is requested [5, 6].

1.1 Minimally Invasive Surgical Technique for PCF

The percutaneous placement of cages between the cervical facet joints may be indicated for adult patients with cervical radiculopathy encompassing the C3–C7 levels. The patient is placed in the prone position with their head supported by a face cushion. Lateral fluoroscopy is obtained to check that the neck is in a neutral position with the front parallel to the floor.

After the head is positioned, gently pull down their shoulders with tape to allow the optimum fluoroscopic view of the entire cervical spine. As for any other MISSs, a clear visualization of perfectly aligned facet joints on lateral fluoroscopy is crucial to proceed with the surgery. The upward trajectory of the surgical approach should match the angle of the facet joints and project onto the skin as the entry point. Next, on anteroposterior (AP) fluoroscopy, the medial and lateral borders of the facets and the operative level should be marked by using a surgical pen. A more medial entry point is chosen to allow a medial to lateral surgical trajectory. Local anesthesia and epinephrine may be locally applied for pain and bleeding control. Bilateral paramedian incisions that are approximately 1–1.5 cm wide should be made on the predetermined entry points at each surgical level (Fig. 2). Under fluoro-

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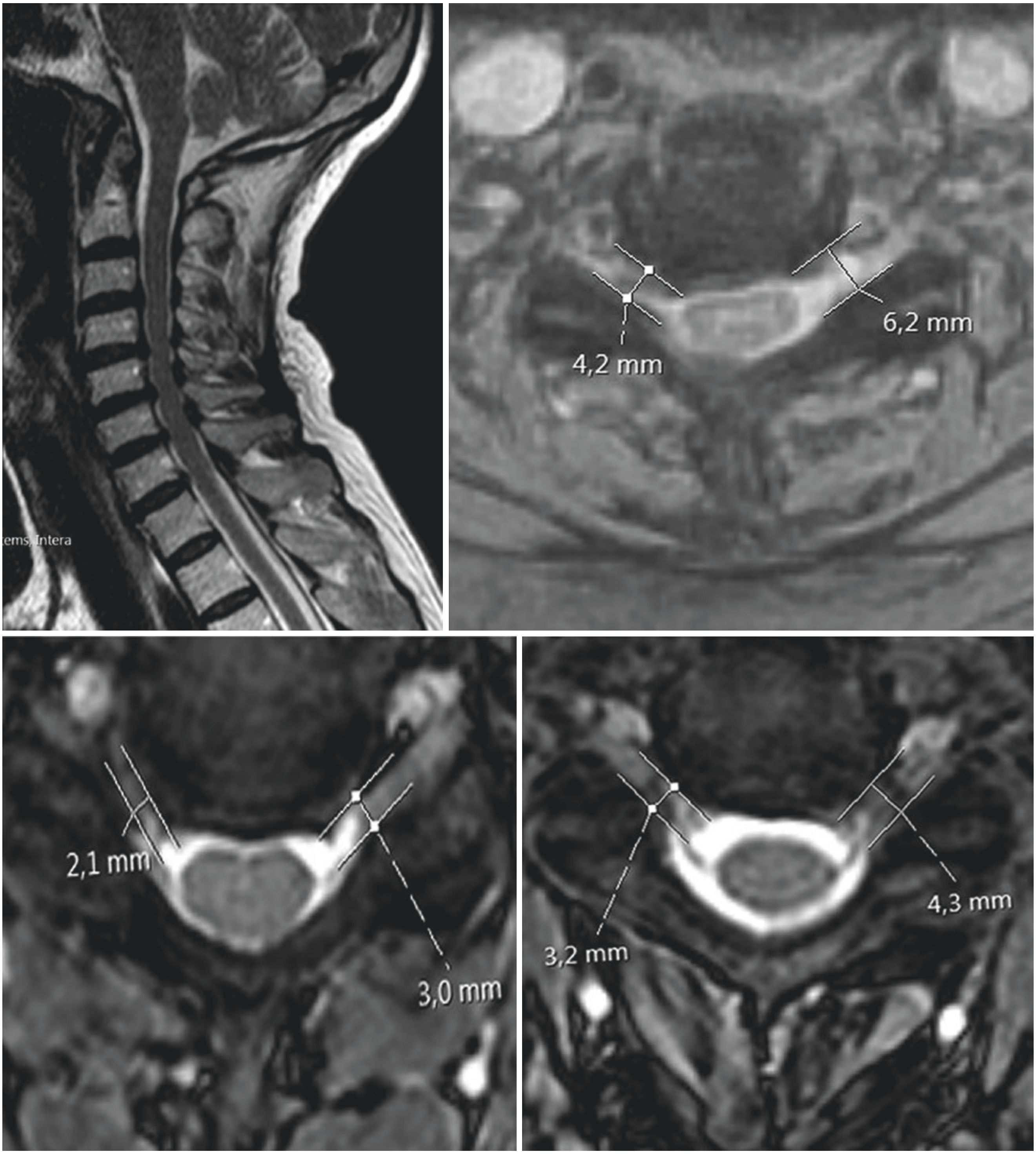

Fig. 1 T2-weighted images of a patient with cervical spondylosis presenting with complaints of cervical radiculopathy and arm and neck pain: from left to right and top to bottom are shown magnetic resonance images from the sagittal plane and axial images of the C4, C5, and C6 levels, respectively, with foraminal stenosis

scopic guidance, a chisel with a verticalized blade is inserted, and upon reaching the bone, it should be rotated by 90° to cut the joint capsule and advance through the facet joint with controlled malleating. The posterior surface of the lateral mass is decorticated with a trephine advancing over the access chisel. After this process has been completed, the trephine should be retracted, and a guide tube should be placed instead to establish a working channel. After the guiding tube

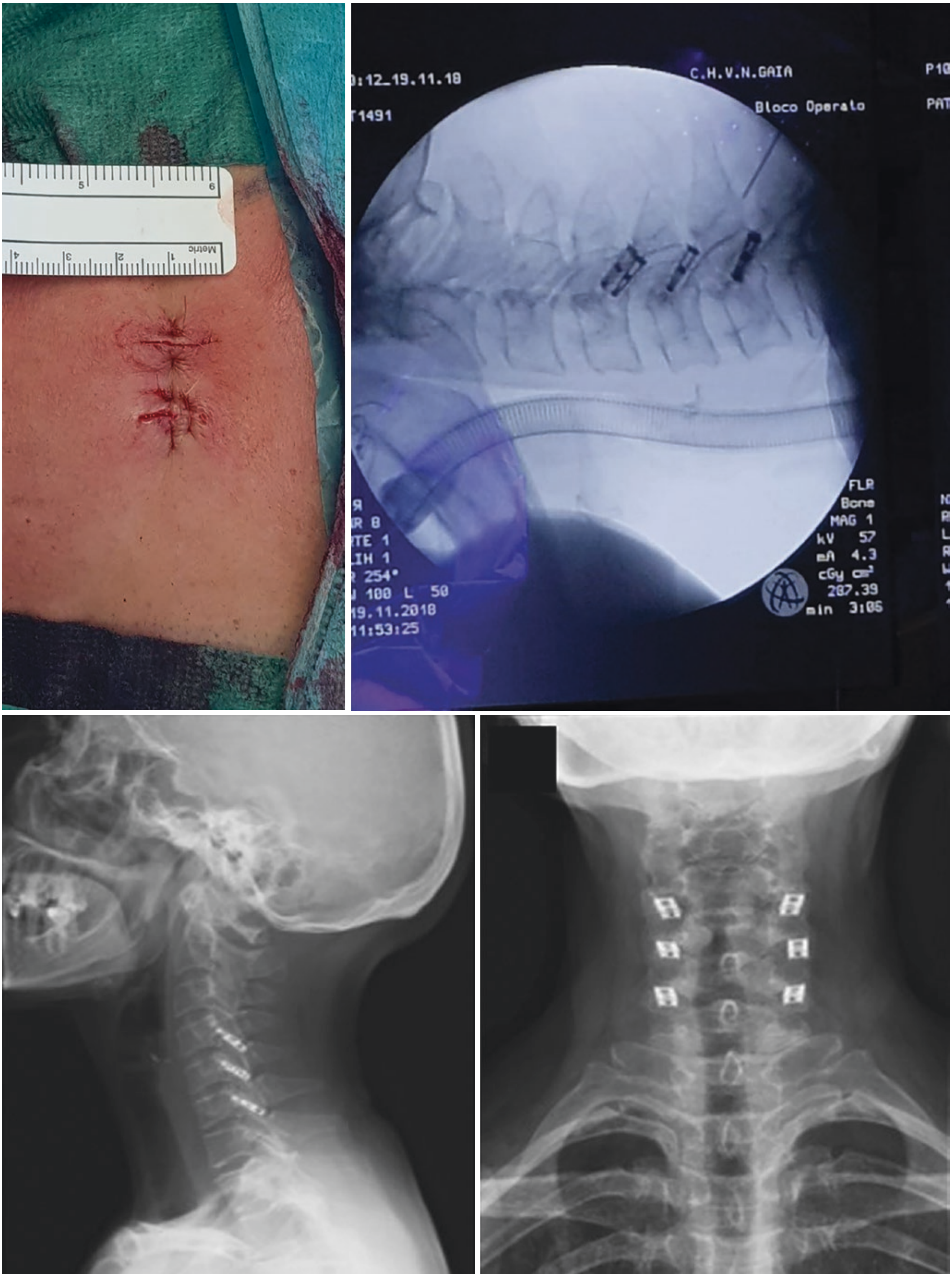

Fig. 2 Peri- and postoperative images from the patient presented in Fig. 1: on top is a perioperative photograph of a representative surgical incision and a fluoroscopic image of the posterior interfacet implants placed in the C4, C5, and C6 vertebrae; on bottom are postoperative control radiographs obtained while in the lateral and anteroposterior views, respectively, after 2-year follow-ups

has been secured at the entry point of the facet joint, the access chisel can be removed. The joint should next be decorticated by using a rasp turned 180° and be advanced into the joint several times to allow the complete decortication essential to promoting fusion. The interfacet cage is then inserted, distracting the target joint. Before releasing the guiding tube, bone graft material should be pushed into the decorticated lateral masses. The final position of the cage should be confirmed via lateral and AP fluoroscopy, and its position should be in the middle of the facet joint, centered between the medial and lateral borders (Fig. 2).

2 Clinical Indications

Suitable indications for percutaneous PCF include indirect foraminal decompression and fusion in cases of cervical radiculopathy [7], symptomatic pseudarthrosis [8], ASD after an index ACDF [9], and failed total disk replacement, as an adjunct for circumferential fusion to ACDF [8] and as a fusion to supplement laminectomy [10]—as depicted in Table 1.

Table 1 Clinical indications for percutaneous posterior cervical fusion through bilateral facet cages

Symptomatic pseudoarthrosis
Symptomatic adjacent-level disease
Failed total disk replacement
Circumferential fusion (360°)
Laminectomy and fusion with posterior cervical cages
Indirect foraminal decompression and fusion

3 Discussion

As a tissue-sparing technique, percutaneous PCF, when compared to the classical open techniques, is linked with favorable surrogate end points for outcomes, such as less muscle damage, which correlates with less postoperative cervical pain, less estimated blood loss (75 mL vs. 225–480 mL), a shorter procedural time (88 min vs. 110–270 min) and a reduction in the length of stay by at least 3 days [8].

PCF allows facet joint distraction and fusion, resulting in a combined enlargement of the intervertebral foramen area and the restriction of the segment's range of motion [11]. As reported by Siemionow et al., these simultaneous features are essential in controlling radicular pain from isolated foraminal stenosis, especially in bilateral cases where foraminotomy is contraindicated [11]. Moreover, as several studies have shown, there was a significant improvement in the Neck Disability Index, short-form-12 version 2, and visual analog scale scores for patients subjected to surgery and followed for 1 year [7] and 2 years [12].

Symptom relief is observed in very early postoperative time points because facet joint cages demonstrated very sound primary stability. The biomechanical effectiveness of bilateral posterior cervical cage stabilization is comparable to single-level plated ACDF, even exceeding it in lateral bending (LB) and axial rotation stabilization [13]. This effect is probably due to the lateral position of the cages. When compared to classical lateral mass screw (LMS) fixation, bilateral posterior cervical cages also provide similar cervical stability, once again with slightly superior results in LB stability [6]. Furthermore, when supplementing single- or multilevel ACDF, posterior cervical cages also provide a significant complement in range of motion suppression [6, 13], which renders this technology suitable to achieve circumferential fusion.

In patients with symptomatic pseudarthrosis, or in those at risk thereof, solid fusion is the ultimate goal. At 24 months, PCF achieved evidence of bridging the trabecular bone in 98.1% of cases and <2 mm translational motion in 100% of cases, denoting high fusion rates [12]. When compared to the anterior interbody cage surface area, the bilateral facet cages' surface area has relatively similar dimensions for bone grafts. Together with a shorter distance for bone bridging, because the facet articular height is shorter than the disk height [14], it enables extremely effective fusion.

As the natural alignment of the cervical spine is commonly lordotic [15], cervical kyphosis is one of the major postoperative concerns typically associated with posterior cervical surgical approaches. The detachment of the posterior cervical muscles is thought to contribute to postoperative cervical kyphosis, axial pain, and disease progression [16]. Similarly, one concern with the use of interfacet spacers is the theoretical risk of inducing iatrogenic kyphosis. However, several reports have shown no evidence of a significant loss of cervical index level lordosis associated with PCF [7, 12, 17]. Although this technique consists of introducing implants between the facet joints located posterior to the segment center of rotation, the leverage arm is very short. One report has even shown that facet spacer insertion, for up to six levels, does not significantly impact global cervical alignment [17].

Fusion in any segment of the cervical spine is known to influence adjacent segments [18], leading to ASD. Indeed, in 2016, Siemionow et al. [19] showed, in their 2-year follow-up study enrolling 53 patients subjected to percutaneous PCF, that 17.6% of subjects developed ASD. However, when comparing their study with published data on ACDF, the authors found that ASD ranged from 24.1% to 44.7% in ACDF-treated patients. Therefore, it appears that PCF, in line with its reduced impact on cervical lordosis, has a lower impact on ASD.

As a consequence of the above, in patients treated with PCF, perioperative complications were also found to be less prevalent than in either ACDF or LMS. In 2017, Siemionow et al. [20] found that posterior cage fixation with bilateral cages showed an overall complication rate of 3.4%, whereas 17.41% was reported for ACDF and 19.4% reported for LMS.

4 Conclusion

Percutaneous PCF with bilateral facet joint cages is a tissue-sparing technique avoiding many of the approach-related complications of open lateral mass fixation and ACDF. It is an elegant resource, which can accomplish in a single operation indirect foraminal decompression and sound primary cervical stability, while solid fusion is achieved without compromising proper sagittal balance. Clinical results are promising in different clinical scenarios, but more-robust evidence from larger trials is warranted.

Conflicts of Interest All authors declare that no conflicts of interest in the publication of this article.

References

1. Yalamanchili PK, Vives MJ, Chaudhary SB. Cervical spondylotic myelopathy: factors in choosing the surgical approach. Adv Orthop. 2012;2012:783762. https://doi.org/10.1155/2012/783762.
2. El-Ghandour NMF, Soliman MAR, Ezzat AAM, Mohsen A, Zein-Elabedin M. The safety and efficacy of anterior versus posterior decompression surgery in degenerative cervical myelopathy: a prospective randomized trial. J Neurosurg Spine. 2020;1:1–9. https://doi.org/10.3171/2020.2.SPINE191272.
3. Badiee RK, Mayer R, Pennicooke B, Chou D, Mummaneni PV, Tan LA. Complications following posterior cervical decompression and fusion: a review of incidence, risk factors, and prevention strategies. J Spine Surg. 2020;6:323–33. https://doi.org/10.21037/jss.2019.11.01.
4. Oppenheimer JH, DeCastro I, McDonnell DE. Minimally invasive spine technology and minimally invasive spine surgery: a historical review. Neurosurg Focus. 2009;27:E9. https://doi.org/10.3171/2009.7.FOCUS09121.
5. Siemionow KB, McCormack BM, Menchetti PPM. Tissue sparing posterior cervical indirect decompression and fusion in foraminal stenosis. In: Menchetti P, editor. Cervical spine. Cham: Springer; 2016. p. 135–49. https://doi.org/10.1007/978-3-319-21608-9_11.
6. Voronov LI, Siemionow KB, Havey RM, Carandang G, Patwardhan AG. Biomechanical evaluation of DTRAX® posterior cervical cage stabilization with and without lateral mass fixation. Med Dev. 2016;23:285–90. https://doi.org/10.2147/MDER.S111031.
7. McCormack BM, Bundoc RC, Ver MR, Ignacio JMF, Berven SH, Eyster EF. Percutaneous posterior cervical fusion with the DTRAX facet system for single-level radiculopathy: results in 60 patients. J Neurosurg Spine. 2013;18:245–54. https://doi.org/10.3171/2012.12.SPINE12477.
8. Siemionow K, Smith W, Gillespy M, McCormack BM, Gundanna MI, Block JE. Length of stay associated with posterior cervical fusion with intervertebral cages: experience from a device registry. J Spine Surg. 2018;4:281–6. https://doi.org/10.21037/jss.2018.05.27.
9. Cheng L, McCormack B, Eyster EF. Posterior cervical fusion utilizing cages placed bilaterally in the facets for the treatment of the upper cervical adjacent segment disease in the elderly. J Clin Neurosci. 2019;63:149–54. https://doi.org/10.1016/j.jocn.2019.01.018.
10. Bou Monsef JN, Siemionow KB. Multilevel cervical laminectomy and fusion with posterior cervical cages. J Craniovertebr Junct Spine. 2017;8:316–21. https://doi.org/10.4103/jcvjs.JCVJS_69_17.
11. Siemionow K, Janusz P, Glowka P. Cervical cages placed bilaterally in the facet joints from a posterior approach significantly increase foraminal area. Eur Spine J. 2016;25:2279–85. https://doi.org/10.1007/s00586-016-4430-7.
12. Siemionow K, Janusz P, Phillips FM, Youssef JA, Isaacs R, Tyrakowski M, McCormack B. Clinical and radiographic results of indirect decompression and posterior cervical fusion for single-level cervical radiculopathy using an expandable implant with 2-year

follow-up. J Neurol Surg A Cent Eur Neurosurg. 2016;77:482–8. https://doi.org/10.1055/s-0036-1584210.

13. Voronov LI, Siemionow KB, Havey RM, Carandang G, Phillips FM, Patwardhan AG. Bilateral posterior cervical cages provide biomechanical stability: assessment of stand-alone and supplemental fixation for anterior cervical discectomy and fusion. Med Dev. 2016;13:223–30. https://doi.org/10.2147/MDER.S109588.
14. Panzer MB, Cronin DS. C4-C5 segment finite element model development, validation, and load-sharing investigation. J Biomech. 2009;42:480–90. https://doi.org/10.1016/j.jbiomech.2008.11.036.
15. Pal GP, Sherk HH. The vertical stability of the cervical spine. Spine. 1988;13:447–9. https://doi.org/10.1097/00007632-198805000-00001.
16. Minamide A, Yoshida M, Simpson AK, Yamada H, Hashizume H, Nakagawa Y, Iwasaki H, Tsutsui S, Okada M, Takami M, Nakao S. Microendoscopic laminotomy versus conventional laminoplasty for cervical spondylotic myelopathy: 5-year follow-up study. J Neurosurg Spine. 2017;27:403–9. https://doi.org/10.3171/2017.2.SPINE16939.
17. Tan LA, Straus DC, Traynelis VC. Cervical interfacet spacers and maintenance of cervical lordosis. J Neurosurg Spine. 2015;22:466–9. https://doi.org/10.3171/2014.10.SPINE14192.
18. Virk SS, Niedermeier S, Yu E, Khan SN. Adjacent segment disease. Orthopedics. 2014;37:547–55. https://doi.org/10.3928/01477447-20140728-08.
19. Siemionow K, Monsef JB, Janusz P. Preliminary analysis of adjacent segment degeneration in patients treated with posterior cervical cages: 2-year follow-up. World Neurosurg. 2016;89:730–7. https://doi.org/10.1016/j.wneu.2016.01.053.
20. Siemionow KB, Glowka P, Blok RJ, Gillespy MC, Gundanna MI, Smith WD, Hyder Z, McCormack BM. Perioperative complications in patients treated with posterior cervical fusion and bilateral cages. J Craniovertebr Junct Spine. 2017;8:342–9. https://doi.org/10.4103/jcvjs.JCVJS_61_17.

Spinal Intradural Extramedullary Tumors: A Retrospective Analysis on Ten-Years' Experience of Minimally Invasive Surgery and a Comparison with the Open Approach

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1 Introduction

Spinal tumors are considered rare pathologies, corresponding to less than 15% of all central nervous system tumors. Intradural extramedullary (ID-EM) tumors are even rarer, comprising 40–45% of spinal tumors with a predominance of meningiomas and nerve sheath tumors [1, 2]. Because of this low incidence, no gold standard for surgical technique exists, and significant heterogeneity is present in the literature concerning the type of tumors included and the differences among techniques compared. Otherwise, "smart" microsurgical and gross total resection (GTR), combined with different intraoperative monitoring modalities, should be used to improve surgical outcomes alongside adjuvant treatments when needed [3]. Most surgeons are comfortable with the classical open approach, which is performed through a midline incision and laminectomy, generally two levels above and below the tumor, with excellent exposure and rate of tumor removal. However, the drawbacks are the soft tissue and posterior tension band and bony element disruption associated with intraoperative bleeding, postoperative pain, increased LOS, and the risk of instability associated with this technique [4, 5]. Interest continues to grow in different minimally invasive surgical (MIS) approaches, from those through a midline incision with the transpinous approach to others with a paramedian incision, and in progression through an interfascial corridor requiring hemilaminectomy to expose the pathology. However, data comparing the standardized paramedian MIS with the open approach are still lacking [6–10]. Minimally invasive surgical approaches may increase the likelihood of nontotal resection and in some cases increase the risk of postoperative complications, such as tumor seeding (e.g., ependymoma and epidermoid) [11]. In this study, we aimed to compare the clinical and functional outcomes of open approaches with those of minimally invasive approaches for patients with ID-EM tumors.

2 Materials and Methods

This is a retrospective analysis of prospectively collected data from June 2009 to July 2019 from patients with intradural extramedullary tumors submitted to surgical removal. We included patients with magnetic resonance imaging (MRI) and intraoperative findings of intradural extramedullary tumors throughout the spinal canal, excluding patients with secondary, infectious, inflammatory, or extradural lesions.

3 Surgical Technique

Each patient was operated while they were in a prone position over a radiolucent table. Radiographically confirming the correct level is the primary step to avoid complications, specifically for minimally invasive approaches. Intraoperative neurophysiological monitoring was used in all cases.

For the open approach, a midline skin incision and subperiosteal muscle dissection was performed at least a level above and below the pathology, followed by total laminectomy (Fig. 1), where the extent of the facetectomy was defined by the axial laterality of the lesion, flavectomy, and midline durotomy with the broad exposure of the upper and

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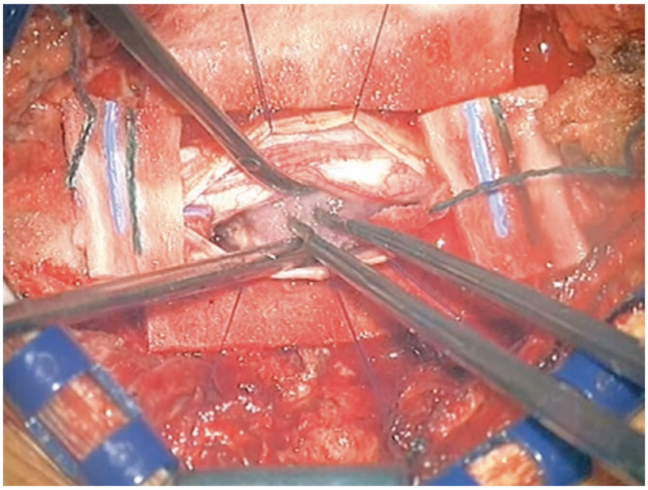

Fig. 1 Intraoperative image of a dorsal meningioma that is being removed through an open midline approach

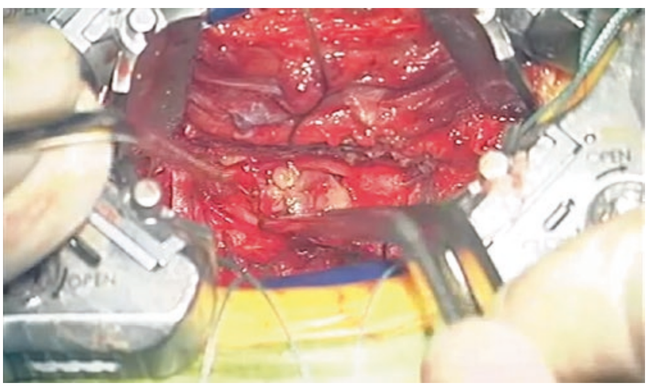

Fig. 2 Intraoperative image of a lumbar schwannoma that is being excised through a paramedian translaminar MIS approach

lower limits of the tumor. The resection of the lesion would follow a standard microsurgical technique, aided by ultrasonic surgical aspiration if needed.

On the MIS approach, small vertical paramedian skin and fascia incisions were carried out; subsequently, larger tubes were applied to create the intermuscle corridor; finally, a tubular retractor was docked between the lamina of the affected level. Through muscle dissection, these tubes allowed for approaching at least two contiguous levels. Generous bone removal, including over-the-top laminectomy and facetectomy as needed, tumor exposure, and resection followed the same steps as those for the open counterpart (Fig. 2). Because a small work channel and a tight dural closure were possible with a 4-0 Prolene running suture, the usage of fibrin glue was not always necessary. After retractor removal, muscle approximation was observed with a reduction in dead space, and a drain was never used.

4 Data Extraction

Electronic medical records were used to extract demographics (age at surgery and sex), preoperative neurological statuses were assessed according to the Medical Research Council (MRC) scale, and preoperative MRIs were reviewed for tumor characteristics (topography and dimension). The operative variables included the type of approach employed (open or minimally invasive), surgery duration, and estimated blood loss (EBL). Postoperative data included tumor histology, length of stay (LOS), complication(s), discharge destination, neurological status (MRC scale) at the last follow-up, and follow-up duration.

Numeric variables are presented as means and standard deviations if normally distributed and otherwise as median and variances. Dichotomous variables are presented as percentages.

A two-tailed independent sample *t*-test was used to compare groups ($p < 0.05$ was considered statistically significant). In addition, the Levene test was used to assess the equal variance assumption. IBM SPSS version 27 was used for statistical analysis.

5 Results

In total, 46 patients with a mean age of 58.7 years (±14.03) with purely ID-EM tumors were included in the analysis. Here, 30 (65.2%) patients were operated through an open approach and 16 (34.8%) through a paramedian minimally invasive approach; 56.5% were women; and all were followed up with after a median time of 24 months. The most predominant histological types were schwannomas (43.5%), followed by ependymomas and meningiomas, at 26.1% and 23.9%, respectively. In addition, these lesions more frequently affected the lumbar (34.8%) and thoracic spine (26.1%).

Patients included in the two cohorts were not significantly different in age ($p = 0.430$). Tumors in the open cohort were relatively larger, with a mean diameter of 35.37 mm, than those in the MIS group, with a mean diameter of 23.44 mm, but this difference did not reach statistical significance ($p = 0.080$). In regard to topography, the respective distributions were very similar between both groups (Table 1). Regarding operative data, the surgical procedure was faster when the minimally invasive approach was used, with a duration of 164.69 min (±55.21), whereas the open approach lasted on average 241.43 min (±122.68); this difference reached statistical significance ($p = 0.006$).

Table 1 Case distribution according to spine topography

	Open		MIS	
Spine level	*n*	%	*n*	%
Cervical	7	23.3	2	12.5
Cervicothoracic	1	3.3	–	–
Thoracic	8	26.7	4	25
Thoracolumbar	4	13.3	2	12.5
Lumbar	9	30	8	50
Sacrum	1	3.3	–	–
Total	30	100	16	100

Another significant difference was seen in the estimated blood loss ($p = 0.026$), where the minimally invasive cohort individuals perioperatively lost on average 144.55 mL (range: 50–350 mL) and the open approach group perioperatively lost 284.58 mL (range: 50–900 mL). The MIS patients had a mean LOS of 5.63 days (range: 1–17 days), and the open group had a higher mean LOS of 17.27 days (range: 2–78 days); this difference was statistically significant ($p = 0.010$). Even though a difference was seen in the incidence of postoperative complications in disfavor of the open approach (41.2% vs. 16.67%), this difference was marginally statistically significant ($p = 0.0489$). Regarding neurological status, assessed according to the MRC scale, preoperative motor strength was similar between the MIS and open approaches ($p = 0.882$). However, the MIS cohort fared better in the postoperative period, with grade of 5/5 on 91.7% vs. 67.6% for the open cohort. The longer the procedure duration, the more likely it was for the patients to experience a longer length of stay ($R = 0.327$, $p = 0.029$). Likewise, surgery duration had a positive and significant correlation with blood loss ($R = 0.555$, $p < 0.001$) and tumor size ($R = 0.324$, $p = 0.032$). Moreover, as expected, blood loss was positively related to tumor size ($R = 0.493$, $p = 0.003$) in both groups.

6 Discussion

ID-EM tumors are rare entities that are consensually treated with a function-preserving approach when GTR is performed [12]. A classical open approach and many minimally invasive techniques are used to treat ID-EM tumors [6–9, 12–19]. Although isolated studies have reported on different MIS techniques to remove ID-EM tumors, this is to the best of our knowledge the first study comparing the classical open approach with only the paramedian MIS approach in all spine levels, avoiding midline muscle denervation.

We contrasted the functional results of the classical midline open approach against a paramedian MIS approach using a tubular retractor. MIS approach is as effective and safe as the classical midline open approach for the total removal of ID-EM tumors, with no difference in the removal grade for similarly located and sized tumors, as reported previously [8, 16, 17, 20]. Compared with previous studies reporting on the MIS removal of ID-EM, we report a superior GTR rate (100%) in all spine levels.

In different published cohorts, the substantial size of tumors was a significant limitation of the MIS approaches. In a comparison study on 42 patients with ID-EM tumors, 31 operated by MIS, the authors found that tumors were smaller in the MIS cohort ($p = 0.01$), predominantly located in the lumbar spine and with less foraminal extension [21]. These differences were not significant in the present study, as patients were well matched in terms of location and tumor extension in both cohorts. Therefore, MIS may suitably manage tumors that extend no longer than two vertebral segments [7].

Regarding the operative aspects, the MIS approach was superior in reducing surgery duration (mean difference of 76.7 min between the two techniques), positively correlated with shorter hospital LOSs. Those two variables must be especially considered for patients of advanced age and with comorbidities that pose greater risks from undergoing major procedures. Diverging results may be found in the literature concerning surgery duration. The experience gathered on performing MIS surgery in degenerative cases may have contributed to improving outcomes and shortening the surgery duration of surgery.

Another factor that is consistently different between these techniques is the EBL, which is significantly superior in the open approach, as expected, with a more disruptive procedure, characterized by bilateral muscle dissection, laminectomy, and sometimes facetectomy, leading to screw fixation and arthrodesis in some cases. No patients in either group needed a transfusion, but blood loss was positively correlated with surgery duration, which again supports taking the MIS approach.

After comparing the incidence of complications between the two groups of patients, we did not find any significant differences, even though there was a trend toward fewer complications in the MIS group. Infections and cerebrospinal fluid (CSF) leaks were the major adverse events in the open group (17.65% vs. 8.3%). However, other functional outcomes were observed: These patients experienced more postoperative pain and worsening motor strength.

Furthermore, the cost–benefit analysis relies a recent study that was performed to compare open and MIS approaches and that found that the latter costs significantly less in terms of hospital costs (USD 21,307.80 for open, USD 15,015.20 for MIS, $p < 0.01$), postoperative charges (USD 75,383.48 for open and USD 56006.88 for MIS, $p < 0.01$), and total charges (USD 100,779.38 for open and USD 76,100.92 for MIS, $p < 0.01$) [21]. It is relevant to consider the costs of surgery in an environment of limited resources, especially when there are no clinical and functional differences in results.

This study has limitations intrinsic to a retrospective design and a relatively small sample size for the final analysis, although reference studies in the literature on this topic have presented similar numbers. Nevertheless, both techniques might be comparable in terms of their efficacies in treating ID-EM tumors, but more research, such as a randomized controlled study, is required to resolve this surgical treatment dilemma.

7 Conclusions

The development of MIS tools is expected to be associated with expanding their techniques, as in the case of ID-EM tumor surgery. The iatrogenic morbidity associated with open approaches should be a concern for surgeons and patients. The paramedian translaminar MIS approach is as effective as the open approach in the GTR of ID-EM tumors, with advantages such as short surgery duration, less blood loss, and shorter hospital length of stay. More controlled clinical trials with larger sample sizes should be performed to better elucidate the benefits of one technique over the other.

Conflicts of Interest The authors declare no conflicts of interest.

References

1. Arnautovic K, Arnautovic A. Extramedullary intradural spinal tumors: a review of modern diagnostic and treatment options and a report of a series. Bosn J Basic Med Sci. 2009;9(Suppl 1):40–5.
2. Traul DE, Shaffrey ME, Schiff D. Part I: spinal-cord neoplasms—intradural neoplasms. Lancet Oncol. 2007;8(1):35–45.
3. Cofano F, Giambra C, Costa P, et al. Management of extramedullary intradural spinal tumors: the impact of clinical status, intraoperative neurophysiological monitoring and surgical approach on outcomes in a 12-year double-center experience. Front Neurol. 2020;11:598619.
4. McGirt MJ, Garcés-Ambrossi GL, Parker SL, Sciubba DM, Bydon A, Wolinksy J-P, Gokaslan ZL, Jallo G, Witham TF. Short-term progressive spinal deformity following laminoplasty versus laminectomy for resection of intradural spinal tumors: analysis of 238 patients. Neurosurgery. 2010;66(5):1005–12.
5. Sciubba DM, Chaichana KL, Woodworth GF, McGirt MJ, Gokaslan ZL, Jallo GI. Factors associated with cervical instability requiring fusion after cervical laminectomy for intradural tumor resection. J Neurosurg Spine. 2008;8(5):413–9.
6. Byvaltsev VA, Stepanov IA, Aliyev MA. Comparison of open and minimally invasive techniques in the surgical treatment of intradural extramedullary spinal tumors in elderly and senile patients. Adv Gerontol Uspekhi Gerontol. 2018;31(3):400–7.
7. Raygor KP, Than KD, Chou D, Mummaneni PV. Comparison of minimally invasive transspinous and open approaches for thoracolumbar intradural-extramedullary spinal tumors. Neurosurg Focus. 2015;39(2):E12.
8. Wong AP, Lall RR, Dahdaleh NS, Lawton CD, Smith ZA, Wong RH, Harvey MJ, Lam S, Koski TR, Fessler RG. Comparison of open and minimally invasive surgery for intradural-extramedullary spine tumors. Neurosurg Focus. 2015;39(2):E11.
9. Yu Y, Zhang X, Hu F, Xie T, Gu Y. Minimally invasive microsurgical treatment of cervical intraspinal extramedullary tumors. J Clin Neurosci. 2011;18(9):1168–73.
10. Zong S, Zeng G, Du L, Fang Y, Gao T, Zhao J. Treatment results in the different surgery of intradural extramedullary tumor of 122 cases. PLoS One. 2014;9(11):e111495.
11. Ottenhausen M, Ntoulias G, Bodhinayake I, Ruppert F-H, Schreiber S, Förschler A, Boockvar JA, Jödicke A. Intradural spinal tumors in adults-update on management and outcome. Neurosurg Rev. 2019;42(2):371–88.
12. González-Martínez EL, García-Cosamalón PJ, Fernández-Fernández JJ, Ibáñez-Plágaro FJ, Alvarez B. Minimally invasive approach of extramedullary intradural spinal tumours. Review of 30 cases. Neurocirugia (Astur). 2012;23(5):175–81.
13. Formo M, Halvorsen CM, Dahlberg D, Brommeland T, Fredø H, Hald J, Scheie D, Langmoen IA, Lied B, Helseth E. Minimally invasive microsurgical resection of primary, intradural spinal tumors is feasible and safe: a consecutive series of 83 patients. Neurosurgery. 2018;82(3):365–71.
14. Iacoangeli M, Gladi M, Di Rienzo A, Dobran M, Alvaro L, Nocchi N, Maria LG, Somma D, Colasanti R, Scerrati M. Minimally invasive surgery for benign intradural extramedullary spinal meningiomas: experience of a single institution in a cohort of elderly patients and review of the literature. Clin Interv Aging. 2012;7:557–64.
15. Konovalov NA, Shevelev IN, Nazarenko AG, Asiutin DS, Korolishin VA, Timonin SI, Zakirov BA, Onoprienko RA. The use of minimally invasive approaches to resect intradural extramedullary spinal cord tumors. Zh Vopr Neirokhir Im N N Burdenko. 2014;78(6):24–36.
16. Lee B, Hsieh PC. Minimally invasive lumbar intradural extramedullary tumor resection. Neurosurg Focus. 2012;33(1):1.
17. Mannion RJ, Nowitzke AM, Efendy J, Wood MJ. Safety and efficacy of intradural extramedullary spinal tumor removal using a minimally invasive approach. Neurosurgery. 2011;68(1):208–16; discussion 216.
18. Nzokou A, Weil AG, Shedid D. Minimally invasive removal of thoracic and lumbar spinal tumors using a nonexpandable tubular retractor. J Neurosurg Spine. 2013;19(6):708–15.
19. Pompili A, Caroli F, Telera S, Occhipinti E. Minimally invasive resection of intradural-extramedullary spinal neoplasms. Neurosurgery. 2006;59(5):E1152.
20. Zhu Y-J, Ying G-Y, Chen A-Q, et al. Minimally invasive removal of lumbar intradural extramedullary lesions using the interlaminar approach. Neurosurg Focus. 2015;39(2):E10.
21. Fontes RBV, Wewel JT, O'Toole JE. Perioperative cost analysis of minimally invasive vs open resection of intradural extramedullary spinal cord tumors. Neurosurgery. 2016;78(4):531–9.

Correlation Between Cervical Spine Sagittal Alignment and Clinical Outcome After Standalone Intersomatic Titanium Cage CeSPACE for Cervical Anterior Discectomy and Fusion in Cervical Degenerative Disk Diseases

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1 Introduction

Degenerative cervical spinal diseases are frequently seen in clinical practice. Although they may be initially asymptomatic, the common association with disk herniation, osteophytes, and hypertrophied ligaments can compress the spinal cord and cause the consequent onset of cervical pain, radiculopathy, or myelopathy. An alteration of the sagittal alignment of the cervical spine is, moreover, frequently associated with these degenerative pathologies. This can be a direct consequence of the degenerative disease but can also be linked to mechanical alterations to the nearby spinal regions. The surgical treatment must aim to decompress the nerve structures, to restore the correct alignment of the spine, and, if necessary, allow vertebral stabilization. Anterior cervical discectomy and fusion (ACDF) with a standalone intersomatic cage for cervical degenerative disease allows for an optimal decompression of the myeloradicular structures, the restoration of the height of disk, the correction of cervical kyphosis, and giving immediate load support to the anterior column [1, 2]. The innovation of the titanium CeSPACE cage is essentially its design, which is made of pure titanium powder embedded onto the oxide-free surface to form a rough, microporous Plasmapore surface, which facilities bone growth and can be successfully used for joint replacement arthroplasty. The use of these cages also permits a physiologic metameric alignment and fusion in one- and multilevel procedures [3–5].

In the literature, few studies have reported a relationship between postoperative radiographic cervical spine results and clinical outcomes [6–8]. Therefore, the aim of this study is to determine the degree of correlation between cervical sagittal alignment after ACDF with a standalone intersomatic cage and improvement in visual analog scale (VAS) scores and Oswestry Neck Disability Index (NDI) values in a consecutive series of patients treated at our institution with cervical anterior discectomy and fusion for degenerative diseases.

2 Materials and Methods

2.1 Patient Selection and Data Collection

A retrospective analysis was conducted in a consecutive series of 180 patients with cervical degenerative diseases, who underwent ACDF with a standalone intersomatic titanium cage implant, from 2013 to 2017 at our institution. General information, clinical presentations, the durations of symptoms, the metameric levels, and postoperative final clinical outcomes were evaluated. All patients underwent preoperative radiological studies on the cervical spine that included X-rays in the lateral, anteroposterior, and flexion/extension views; computed tomography (CT) scans; and magnetic resonance imaging (MRI) scans with T1- and T2-weighted sequences in the transverse and sagittal planes (Fig. 1). VAS scores were used for neck and radicular pain and Oswestry Neck Disability Index (NDI) scores for myelopathy. The indication for surgery was cervical pain associated with intractable radiculopathy that did not respond to conservative treatment for at least 5 weeks or evidence of a progressive neurologic deficit. Patients previously treated via another cervical surgical procedure, those

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Fig. 1 Preoperative T2-weighted sagittal MRI revealing disk prolapse and spinal cord compression at the C5-C6 level

affected by traumatic injuries, and those with other concomitant spinal diseases (tumors or infections) were excluded from the study.

2.2 Surgical Technique

In all patients, we performed a standard anterior cervical approach through a right-side anterolateral retropharyngeal approach. Under general anesthesia and antibiotic prophylaxis with 2 g of ceftriaxone IV 60 min before incision, each patient was placed in a supine position with their head slightly reclined. A horizontal skin incision for one or two levels was performed in the right paramedian cervical area. The surgical exposure involved gaining access to the operating site and retracting the tissues by using minimal instrumentation; the trachea and the esophagus were retracted in order to better see the vertebral bodies. After fluoroscopic control, we performed the decompression of the spinal cord and/or nerve roots, including complete discectomy, the removal of the posterior longitudinal ligament, and the removal of osteophytes that were in contact with and/or compressed the neural elements. The optimal decompression of neural structures was verified by using a blunt probe. The bony surface of both vertebral end plates was preserved as much as possible during discectomy. Implant selection and CeSPACE positioning were obtained under lateral fluoroscopy. The implant design correlates with the anatomy of the cervical spine.

2.3 Clinical and Radiological Evaluations

Patients' clinical outcomes were pre- and postoperatively assessed at 12-month follow-ups by using their VAS scores and NDI values.

All patients underwent anteroposterior, lateral, and flexion/extension radiographs 3 and 6 months after surgery (Fig. 2). We looked for radiological evidence of (a) cervical spine alignment; (b) subsidence, defined as a cage migration of more than 2 mm into the adjacent vertebral body; (c) migration along the superior and/or inferior end plates; and (d) the settling of the implant. Cervical spine alignment was assessed according to the following three parameters: the C2–7 Cobb angle, the C2–7 sagittal vertical axis (SVA), and the T1 slope minus the C2–7 Cobb angle. The change in cervical sagittal alignment was defined as the difference between the post- and preoperative C2–7 Cobb angles, the C2–7 SVAs, and the T1 slope minus the C2–7 Cobb angles. T2-weighted magnetic resonance (MR) images were used to evaluate the high signal intensity of the spinal cord.

2.4 Statistical Analysis

All the statistical analyses were performed in Microsoft Excel (Office 2016) with paired Student *t*-tests, paired *t*-tests, chi-square tests, linear regression analyses, and analyses of variance (ANOVAs). The alpha level was set a priori at 0.05.

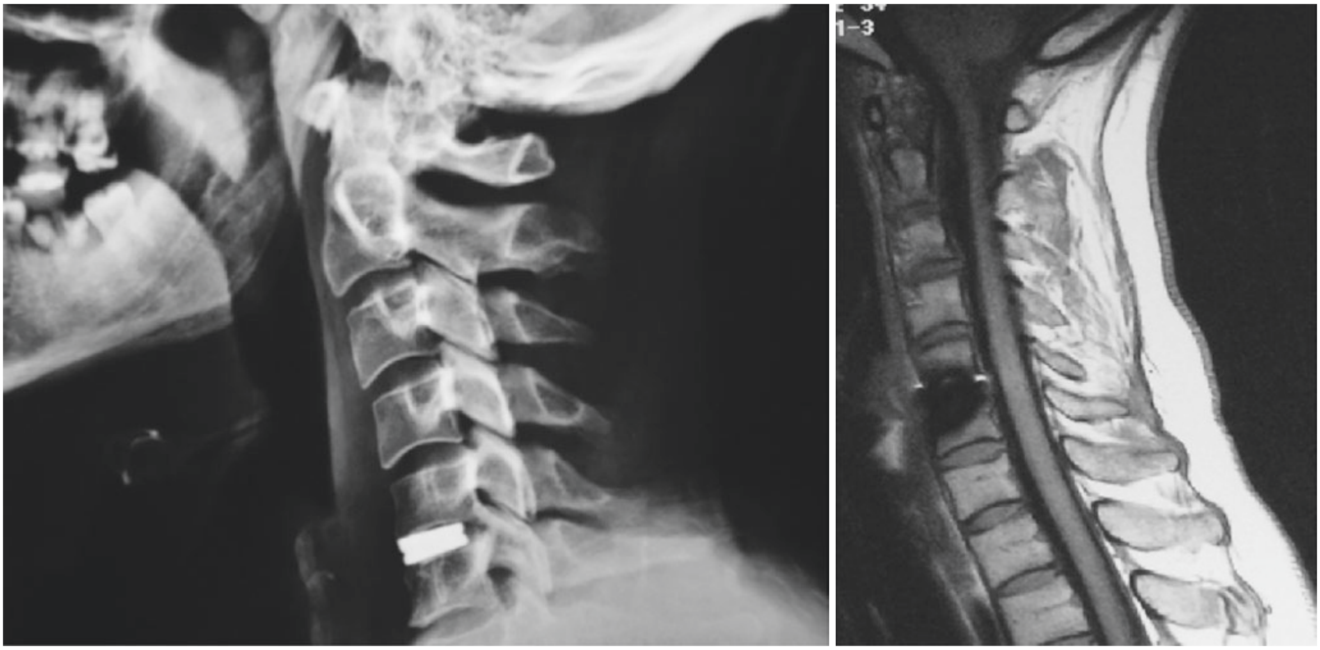

Fig. 2 On the left, plain postoperative lateral X-ray at 6 months presenting the implant; on the right, in the same case, control T2-weighted sagittal MRI

3 Results

This study included 180 patients, 97 (53.89%) male and 83 (46.11%) female, aged between 39 and 72 years (mean age: 56.6 years). There were 135 (75%) single-level, 40 (22.22%) two-level, and five (2.77%) three-level diseases. The preoperative clinical evaluation showed cervical pain in 58 patients (32.22%), radicular pain in 29 (16.11%), both pains in 93 (51.67%). The C3–C4 level was affected in 34 patients (14.47%), C4–C5 in 78 patients (33.19%), C5–C6 in 85 patients (36.17%), and C6–C7 in 38 patients (16.17%) (Table 1). Preoperatively, the mean VAS score for neck pain was 7.71 (range: 4–10), 8.07 (range: 5–10) for radicular pain, and 7.75 (range: 5–10) for both pains. Postoperatively, we obtained a significant improvement in these parameters at the 12-month follow-up time ($p < 0.001$). At this point, 2.71 was the mean VAS score for neck pain (range: 0–6), 2.17 (range: 0–6) for radicular pain, and 2.08 (range: 0–7) for both pains (Table 2). The clinical and neurological statuses of patients were evaluated by using their NDI scores. The average preoperative score was 47.24% for patients with only cervical pain or only radicular pain, while it was 56.7% for patients with both pains. In the follow-up, the score improved to 24.13% in patients with only cervical pain, 31.72% in patients with only radicular pain, and 37.31% in patients with both pains. Overall, we documented a clear progressive resolution of the symptoms, highlighted in the preoperative phase, in 160 patients (88.8%). For the preoperative cervical curvature, 62 (68%) of the 91 patients had lordosis and 29 (32%) a straight curve (Table 3). Additionally, 140 (78%) maintained their original curvature or experienced an improved curvature (from straight to lordosis or from kyphosis to lordosis). Specifically, 11 patients in the straight group changed to kyphosis, whereas 29 patients in the lordotic group changed to straight (Table 4). However, cervical sagittal alignment after surgery was not significantly associated with clinical outcomes in terms of postoperative improvement in the VAS neck scores or the NDI scores ($p > 0.05$). Similarly, the change in cervical sagittal alignment

Table 1 Data on the population, the level, and the type of the disease

No. of patients	180
Age (year)	56.6
Sex	
Female	83 (53.89%)
Male	97 (46.11%)
Time with symptoms (m) 12.8 ± 8	
Levels	
Single level	135 (75.00%)
Two levels	40 (22.22%)
Three levels	5 (2.77%)
C3–C4	34 (14.47%)
C4–C5	78 (33.19%)
C5–C6	85 (36.17%)
C6–C7	38 (16.17%)
Tot.	235
Type of pain	
Cervical	58 (32.22%)
Radicular	29 (16.11%)
Both	93 (51.67%)

Table 2 Clinical outcomes evaluated with VAS scores and NDI % scores on three kinds of pain before surgical treatment and after a 12-month follow-up

	No. of patients	Before surgery	12-month follow-up	*p*-value
VAS score cervical pain	58	7.54	2.71	<0.001
VAS score radicular pain	29	8.07	2.17	<0.001
VAS score both pains	93	7.75	2.08	<0.001
NDI % cervical pain	58	47.24	24.13	<0.001
NDI % radicular pain	29	47.24	31.72	<0.001
NDI % both pains	93	56.66	37.31	<0.001

Table 3 Data on radiological parameters of the population

Variable	Kyphosis	Straight	Lordosis	Total	*p*-value
No. of patients	27	62	91	180	
Age (year)	55.1 ± 7.5	56.3 ± 7.6	58.2 ± 8.5	56.6 ± 7.8	0.226
Sex (M:F)	11:16	37:25	49:42	97:83	
C2-7 Cobb angle (°)	−5.3 ± 4.1	5.9 ± 2.8	17.1 ± 5.6	9.4 ± 9.6	0.001
C2-7 SVA (mm)	24.8 ± 11.6	23.9 ±15.1	16.9 ± 9.1	21.9 ± 12.5	0.126
T1 slope (°)	18.4 ± 7.1	25.4 ±7.8	27.8 ± 7.7	29.9 ± 9.4	0.013
T2-weighted MR image cord signal change (no. of patient)	12 (44%)	29 (48%)	46 (51%)		

Table 4 Postoperative changes in cervical curvature

	Preoperative cervical curvature			
Postoperative cervical curvature	Lordosis	Straight	Kyphosis	Total
Lordosis	62	3	0	65
Straight	29	48	11	88
Kyphosis	0	11	16	27
Total	91	62	27	180

was not related to the VAS neck ($p > 0.05$) or NDI ($p > 0.05$) scores. We reported eight (4.4%) cases of subsidence. In four (2.2%) cases, migration was less than 2 mm. In two cases, we documented a kyphotic reduction less than 4°. We did not note cases of cage migration either during the immediate postoperative period or at follow-up. A rate of 97% fusion was documented between adjacent vertebral bodies. The MRI evaluation was performed during follow-ups (Fig. 2), which detected 12 cases of adjacent segment disease.

4 Discussion

Cervical degenerative diseases are chronic, progressive conditions characterized by an initial loss of elasticity in the disk and its progressive alteration of the ability to reduce and distribute pressure forces on the vertebral end plates. The loss of compactness in the disk also causes a decrease in vertebral heights and the thickening of the ligamentum flavum. The combination of all these phenomena can cause incorrect cervical alignment. The presence of disk herniation, osteophytes, and hypertrophied ligaments may compress the spinal cord, resulting in the onset of cervical pain, radiculopathy, or myelopathy [9]. The surgical treatment must aim to decompress the nerve structures and, where possible, to restore the correct vertebral alignment; surprisingly, to date, few studies have specifically examined the degree of correlation between sagittal cervical spinal alignment and improvements in clinical outcomes [8]. Many procedures have been proposed for the surgical treatment of cervical degenerative diseases, such as anterior decompression, laminectomy, laminoplasty, and instrumented anterior and posterior fusion with plates or screws. Anterior approaches are effective for neural decompression, showing better clinical outcomes with less surgical trauma when compared with posterior approaches. Husag et al. reported in their series of patients who underwent anterior cervical discectomy without fusion an excellent overall benefit in 95% of cases. However, at the same time, the fusion rate of 70%, after the procedure, led to an increase in segmental motion, subsidence, and cervical kyphosis, leading to instability and degenerative disk disease in adjacent levels [10].

The microsurgical ACDF through the placement of autografts or heterografts in the intersomatic space is the operative procedure of choice for degenerative disk disease and cervical spondylosis associated with radiculopathy or myelopathy. This procedure improves fusion, restores vertebral alignment, and significantly reduces the incidence of subsidence, thus overcoming the limitations associated with the use of anterior plates and screws [11]. Although ACDF represents a well-established technique in the treatment of degenerative cervical pathologies, there are still questions about the most suitable technique of fusion to adopt.

The use of autologous grafts from the iliac crest has represented the ideal treatment for many years. However, this technique is burdened by a series of complications, such as graft collapse, the loss of disk space height, kyphosis, and possible morbidities at the donor site, such as pain, hematomas, and infections [12, 13]. In order to overcome these limitations, intersomatic fusion cages of various shapes and compositions have been developed. Cages are cubical implants that are designed to restore physiological disk height and allow bone growth, favoring a faster fusion and allowing the correct realignment of the cervical spine [14]. Moreover, the presence of dislocation and subsidence has been described as significantly reduced [15]. Different types of cages are available to perform ACDF, including titanium cages, carbon-fiber-reinforced polymer cages, polyetheretherketone (PEEK) cages, and cages integrated with and without synthetic bone grafts [15–18].

In 2004, Meier et al., comparing six spacers for spondylosis of the cervical spine in a series of 267 patients, reported an increased tendency toward the dislocation of PEEK cages when compared to that of other implants, such as Plasmapore-coated titanium cages [19]. The Plasmapore pore sizes range from 50 to 200 μm, with a microporosity of 35% and a thickness of 0.35 mm, leading to a large surface area optimal for bone growth. Moreover, Plasmapore is a very rough surface and may support the primary stability of the cage; consequently, the cages are not filled with any form of bone or other material. At the end of the discectomy, determining the cage dimensions requires using special measuring devices, which are housed in the now-empty interbody space of the disk. Choosing the correct cage height is crucial. In fact, the implant of too large a cage may cause iatrogenic damage by stretching the nerve roots. On the other hand, too small a cage can cause the kyphosis of the vertebral tract and the loss of spinal balance. Krayenbuhl et al., in their series of patients affected by cervical myeloradiculopathies, described a 98% fusion rate with only 2% subsidence [20]. Arregui et al. implanted CeSPACE into a series of 104 patients. The bone fusion rate was 66.3% 6 months after the surgical procedure, while it was 91% at the end of the first year of follow-up [16]. Our data are in line with those in the reported literature. The bone fusion rate was 97%, while subsidence cases were documented in only eight (4.4%). In our study, according to Gum et al., no significant difference between pre- and postoperative cervical lordosis was observed [8]. However, our study takes into consideration only a cohort of one- and two-level ACDFs, and the aim of the procedure is not mainly sagittal correction. VAS and NDI scores, used to measure clinical statuses, showed significant improvements from baselines to follow-ups at 2 years, but there were no significant correlations between improvements in clinical outcomes and cervical sagittal alignment. Pitzen et al., with a multicenter randomized controlled study investigating the use of dynamic vs. rigid anterior cervical plates, demonstrated that a loss of up to 4.3° of segmental cervical lordosis had no correlation with NDI or VAS scores at 2-year follow-ups [21]. Although all the segmental curves act together to optimize sagittal balance, the cervical spine provides a smaller contribution than that of the lumbar spine or pelvis [22]. To the best of our knowledge, few studies have specifically investigated the level of correlation between cervical spine sagittal alignment and clinical outcome measures. The maintenance or restoration of cervical sagittal profile is not essential after ACDF, and it is not correlated with improvements in clinical outcomes. It appears that small deviations at 2-year follow-ups are tolerated and are not the driving factors behind patient-perceived improvements. Anterior discectomy and interbody fusion by positioning the CeSPACE device have been demonstrated to be safe and valid alternatives to other methods of treatment for cervical degenerative disk disease, such as anterior decompression, laminectomy, laminoplasty, and instrumented anterior and posterior fusion with plates or screws. It constitutes an effective method for the treatment of cervical disk herniation for improving neurological deficits, reducing postoperative pain, and improving quality of life. Furthermore, the standalone intersomatic titanium cage implants have proven to be effective and safe for the restoration of the physiological height of the disk, and they allow bone growth for obtaining fusion while allowing the correct realignment of the cervical spine, preserving cervical lordosis.

References

1. Bose B. Anterior cervical instrumentation enhances fusion rates in multilevel reconstruction in smokers. J Spinal Disord. 2001;14(1):3–9.
2. Tureyen K. Disc height loss after cervical anterior microdiscectomy with titanium intervertebral cage fusion. Acta Neurochir. 2003;145:565–70.
3. Hwang S, Lin C, Lieu A, et al. Three-level and four-level anterior cervical discectomies and titanium cage-augmented fusion with and without plate fixation. J Neurosurg Spine. 2004;2:160–7.
4. Marbacher S. Long-term outcome after adjacent two-level anterior cervical discectomy and fusion using stand-alone plasmaphore-covered titanium cages. J Neurol Surg A Cent Eur Neurosurg. 2015;76(3):199–204.
5. Wang B, Lü G, Kuang L. Anterior cervical discectomy and fusion with stand-alone anchored cages versus posterior laminectomy and fusion for four-level cervical spondylotic myelopathy: a retrospective study with 2-year follow-up. BMC Musculoskelet Disord. 2018;19:216.

6. Djurasovic M, Glassman SD. Correlation of radiographic and clinical findings in spinal deformities. Neurosurg Clin N Am. 2007;18:223–7.
7. Glassman SD, Berven S, Bridwell K, Horton W, Dimar JR. Correlation of radiographic parameters and clinical symptoms in adult scoliosis. Spine. 2005;30:682–8.
8. Gum JL, Glassman SD, Douglas LR, Carreon LY. Correlation between cervical spine sagittal alignment and clinical outcome after anterior cervical discectomy and fusion. Am J Orthop. 2012;41:E81–4.
9. Han SY, Kim HW, Lee CY, Kim HR, Park DH. Stand-alone cages for anterior cervical fusion: are there no problems? Korean J Spine. 2016;13:13–9.
10. Husag L, Probst C. Microsurgical anterior approach to cervical discs. Review of 60 consecutive cases of discectomy without fusion. Acta Neurochir. 1984;73:229–42.
11. Song K, Song J, Kim D, Shim DG, Lee K. Efficacy of combined anteroposterior fusion with no plate versus anterior fusion alone with cage and plate for multilevel degenerative cervical disease. Spine J. 2014;14(4):598–603.
12. Shamsaldin M, Mouchaty H, Desogus N, Costagliola C, Di Lorenzo N. Evaluation of donor site pain after anterior iliac crest harvesting for cervical fusion: a prospective study on 50 patients. Acta Neurochir. 2006;148:1071–4.
13. Zevgaridis D. Prospective controlled study of rectangular titanium cage fusion compared with iliac crest autograft fusion in anterior cervical discectomy. Neurosurg Focus. 2002;12(1):E2.
14. Assietti R, Beretta F, Arienta C. Two-level anterior cervical discectomy and cage-assisted fusion without plates. Neurosurg Focus. 2002;12(1):E3.
15. Kapetanakis S, Thomaidis T, Charitoudis G, Pavlidis P, Theodosiadis P, Gkasdaris G. Single anterior cervical discectomy and fusion (ACDF) using self-locking stand-alone polyetheretherketone (PEEK) cage: evaluation of pain and health-related quality of life. J Spine Surg. 2017;3(3):312–22.
16. Arregui R. CeSPACE. Cervical interbody fusion system. Preliminary retrospective study in 104 cases (120 implants). Neurocirugia. 2011;22:542–53.
17. El Abed K, Shawky A, Barakat M, Ainscow D. Anterior cervical discectomy and fusion with stand-alone trabecular metal cages as a surgical treatment for cervical radiculopathy: mid-term outcomes. Asian Spine J. 2016;10(2):245–50.
18. Sugawara T. β-tricalcium phosphate promotes bony fusion after anterior cervical discectomy and fusion using titanium cages. Spine. 2011;36:1509–14.
19. Meier U, Kemmesies D. Experiences with six different intervertebral disc spacers for spondylodesis of the cervical spine. Orthopade. 2004;33(11):1290–9.
20. Krayenbühl N. Use of an empty, Plasmapore-covered titanium cage for interbody fusion after anterior cervical microdiscectomy. J Clin Neurosci. 2008;15:11–7.
21. Pitzen T. Loss of lordosis and loss of segmental height do not affect clinical results following ACDF: secondary endpoint results from a multicentric, randomized, controlled study. Spine J. 2010;10(9):33S.
22. Knott PT, Mardjetko SM, Techy F. The use of the T1 sagittal angle in predicting overall sagittal balance of the spine. Spine J. 2010;10(11):994–8.

Part IV

Dorsal

Spinal Epidural Atypical Meningioma: Case Report and Review of the Literature

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1 Introduction

Spinal meningiomas (SMs) typically arise into intradural extramedullary space. Rarely, they may originate extradurally, which is more likely the origin site of malignant neoplasms such as metastases or lymphoma [1]. About 10% of all spinal meningiomatous lesions have an extradural extension, while those originating purely extradurally are extremely rare [2]. The occurrence of high-grade epidural SMs is almost anecdotal. Herein, we describe the case of a young woman presenting with sensory disturbances attributable to a sleeve-like epidural thoracic mass. The clinical, intraoperative, and pathological findings of this rare entity are reported. A search of the English literature via PubMed was conducted to find studies on spinal epidural atypical meningiomas.

2 Materials and Methods

The case of an epidural atypical spinal tumor was described through clinical and surgical reports from onset to 24 months after surgery. The main radiological and histopathological features are highlighted to make the case representative.

A search of studies in the English literature was conducted on PubMed to identify previous reports on spinal epidural atypical meningiomas. We used the following keywords alone or a combination of them: "atypical"; "grade II"; "epidural"; "extradural"; and "meningioma."

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3 Results

3.1 Case Report

In January 2020, a 24-year-old woman was admitted to the Neurosurgery of Fondazione Policlinico Agostino Gemelli IRCCS in Rome, Italy, with a 6-month history of dysesthesia and paresthesia in the lower limbs. Her symptoms had progressively exacerbated over time and eventually irradiated to the abdomen. A neurological examination upon admission revealed bilateral tactile hypoesthesia (5/10) and paresthesia below Th4. She presented with exaggerated knee and ankle reflexes, bilaterally. Her extensor plantar response and patellar clonus were elicited on the left side. Her motor function was preserved, as was her control of voluntary sphincters. Her medical history included only therapy with Aldactone for hirsutism related to polycystic ovary syndrome.

Magnetic resonance imaging (MRI) showed an expansive and infiltrating lesion in the extradural, subarachnoid space at Th4-Th5. The mass extended caudally for approximately 34 mm from the superior end plate of Th4 to the upper half of the Th5 vertebral body. The pathological tissue was located posteriorly with increased thickness on the right side, and it caused the segmental stenosis of the spinal canal, the obliteration of the perimedullary cerebrospinal fluid (CSF) spaces, spinal cord compression, and displacement to the left. On T2-weighted images, the spinal cord showed slight hyperintensity, possibly due to ischemic events. The pathological tissue appeared isointense on T1-weighted images and mildly hyperintense on T2-weighted images, with restricted proton motion on diffusion-weighted images (DWI) and a diffuse and homogenous contrast uptake. Following the injection of the contrast medium, the lesion had a sleeve-like appearance causing spinal cord compression. In addition, the lesion presented an initial extension toward the neural foramina, mainly in the right Th4-Th5 intervertebral foramen. There was no evidence of signal

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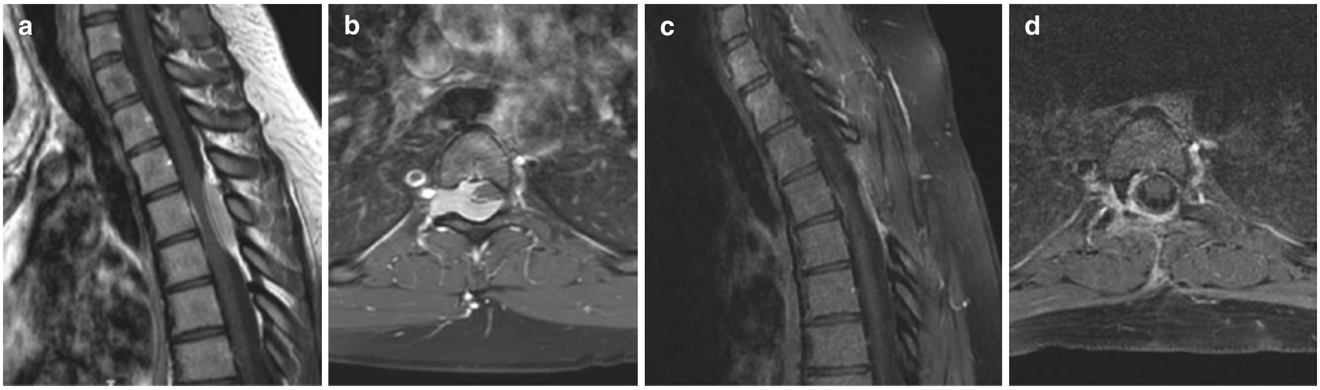

Fig. 1 MRI imaging: (**a**) preoperative sagittal MRI with contrast showing the contrast-enhancing dorsal spinal epidural lesion; (**b**) preoperative axial MRI documenting the sleeve-like epidural lesion; (**c**, **d**) 2-year follow-up T1-weighted sagittal and axial postoperative MRI with contrast documenting recurrence-free dorsal spinal canal

alterations on the adjacent skeletal segments consistent with bone swelling. The pathological tissue was not of unequivocal interpretation, and a lymphoproliferative disorder was included in the differential diagnosis. A coexisting myelopathic area was evident (Fig. 1a).

Surgery was performed with intraoperative neurophysiological monitoring to assess the motor- and somatosensory-evoked potentials of the inferior limbs. Following the exposure of the Th4-Th5 laminae and joints, we performed a bilateral Th4 laminectomy by using the high-speed drill and the bone punches. The dura appeared covered by a gray-reddish, elastic, and hard tissue, tightly adherent to and infiltrating the right anterolateral dural sleeve and the emerging nerve root (Fig. 2).

The intraoperative frozen-section examination was suggestive of meningioma. During the delicate removal of the anterolateral component of the tumor, a sudden the reduction in the Motor Evoked Potentials (MEPs) and Somatosensory Evoked Potentials (SEPs) occurred, which was treated with the prompt intravenous injection of methylprednisolone, which helped maintain high arterial pressure and prevent ischemia. The corticospinal D wave exhibited a reduction in the amplitude caudal to the lesion. By that point, the dorsal and the lateral right intraforaminal Th4-Th5 portions of the extradural mass had been successfully and completed resected. Given the decreased neurophysiological pattern recorded during surgery and given that the frozen-section examination suggested meningioma, we decided to avoid any further cauterization on the sites of dural infiltration, in particular the ventrolateral side of the spinal cord. The decision was taken to avoid surgically manipulating the spinal cord, which would have been necessary for the excision of the tumoral component anterior to the dural sac.

In the immediate postoperative period, the patient exhibited proprioceptive disturbances and motor deficits on the right inferior limb (3/5), with worse proximal weakness. Sensory functions and sphincter control were not affected.

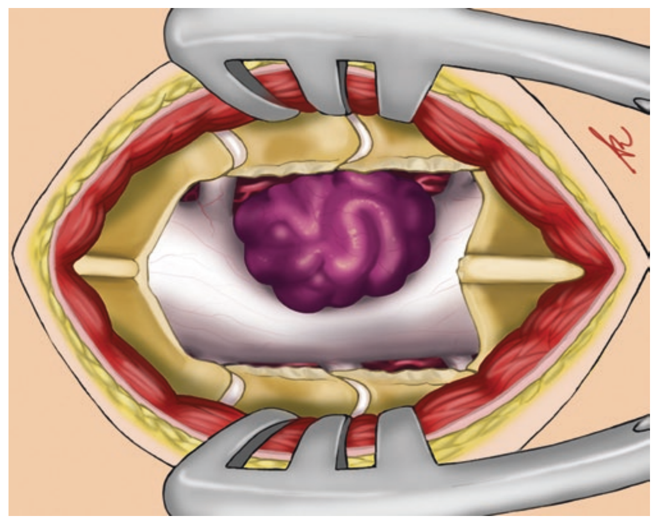

Fig. 2 Representational drawing of the surgical field

Postoperative MRI confirmed the gross total resection of the tumor and the findings were negative for spinal canal compression (Fig. 1b). Nonetheless, small T2-hyperintense foci located between Th4 and Th5 persisted on the spinal cord. Compared to the preoperative MRI, the hyperintensity's extension was substantially unmodified, and only minimal signs of swelling, ascribable to a myelopathic lesion, were present. On the fourth postoperative day, the patient was transferred to a rehabilitation clinic in good clinical condition and reported rapid neurological improvement.

4 Histopathology

Histological specimens consisted of meningothelial tumor fragments. The tumor cells were arranged in chords, nest and whorls (Fig. 3a). Scattered psammomatous bodies were present in the tumor tissue (Fig. 3a). The tumor did not show significant nuclear polymorphism nor areas with necrosis or diffuse growth pattern. However, mitotic activity was significantly high (up to 5 mitoses/10 high-power fields (HPFs)), granting the diagnosis of atypical meningioma (World Health Organization (WHO) grade II, WHO 2016). The tumor infiltrated the epidural tissue at its periphery (Fig. 3b). No infiltration of nervous tissue was found.

At the 3-month follow-up, she presented with complete neurologic recovery. Radiologic follow-ups at 6 and 12 months showed no recurrence of the disease. Spinal cord MRI at the 2-year follow-up showed no recurrence of the disease (Fig. 1c).

We methodically reviewed the English literature on spinal epidural atypical meningioma, and we found out that the occurrence of epidural atypical SMs (WHO grade II) was almost anecdotal. Only two cases have been previously reported (Table 1). Rutherford et al. [3] described the case of a 29-year-old man with exacerbating neuropathic pain, dysesthesia, and paresthesia in the coccygeal, buttock, and thigh regions due to a sacral epidural atypical meningioma. Despite the apparent complete resection, the patient presented with a recurrence of the original symptoms 9 months after surgery: the local recurrence of the meningioma was evident on MRI, extending through the S2 foramen into the presacral soft tissues. At 6 months after second surgery, local and systemic recurrence occurred with multiple pulmonary metastases, so the patient was referred to palliative chemotherapy.

Ben Nsir et al. [1] reported the case of a 70-year-old man who presented with lower-limb paresthesia, dysesthesia, and motor deficits, owing to an anterior lateral extradural lesion at the Th5 level revealed by the MRI. The patient underwent a posterolateral approach in emergency, and his histopathology revealed a diagnosis of epidural atypical meningioma. Despite the complete excision and cauterization of invasion sites, followed by adjuvant radiotherapy, local recurrence occurred 7 years after surgery. The patient presented with severe symptoms of spinal cord compression and MRI evidence of anterolateral progression of the tumor, which involved the soma of Th5 and extended into the posterior mediastinum. Thus, the patient was submitted to a second surgical removal of the recurrent lesion and was successively submitted to rehabilitation, following a good recovery. The scarce available literature on cases of epidural atypical meningioma made it hard to draw conclusions on the epidemiology, prognosis, and optimal management of this disease.

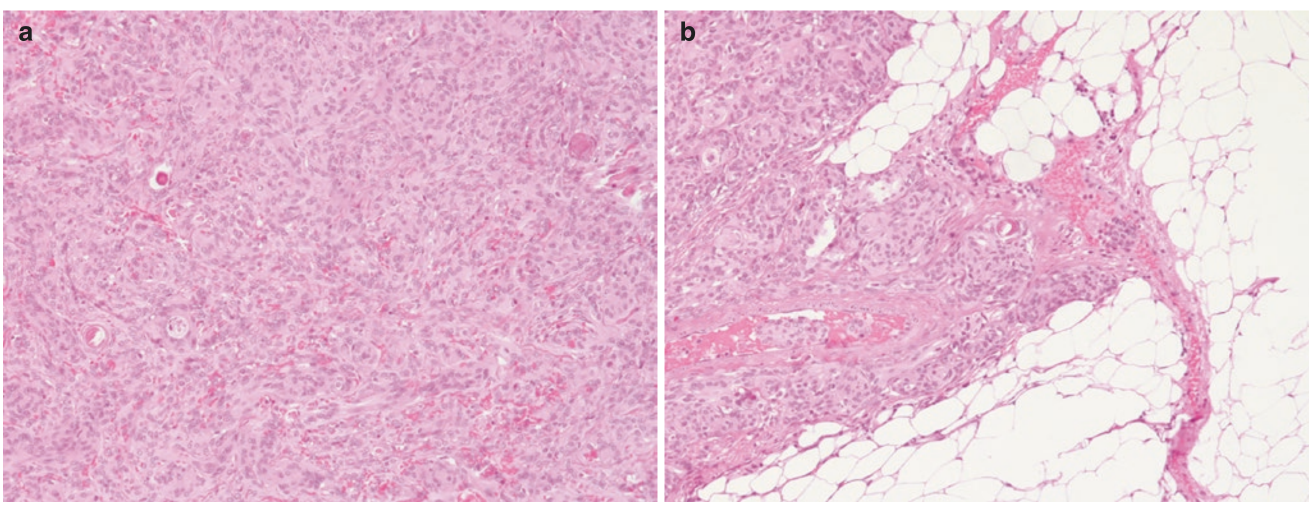

Fig. 3 Neuropathological features of the case reported here: (**a**) cells arranged in chords, nests, and whorls and scattered psammomatous bodies in tumor tissue; (**b**) the tumor infiltrating the epidural adipose tissue at its periphery (hematoxylin and eosin stain 100×)

Table 1 Cases of epidural atypical meningiomas in the English literature

Author (year)	Age	Sex	Location	Clinical onset	Surgical approach	EOR	Ki67	RT	Recurrence (PFS)/ treatment	FU (m)	State of disease at LFU
Rutherford (2006)	29	M	S2–S3	Neuropathic pain	Posterior	GTR	10%	No	9 months/ surgery	15	Recurrence and metastasis (palliative chemotherapy)
Ben Nsir (2014)	70	M	Th5	Paraparesis	Posterolateral	GTR	N/A	Adjuvant RT, 50 Gy	7 years/ surgery	108	No recurrence
Present case	24	F	Th4-Th5	Lower-limb hypesthesia	Posterior	GTR	7%	No	No	24	No recurrence

(*M* Male; *F* Female; *EOR* Extent of Resection; *GTR* Gross Total Removal; *N/A* Not Available; *RT* Radiation Therapy; *PFS* Progression-Free Survival; *FU* Follow-Up; *LFU* Last-available Follow-Up)

5 Discussion

Meningiomas represent the most common primary spinal tumor in adults, accounting for 39% of all tumors [4]. They are generally well-circumscribed lesions with broad-based dural attachments; the typical dural tail sign is clearly seen in 60–70% of the cases, and sometimes its relationships with the spinal cord and the denticulate ligament cause the so-called ginkgo leaf sign in those meningeal lesions arising laterally or ventrolaterally to the spinal cord [5].

Extradural meningiomas are rare entities, accounting for 2.5–3.5% of all spinal meningiomas and generally involving the thoracic and cervical spine [4, 6]. According to the review by Bettaswamy et al. [2]. Only seven cases of pure extradural spinal meningioma had been reported as of 2016. Due to the rarity of purely extradural meningiomas, these tumors can be misdiagnosed on radiological imaging as spinal metastases [7–9] even if radiological features, especially signal intensity on MRI, seem typical of meningiomas. Many authors have highlighted the value of intraoperative histology in adequate surgical management [1, 10].

Epidural meningiomas pose challenges for the surgeon not only because they can be misdiagnosed as other aggressive extramedullary malignancies but also because their surgical management is difficult. Extension over multiple spinal segments, adherence to nerve roots, and dural invasion have been reported in the vast majority of cases [6]. Pathologically, atypical SMs feature elevated mitotic activity (a mitotic index of at least 4 and 20 mitoses/10 HPFs), and/or for atypical SMs, three of the following five histological features are present: spontaneous necrosis, sheeting, prominent nucleoli, high cellularity, and/or small cells [11]. According to some authors SMs' prognoses are unfavorable because of their invasiveness and vascularization [12–15]. The gross total resection of the tumor may be difficult to achieve because of bone involvement and/or paraspinal extension. Because of the difficulties in achieving the gross total removal of the tumors, the recurrence rate after surgery seems to be up to four times higher than that in cases of intradural meningiomas [16].

Several pathogenic theories exist: Most likely, epidural SMs arise from the arachnoid tissue lying around the periradicular nerve root sleeve, where spinal leptomeninges merge directly into the dura. As demonstrated by Savardekar et al. [10], this theory provides a rationale to resect the tumor by detaching it from the spinal dura, without needing to excise the dura itself.

These findings refer mostly to a series of WHO grade I epidural SMs, so their value on WHO grade II epidural spinal meningioma is questionable. Indeed, the available knowledge about grade II epidural SMs is very limited because of their rarity. Nevertheless, grade II SMs account for approximately 6% of SMs, mostly intradural lesions. A recent clinical series and literature review [17] focused on atypical meningiomas' high recurrence risk, ranging from 15% to 61%. Among epidural spinal meningiomas, atypical lesions are very rare. The presented case is the first one diagnosed at our institution, which is a high-volume center for meningiomas in our country. Because of its rarity, it is not yet possible to draw significative conclusions on epidural atypical SMs as nosological entities, but several factors contribute to making them clinical, diagnostic, and surgical dilemmas: They can be preoperatively mistaken for secondary lesions; intraoperative management can be challenging because of the involvement of the surrounding tissues; and gross total resection should be advocated but can be associated with higher morbidity, causing functional deficits, as both in our case and the case described by Ben Nsir et al. [1]. The risk for recurrence seems to be high because of a combination of both their anatomical extension (which often prevents radical excision) and their grading. Furthermore, even without any histological evidence of malignancy, atypical meningioma can metastasize [1]. On the other hand, there's no evidence that adjuvant radiotherapy is mandatory for the long-term control of the disease [18].

6 Conclusions

Epidural atypical spinal meningiomas are unique owing to a combination of factors. Apart from this case, just two other cases have been previously reported in literature, with relapses and the progression of the disease occurring in both. In our case, gross total resection was achieved, and no signs of local or distant recurrence were observed at the 24-month follow-up. Despite their rarity, epidural atypical meningiomas represent clinicopathological entities that deserve recognition. Further experience is needed to accurately define the prognosis and optimal management of this rare entity.

Conflicts of Interest The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter or materials discussed in this manuscript.

References

1. Ben Nsir A, Boughamoura M, Mahmoudi H, Kilani M, Hattab N. Uncommon progression of an extradural spinal meningioma. Case Rep Surg. 2014;2014:630876.
2. Bettaswamy G, Ambesh P, Das KK, Sahu R, Srivastava A, Mehrotra A, Behari S. Extradural spinal meningioma: revisiting a rare entity. J Craniovertebral Junction Spine. 2016;7(1):65.
3. Rutherford SA, Linton KM, Durnian JM, Cowie RA. Epidural meningioma of the sacral canal: case report. J Neurosurg Spine. 2006;4(1):71–4.

4. Pant I, Gautam VKS, Kumari R, Chaturvedi S. Spinal tumour: primary cervical extradural meningioma at an unusual location. J Spine Surg. 2017;3(3):509.
5. Yamaguchi S, Takeda M, Takahashi T, Yamahata H, Mitsuhara T, Niiro T, Kurisu K. Ginkgo leaf sign: a highly predictive imaging feature of spinal meningioma. J Neurosurg Spine. 2015;23(5):642–6.
6. Zhang LH, Yuan HS. Imaging appearances and pathologic characteristics of spinal epidural meningioma. Am J Neuroradiol. 2018;39(1):199–204.
7. Ito K, Imagama S, Ando K, Kobayashi K, Hida T, Tsushima M, Matsumoto A, Morozumi M, Tanaka S, Nishida Y, Ishiguro N. Discrimination between spinal extradural meningioma and both intra and extradural meningioma: case report. Nagoya J Med Sci. 2017;79(1):115–21.
8. Wu L, Yang T, Deng X, Yang C, Zhao L, Yao N, Xu Y. Spinal extradural en plaque meningiomas: clinical features and long-term outcomes of 12 cases. J Neurosurg Spine. 2014;21(6):892–8.
9. Zevgaridis D, Thomé C. Purely epidural spinal meningioma mimicking metastatic tumor: case report and review of the literature. Spine. 2002;27(18):E403–5.
10. Savardekar A, Chatterjee D, Chatterjee D, Dhandapani S, Mohindra S, Salunke P. Totally extradural spinal en plaque meningiomas–diagnostic dilemmas and treatment strategies. Surg Neurol Int. 2014;5(7):S291.
11. Louis DN, Perry A, Reifenberger G, Von Deimling A, Figarella-Branger D, Cavenee WK, Ellison DW. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol. 2016;131(6):803–20.
12. Cohen-Gadol AA, Zikel OM, Koch CA, Scheithauer BW, Krauss WE. Spinal meningiomas in patients younger than 50 years of age: a 21-year experience. J Neurosurg. 2003;98(3):258–63.
13. Cramer P, Thomale UW, Okuducu AF, Lemke AJ, Stockhammer F, Woiciechowsky C. An atypical spinal meningioma with CSF metastasis: fatal progression despite aggressive treatment. Case report. J Neurosurg Spine. 2005;3:153–8.
14. Maiti TK, Bir SC, Patra DP, Kalakoti P, Guthikonda B, Nanda A. Spinal meningiomas: clinicoradiological factors predicting recurrence and functional outcome. Neurosurg Focus. 2016;41:E6.
15. Noh SH, Kim KH, Shin DA, et al. Treatment outcomes of 17 patients with atypical spinal meningioma, including 4 with metastases: a retrospective observational study. Spine J. 2018;19(2):276–84.
16. Klekamp J, Samii M. Surgical results for spinal meningiomas. Surg Neurol. 1999;52(6):552–62.
17. Han B, Zhang L, Jia W, Yang J. Clinical features and surgical outcomes of high-grade spinal meningiomas: report of 19 cases and literature review. J Clin Neurosci. 2020;72:264–9.
18. Sun SQ, Cai C, Ravindra VM, Gamble P, Yarbrough CK, Dacey RG, Ray WZ. Simpson grade I-III resection of spinal atypical (World Health Organization Grade II) meningiomas is associated with symptom resolution and low recurrence. Neurosurgery. 2015;76(6):739–46.

Costotransversectomy in the Surgical Treatment of Mediolateral Thoracic Disk Herniations: Long-Term Results and Recent Minimally Invasive Technical Adjuncts

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1 Introduction

Thoracic herniated disks are relatively rare. They account for approximately 2% of all intervertebral herniated disks in large series [1–3]. Their rarity is well explained by the fact that they occur in the less mobile part of the spine. Also, calcifications, unlike in other discogenic pathologies and spine levels, are not infrequent in thoracic disk disease. Traditional surgery via laminectomy has frequently yielded disappointing results [2–5], although the recent literature has reported anterior calcified thoracic herniation successfully treated with this approach [6, 7]. This issue has encouraged a search for alternatives, such as anterolateral [8], lateral [9–11], or posterolateral [12–15] approaches to the thoracic spine. Classically, costotransversectomy represents one of the most used alternative approaches with the advantage to spare, as a rule, the pleura while allowing a convenient tangential view of the anterior part of the thoracic spine. Its learning curve is straightforward, and an expert spinal surgeon would require only a few training sessions and cadaver labs to start to feel confident enough to introduce it into their clinical practice. Moreover, its results are quite comparable to those of the other available approaches [16, 17]. However, shortcomings of this approach (pleural lesions, postoperative dysesthesia as a consequence of extensive neuromuscular bundle dissection, and/or intercostal muscle division) lead the neurosurgical community to search for less-invasive but still-effective approaches to the thoracic spine. Taking into consideration this emerging minimally invasive philosophy, we more recently shifted to a less invasive, navigation-guided, and endoscopic-assisted approach, which still keeps the same philosophy of the original costotransversectomy approach: tangential, extrapleural, and posterolateral [3, 18].

We report here the long-term results of a series of 66 thoracic disk herniation patients surgically treated during a 10-year period.

2 Materials and Methods

From January 2009 to December 2019, we selected 66 patients harboring a symptomatic median-paramedian herniated disk at the level of thoracic spine, treated at the authors' institutions.

In three patients, disk herniations were present on two adjacent levels, totalizing 68 procedures. Two of these patients underwent a second surgery a few months after the first procedure. Neurological examinations at admission, neurophysiological examinations, pre- and postoperative examinations, and 6-month and 12-month follow-up images, including computed tomography (CT) scans with three-dimensional (3D) reconstructions and/or magnetic resonance imaging (MRI) scans, were reviewed.

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3 Clinical Symptoms

The most common clinical presentation included drug-resistant radicular pain at the appropriate level, accompanied by lower-limb hyperreflexia and gait disorders. Radicular pain and/or impairment was detected in 60 out of 66 patients (90%). Clinical signs of myelopathy, such as hyperreflexia, clones, and noticeable fatigue while walking, were detected in 26 out of 66 patients (39.3%). These patients came to surgery earlier than those without myelopathy. The two most frequent levels of disease were T9 and T11.

4 Radiological Signs

A thoracic X-ray could sometimes show a calcified disk. CT scans, in addition to MRI scans, represent the main diagnostic tools in thoracic disk pathology. Out of the 66 cases, 46 showed some areas of calcifications (69.6%); of these, 23 were calcified disks of significant size. MRI represents the main diagnostic test because it shows both the entity and the consistency of the lesion and the severity of the neural compression, but a 1 mm CT scan with 3D reconstruction is more useful for surgical planning and neuronavigation (Fig. 1).

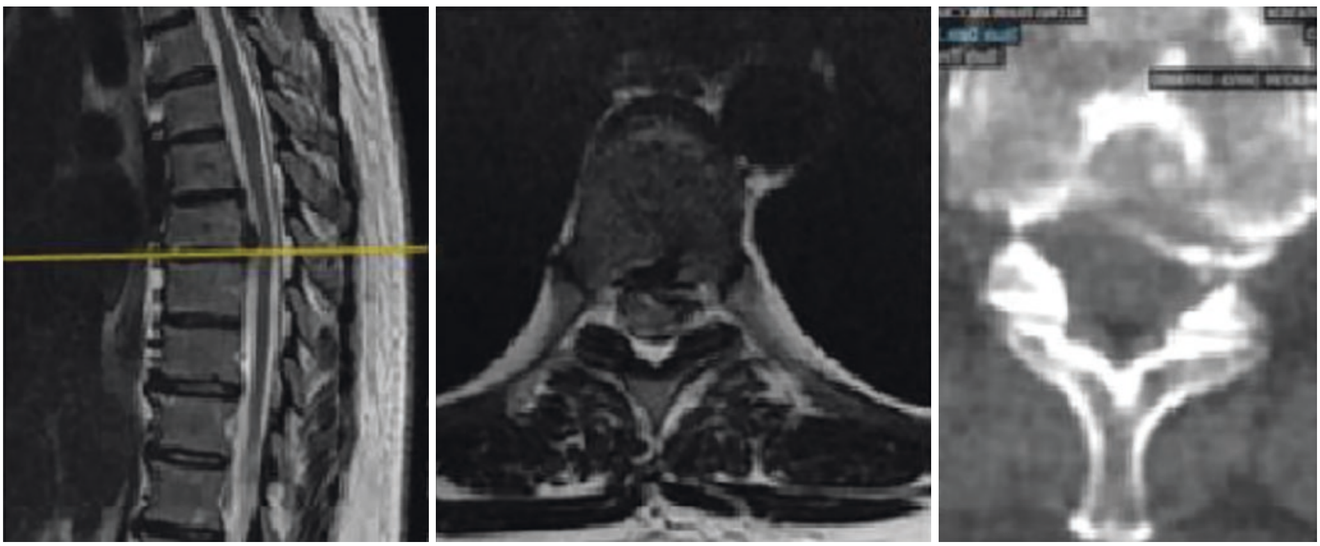

Fig. 1 CT scan and MRI preoperative studies showing a mediolateral partially calcified disk herniation

5 Surgical Technique

A posterolateral extracavitary approach was routinely used in this study. In brief, a hockey-stick skin incision extended one space below the symptomatic side was performed. In the most recent cases, we performed a customized median epispinous skin incision limited to the involved level, as verified by the neuronavigation. Intervertebral muscles were subperiosteally sectioned along the course of the corresponding rib and were retracted superiorly and inferomedially by using self-retaining retractors and skin hooks or retracted longitudinally, centered to the costotransverse joint, in the most recent cases. Careful soft tissue dissection and rib exposure are mandatory to adequately surgically expose the disk, in order to obtain a safe dissection of the pleura, thus reducing the risk of its accidentally opening [16]. The site was freed from pleural adhesions, and the nerve root became visible in the lower edge of the rib. In the first cases, a limited costectomy was then performed by using appropriate thoracic surgical instruments [19]. Because pleural adhesion can be significant at this level, the removal of the transverse process and joint was performed with the judicious use of a drill and careful microdissection. Once the joint had been reduced, the nerve root was followed up to the neural foramen, and the discal space was identified. The disk was removed, and the interdiscal space was enlarged with spacers. This maneuver facilitates further discectomy and allows the adequate removal of marginal osteophytes from the anterior portion of the adjacent vertebrae. This should be carried out with the careful use of a diamond burr. Finally, the epidural space was entered while the spinal canal remained protected by the posterior longitudinal ligament. At this stage, some epidural bleeding can occur, which can be easily controlled with low-power bipolar coagulation or the judicious use of hemostatic material. Once the adequate decompression of the neural elements had been obtained, the discal space was eventually filled with the autologous bone obtained from the removed rib. The integrity of the pleura was carefully checked (in the case of pleural violation, a chest drainage system was inserted), and the wound closed layer by layer.

In the last cases, the surgical technique was modified, thanks to the availability of modern technologies—i.e., endoscopies, spinal neuronavigators, and piezoelectric osteotomes (MECTRON, Italy). Briefly, through a tailored median epispinous incision and unilateral subperiosteal muscle dissection, the rib was reduced down to one thin bone layer thanks to the use of a piezoelectric bone scalpel (Fig. 2).

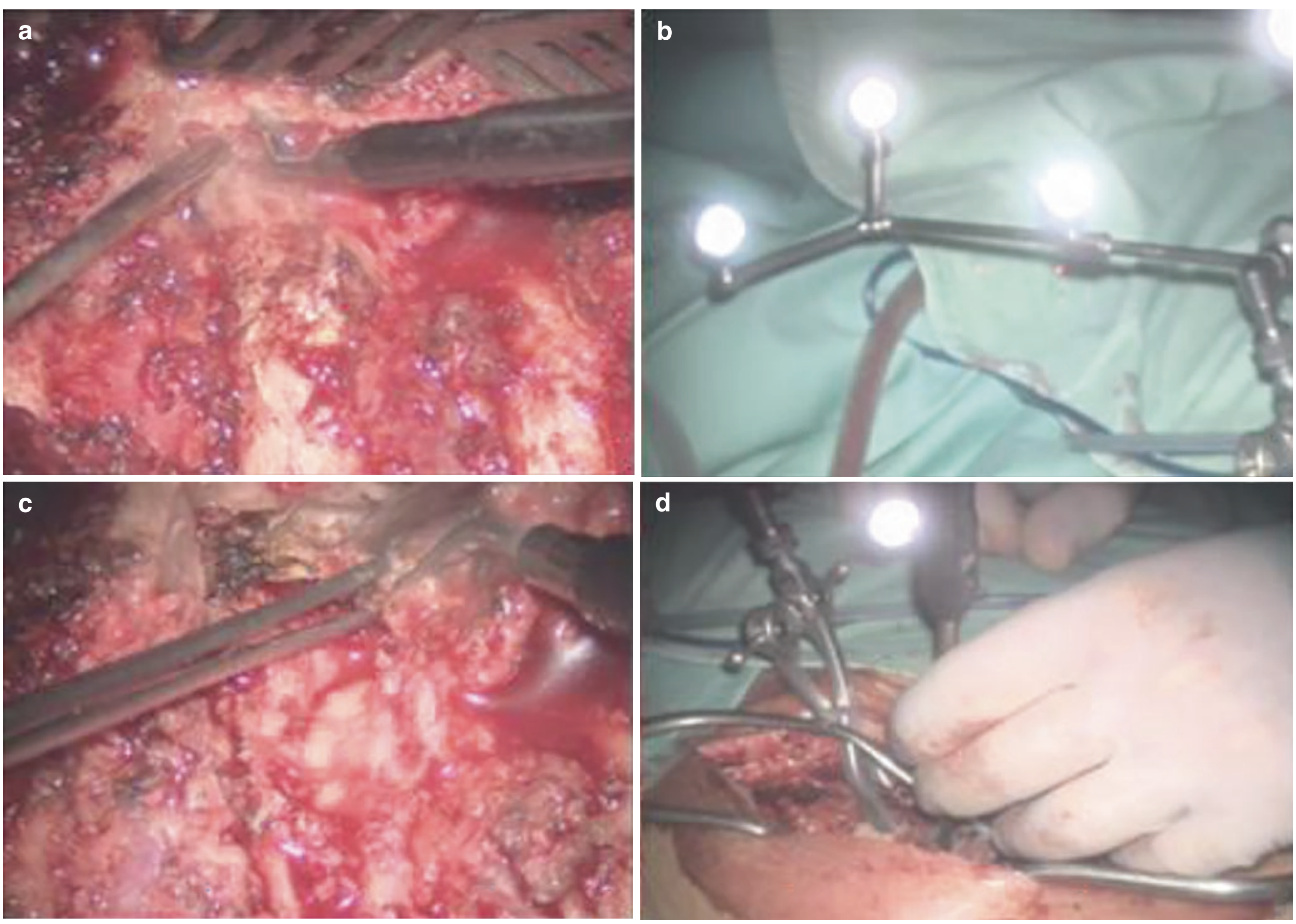

Fig. 2 (**a**–**c**) Piezoelectric scalpel used for safe bone removal in costotransversectomy; (**b**–**d**) intraoperative neuronavigation control and surgical targeting to minimize the unnecessary approach-related manipulation of healthy tissues and minimize complications

The rib was therefore easily mobilized to expose the nerve root at its foraminal exit without any risk of exposing or damaging the microvascular bundle, which was left unviolated, or the pleura underneath. Spinal neuronavigation is quite helpful in limiting the approach and healthy tissue manipulation while maintaining the surgical orientation in this sort of keyhole approach [16, 20]. Although the surgical exposure is obviously more limited, if it is compared to the approach previously used, then the angle of vision is almost the same, eventually augmented by the endoscope to look around the blind corners [13, 21, 22]. The careful and partial removal of the joint, sometimes leaving part of the transverse process, adequately exposes the affected neural foramen and the discal space, and then surgery proceeds as described above (Fig. 3), apart from the autologous bone graft, which is not routinely used. Again, piezoelectric technology is quite helpful in allowing adequate bone tissue removal while minimizing the risks of accidental pleural and/or dural openings and that of nerve damage.

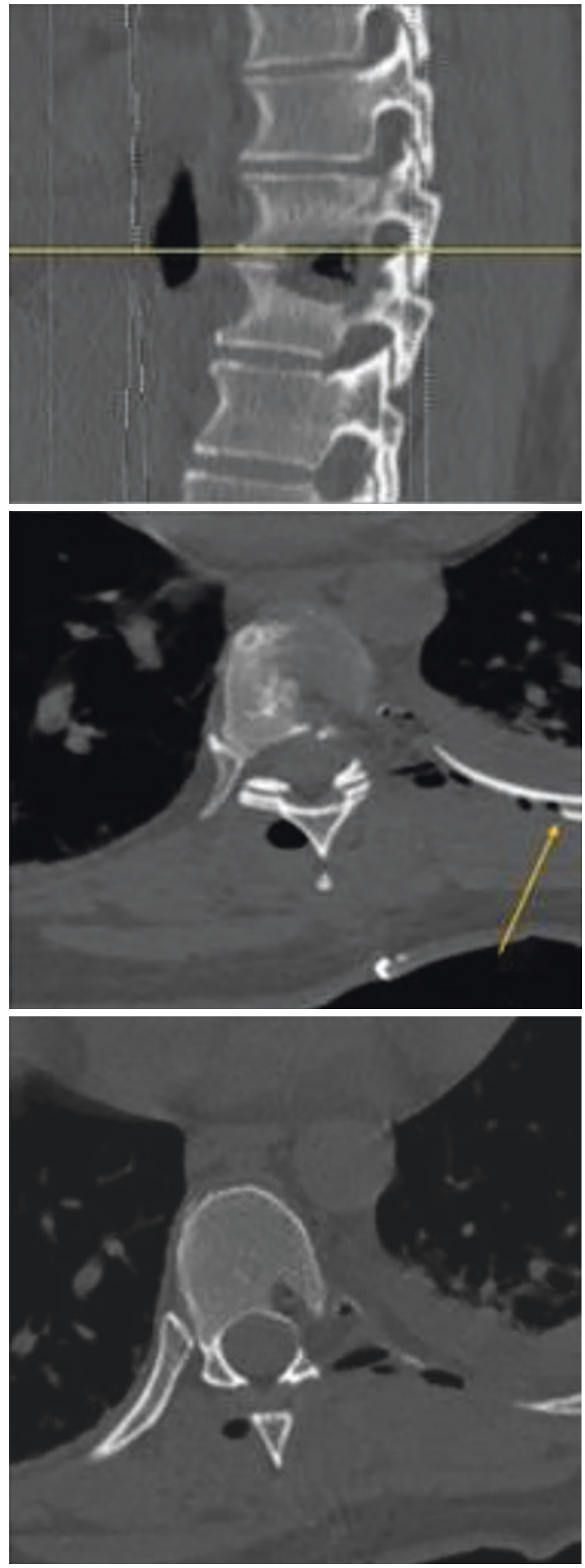

Fig. 3 Postoperative CT scan: yellow arrow shows the flattened outer layer of the rib, via piezosurgery, which protects the pleura, while displacing down the rib provides an adequate and almost-tangential working angle to reach the medial part of the discal space

6 Methods

In evaluating the long-term results, we considered three clinical parameters: (a) radicular pain; (b) radicular hypodysesthesia; (c) radiological decompression and spinal stability; and (d) myelopathy. The latter one was classified as significant when gait fatigue, abnormal lower-limb reflexes, and clones were present. Even when present, a mild increase in the lower limbs' reflexes was not on its own considered a definite sign of myelopathy. Spinal trauma patients were not considered for the present study. The analysis of variance (ANOVA) test was used for statistical analysis, and a *p*-value < 0.05 was considered significant.

7 Results

Patients with signs of myelopathy (29 cases) exhibited a shorter clinical history when compared to the remaining ones (4–12 months while averaging 5.7 months vs. 6–14 months while averaging 7.8 months, $p < 0.05$). Postoperative CT scans were routinely performed, and in all cases, they showed adequate spinal cord and canal decompression, with different volumes of bone removal (Fig. 3). The intraoperative violation of the pleura required the placement of a chest tube draining system in three patients (all but one among the oldest operated-on patients). Two patients among the first patients (and one in the last), submitted to a "regular" costotransversectomy and showed postoperative neurosurgical worsening. However, most of them reported significant wound discomfort, which required about 2–3 weeks for it to subside if so (none of those operated on with the minimally invasive technical refinements). No cases of deep-wound infection occurred. However, superficial wound infection requiring 10 days of local medications occurred in one patient, who developed pneumothorax 2 weeks after surgery.

We wonder whether infection played a role in the development of this unusual complication. A long-term follow-up (2–10 years) was available for all cases. Seven patients died from unrelated causes; however, their follow-ups were adequate (5 and 10 years). Two patients operated at two adjacent levels developed iatrogenic scoliosis and required subsequent arthrodesis. In all but two patients, radicular symptoms improved. Hypoesthesia in the related dermatomes was postoperatively noticed in 22 cases. This was not reported as a quality-of-life-affecting symptom. Almost all the first patients reported local dysesthesia at the level of the surgical wound (probably because of the hockey-stick skin incision) and almost none of the last cases. The average follow-up time in these cases was relatively short: 4 years vs. 7 years for the whole group. Thus, in addition to the local dysesthesia from the type of skin incision, a process of adaption could occur in the longer term, making dysesthesia less distressing to patients.

Clinical signs of lower-limb myelopathy were detected in 26 cases. These cases exhibited shorter clinical histories compared to those of the remaining patients (4–12 months while averaging 5.8 months vs. 6–14 months while averaging 7.9 months, $p < 0.05$). All cases were operated within 6 months from the clinical onset. Out of the 26 cases, 21 improved, even if to different degrees.

7.1 Illustrative Case

A 45-year-old woman presented with a 1-month history of gait disturbances, left-sided D7 sensory level, and mild right lower-limb hyperreflexia. A CT and MRI study showed a D7-D8 calcified disk herniation with concomitant spinal cord compression (Fig. 1). In order to adequately expose the anterolateral part of the canal, a left-sided D7-8 costotransversectomy approach was selected. Under neuronavigation control, a mini-invasive and targeted surgical trajectory was obtained (Fig. 2b–d), with very limited skin incision and muscle manipulation. The bone removal was also tailored, under neuronavigation guidance, to limit the bone removal while not exposing unnecessary anatomical structures. Thereafter, the disk was easily removed under microscopic magnification and endoscopy assistance [13, 23, 24]. The entire surgical procedure was under SEP/MEP monitoring. Furthermore, in our experience, the piezoelectric bone scalpel revealed its advantages during the costotransversectomy, where after the initial use of the high-speed drill aimed at speeding up the procedure, the inner layer of the rib bone was removed, like a thin eggshell, to leave only a bony shield on the underlying pleura while offering the possibility to lower the rib and widen the essential exposure. The costotransversectomy was not found to cause any damage to the adjacent pleural and/or neurovascular structures. The piezoelectric osteotome was also used to safely remove the circumferential vertebral bony spurs and the calcified disk without causing any unwanted accidental dural or spinal cord damage.

Postoperative radiological findings showed the preciseness of bone cutting together with calcified hernia removal and spine cord decompression (Fig. 3). The patient experienced satisfying neurological improvements at the 3-, 6-, and 12-month clinical follow-ups, especially for her sensory deficit, from which she completely recovered.

8 Discussion

Alternative surgical approaches to laminectomy have proved to be effective in the surgical management of thoracic disk herniation [1, 25]. Indeed, many studies have analyzed the results of these different approaches, such as anterior [26], anterolateral transthoracic [8], lateral extracavitary [9], costotrasversectomy [16, 17], and transfacet–transpeduncular [9, 22, 27]. Generally, little difference has been observed in the comparative evaluation of the surgical results of all these approaches [3, 28].

Microsurgical approaches for the treatment of pathology located in the ventral thoracic spine that use video-assisted thoracic surgery (VATS) allow neurosurgeons to access the discal spaces, vertebral bodies, paravertebral soft tissues, spinal cord, spinal nerves, and sympathetic chain through minimally invasive surgery. This has been associated with substantial clinical benefits, including reduced postoperative pain, lower complication rates, and shorter recovery times when compared with standard thoracotomy techniques [29, 30].

However, even today, no significant difference has been observed in studies that have compared the postoperative results of thoracic endoscopy versus those of the already-established techniques in clinical routines—i.e., either anterolateral or posterolateral approaches [8, 9, 31].

Our study analyzed the long-term results of a relatively consistent experience with thoracic disk herniations approached via a costotransversectomy and analyzed the impact of its modern, less aggressive modification, which, however, respects the original principle of lateral-tangential extrapleural approach to the most anteromedial part of the discal space [24, 32, 33]. This has also been used in a few cases of anteriorly located extradural spinal tumors because it offers a convenient view of that region without dural and spinal cord retraction. Our data well matches with the literature in terms of patient characteristics, preoperative symptoms, diagnostic strategies, and indications for surgery. We observed that patients with noticeable signs of myelopathy had significantly longer clinical histories when compared with those in whom myelopathy was either absent or insignificant.

Moreover, our postoperative results are comparable to those of the largest series reported in the literature in terms of postoperative improvements in symptoms and complication rates [11, 33, 34]. For this reason, using costotransversectomy, which, as stated above, does not require a long learning curve, as the routine approach for thoracic herniated disk disease has become a conceptual strategic choice during the past 10 years. Our goal was to outline some conceptual advantages over other techniques and to consider the potential disadvantages of costotransversectomy. The potential lack of pleural violation represents a noticeable advantage over the transthoracic approaches, and this lack requires opening the chest, even in endoscopic mini-thoracotomy; the lateral extracavitary approach would be more likely to cause this complication [9, 10, 33]. Respecting the pleura requires taking particular care when removing the facet joint, to which pleura may strongly adhere. We regularly perform this surgical step under microscopic magnification and with piezosurgery. Nevertheless, pleural injury and the subsequent necessary implementation of a chest tube occurred in approximately 15% of the patients, although in none of the last operated-on patients.

Adequate rib removal allows the prompt availability of autologous bone material to fill in the emptied discal space and/or the cavity created by the partial removal of the vertebral body, when required, to obtain the fusion. We had to perform transpedicular fixation only in the two patients: One with a second herniation occurred in an adjacent space on the same side a couple of months after the first surgery; the other, with symptomatic iatrogenic scoliosis, occurred in spite of bony fusion, as a likely result of the extensive removal of two adjacent facets [34, 35].

To manage the cases of calcified, centrally located thoracic hernia, we enlarged the hemilaminectomy, which as a rule is very small, to decompress the spinal cord; otherwise, a not negligible contralateral portion of the calcified disk would have been left in situ owing to a lack of full, adequate visualization, even under endoscopic magnification [7, 32]. In the long term, this strategy was effective in all cases. However, rib removal necessitated a hockey-stick type of incision with the division of the intercostal muscles, which caused a not minor amount of discomfort in the patient who required a few weeks to subside.

Our experience has confirmed the similar decompressive efficacy of transfacet–transpeduncular, or midline calcified, lesions, as shown in Figs. 4 and 5.

We already mentioned the advantage of costotransversectomy over the other routinely used approaches for thoracic disk herniation: Costotransversectomy does not require violating the pleura, and its surgical anatomy makes this eventuality quite unlikely. However, we cannot overlook the fact that a significant proportion of patients, when specifically asked about comfort levels, reported discomfort at the operative site, sometimes radicular and pain-like and sometimes also a long time after the operation [9, 19]. Only a minority of those patients required pain medication, so the subjective patient's perception played a significant role in this issue. Although this must not be underemphasized, it should be balanced against the safety of the approach for preventing surgery-related spinal cord injury. We wonder whether not only the manipulation of the lateral thoracic muscles but also local postoperative microinstability, which is difficult to

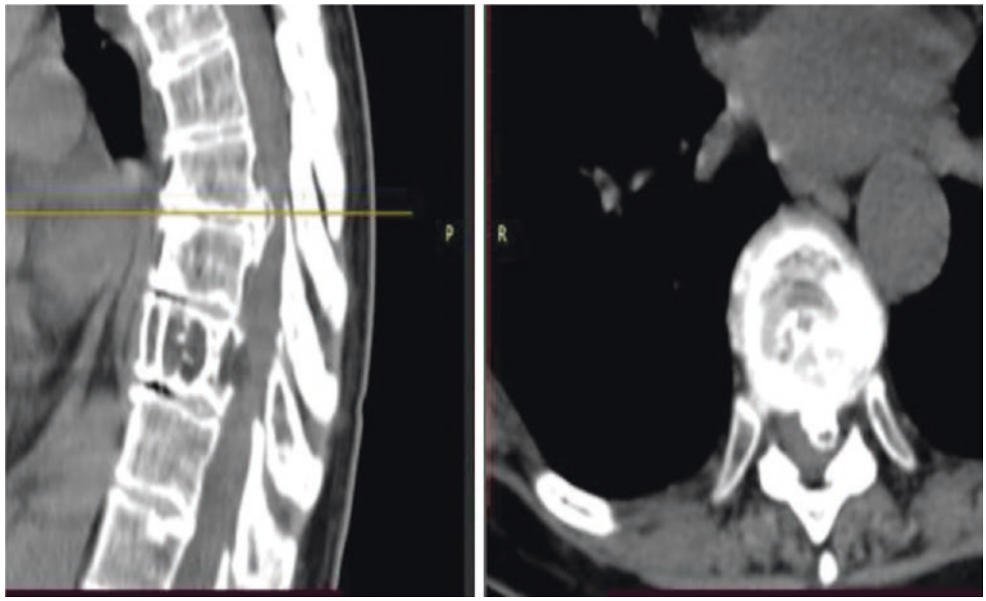

Fig. 4 Preoperative CT scan showing a mediolateral partially calcified disk herniation

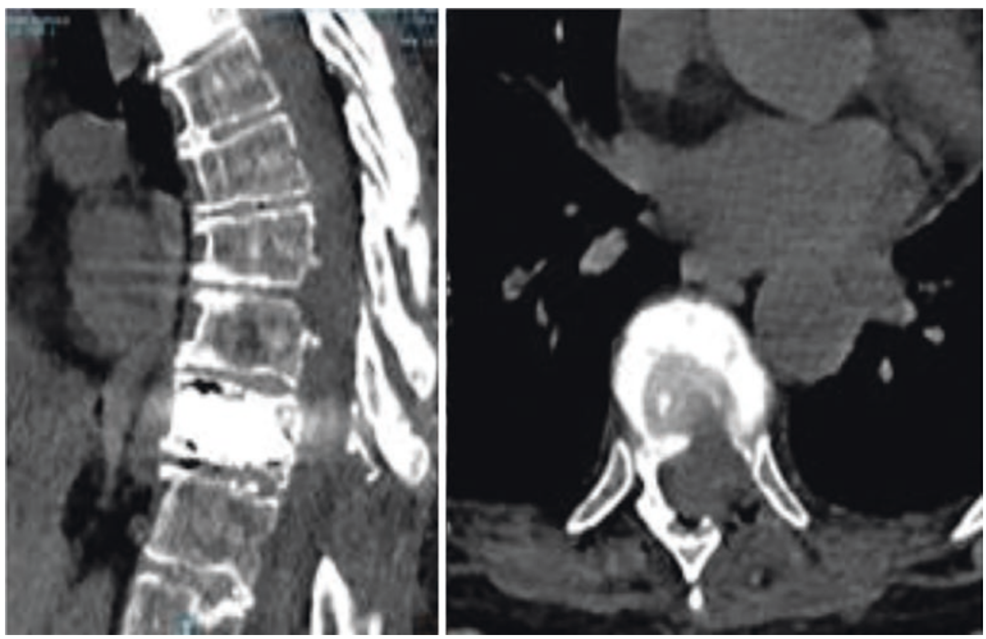

Fig. 5 An adequate and almost-tangential working angle to reach the most medial part of the discal space with simple transfacet–transpeduncular decompression (note the vertebroplasty for angioma above and below the decompression)

demonstrate radiologically because of the peculiar characteristics of the thoracic spine, could have played roles in this issue [17]. Concerning the postoperative instability, we already stated that the patients who experienced this complication underwent the removal of two-adjacent-level facets and that each one's postoperative symptomatic scoliosis resolved with instrumented surgery.

Our quite recent experience with the mini-invasive approach directly targeting the affected disk and the neural foramen has apparently solved the problem of postoperative dysesthesia and/or microinstability, which had become serious in the previously operated-on patients. Our experience with the traditional posterolateral approach and the availability and judicious use of modern technologies, such as spinal navigators and piezoelectric instruments for bone dissection, enabled us to gain some better results in the most recent cases [13, 23]. However, the number of operated-on patients is still limited, and these encouraging results await confirmation from a larger number of cases.

9 Conclusions

The present experience gives further support to the use of costotransversectomy, along with its mini-invasive modifications, as a suitable and safe approach for thoracic disk disease. Although we must admit that endoscopy is likely to become the gold-standard surgical method in the future and that the anterior approach with mini-thoracotomy without rib removal will become popular, the future scenario could certainly reserve an important place for the approach we have used in the surgical management of this challenging spinal pathology, mainly because of the approach's versatility and short learning curve.

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References

1. Bouthors C, Benzakour A, Court C. Surgical treatment of thoracic disc herniation: an overview. Int Orthop. 2019;43(4):807–16. https://doi.org/10.1007/s00264-018-4224-0. Epub 2018 Nov 8.
2. Ridenour TR, Haddad SF, Hitchon PW, et al. Herniated thoracic disks: treatment and outcome. J Spinal Disord. 1993;6(3):218–24.
3. Sagar B, Sharma, Kim J-S. A review of minimally invasive surgical techniques for the management of thoracic disk herniations. Neurospine. 2019;16(1):24–33.
4. El-Kalliny M, Tew JM, van Loveren H, et al. Surgical approaches to thoracic disc herniations. Acta Neurochir. 1991;111(1-2):22–32.
5. Rossitti S, Stephensen H, Ekholm S, von Essen C. The anterior approach to high thoracic (T1-T2) disc herniation. Br J Neurosurg. 1993;7(2):189–92.
6. Arts MP, Bartels RH. Anterior or posterior approach of thoracic disc herniation. A comparative cohort of mini-transthoracic versus transpedicular discectomies. Spine J. 2014;14(8):1654–62. https://doi.org/10.1016/j.spinee.2013.09.053.
7. Nakhla J, Bhashyam N, De la Garza RR, Nasser R, Kinon MD, Yassari R. Minimally invasive transpedicular approach for the treatment of central calcified thoracic disc disease: a technical note. Eur Spine J. 2018;27(7):1575–85. https://doi.org/10.1007/s00586-017-5406-y. Epub 2017 Dec 15.
8. Deviren V, Kuelling FA, Poulter G, Pekmezci M. Minimal invasive anterolateral transthoracic transpleural approach: a novel technique for thoracic disc herniation. A review of the literature, description of new surgical technique and experience with first 12 consecutive patients. J Spinal Disord Tech. 2011;24(5):E40–8. https://doi.org/10.1097/BSD.0b013e31822af6f.
9. Lubelski D, Abdullah KG, Mroz TE, et al. Lateral extracavitary vs.costotrasversectomy approaches to the thoracic spine: reflections on lessons learned. Neurosurgery. 2012;71(6):1096–102. https://doi.org/10.1227/NEU.0b013e3182706102.
10. Oltulu I, Cil H, Ulu MO, Deviren V. Clinical outcomes of symptomatic thoracic disk herniations treated surgically through minimally invasive lateral transthoracic approach. Neurosurg Rev. 2019;42(4):885–94. https://doi.org/10.1007/s10143-018-01064-2. Epub 2019 Jan 8.
11. Uribe JS, Smith WD, Pimenta L, et al. Minimally invasive lateral approach for symptomatic thoracic disc herniation: initial multicentre clinical experience. J Neurosurg Spine. 2012;16(3):264–79. https://doi.org/10.3171/2011.10.SPINE11291.
12. Baranowska A, Baranowski P, Baranowska J, Jarzyński T. Evaluation of the results of posterior approach in thoracic disc herniation surgery. Pol Merkur Lekarski. 2020;48(287):318–22.
13. Liu W, Yao L, Li X, Tian Z, Ning C, Yan M, Wang Y. Percutaneous endoscopic thoracic discectomy via posterolateral approach: a case report of migrated thoracic disc herniation. Medicine. 2019;98(41):e17579. https://doi.org/10.1097/MD.0000000000017579.
14. Quillo-Olvera J, Kim JS. A novel, minimally invasive hybrid technique to approach intracanal herniated thoracic discs. Oper Neurosurg. 2020;19(2):E106–16. https://doi.org/10.1093/ons/opz362.
15. Sagan LM, Madany L, Lickendorf M. Costotrasversectomy and interbody fusion for treatment of thoracic dyscopathy. Ann Acad Med Stetin. 2007;53(1):23–6.
16. Kim KD, Babbitz JD, Mimbs J. Imaging-guided costotrasversectomy for thoracic disc herniation. Neurosurg Focus. 2000;9(4):e7.
17. Pei B, Sun C, Xue R, Xue Y, Zhao Y, Zong YQ, Lin W, Wang P. Circumferential decompression via a modified costotransversectomy approach for the treatment of single level hard herniated disc between T10-L1. Orthop Surg. 2016;8(1):34–43. https://doi.org/10.1111/os.12223.
18. Falavigna A, Piccoli CL. Minimally invasive approaches for thoracic decompression from discectomy to corpectomy. J Neurosurg Sci. 2013;57(3):175–92.
19. Wagner R, Telfeian AE, Iprenburg M, Krzok G, Gokaslan Z, Choi DB, Pucci FG, Oyelese A. Transforaminal endoscopic foraminoplasty and discectomy for the treatment of a thoracic disc herniation. World Neurosurg. 2016;90:194–8. https://doi.org/10.1016/j.wneu.2016.02.086. Epub 2016 Feb 28.
20. Hur JW, Kim JS, Cho DY, Shin JM, Lee JH, Lee SH. Video-assisted thoracoscopic surgery under O-arm navigation system guidance for the treatment of thoracic disk herniations: surgical techniques and early clinical results. J Neurol Surg A Cent Eur Neurosurg. 2014;75(6):415–21. https://doi.org/10.1055/s-0034-1368690. Epub 2014 Feb 25.
21. Chiu JC, Clifford TJ, Sison R. Percutaneous microdecompressive endoscopic thoracic discectomy for herniated thoracic discs. Surg Technol Int. 2002;10:266–9.
22. Li ZZ, Zhao HL, Cao Z, Shang WL, Hou SX. Technical notes and clinical efficacy analysis of full-endoscopic thoracic discectomy via transforaminal approach. Zhonghua Yi Xue Za Zhi. 2020;100(4):279–85. https://doi.org/10.3760/cma.j.issn.0376-2491.2020.04.008.
23. Roselli R, Iacoangeli M, Pompucci A, Trignani R, Restuccia D, Di Lazzaro V, Scerrati M. Anterior cervical epidural abscess treated by endoscopy-assisted minimally invasive microsurgery via posterior approach. Minim Invasive Neurosurg. 1998;41(3):161–5. https://doi.org/10.1055/s-2008-1052034.
24. Ruetten S, Hahn P, Oezdemir S, Baraliakos X, Merk H, Godolias G, Komp M. Full-endoscopic uniportal decompression in disc herniations and stenosis of the thoracic spine using the interlaminar, extraforaminal, or transthoracic retropleural approach. J Neurosurg Spine. 2018;29(2):157–68. https://doi.org/10.3171/2017.12.SPINE171096. Epub 2018 Jun 1.
25. Court C, Mansour E, Bouthors C. Thoracic disc herniation: surgical treatment. Orthop Traumatol Surg Res. 2018;104(1S):S31–40. https://doi.org/10.1016/j.otsr.2017.04.022. Epub 2017 Dec 7.
26. Otani K, Nakai S, Fujimura Y, et al. Surgical treatment of thoracic disc herniation using the anterior approach. J Bone Joint Surg Br. 1982;64(3):340–3.
27. Nishimura Y, Thani NB, Tochige S, et al. Thoracic discectomy by posterior pedicle-sparing, transfacet approach with real-time intraoperative ultrasonography: clinical article. J Neurosurg Spine. 2014;21(4):568–76. https://doi.org/10.3171/2014.6.SPINE13682.
28. Noureldine MHA, Pressman E, Krafft PR, Molcanyi M, Tran ND, Greenberg MS, Alikhani P. Management of thoracic disc herniation using the mini-open retropleural approach: technique illustration and clinical outcomes of 33 patients from a single academic center. Oper Neurosurg. 2020;19(5):567–81. https://doi.org/10.1093/ons/opaa228.

29. Russo A, Balamurali G, Nowicki R, et al. Anterior thoracic foraminotomy through mini-thoracotomy for the treatment of giant thoracic disc herniations. Eur Spine J. 2012;21(Suppl 2):212–20. https://doi.org/10.1007/s00586-012-2263-6.
30. Visocchi M, Masferrer R, Sonntag VHK, Dickman CA. Thoracoscopic approaches to the thoracic spine. Acta Neurochir. 1998;140(8):737–43; discussion 743–744. https://doi.org/10.1007/s007010050174.
31. Ogden TA, Kaiser M, Fessler RG. Minimally invasive approaches to thoracic disk herniations. Best evidence for spine surgery: cardinal cases. 2012.
32. Lowe SR, Alshareef MA, Kellogg RT, Eriksson EA, Kalhorn SP. A novel surgical technique for management of giant central calcified thoracic disk herniations: a dual corridor method involving tubular transthoracic/retropleural approach followed by a posterior transdural diskectomy. Oper Neurosurg. 2019;16(5):626–32. https://doi.org/10.1093/ons/opy225.
33. Soda C, Faccioli F, Marchesini N, Ricci UM, Brollo M, Annicchiarico L, Benato C, Tomasi I, Pinna GP, Teli M. Transthoracic versus retropleural approach for symptomatic thoracic disc herniations: comparative analysis of 94 consecutive cases. Br J Neurosurg. 2021;35(2):195–202. https://doi.org/10.1080/02688697.2020.1779660. Epub 2020 Jun 19.
34. Brotis AG, Tasiou A, Paterakis K, Tzerefos C, Fountas KN. Complications associated with surgery for thoracic disc herniation: a systematic review and network meta-analysis. World Neurosurg. 2019;132:334–42. https://doi.org/10.1016/j.wneu.2019.08.202. Epub 2019 Sep 5.
35. Wessell A, Mushlin H, Fleming C, Lewis E, Sansur C. Thoracic discectomy through a unilateral transpedicular or costotransversectomy approach with intraoperative ultrasound guidance. Open Neurosurg. 2019;17(3):332–7. https://doi.org/10.1093/ons/opy348.

The Thoracoscopic Approach in Spinal Cord Disease

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1 Introduction

Video-assisted thoracic surgery (VATS) as a minimally invasive procedure has recently been growing in popularity as an alternative option to open thoracotomy for the treatment of several spinal conditions. The first report of a thoracoscopic approach was published by Jacobaeus in 1910, where it was used to diagnose and lyse tuberculosis lung adhesion [1–3]. With the discovery of streptomycin in 1945 for tuberculosis treatment, there was a decrease in the clinical application of thoracoscopy for such a condition [4]. In 1993, Mack published the first study on endoscopic approaches to spinal disorders, reporting ten patients with various thoracic spinal pathologies that were effectively operated on endoscopically [5]. Thereafter, VATS has been extensively used in spinal deformities such as scoliosis. The use of VATS in spine surgery includes the treatment of thoracic prolapsed disk diseases [6, 7], vertebral osteomyelitis [8–11], fracture management [12], vertebral interbody fusion [6], tissue biopsy [8–13], anterior spinal release and fusion without [4–22] or with [23–25] instrumentation (VAT-I) for spinal deformity correction. As the knowledge and the comfort of using such techniques have expanded, the indications have extended to corpectomy for tumor resections [26–32].

The absolute contraindication for VATS includes a patient's inability to tolerate single-lung ventilation; a value for forced expiratory volume in 1 s (FEV1) that is less than 50% [13]; dense pleural adhesion; respiratory insufficiency; empyema; and failed prior thoracotomy surgery.

Herein, we report on an overview of the technical aspects and clinical applications of VATS.

2 Methods

2.1 Surgical Anatomy and Technique

Most VATS approaches are from the right side for pathologies involving the middle and upper thoracic spine because there is a greater working spinal surface area lateral to the azygos vein than that lateral to the aorta [26]. Below T-9, a left-sided approach is made possible because the aorta moves away from the left posterolateral aspect of the spine to an anterior position as it passes through the diaphragm.

Following the induction of anesthesia with the placement of a double-lumen intubation tube, the patient is turned to the left lateral position, with the right side of the chest pointing upward. This position is maintained via the flexion of the downside hip and knee and is secured by using surgical tape. An axillary roll is positioned to prevent putting pressure on the dependent shoulder [33].

Following the deflation of the lung and the introduction of the thoracoscopy instruments, the involved vertebra is identified under fluoroscopy and the segmental artery also identified.

Regarding the placement of thoracoscopic instruments, several strategies are possible:

- In the anterolateral approach, the surgeon stands on the patient's ventral side, where more spinal levels can be approached between the azygos vein and the vertebrae from each portal.
- In the combined anterolateral and posterolateral approach, the portals are first placed along the anterior axillary line for spinal release and fusion [16, 20, 22] and then replaced

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posterolaterally for spinal instrumentation [23]. A disadvantage of this approach is the potential danger of working with instruments from an anterior to a posterior direction into the spinal canal.

- In the posterolateral approach, all access portals are placed between the mid and posterior axillary lines [24, 25]. The surgeon stands to face the back of the patient; both discectomy with fusion and discectomy with instrumentation can be performed via these posterolateral portals without needing additional anterolateral portals. Comparing it with conventional posterior instrumentation and fusion, an all-posterolateral approach carries increased technical difficulties in performing a thorough discectomy and comes with a lack of protection to the anterior vascular structure during the anterior longitudinal ligament release.

2.2 Discectomy

The successful correction of the intervertebral fusion and deformity requires a thorough discectomy [13] and end-plate clearance. The parietal pleura on the spinal column is longitudinally incised along the peak of the disk where it is most avascular. Intervertebral segmental vessels should be cauterized slowly, layer by layer; having a clear surgical field with minimal bleeding facilitates the thoracoscopic procedure. Once the intervertebral disk has been exposed beneath the pleura, the annulus is incised by a long-handled no. 15 scalpel blade. A pituitary rongeur is used to remove the annulus disk complex. The cartilaginous end plates are separated from the subchondral vertebral bone by using a sharp, cutting Cobb elevator, and the final clearance of the discal space is carried out by a combination of straight and angled pituitary rongeurs and cup curettes. The resection of the proximal 2 cm of rib head (except when the level is below T11) is required to achieve a thorough clearance at the posterolateral corner of the disk [6]. The foraminal ligaments are then cut to expose the superior edge of the pedicle. The superior part of the pedicle is resected to expose the spinal canal.

2.3 Spinal Fusion

After the discectomies, the segments of the rib under the skin incisions are removed via the open-rib harvesting technique and by using a rib cutter. This provides an autogenous rib graft for intervertebral body fusion and a possible thoracoplasty effect. Alternatively, the rib graft can be harvested via a closed endoscopic technique [34], or iliac crest graft could be used [17].

2.4 Vertebral Bone Screw Insertion

The vertebral screw entry point is located just anterior and inferior to the corresponding rib head. The instrument directed into the spine should be placed perpendicular to the imaginary plane between the X-ray tube and the image intensifier on either end of the C-arm. This should prevent instruments from penetrating the iatrogenic spinal canal [34–36]. The final screw position should be in the middle of the vertebral body and parallel to its vertebral end plates. Bicortical screw purchase is preferable. It is critical to ensure that each screw head is placed against the near cortex of each vertebra.

3 Results

Rosenthal and Dickman reported the results of 55 consecutive patients undergoing VATS discectomy [7]. Of the radiculopathic patients, 79% completely recovered. When comparing the VATS results to their patients treated via costotransversectomy or thoracotomy, they found that VATS was associated with 50% less blood loss and 1 hour less operative time. Anand and Regan [6] reported their results of 100 consecutive cases of thoracic disease treated via VATS. The overall subjective patient satisfactory rate was 84%, and the objective's long-term clinical success was obtained in 70% of patients at 2-year follow-ups.

Dickman et al. reported a comparable outcome in fracture management between a VATS- vertebrectomy group and an open-thoracotomy group [26]. Many authors have described the use of VATS in the management of primary and metastatic spinal tumors [9–32]. In a series of 41 patients with metastatic tumors decompressed via VATS, there were two (5%) perioperative deaths, and both were related to respiratory complications [29]. The use of VATS to obtain tissue confirmation for a faster and more reliable diagnosis of thoracic spinal tuberculosis has been reported [8]. The endoscopic approach to the treatment of thoracic vertebral osteomyelitis may reduce the surgical morbidity that is otherwise not tolerated in these sick patients [9–29]. Vertebral tuberculosis constitutes 50% of all cases, 44% of which occur in the dorsal spine [37]. Thoracoscopic surgery obtains radical debridement, leading to a direct visualization of the dural sac and kyphotic deformity correction with an interbody cage and anterior screwing [9]. Huang et al. showed the reliability and effectiveness of thoracoscopy in the management of ten patients with dorsal tuberculous spondylitis [38]. There was no recurrence of infection at the 24-month follow-up examinations.

4 Discussion and Conclusion

Although VATS can be performed in many spinal conditions, it is most beneficial in the treatment of scoliotic deformity, which requires taking a multilevel approach, from the upper to the lower thoracic spine. On the contrary, other conditions where the pathology is localized to one or two segmental levels, such as in thoracic disk prolapse or infection, can be managed with a mini open thoracotomy, as an alternative to the traditional open procedure.

As the knowledge and the comfort of using such techniques have expanded, the indications have extended to vertebrectomy for tumor resections [26, 27]. The improved exposure, reduction in operative time and blood loss, and improved recovery times were notable. As a matter of fact, a thoracoscopic-assisted anterior approach could reduce the duration and the morbidity of a vertebrectomy without affecting oncological management.

The complications associated with thoracoscopic procedures are similar to those associated with open thoracotomy, with variations in the incidence. In addition, anesthesia, patient positioning, port placement and access, and instrument manipulation also contribute to other specific complications [39].

The complications related to anesthesia are mainly from single-lung ventilation: incorrect placement, inaccurate tubing size, and the over- or underinflation of the bronchial cuff, which can cause air leaks that allow air into the operated-on lung [40]. Some patients may also have pulmonary blebs, which spontaneously burst and cause pneumothoraxes, resulting in hypercarbia, hemodynamic instability, and even venous gas embolisms. Ventilation–perfusion mismatch resulting in arterial desaturation may occur secondary to both lungs' being perfused while one lung is ventilated [40].

Regarding the complications related to endoscope placement, injury to the lung parenchyma and other vessels may occur [10, 40] because the initial port is placed blindly. Injury to large intrathoracic vessels may also occur with instrumentation. Endoscopic instruments and retractors placed in the chest cavity can cause injury to the lung parenchyma and to large vessels in the chest cavity, leading to air leaks postoperatively and excessive blood loss intraoperatively [41].

In conclusion, according to the data from the literature, video-assisted thoracoscopic surgery (VATS), in experienced hands, has advantages over open thoracotomy, such as less postoperative pain and morbidity, earlier mobilization leading to shorter hospital stays and lower costs, and smaller scars, with minimal peri- and postoperative complications. On the other hand, the approach comes with a learning curve, and experience in endoscopic surgery is mandatory to safely perform the approach.

References

1. Jacobaeus HC. Endopleural operations by means of a thoracoscope. Beitr Klin Tuberk. 1915;35:1.
2. Jacobaeus HC. Possibility of the use of the crytoscope for investigation of serious cavities. Munch Med Wochenchr. 1910;57:2090–2.
3. Jacobaeus HC. The practical importance of thoracoscopy in surgery of the chest. Surg Gynecol Obstet. 1922;34:289–96.
4. King AG, Mills TE, Leo WA Jr, Chutkan NG, Revels TS. Video-assisted thoracoscopic surgery in the prone position. Spine. 2000;25:2403–6.
5. Mack MJ, Regan JJ, Bobechko WP, Acuff TE. Application of thoracoscopy for disease of the spine. Ann Thorac Surg. 1993;56:736–8.
6. Anand N, Regan JJ. Video-assisted thoracoscopic surgery for thoracic disc disease: classification and outcome study of 100 consecutive cases with a 2-year minimum follow-up period. Spine. 2002;27:871–9.
7. Rosenthal D, Dickman CA. Thoracoscopic microsurgical excision of herniated thoracic discs. J Neurosurg. 1998;89:224–35.
8. Dusmet M, Halkic N, Corpataux J. Video-assisted thoracic surgery diagnosis of thoracic spinal tuberculosis. Chest. 1999;116:1471–2.
9. Huang TJ, Hsu R, Chen SH, Liu HP. Video-assisted thoracoscopic surgery in managing Tuberculous spondylitis. Clin Orthop Relat Res. 2000;379:143–53.
10. McAfee PC, Regan JJ, Zdeblick T, Zukerman J, Picetti GD, Heim S, et al. The incidence of complications in endoscopic anterior thoracolumbar spinal reconstructive surgery. A prospective multicenter study comprising the first 100 consecutive cases. Spine. 1995;20:1624–32.
11. Muckley T, Schutz T, Schmidt M, Potulski M, Buhren V, Beisse R. The role of thoracoscopic spinal surgery in the management of pyogenic vertebral osteomyelitis. Spine. 2004;29:227–33.
12. Huang TJ, Hsu RW, Liu HP, Hsu KY, Liao YS, Shih HN, et al. Video-assisted thoracoscopic treatment of spinal lesions in the thoracolumbar junction. Surg Endosc. 1997;11:1189–93.
13. Kuklo TR, Lenke LG. Thoracoscopic spine surgery: current indications and techniques. Orthop Nurs. 2000;19:15–22.
14. Al-Sayyad M, Crawford A, Wolf R. Early experiences with video-assisted thoracoscopic surgery: our first 70 cases. Spine. 2004;29:1945–51.
15. Al-Sayyad M, Crawford A, Wolf R. Video-assisted thoracoscopic surgery. The Cincinnati experience. CORR. 2005;434:61–70.
16. Crawford AH, Wall EJ, Wolf R. Video-assisted thoracoscopy. Orthop Clin North Am. 1999;30:367–85.
17. Lenke LG. Anterior endoscopic discectomy and fusion for adolescent idiopathic scoliosis. Spine. 2003;28:36–43.
18. Newton P, Shae KG, Granlund KF. Defining the pediatric spinal thoracoscopy learning curve: sixty-five consecutive cases. Spine. 2000;25:1028–35.
19. Newton PO, Marks M, Faro F, Betz R, Clements D, Haher T, et al. Use of video-assisted thoracoscopic surgery to reduce perioperative morbidity in scoliosis surgery. Spine. 2003;28:249–54.
20. Newton P, White K, Faro F, Gaynor T. The success of thoracoscopic anterior fusion in a consecutive series of 112 pediatric spinal deformity cases. Spine. 2005;30:392–8.
21. Sucato D, Elerson E. A comparison between the prone and lateral position for performing a thoracoscopic anterior release and fusion for pediatric spinal deformity. Spine. 2003;28:2176–80.
22. Waisman M, Saute M. Thoracoscopic spine release before posterior instrumentation in scoliosis. Clin Orthop. 1997;336:130–6.
23. Newton P, Parent S, Marks M, Pawelek J. Prospective evaluation of 50 consecutive scoliosis patient surgically treated with thoracoscopic anterior instrumentation. Spine. 2005;30:100–9.
24. Picetti G, Pang D. Thoracoscopic techniques for the treatment of scoliosis. Childs Nerv Syst. 2004;20:802–10.

25. Wong HK, Hee HT, Yu Z, Wong D. Results of thoracoscopic instrumented fusion versus conventional posterior instrumented fusion in adolescent idiopathic scoliosis undergoing selective thoracic fusion. Spine. 2004;29:2031–8.
26. Dickman CA, Rosenthal D, Karahalios DG, Paramore CG, Mican CA, Apostolides PJ, et al. Thoracic vertebrectomy and reconstruction using a microsurgical thoracoscopic approach. Neurosurgery. 1996;38(2):279–93.
27. Verheyden AP, Hoelzl A, Lill H, Katscher S, Glasmachera S, Josten C. The endoscopically assisted simultaneous posteroanterior reconstruction of the thoracolumbar spine in prone position. Spine J. 2004;4(5):540–9.
28. Citow JS, MacDonald RL, Ferguson MK. Combined laminectomy and thoracoscopic resection of a dumbbell neurofibroma. Technical case report. Neurosurgery. 1999;45:1263–6.
29. Huang TJ, Hsu RW, Sum CW, Liu HP. Complications in thoracoscopic spinal surgery. A study of 90 consecutive patients. Surg Endosc. 1999;13:346–50.
30. Konno S, Yabuki S, Kinoshita T, Kikuchi S. Combined laminectomy and thoracoscopic resection of dumbbell-type thoracic cord tumor. Spine. 2001;26:130–4.
31. McLain R, Lieberman H. Controversy. Endoscopic approaches to metastatic thoracic disease. Spine. 2000;25:1855–8.
32. Rosenthal D. Endoscopic internal fixation of the thoracic spine. Eur Spine J. 2000;9:8–16.
33. Visocchi M, Masferrer R, Sonntag VKH, Dickman CA. Thoracoscopic approaches to the thoracic spine. Acta Neurochir. 1998;140:737–44.
34. Mehlman CT, Crawford AH, Wolf RK. Video-assisted thoracoscopic surgery (VATS). Endoscopic thoracoplasty technique. Spine. 1997;22:2178–82.
35. Liu GKP, Kit WH. Video assisted thoracoscopic surgery for spinal conditions. Neurology. 2005;53(4):489–98.
36. Kapoor SK, Agarwal PN, Jain BR, Kumar R. Video assisted thoracoscopic decompression of tubercular spondylitis: clinical evaluation. Spine. 2005;30:E605–10.
37. Sasani M, Ozer AF, Oktenoglu T, Kaner T, Aydin S, Canbulat N, Carilli S, Sarioglu AC. Thoracoscopic surgical approaches for treating various thoracic spinal region diseases. Turk Neurosurg. 2010;20(3):373–81.
38. Arlet V. Anterior thoracoscopic spine release in deformity surgery: a meta-analysis and review. Eur Spine J. 2000;9:17–23.
39. Perez-Cruet MJ, Fessler RG, Perin NI. Review: complications of minimally invasive spinal surgery. Neurosurgery. 2002;51(5 Suppl):26–36.
40. Levin R, Matusz D, Hasharoni A, Scharf C, Lonner B, Errico T. Mini-open thoracoscopically assisted thoracotomy versus video-assisted thoracoscopic surgery for anterior release in thoracic scoliosis and kyphosis: a comparison of operative and radiographic results. Spine J. 2005;5:632–8.
41. Roush T, Crawford AH, Berlin RE, Wolf RK. Tension pneumothorax as a complication of video- assisted thoracoscopic surgery for anterior correction of idiopathic scoliosis in an adolescent female. Spine. 2001;26:448–50.

Cirq Robotic Assistance for Thoracolumbar Pedicle Screw Placement: Overcoming the Disadvantages of Minimally Invasive Spine Surgery

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1 Introduction

Various minimally invasive spine surgery (MISS) techniques have been developed with the goal of reducing approach-related soft-tissue trauma and its associated complications. With the evolution of modern MISS instrumentations, the possibilities for reduction, distraction, compression, and reclination on multiple levels have substantially increased and MISS have become a therapeutic option even for complex spinal pathologies, trauma, and deformities. However, there is still controversy over some of the possible disadvantages of MISS techniques, such as their longer operating times, higher intraoperative radiation, a challenging learning curve [1, 2], and a potentially higher risk for pedicle screw misplacements [3]. A solution to these disadvantages could be the implementation of new technologies, such as computer-assisted navigation (CAN) and surgical robotics. We compare standard fluoroscopy MISS technique for pedicle screw fixation with our experience with time per screw and X-ray exposure for pedicle screw placement by using Brainlab Cirq passive robotic arm assistance coupled with Brainlab Curve navigation system.

2 Materials and Methods

This is a prospective study that includes 109 screws in 24 patients who underwent minimally invasive robot-assisted pedicle fixation utilizing the Brainlab Cirq arm coupled with the Brainlab Curve navigation system (Group I). The study included all consecutively admitted patients who planned to undergo a stabilization procedure that involves pedicle screw placement between February 2021 and December 2021. The control group includes 108 screws placed with a conventional minimally invasive technique and fluoroscopic guidance in 20 consecutive patients, according to retrospectively collected data (Group II).

The duration of surgery, the time to place one screw, the X-ray exposition, and the pedicle screw accuracy for each patient were recorded and reviewed. The time to place one screw was measured intraoperatively from the moment that Cirq was engaged until the screw was securely seated. The radiation exposure time for each patient was measured and recorded automatically by the C-arm. Pedicle screw placement accuracy was assessed by the Gertzbein-Robbins's method of measuring screw placement deviation, with grades from A to E. Grade A referred to no breach/deviation, grade B to breach <2 mm, grade C to breach <4 mm, grade D to breach <6 mm, and grade E to breach >6 mm [4]. The breach direction (cranial, lateral, caudal, or medial) was also recorded. A rating of grade A or B was considered clinically acceptable.

2.1 Robot-Assisted Technique

The equipment used consisted of an intraoperative Siemens Arcadis Orbic 3D C-arm in conjunction with Curve Navigation and a Cirq Alignment spine (Brainlab AG, Munich, Germany) and with a cannulated transpedicular screw system (Armada, Nuvaisive). Under general anesthesia, the patient is placed prone on a radiolucent table. Cirq is directly mounted to the operating room (OR) table rail. The surgical field and the Cirq arm are prepared and draped. A reference array is fixated on a spinous process, using a minimal skin incision usually caudal to the operative field (Fig. 1).

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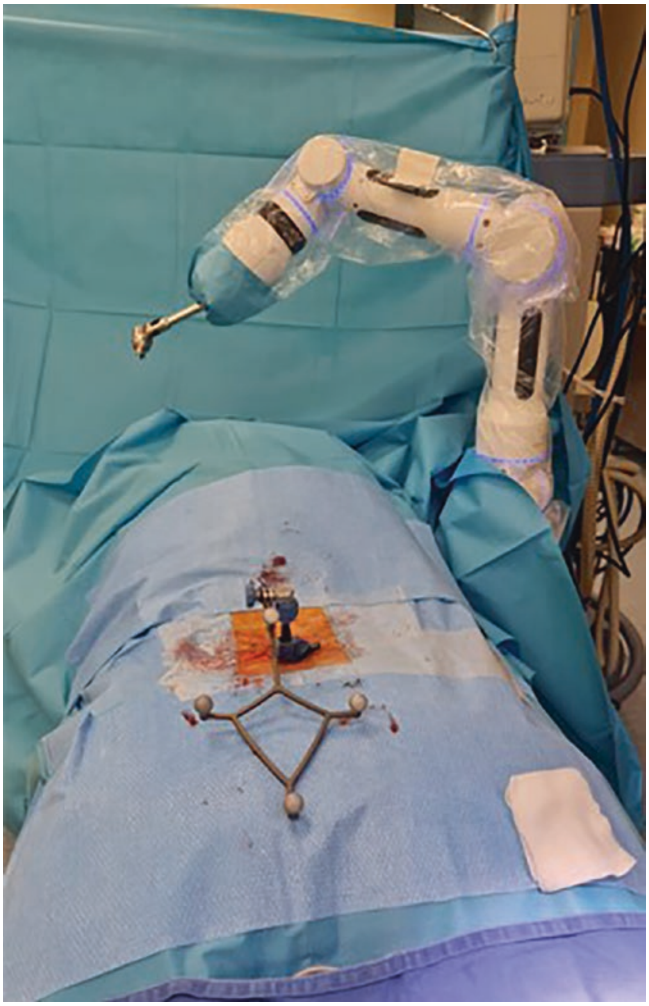

Fig. 1 A reference array is fixated on a spinous process, usually caudal to the operative field; Cirq is aligned and locked in at the desired screw trajectory

A 3D X-ray scan is completed, and the images are automatically transferred to the Curve Navigation system. Navigation tools are then registered. In cases of a minimally invasive spinal surgery (MISS) procedure, a navigated probe is used to plan the skin incisions. Cirq is then engaged, aligned, and locked in at the desired screw trajectory. A 3.2 mm drill is used through the cannula on the robotic arm to create a pilot hole, after which a K-wire is inserted. The procedure is repeated for each pedicle. The position of the K-wires is confirmed with anterior–posterior (AP) and lateral fluoroscopy. Once good positioning has been confirmed, canulated screw insertion is performed along the K-wire by using the standard MISS technique. The position of the screws is reconfirmed either with AP/lateral fluoroscopy or with a new 3D scan.

2.2 Fluoroscopy-Guided Technique

In the fluoroscopy-guided group (Group II), the pedicles were tapped, and the screws were inserted by using anatomical landmarks and AP/lateral fluoroscopic guidance.

3 Statistical Analyses

Statistical analyses were performed by using IBM SPSS Statistics version 22.0. A Mann–Whitney U test was used to compare the differences in operation length, radiation exposure, and the accuracy of screw insertion between Group I and Group II.

4 Results

In total, 217 screws were placed into 44 patients. The treated levels ranged from T10 to S1. The average patient age at the time of surgery was 53.7 years (range 13–78 years); 20 were male and 24 female. The pathology was trauma in 18 cases, degeneration in 14, cancer in eight, and infection in four. In the robot-assisted group (Group I; $n = 24$; 109 screws), 104 screw placements were grade A (95.4%); five were grade B (4.6%)—two lateral, one medial and two cranial; and zero were grades C or D. No revision surgeries were needed, the postoperative period for all patients was uneventful, and all patients were verticalized, mobilized, and discharged according to the standard protocol of the department. In the conventional group (Group II, $n = 20$; 108 screws), 96 screw placements were grade A (88.89%); ten were grade B (9.26%)—seven lateral and three medial; one was grade C (0.93%)—lateral; and one was grade D (0.93%)—lateral. When comparing the two groups by using a nonparametric Mann–Whitney U test, we found better accuracy with the use of the Cirq robotic arm, but no statistical significance was yielded with our current sample, $p = 0.3724$.

There was a significant difference in the operation time length between Group I—114.3 min [70.00–210.00]—and Group II—127.7 min [90.00–240.00], $p = 0.0183$)—and in the time to place one screw between Group I—4.04 min [2.35–6.30]—and Group II—8.4 min [6.20–10.5], $p = 0.0001$. There was no significant difference in the radiation exposure time between Group I—95.00 s [78.00–159.00]—and Group II—108.0 s [53.00–121.00], $p = 0.5482$). However, the radiation exposure for the surgical team in Group I was very limited because they were outside of the operation room during the 3D-image acquisition.

5 Discussion

Minimally invasive percutaneous spinal fixation techniques have some clear advantages, such as a reduction in iatrogenic intraoperative tissue trauma, thus minimizing the blood loss and postoperative pain and shortening the period of hospital stay for patients. However, there is still a debate on some of the potential drawbacks of MISS techniques, such as their longer operating times, increased intraoperative radiation, and higher risk for screw malposition.

Regarding comparisons of MISS techniques with conventional open techniques to determine the shortest operative time, the literature is not conclusive about which is superior. Some studies have reported shorter operation times for open surgery groups, ranging from 90 to 250 min, compared to 135 to 375 min in the minimally invasive group [5]. However, other studies, such as those conducted by Schizas et al. and Brodano et al., have found no significant difference in the duration of surgery [6, 7]. Several studies have attempted to compare the total operative time and time required per screw insertion when using robot-assisted versus freehand techniques. Specific studies applicable to minimally invasive spinal surgery (MISS) have compared percutaneous pedicle screw placement using a robot versus following fluoroscopy-based techniques, but they unfortunately did not report operative time [8, 9]. A cadaveric study conducted by Vaccaro et al. demonstrated that the overall surgical time was similar between MISS pedicle screw placement using conventional fluoroscopy and pedicle screw placement using robot assistance [10]. Our experience, however, suggests that robotic assistance could significantly reduce the operative time and the time to place one screw for cases featuring MISS.

Robotic surgery offers a significant advantage over traditional techniques in terms of radiation exposure reduction, particularly for surgeons. Spinal surgery is associated with higher ionizing radiation exposure for all operating room staff compared with other subspecialties, a concern compounded by the increasing use of minimally invasive techniques in recent years. However, computer-assisted navigation and robotic spinal surgery have the potential to significantly reduce X-ray exposure for both patients and surgeons without significantly increasing operative time [3, 11]. Fomekong et al. proved that the cumulative radiation exposure remained below measurable levels with the use of robotic systems [12]. Fan et al. reported that the average fluoroscopy time for screw placement with robotic assistance was 4.02 ± 1.6 min vs. 8.89 ± 3.1 with the free hand technique [13]. In our study, there was also no significant difference in radiation exposure time for the patient between the robot-assisted group and the fluoroscopy-guided group. The radiation exposure time for the patients in the robotic group (Group I) was mostly due to the 3D fluoroscopic preregistration. Also, the radiation exposure for the surgical team in this group was very limited because they were outside of the operation room during the image acquisition.

One of the most widely discussed issues in the literature concerning spinal robot-assisted surgery pertains to screw accuracy because even a slight deviation from the optimal position could result in injuring the neural or vascular structures or reducing the stability of the instrumentation [14]. With conventional fluoroscopy-guided and freehand techniques, the accuracy of pedicle screw placement relies heavily on the surgeon's experience and their identification of anatomical landmarks. Malposition rates in conventional screw placement series can be significant: In studies analyzing postoperative computerized tomography (CT) scans, these rates could reach up to 15.7%, although the frequency of symptomatic cases is still relatively low [15]. In minimally invasive spine surgery, the rate of this complication could be even higher because of the lack of visible anatomical landmarks. The computer-assisted navigation systems and emerging robotic platforms have the potential to reduce screw misplacement rates, including in minimally invasive procedures. Several studies comparatively examining the safety and accuracy of robot-assisted pedicle screw placement with that of fluoroscopy-guided and freehand placement have been published in recent years. Lonjon et al. achieved 97.3% accuracy in the robotic group versus 92% in the conventional group [16]. Several other studies have also demonstrated over 95% accuracy with robot-assisted pedicle screw placement utilizing different platforms [13, 17]. In this study, we found all the screws placed with the robot-assisted technique to be clinically acceptable (Gertzbein-Robbins's grades A and B). Despite the limitation of the small series, we can conclude that pedicle screw placement with the Cirq is safe and at least as accurate as fluoroscopic guidance. Given that these results were achieved during the first cases with the technique, we could conclude that two important additional advantages of Cirq and other robotic platforms are that screw accuracy is less dependent on the surgeon's level of experience and that good results could be achieved early on. This would largely diminish the challenging learning curve of MISS for a less-experienced spinal surgeon.

6 Conclusion

Our initial experience suggests that Cirq robotic arm–assisted pedicle screw placement is feasible and is at least as accurate and safe as fluoroscopic guidance. Good results and proficiency with the technique were achieved even in the initial cases. We believe that the CAN systems and emerging robotic platforms have the potential to diminish the main disadvantages of MISS techniques—longer operation times and X-ray exposure, at least for the surgical team.

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Ethical Approval All procedures performed in studies involving human participants were carried out in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the local institutional ethics committee of University Hospital "Pirogov."

References

1. Burneikiene S, Roeca C, Nelson L, Mason A, Villavicencio A. Minimally invasive versus open transforaminal lumbar interbody fusion. Surg Neurol Int. 2010;1(1):12. https://doi.org/10.4103/2152-7806.63905.
2. Walker CT, Xu DS, Godzik J, Turner JD, Uribe JS, Smith WD. Minimally invasive surgery for thoracolumbar spinal trauma. Ann Transl Med. 2018;6(6):102. https://doi.org/10.21037/atm.2018.02.10.
3. Phan K, Rao PJ, Kam AC, Mobbs RJ. Minimally invasive versus open transforaminal lumbar interbody fusion for treatment of degenerative lumbar disease: systematic review and meta-analysis. Eur Spine J. 2015;24(5):1017–30. https://doi.org/10.1007/s00586-015-3903-4.
4. Gertzbein SD, Robbins SE. Accuracy of pedicular screw placement in vivo. Spine. 1990;15(1):11–4. https://doi.org/10.1097/00007632-199001000-00004.
5. Vazan M, Gempt J, Meyer B, Buchmann N, Ryang Y-M. Minimally invasive transforaminal lumbar interbody fusion versus open transforaminal lumbar interbody fusion: a technical description and review of the literature. Acta Neurochir. 2017;159(6):1137–46. https://doi.org/10.1007/s00701-017-3078-3.
6. Brodano GB, Martikos K, Lolli F, et al. Transforaminal lumbar interbody fusion in degenerative disk disease and spondylolisthesis grade I. J Spinal Disord Tech. 2015;28(10):E559–64. https://doi.org/10.1097/BSD.0000000000000034.
7. Schizas C, Tzinieris N, Tsiridis E, Kosmopoulos V. Minimally invasive versus open transforaminal lumbar interbody fusion: evaluating initial experience. Int Orthop. 2009;33(6):1683–8. https://doi.org/10.1007/s00264-008-0687-8.
8. Fayed I, Tai A, Triano M, et al. Robot-assisted percutaneous pedicle screw placement: evaluation of accuracy of the first 100 screws and comparison with cohort of fluoroscopy-guided screws. World Neurosurg. 2020;143:e492–502.
9. Yang JS, He B, Tian F, et al. Accuracy of robot-assisted percutaneous pedicle screw placement for treatment of lumbar spondylolisthesis: a comparative cohort study. Med Sci Monit. 2019;25:2479–87.
10. Vaccaro AR, Harris JA, Hussain MM, et al. Assessment of surgical procedural time, pedicle screw accuracy, and clinician radiation exposure of a novel robotic navigation system compared with conventional open and percutaneous freehand techniques: a cadaveric investigation. Glob Spine J. 2020;10(7):814–25.
11. Kim CW, Lee Y-P, Taylor W, Oygar A, Kim WK. Use of navigation-assisted fluoroscopy to decrease radiation exposure during minimally invasive spine surgery. Spine J. 2008;8(4):584–90. https://doi.org/10.1016/j.spinee.2006.12.012.
12. Fomekong E, Safi SE, Raftopoulos C. Spine navigation based on 3-dimensional robotic fluoroscopy for accurate percutaneous pedicle screw placement: a prospective study of 66 consecutive cases. World Neurosurg. 2017;108:76–83. https://doi.org/10.1016/j.wneu.2017.08.149.
13. Fan Y, Du J, Zhang J, Liu S, Xue X, Huang Y, Zhang J, Hao D. Comparison of accuracy of pedicle screw insertion among 4 guided technologies in spine surgery. Med Sci Monit. 2017;23:5960–8. https://doi.org/10.12659/MSM.905713.
14. Hicks JM, Singla A, Shen FH, Arlet V. Complications of pedicle screw fixation in scoliosis surgery. Spine. 2010;35(11):E465–70. https://doi.org/10.1097/BRS.0b013e3181d1021a.
15. Gautschi OP, Schatlo B, Schaller K, Tessitore E. Clinically relevant complications related to pedicle screw placement in thoracolumbar surgery and their management: a literature review of 35,630 pedicle screws. Neurosurgical Focus. 2011;31(4):E8. https://doi.org/10.3171/2011.7.FOCUS11168.
16. Lonjon N, Chan-Seng E, Costalat V, Bonnafoux B, Vassal M, Boetto J. Robot-assisted spine surgery: feasibility study through a prospective case-matched analysis. Eur Spine J. 2016;25(3):947–55. https://doi.org/10.1007/s00586-015-3758-8.

Li H-M, Zhang R-J, Shen C-L. Accuracy of pedicle screw placement and clinical outcomes of robot-assisted technique versus conventional freehand technique in spine surgery from nine randomized controlled trials. Spine. 2020;45(2):E111–9. https://doi.org/10.1097/BRS.0000000000003193.

Further Reading

Theocharopoulos N, Perisinakis K, Damilakis J, Papadokostakis G, Hadjipavlou A, Gourtsoyiannis N. Occupational exposure from common fluoroscopic projections used in orthopaedic surgery. J Bone Jt Surg Am. 2003;85(9):1698–703. https://doi.org/10.2106/00004623-200309000-00007.

Part V

Lumbar

Toward the End of the Funnel: The Ventriculus Terminalis—The State of Art of an Ancient Entity with a Recent History

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1 Introduction

The ventriculus terminalis, also called the fifth ventricle, is a small cavity lined by normal ependymal tissue that is in the conus medullaris below the emergence of the last two coccygeal nerves with extension down into the upper end of the filum terminale [1].

This cavity was first described in 1859 by Stilling as a dilation of the central spinal canal at the bottom and in communication with the subarachnoid space [2].

The name *ventriculus terminalis* (VT) was given by Krause, who, contrary to Stilling, described this entity as a true cavity that did not open into the subarachnoid space [3].

Normally, the VT presents during fetal development, appearing between the 43rd and 48th day of embryogenesis, and it typically regresses after birth [4]. In this situation, it is supposed to communicate with the central canal of the inferior portion of the spinal cord containing cerebrospinal fluid (CSF). Nevertheless, cases of asymptomatic dilated VT during the first 5 years of life have been reported in the literature as a normal developmental phenomenon without pathological significance [5].

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The pathogenesis of this lesion's persistence into adulthood remains unknown.

Various theories have been adopted to explain the etiopathogenesis of the persistence of a symptomatic VT into adulthood, proposing vascular disturbance, inflammation, and the compression or ischemic necrosis of the spinal cord as concurrent mechanisms [6].

The symptoms, when present, may vary from aspecific signs to sphincter dysfunctions and focal neurological deficits. Although different cases have been described in the literature, the treatment is still an object of debate. Conservative management, marsupialization, or the placement of a T drain have been described [7]. Currently, to the best of our knowledge, only 57 cases have been reported in the literature [8].

2 Embryological Basis

The VT is a small cavity of the conus medullaris that forms during fetal life. The embryonic development of the spinal cord is characterized by three phases: neurulation, canalization, and regressive differentiation. The neurulation phase is a dynamic process that takes place early during embryogenesis, between weeks 3 and 4 of human gestation [9] with neural tube formation. During the subsequent phase (canalization), the caudal end of the neural tube and the notochord combine to become an aggregate of undifferentiated cells. This caudal mass, after cytoplasmic vacuolization, is replaced by a wide canal lined by ependyma. Finally, during the last phase, retrogressive differentiation, the upper part of the ependyma-lined canal dilates and becomes the ventriculus terminalis within the conus terminalis [10]. According to Kernohan's study, the VT appears on approximately the 45th day (range: between the 43rd and 48th day) after conception [1]. During the process of regressive differentiation, a major

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portion of the distal cord involutes to form a glioependymal strand, called filum terminale [11].

The dilated VT can be observed at any age. In the literature, cases of a persistent dilated VT during the first 5 years of life have been described without pathological correlation [5].

3 Clinical Pathophysiology

Among adults, the isolated dilatation of the VT is a rare phenomenon, documented in only 57 cases, as reported in the updated literature [8]. Although several theories exist on the mechanism that determines the persistence of a symptomatic VT into adult life, it is still unknown. Sigal et al. proposed that the enlargement of VT could be secondary to the isolation of VT from the central canal, due to an absence of communication between the ependymal canal of the upper spinal cord and the central canal of the lower spinal cord, which could occur as a result of ischemia or trauma [10].

Clinical presentation can be various, including nonspecific symptoms, such as lower-back pain or a focal neurological deficit, with the progressive loss of strength, gait disturbances, sensory disturbances, and sphincter dysfunctions. Clinical symptoms are usually progressively insidious; however, sudden onset has been reported with acute cauda syndrome [12].

4 Diagnosis

Magnetic resonance (MR) is the investigation of choice for the diagnosis of these lesions [13]. In these cases, MR usually shows a well-circumscribed ovoid cystic lesion, without a septated structure, localized at the level of the cauda. The cystic fluid has a similar signal to that of CSF in all sequences, and no enhancement is observed after gadolinium-contrast injection [5, 13]. Differential diagnoses include syringomyelia, hydromyelia, intramedullary cysts, or tumors such as ependymoma, astrocytoma, oligodendroglioma, and hemangioblastoma.

In the case of hydromyelia, the dilation is generally localized above the filum terminale; in terminal syringomyelia, there is no ependymal lining; and tumors demonstrate impregnation after contrast administration [11]. MR is also useful in detecting other cranial or spinal conditions, such as spinal dysraphisms, Chiari malformation, or tethered cord syndrome, which are rare comorbidities in VT patients.

5 Therapeutic Strategies

Given the rarity of the disease, the standard management of adult VT is controversial and has yet to be defined. Two types of approaches are possible: conservative and surgical. The choice between these approaches should be based on clinical manifestations.

In 2008, Demoura et al. proposed a classification based on clinical symptoms that splits the affected patients into three groups: type I patients with nonspecific symptoms like lower-back pain or radicular pain, type II patients with focal neurological deficits without sphincter dysfunction, and type III patients reporting sphincter dysfunction.

According to this, the patients with type I lesions should be treated conservatively, while for the patients with type II or type III VTs, the surgical option seems to be the treatment of choice, achieving an improvement in the clinical outcome [14].

The classification by Demoura has been subsequently revised by Ganau et al., introducing a further subdivision of the type I into two subgroups: type Ia features clinical symptoms stable at follow-up and type Ib features progressive worsening. The latter group would be a candidate for surgical treatment, while for the type Ia, a conservative policy can be adopted, with clinical and radiological follow-up [15].

The surgical treatment consists of laminectomy, midline myelotomy, cystic drainage, and/or fenestration (Fig. 1). Shunt placement, although it is described in the literature [16], is not recommended, because of the lack of any evident advantage in clinical outcomes compared to those of other surgical techniques and to the possible complications of implanting a prosthetic device.

In fact, no significative differences in outcomes have been observed when comparing the different surgical strategies [14]. Surgical treatment has been associated with good outcomes for motor and sphincter disorders, while controversial effectiveness has been observed in pain relief [15].

One alternative procedure described in recent years is the percutaneous aspiration of CSF under MR guidance. This is a recently introduced technique that as shown good results, but only three patients have been treated so far [17].

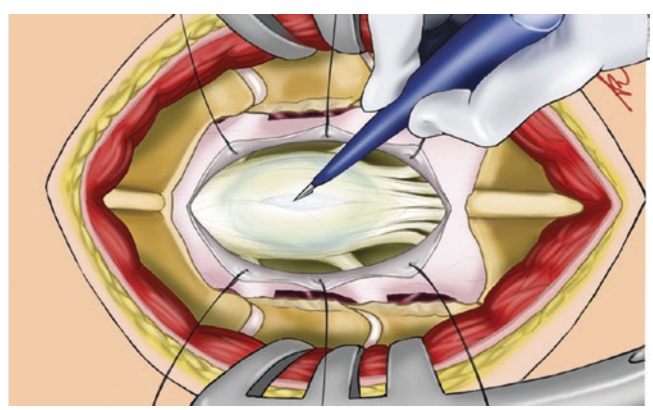

Fig. 1 Artistic representation of the surgical treatment of a dilated ventriculus terminalis: laminectomy/laminotomy, midline myelotomy, and cystic fenestration

In the literature, complete or partial recovery has been observed even in patients with neurological and/or sphincteric disorders that were surgically treated [18]. However, an aspect that does not emerge from the literature is the clinical impact of the delay from the onset of symptoms to the surgical treatment.

6 Conclusion

An isolated VT in an adult is a rare pathology that falls into a differential diagnosis with neoplastic lesions of the conus. Although VT may be considered an incidental finding in pediatric age and can be a scarcely symptomatic finding in adulthood, results from our experience and those in the literature suggest treating VT whenever symptomatic or in progressively worsening cases. In the literature, the surgical treatment proved to lead to complete or near-complete recovery, even in the patients with neurological and sphincteric disorders. Direct decompression is the gold standard, and it consists of laminectomy or laminotomy, midline myelotomy, and cyst fenestration with or without positioning an intracystic catheter.

Conflicts of Interest The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

1. Kernohan JW. The ventriculus terminalis: its growth and development. J Comp Neurol. 1924;38:107–25.
2. Stilling B. Neue Untersuchungen uber den Bau des Ruchenmarks. Kassel: H Hotop; 1859.
3. Krause Krause W. Der ventriculus terminalis des Rückenmarks. Arch Mikrosk Anat. 1875;11(1):216–30.
4. Van Rillaer O, Vandaele P, Ramboer K. Malformative persistence of terminal ventricle. JBR. 2009;92(3):178–9.
5. Coleman LT, Zimmerman RA, Rorke LB. Ventriculus terminalis of the conus medullaris: MR findings in children. Am J Neuroradiol. 1995;16:1421–6.
6. Nassar SI, Correll JW, Housepian EM. Intramedullary cystic lesions of the conus medullaris. J Neurol Neurosurg Psychiatry. 1968. https://doi.org/10.1136/jnnp.31.2.106.
7. Borius PY, Cintas P, Lagarrigue J. Ventriculus terminalis dilatation in adults: a case report and review of the literature. Neurochirurgie. 2010;56(5):386–90.
8. Severino R, Severino P. Surgery or not? A case of ventriculus terminalis in an adult patient. J Spine Surg. 2017. https://doi.org/10.21037/jss.2017.06.22.
9. Raybaud C, Naidich TP, Melone DG. Developpement de Ia moelle et du rachis. In: Manelfe C, editor. lmagerie du rachis et de Ia moelle. Paris: Vigot; 1989. p. 93–7.
10. Sigal R, Denys A, Halimi P, Shapeero L, Doyon D, Boudghene F. Ventriculus terminalis of the conus medullaris: MR imaging in four patients with congenital dilatation. Am J Neuroradiol. 1991;12(4):733–7.
11. Ciappetta P, Durso PI, Luzzi S, et al. Cystic dilation of the ventriculus terminalis in adults. J Neurosurg Spine. 2008;8:92–9. https://doi.org/10.3171/SPI-08/01/092.
12. Brisman JL, Li M, Hamilton D, Mayberg MR, Newell DW. Cystic dilation of the conus ventriculus terminalis presenting as an acute cauda equina syndrome relieved by decompression and cyst drainage: case report. Neurosurgery. 2006. https://doi.org/10.1227/01.neu.0000197486.65781.88.
13. Dullerud R, Server A, Berg-Johnsen J. MR imaging of ventriculus terminalis of the conus medullaris. A report of two operated patients and a review of the literature. Acta Radiol. 2003. https://doi.org/10.1034/j.1600-0455.2003.00096.
14. de Moura Batista L, Acioly MA, Carvalho CH, Ebner FH, Tatagiba M. Cystic lesion of the ventriculus terminalis: proposal for a new clinical classification. J Neurosurg Spine. 2008. https://doi.org/10.3171/SPI/2008/8/2/163.
15. Ganau M, Talacchi A, Cecchi PC, Ghimenton C, Gerosa M, Faccioli F. Cystic dilation of the ventriculus terminalis. J Neurosurg Spine. 2012. https://doi.org/10.3171/2012.4.SPINE11504.
16. Stewart DH Jr, King RB, Lourie H. Surgical drainage of cyst of the conus medullaris. Report of three cases. J Neurosurg. 1970. https://doi.org/10.3171/jns.1970.33.1.0106.
17. Takahashi S, Saruhashi Y, Odate S, Matsusue Y, Morikawa S. Percutaneous aspiration of spinal terminal ventricle cysts using real-time magnetic resonance imaging and navigation. Spine. 2009. https://doi.org/10.1097/BRS.0b013e31819b33d6.
18. Zeinali M, Safari H, Rasras S, Bahrami R, Arjipour M, Ostadrahimi N. Cystic dilation of a ventriculus terminalis. Case report and review of the literature. Br J Neurosurg. 2019. https://doi.org/10.1080/02688697.2017.1340585.

Cystic Dilatation of the Ventriculus Terminalis: Examining the Relevance of the Revised Operative Classification Through a Systematic Review of the Literature, 2011–2021

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1 Introduction

Intramedullary cystic lesions of the conus medullaris often pose diagnostic challenges, with a broad range of differential diagnoses, including tumoral and nontumoral cystic lesions. While the former lesions tend to demonstrate an avid contrast uptake, which can be homogeneous or heterogeneous, depending on the nature of the lesion, the lack of contrast enhancement in the event of a hypointense appearance on T1-weighted sequences, an isointense proton-density-weighted sequence, and a hyperintense T2-weighted sequence—all hallmarks of cerebrospinal fluid filled cavities—usually raises the suspicion of a nontumoral cyst. However, even nontumoral cysts may pose challenges to clinicians and neuroradiologists. More specifically, the fifth ventricle, better known as ventriculus terminalis, can represent nonpathological variation in the normal appearance of the conus medullaris, whereas the other end of this spectrum is often represented by its pathological cystic dilatation. In fact, it is well known that the presence of a fifth ventricle can represent a normal developmental phenomenon not only in newborns and childhood, where the prevalence is estimated to be quite high (up to 2.9%), but also in adulthood [1–3]. On the contrary, a cystic dilatation of the ventriculus terminalis (CDVT) is certainly a rare pathological condition, which should always prompt an immediate neurosurgical referral. For a long time, because of the fine line between a normal remnant of the fifth ventricle and a pathological CDVT, the spinal community has lacked a consensus on the most appropriate management protocols for patients with CDVT, where some groups advocate for the fenestration of the cyst and other groups suggest taking a watchful waiting approach.

The Tubingen group [4], led by Tatagiba, engaged in the first attempt to shed light on the management of CDVT and proposed classifying patients into three types: type I, in the case of nonspecific neurological symptoms or nonspecific complaints, including lower-back pain, sciatica, and inferior limb pain; type II, in the presence of a focal neurological deficit, such as paresis, sensory disturbances, altered deep reflexes, or muscular atrophy; and type III, when a sphincter dysfunction, such as bowel and/or bladder incontinence, is noticed. According to their experience [4], type I patients were best managed conservatively, whereas type II and type III patients were usually considered for surgical intervention. In 2011, a revision of this operative classification of CDVT

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was proposed by Ganau et al. [5], who pointed out that even some type I patients may show very good radiological and clinical outcomes following surgical intervention. Tehrefore, it was suggested that patients with unspecific complaints should be subdivided into two types: type Ia, including patients who report clinical complaints that become stable within a couple of months of observation and who are amenable to conservative management; and type Ib, including patients who have unspecific but worsening symptoms and who require surgical evacuation of their respective cysts. Over the past few years, more surgeons have contributed to the literature on CDVT; however, those single-center experiences limited all the inferences made about the demographics of CDVT, its natural history, and its responses to treatments. The goal of this study is to ascertain which impact such a revised classification had on the management of patients diagnosed over the past 10 years.

2 Materials and Methods

Given such a background, a systematic review of the literature covering the 2011–2021 period, which followed the revision of the CDVT classification proposed by Ganau et al., appeared to be the most appropriate study design. The clinical question for the present study was well articulated according to the following Patient-Investigation-Control-Outcome (PICO) framework: all the CDVTs reported in the literature were aligned with the patients and problems investigated (P); the consideration of conservative treatment or surgical intervention (in the form of cerebrospinal fluid (CSF) diversion, fenestration, or excision) was the intervention assessed (I); a comparison of the natural history reported for type 1a and all other types of CDVT was the control (C); and, finally, the lack of motor or the presence of sphincter disturbances at follow-up in type 1a patients was the clinical outcome of interest (O).

This study's review of the relevant literature was conducted on the following electronic databases: PubMed, Ovid Medline, and Scopus. The following Medical Subject Headings (MeSH) terms were used: "fifth ventricle," "ventriculus terminalis," and "cystic dilatation ventriculus terminalis." No language restrictions were applied. All the case reports and clinical series describing new cases of CDVT were included, and other types of documents, such as any review article (narrative, scoping, or systematic), editorials, letters, and book chapters, if available, were retrieved.

All data pertaining to new cases of CDVT were accurately reviewed for age, sex, presenting symptoms, length of clinical history, neurological examination, radiological findings, surgical techniques, and clinical-radiological outcomes at follow-ups.

To ensure the quality of this review, its design and reporting have been conceived and conducted in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist for systematic review articles (http://prisma-statement.org/), a dedicated flowchart guided us through the identification, screening, and inclusion stages of the search conducted through the aforementioned databases (see Fig. 1). Levels of evidence established by the Oxford Centre for Evidence-Based Medicine (OCEBM) were used to establish the quality of evidence for the study included in the review (https://www.cebm.ox.ac.uk/resources/levels-of-evidence), and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group Criteria for the Strength of Recommendations (https://www.gradeworkinggroup.org/) were applied in drawing our conclusions.

3 Results

Ten new clinical articles presenting a total of 30 cases of CDVT were identified and included for qualitative analysis (see Fig. 1). The documents retrieved were published by surgeons from three macroregional areas: Europe and the Near East (Sweden, Italy, and Israel), Asia (China, Japan, and Iran), and North America (Canada and the US). Apart from three case series [6–8], all the other articles consisted of case reports [9–14] and a surgical video [15].

The results obtained indicate a striking sex-based predisposition (F/M ratio: 28/2) and a median age at the time of neurosurgical referral of 50 years (average: 48.2 years; range: 5–73 years). The dimension of CDVT at the time of diagnosis was not uniformly reported: most authors provided the preoperative cysts' size on T2-weighted magnetic resonance imaging (MRI) scans, using either lateral views or lateral and axial views, whereas one group opted for calculating the cyst volume and reported its change following treatment. Whenever the CDVT classification was not reported by authors, we used the clinical information provided to estimate it. Thus, patients were classified as follows: three in type Ia, three in type Ib, 14 in type II, and ten in type III. The clinical data pertaining to the cohort identified through this systematic review are reported in Table 1.

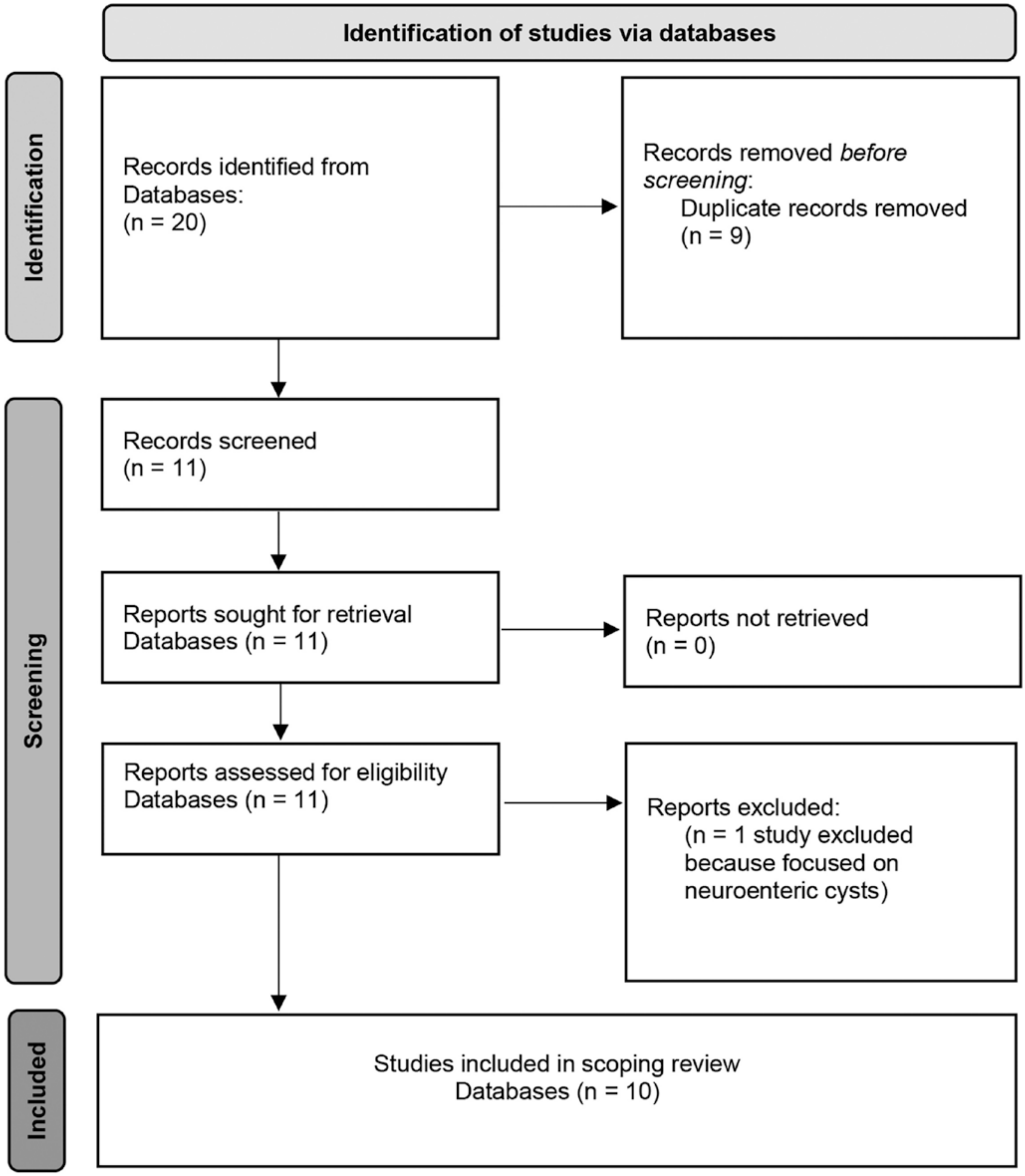

Fig. 1 Flowchart for identification of studies to be included in the systematic review

Table 1 Summary of clinical/surgical series in this review

Study (country, year)	No. of patients	Gender, age	CDVT type	Preop size or volume	Treatment	Outcome and FU length (months)
Bellocchi et al. (Italy, 2013)	1	F, 61	Ib	60 × 13 mm	CF	SI (8)
Pencovich et al. (Israel, 2013)	1	F, 27	III	N/A	CF	SI (4)
Woodley-Cook et al. (Canada, 2016)	1	F, 47	II	N/A	CF	SI (36)
Kawanishi et al. (Japan, 2016)	1	F, 66	II	N/A	CF	SI (36)
Severino et al. (Italy, 2017)	1	F, 52	II	64 × 79 mm	CF	SI (3)
Zhang et al. (China, 2017)	6	F,54	Ia	45 × 10 × 14 mm	SS	UC (72)
		F, 56	II	36 × 14 × 11 mm	SS	SI (44)
		F, 27	II	10 × 6 × 6 mm	SS	PI (36)
		F, 46	II	37 × 13 × 15 mm	SS	SI (24)
		F, 27	II	25 × 19 × 12 mm	SS	PI (16)
		F, 54	III	70 × 13 × 13 mm	SS	SI (52)
Lotfinia et al. (Iran, 2018)	3	F, 62	Ib	N/A	CF	SI (28)
		F, 64	II	N/A	CF	PI (28)
		F, 51	II	N/A	CF	SI (28)
Fletcher-Sandersjoo et al. (Sweden, 2019)	14	F, 40	Ia	3 mL	CF + SS	UN (7)
		F, 38	Ia	1.5 mL	No surgery	UC (124)
		F, 36	Ib	2 mL	CF	SI (85)
		F, 42	II	1 mL	CF	UN (90)
		F, 53	II	1 mL	CF	PI (96)
		F, 35	II	1 mL	CF	PI (11)
		F, 56	II	4 mL	CF	PI (16)
		F, 63	III	12 mL	CF	PI (103)
		F, 50	III	2 mL	CF + SS	SI (16)
		F, 45	III	0.4 mL	CF	PI (60)
		F, 38	III	2 mL	CF	PI (61)
		F, 44	III	9 mL	CF	PI (99)
		M, 71	III	5 mL	CF	PI (59)
		F, 64	III	23 mL	CF + SS	SI (15)
Zeinali et al. (Iran, 2019)	1	M, 5	III	20 × 12 mm	CF	PI (6)
Helal et al. (USA, 2021)	1	F, 73	II	N/A	CF	N/A

F Female, *M* male, *CF* cyst fenestration, *SS* subarachnoid shunting, *SI* significantly improved, *PI* partially improved, *UC* unchanged, *FU* follow-up

4 Discussion

The articles captured by this systematic review confirm the very low incidence of CDVT and highlight once again the challenges to its management.

4.1 Demographics

According to previously published cumulative data, 67 surgical cases of CDVT had been documented until 2019 [6], with only one more case since, published in 2021 [15]. When factoring in also four cases managed conservatively [5, 6], the total cohort of CDVT cases reported so far includes 71 patients. Although unexplained, the female predominance of 82%, as previously reported [8], continues to be confirmed even by our analysis; in fact, the impressive F/M ratio calculated through our systematic review (F/M: 28/2) seems to suggests that the correct figure should probably be >90%.

4.2 Clinical Presentation

Symptoms' duration in patients with CDVT is known to be quite variable; unfortunately, though, such data were not systematically reported in the articles included in this review. Nonetheless, from those authors who did report more-precise figures on the length of clinical history, we could calculate a broad range of symptoms' duration, spanning from a few months [7] to several years (the longest clinical history was 30 years) [8].

Interestingly, the proportion of patients with types Ia and Ib, type II, and type III match very well with the one originally reported by Ganau et al.: 20%, 50%, and 30%, respectively. This suggests that patients with CDVT motor and/or sensory disturbances represent the most common presenting signs and symptoms, whereas one patient out of three shows the most severe form with evidence of sphincter disturbances. Furthermore, patients with CDVT may often present with concurrent spinal pathologies, the most frequent being lumbosacral disc degeneration (or proper herniation) and sacral perineural cysts. This systematic review led to the determination that this might be the case in over 30% of patients.

4.3 Referral Pathways

Only type III patients had an expedited diagnostic workup and treatment; for all other CDVTs, the time that elapsed between the initial diagnosis and the decision to opt for either surgery or taking a watchful waiting approach was very variable. A superficial observer might conclude that such variability is due to the inconsistent degree of clinical complaints, but we argue that differences in referral pathways, particularly in healthcare systems where there is a lack of clearly identifiable specialist centers for the management of patients with ventriculus terminalis, might explain it. On one hand, only the series from Karolinska University (Sweden, 14 cases) and that from Beijing Tiantan Hospital (China, six cases) match or approximate the size of the clinical series previously reported by Verona University Hospital (Italy, 13 cases). On the other hand, most articles published on this topic consist of case reports (12 studies), or small series of two (five articles), three (three articles), or a maximum of four (two articles) patients, respectively.

4.4 Surgical Management and Relevance of the Operative Classification

Our qualitative analysis indicates that almost all patients reported in the past 10 years were treated surgically, via either dorsal myelotomy and cystic fenestration, cyst-subarachnoid shunting, or both. Of note, no cases of the percutaneous aspiration of the cysts, a maneuver previously described in the literature [16], or cases using intraoperative ultrasound [17] were described in the cases reported over the past decade.

Furthermore, not all authors specified whether the original operative classification of CDVT, or its revision, were taken into account in deciding on the management strategy. Of note, the few authors who used the revised classification to retrospectively classify patients and make sense of their postoperative clinical outcomes agreed on its usefulness. Their comments, together with the analysis of all other follow-ups, provide an unprecedented window into the natural history of CDVT and reinforce the appropriateness of the subclassification into types Ia and Ib. In fact, while all patients harboring type Ib, II, and III cysts improved after surgery, although some only partially, the neurological status and clinical complaints of the three patients with type Ia CDVT remained unchanged regardless of their operative (two cases) or nonoperative (one case) management.

Those findings are well in keeping with the original recognition of a high number of false-positive cases in type I CDVTs [4], but they also confirm the recommendation for surgical intervention in type Ib patients proposed by the revised operative classification [5], because all type Ib patients identified in this review demonstrated a significant improvement even at very long follow-up times (range: 8–85 months).

4.5 Level of Evidence and Recommendations

While the level of evidence gathered by this systematic review remains low because the literature on CDVT consists only of retrospective studies based on single-center series (level of evidence 4 according to OCEBM), the strength of recommendation for adopting the revised operative classification of CDVT is moderate. The following is a paraphrase of the GRADE definition for moderate recommendations: Further research is likely to have an important impact on our confidence that adherence to the recommended use of this classification will do more good than harm. Obviously, the current revision might be subject to further improvements should additional evidence be gathered in the future by higher-quality studies. However, we should anticipate that in addition to the designing of multicentric protocols or formal registries, there is an argument for considering randomization only in type Ib patients (but not in type Ia patients, who are more suited to watchful waiting, or in types II and III patients when they present with ongoing neurological deficits).

4.6 Study Limitations

This systematic review answered a very clear PICO question on the usefulness of the revised operative classification of the CDVT; however, it suffers from all the drawbacks related to the nature of this rare pathology. In fact, the evidence gathered and the recommendation produced are affected by the very low prevalence of ventriculus terminalis, the low incidence of CDVT, and the broad range of clinical pictures that such dilatation might induce.

5 Conclusions

The results obtained by this review suggest that CDVT is a rarely reported condition with a broad spectrum of clinical presentations. With only 71 cases described to date, CDVT should effectively be considered an orphan disease; hence, we advocate for its inclusion in the Rare Diseases Registry (RaDaR) program of the National Center for Advancing Translational Sciences (NCATS). The most relevant take-home messages of this systematic review concern the referral pathways and management strategies. On one hand, our results indicate that adequate consideration should be given to designing national pathways for referral to tertiary centers with relevant expertise in the management of lesions on the conus medullaris. On the other hand, we found it appropriate to propose a moderate recommendation for adopting the revised classification of CDVT when managing those patients. Therefore, we suggest that type Ia should be, at least initially, treated conservatively, whereas we reckon that the signs and symptoms described in types Ib, II, and III seem to benefit, although in some patients only partially, from surgical decompression in the form of cystic fenestration, cyst-subarachnoid shunting, or both.

Conflicts of Interest The authors do not report any financial, personal, or professional conflicts of interest concerning the materials and methods used in this study or the findings specified in this chapter.

References

1. Coleman LT, Zimmerman RA, Rorke LB. Ventriculus terminalis of the conus medullaris: MR findings in children. AJNR Am J Neuroradiol. 1995;16(7):1421–6.
2. Liccardo G, Ruggeri F, De Cerchio L, Floris R, Lunardi P. Fifth ventricle: an unusual cystic lesion of the conus medullaris. Spinal Cord. 2005;43(6):381–4. https://doi.org/10.1038/sj.sc.3101712.
3. Unsinn KM, Mader R, Gassner I, Kreczy A, Freund MC. Sonography of the ventriculus terminalis in newborns. AJNR Am J Neuroradiol. 1996;17(5):1003–4.
4. de Moura Batista L, Acioly MA, Carvalho CH, Ebner FH, Tatagiba M. Cystic lesion of the ventriculus terminalis: proposal for a new clinical classification. J Neurosurg Spine. 2008;8(2):163–8. https://doi.org/10.3171/SPI/2008/8/2/163.
5. Ganau M, Talacchi A, Cecchi PC, Ghimenton C, Gerosa M, Faccioli F. Cystic dilation of the ventriculus terminalis. J Neurosurg Spine. 2012;17(1):86–92. https://doi.org/10.3171/2012.4.SPINE11504.
6. Fletcher-Sandersjöö A, Edström E, Bartek J Jr, Elmi-Terander A. Surgical treatment for symptomatic ventriculus terminalis: case series and a literature review. Acta Neurochir. 2019;161(9):1901–8. https://doi.org/10.1007/s00701-019-03996-0.
7. Lotfinia I, Mahdkhah A. The cystic dilation of ventriculus terminalis with neurological symptoms: three case reports and a literature review. J Spinal Cord Med. 2018;41(6):741–7. https://doi.org/10.1080/10790268.2018.1474680.
8. Zhang L, Zhang Z, Yang W, Jia W, Xu Y, Yang J. Cystic dilation of the ventriculus terminalis: report of 6 surgical cases treated with cyst-subarachnoid shunting using a T-catheter. World Neurosurg. 2017;104:522–7. https://doi.org/10.1016/j.wneu.2017.05.017.
9. Bellocchi S, Vidale S, Casiraghi P, Arnaboldi M, Taborelli A. Multilobed cystic dilation of the ventriculus terminalis (CDVT). BMJ Case Rep. 2013;2013:bcr2013008654. https://doi.org/10.1136/bcr-2013-008654.
10. Kawanishi M, Tanaka H, Yokoyama K, Yamada M. Cystic dilation of the ventriculus terminalis. J Neurosci Rural Pract. 2016;7(4):581–3. https://doi.org/10.4103/0976-3147.185504.
11. Pencovich N, Ben-Sira L, Constantini S. Massive cystic dilatation within a tethered filum terminale causing cauda equina compression and mimicking syringomyelia in a young adult patient. Childs Nerv Syst. 2013;29(1):141–4. https://doi.org/10.1007/s00381-012-1911-9.
12. Severino R, Severino P. Surgery or not? A case of ventriculus terminalis in an adult patient. J Spine Surg. 2017;3(3):475–80. https://doi.org/10.21037/jss.2017.06.22.
13. Woodley-Cook J, Konieczny M, Spears J. The slowly enlarging ventriculus terminalis. Pol J Radiol. 2016;81:529–31. https://doi.org/10.12659/PJR.895669.
14. Zeinali M, Safari H, Rasras S, Bahrami R, Arjipour M, Ostadrahimi N. Cystic dilation of a ventriculus terminalis. Case report and review of the literature. Br J Neurosurg. 2019;33(3):294–8. https://doi.org/10.1080/02688697.2017.1340585.
15. Helal A, Pirina A, Sorenson TJ, Palandri G. Fenestration of symptomatic ventriculus terminalis: 2-dimensional operative video. Oper Neurosurg (Hagerstown). 2021;20(4):E293. https://doi.org/10.1093/ons/opaa372.
16. Takahashi S, Saruhashi Y, Odate S, Matsusue Y, Morikawa S. Percutaneous aspiration of spinal terminal ventricle cysts using real-time magnetic resonance imaging and navigation. Spine (Phila Pa 1976). 2009;34(6):629–34. https://doi.org/10.1097/BRS.0b013e31819b33d6.
17. Ganau M, Ligarotti GK, Apostolopoulos V. Real-time intraoperative ultrasound in brain surgery: neuronavigation and use of contrast-enhanced image fusion. Quant Imaging Med Surg. 2019;9(3):350–8. https://doi.org/10.21037/qims.2019.03.06.

Does Laminectomy Affect Spino-Pelvic Balance in Lumbar Spinal Stenosis? A Study Based on the EOS X-Ray Imaging System

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1 Introduction

Lumbar spinal stenosis (LSS) is a frequent disorder in elderly people and the most common reason for patients over 65 years to undergo spinal surgery. The narrowing of the lumbar canal is due to a combination of factors: disc degeneration, the hypertrophy of the yellow ligament and facet joints, spondylolisthesis and the presence of osteophytes. Surgical treatment is intended to enlarge the canal and foramina to decompress the nerve roots with different possible strategies: laminectomy; bilateral or unilateral laminotomy; and the splitting of spinous processes [1]. Our purpose is to determine whether and to what extent the conventional facet-sparing laminectomy affects the spino-pelvic balance, evaluated pre- and postoperatively through the EOS X-ray Imaging System [2, 3].

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2 Methods and Materials

2.1 Patient Population

In total, 26 patients (eight female, 18 male; average age: 69.9, range: 65–80) with symptomatic LSS underwent facet-preserving laminectomy over a period of 3 months. The inclusion criteria were as follows: an almost-6-month history of neurogenic claudication; grade C or D stenosis according to the Schizas scale on magnetic resonance imaging (MRI) images [4]; no other comorbidities or conditions that could affect spino-pelvic parameters, such as spondylolisthesis or instability at the flexion-extension X-ray exam. Patients' clinical conditions were assessed through the Oswestry Disability Index (ODI) [5], the visual analogue scale (VAS) [6] and the modified Japanese Orthopaedic Association (mJOA) scoring system [7]. The clinical evaluation was performed 2 days before and 6 months after surgery (Table 1). Ten patients had two-level lumbar stenosis and 16 patients three-level lumbar stenosis.

2.2 Imaging Evaluation

Before surgery, all the patients underwent a 1.5T MRI of the lumbar spine and flexion-extension radiographs in the standing position. EOS 2D/3D acquisition and 3D reconstructions with sterEOS 3D software (EOS Imaging, France), which were obtained preoperatively and 6 months after surgery, have been used to calculate the spino-pelvic balance parameters and the axial vertebral rotation (AVR) for each vertebra (Fig. 1). Spino-pelvic balance was evaluated according to the following parameters: thoracic kyphosis (TK); lumbar lordosis (LL); pelvic incidence (PI); pelvic tilt (PT) and sacral slope (SS); and the difference between PI and LL. TK is defined as the angle between the upper end plate of the T4

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Table 1 Patients' clinical evaluations before and 6 months after surgery

Patient	Age (years)	Stenosis levels	VAS pre/post	mJOA pre/post	ODI (%) pre/post
1 (M)	69	L3-L4, L4-L5, L5-S1	6/4	7/10	42/28
2 (M)	66	L3-L4, L4-L5	7/3	6/11	42/18
3 (M)	68	L3-L4, L4-L5	9/4	5/10	58/26
4 (M)	65	L4-L5, L5-S1	8/4	10/12	62/16
5 (F)	71	L3-L4, L4-L5	8/3	7/12	60/14
6 (M)	71	L3-L4, L4-L5	8/4	7/12	64/22
7 (F)	70	L3-L4, L4-L5, L5-S1	5/3	8/10	34/20
8 (M)	73	L2-L3, L3-L4, L4-L5	7/4	9/11	28/16
9 (M)	76	L3-L4, L4-L5, L5-S1	7/3	9/12	30/18
10 (M)	65	L3-L4, L4-L5, L5-S1	6/2	10/12	44/30
11 (M)	67	L3-L4, L4-L5, L5-S1	8/3	9/12	60/24
12 (M)	74	L4-L5, L5-S1	6/3	11/14	46/22
13 (M)	73	L3-L4, L4-L5, L5-S1	7/3	12/15	56/24
14 (M)	75	L3-L4, L4-L5, L5-S1	5/3	9/13	32/18
15 (F)	65	L3-L4, L4-L5, L5-S1	6/3	9/13	44/22
16 (F)	67	L2-L3, L3-L4, L4-L5	4/2	11/14	38/16
17 (M)	69	L3-L4, L4-L5, L5-S1	6/4	10/14	48/28
18 (F)	67	L3-L4, L4-L5, L5-S1	4/2	12/15	36/12
19 (F)	65	L3-L4, L4-L5, L5-S1	7/3	9/13	56/22
20 (M)	70	L3-L4, L4-L5	8/4	8/13	74/36
21 (M)	69	L2-L3, L3-L4, L4-L5	5/2	11/16	34/12
22 (M)	69	L3-L4, L4-L5, L5-S1	6/3	10/14	44/22
23 (M)	69	L3-L4, L4-L5, L5-S1	7/3	10/14	52/22
24 (F)	80	L3-L4, L4-L5	8/4	7/11	72/36
25 (M)	78	L3-L4, L4-L5	6/2	10/15	50/20
26 (F)	66	L4-L5, L5-S1	7/3	9/14	54/26

vertebrae and the lower end plate of the T12 vertebrae. LL is the angle between the sacral end plate and the upper end plate of the L1 vertebra. PI is the angle between a line drawn from the centre of the femoral head axis to the midpoint of the sacral plate and perpendicular to the sacral plate. PI defines the relative orientation of the sacrum versus the iliac bone. PT is the angle between a line drawn from the centre of the femoral head axis to the midpoint of the sacral plate and the vertical. SS refers to sagittal inclination of the sacral end plate and is defined as the angle between the end plate of S1 and the horizontal. PT and SS are directly related to the geometrical eq. PI = PT + SS. The difference between PI and the LL angle (PI-LL) quantifies the mismatch between the pelvic morphology and the lumbar curve; spino-pelvic alignment is considered satisfactory when PI-LL is below the 10° threshold [8]. The vertebra orientation in the space is represented by a vector (i.e., AVR) in order to simplify the visualization and to allow mathematical quantification (Fig. 2). The AVR is based on known vertebral landmarks; it appears as a line starting at the midpoint of the straight connecting the two pedicular centroids, parallel to the upper end plate at the level of the pedicles and terminating at the ventral surface of the vertebral body. Therefore, AVR represents the axis of the vertebra in its sagittal median axis, and its length is proportional to its size. The AVRs are placed in a coordinate system: A line connecting the two acetabular centres forms the X-axis of the coordinate system; the Y-axis is perpendicular to the coronal; and the Z-axis is a perpendicular to the horizontal plane that crosses the Y-axis and the X-axis in the midpoint of the interacetabular straight. The calibration scale of the coordinate system is based on the interacetabular distance. After AVRs are placed inside this calibrated coordinate system, the coordinates of each vector point can be determined in all three planes by using basic vector algebra [9]. In this study, we focused only on the vertebral vector projection in the axial plane (Fig. 3).

2.3 Statistical Analysis

Statistical analyses were performed by using Stata software (version 13; StataCorp LP, College Station, Texas, USA). Before each analysis, the Shapiro–Wilk test was used to assess the normality of the distribution of variables. If the normality assumption was satisfied, parametric tests were used (Student's *t*-test, linear regression analysis); otherwise, nonparametric equivalent tests were employed. The results were considered significant if $p < 0.05$.

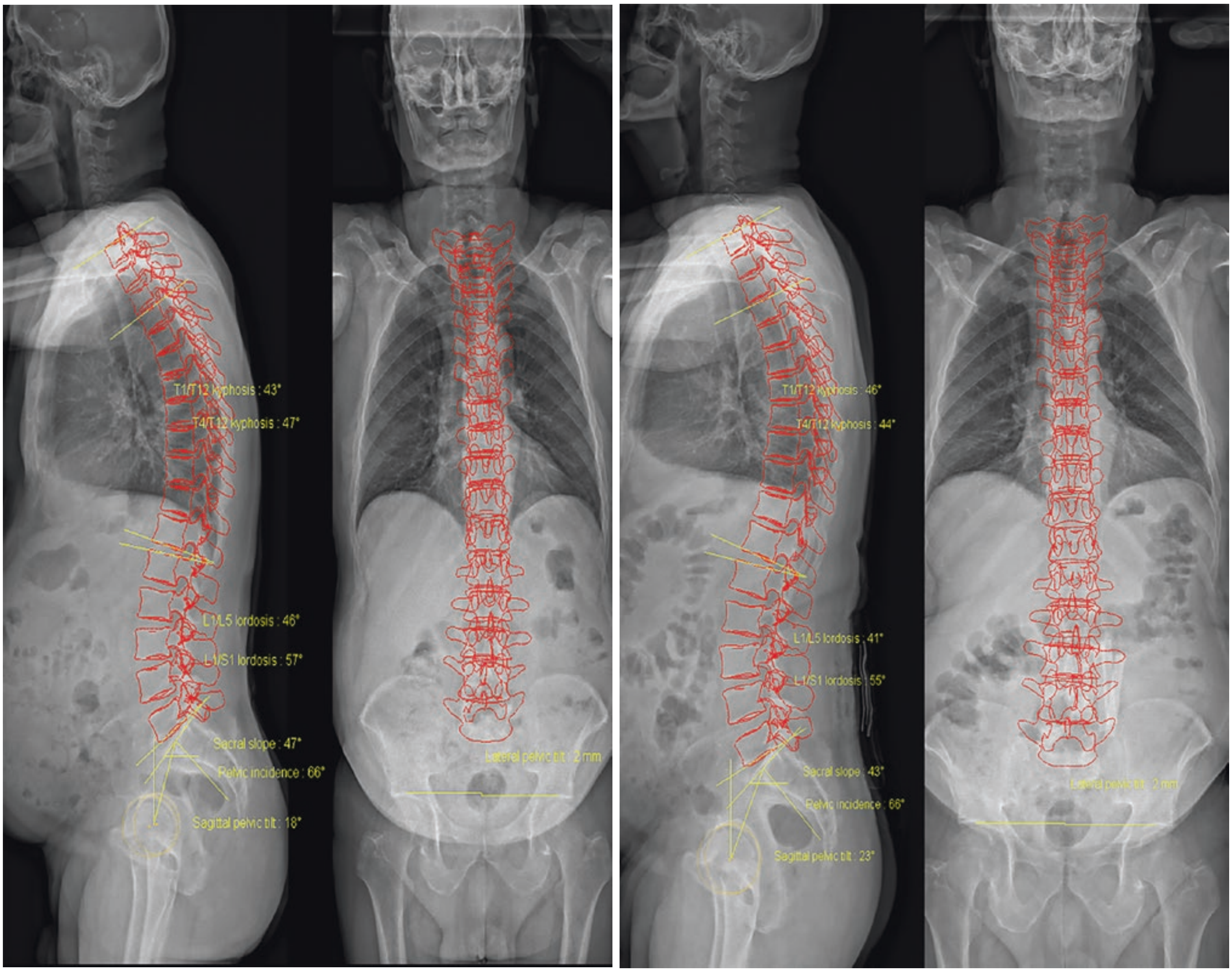

Fig. 1 Pre- and postoperative EOS 3D reconstruction, on which sterEOS 3D software automatically calculates the pelvic and spinal parameters of the sagittal balance (LL,TK, SS, PI, and PT)

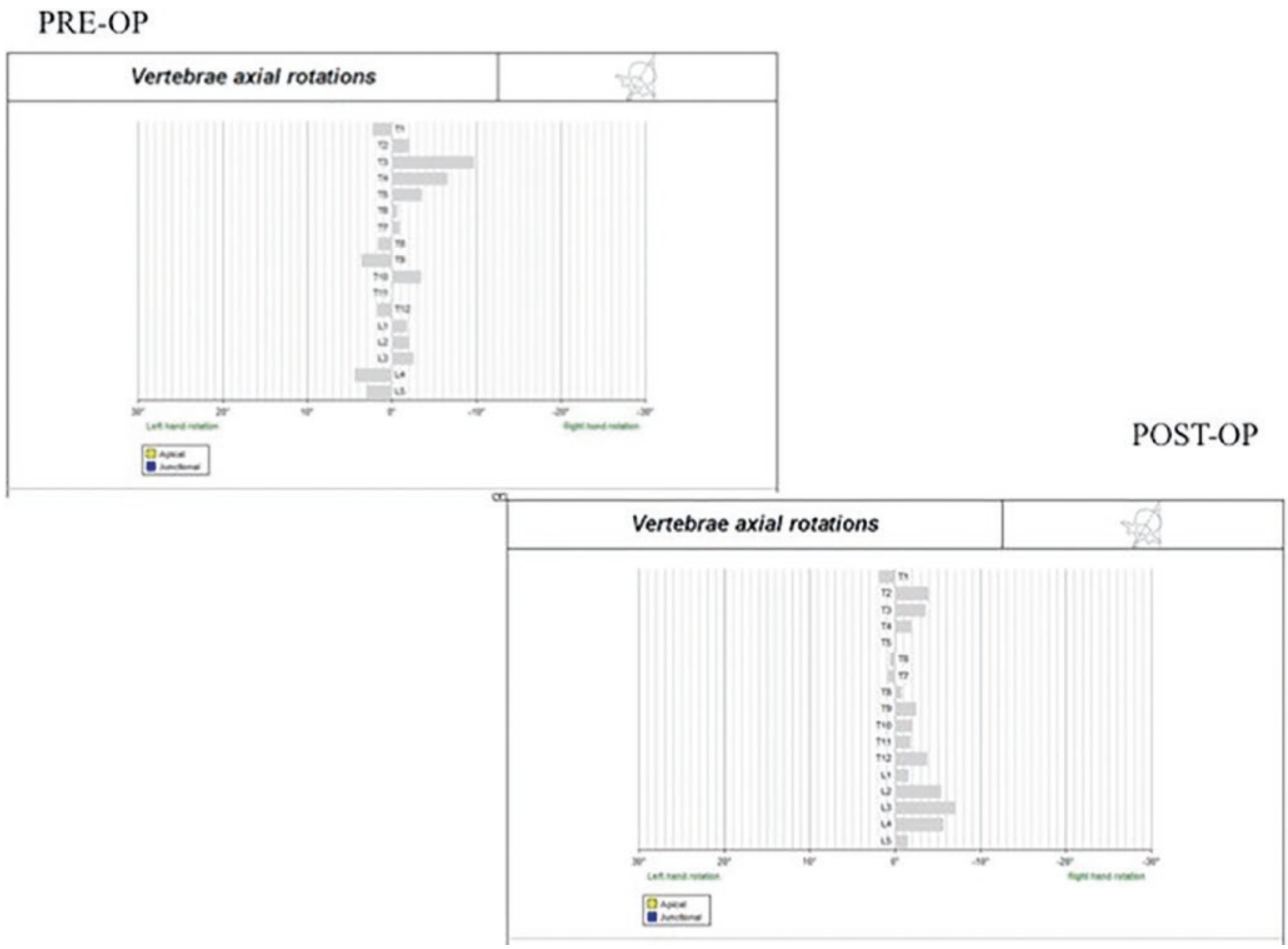

Fig. 2 Pre- and postoperative diagram of the axial rotation of vertebrae

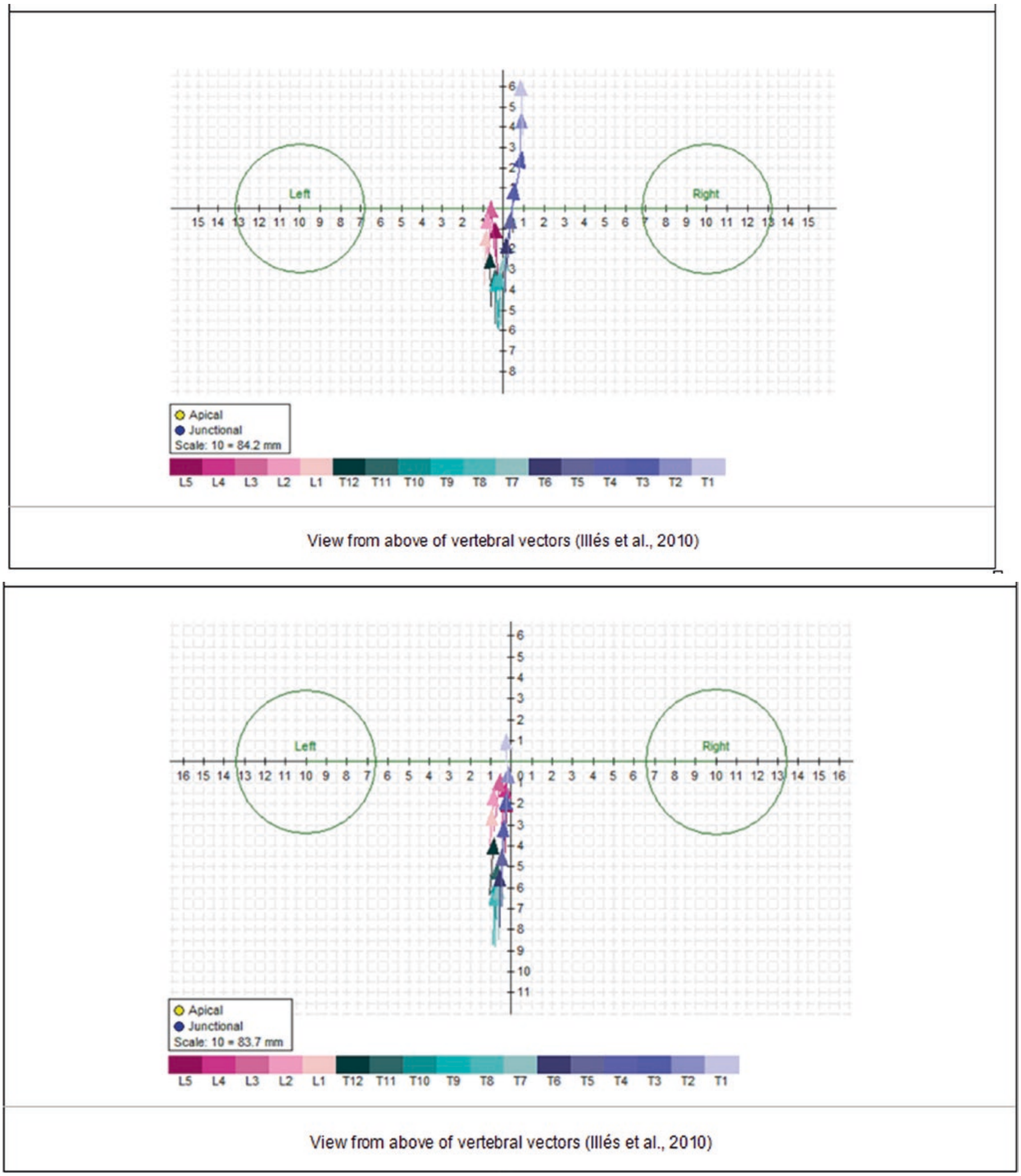

Fig. 3 Pre- and postoperative view from above of the vertebral vectors

3 Results

In all cases, the normality assumption was satisfied, so parametric tests were used. For each parameter, the mean and the standard deviation were calculated, before and 6 months after surgery. We obtained the following results by using Student's *t*-test for paired data:

- TK, LL and PI were not significantly modified by surgery: preoperative TK (was 37.42° (mean) ± 10.45° (standard deviation) vs postoperative 37.38° ± 11.20°, $p = 0.29$; LL 50.19° ± 13.54° vs 47.08° ± 12.08°, $p = 0.10$; and PI (53.03° ± 10.79° vs 53.62° ± 10.57°, $p = 0.59$).
- SS significantly decreased after surgery (39.58° ± 10.40° vs 36.81° ± 10.39°, $p = 0.03$).
- PT significantly increased after surgery (13.50° ± 7.27° vs 16.73° ± 7.84°, $p = 0.002$).

In our series, the postoperative PI-LL value was 6.54° < 10°. The pre- and postoperative axial vertebral rotation (AVR) of each vertebra (T1-L5), automatically calculated by sterEOS 3D software based on reconstructed 3D models, did not show statistically significant results. The VAS and ODI values significantly decreased after surgery (respectively, 6.58 ± 1.30 vs 3.16 ± 0.71, $p < 0.05$; 48.46 ± 12.67 vs 21.92 ± 6.31, $p < 0.05$ on Student's *t*-test for paired data). The mJOA values significantly increased after surgery (9.04 ± 1.78 vs 12.77 ± 1.68, $p < 0.05$ on Student's *t*-test for paired data).

4 Discussion

The gold-standard treatment for symptomatic LSS is a facet-preserving laminectomy [1]. Controversy continues on the extent of resection required to effectively decompress the spinal canal: Because narrowing occurs predominantly at the interlaminar region—due to the arthrosis of facet joints, disc bulging and ligamentous hypertrophy—the resection of the whole vertebral arch may not be necessary. Alternatively, an interlaminar decompression or an undercutting unilateral laminectomy can be performed to decompress the spinal canal. Extensive damage to paraspinous muscles and the resection of the posterior bone and ligaments could increase postoperative pain and long-term instability [10]: Surgical techniques sparing posterior midline structures have been recently proposed with the aim of preserving spinal stability [11], although clear indicators are still lacking. Because most of the translational and rotational resistance is provided by vertebral discs and zygapophyseal joints and because the force exerted by posterior ligaments during flexion is small when compared to that by back muscles [12], spinal stability is minimally affected by conventional laminectomy. Suzuki et al. noticed that patients with LSS usually exhibit a forward bending of the trunk and a pelvic retroversion with a consequent loss of LL [13]: This posture increases the available space in the spinal canal, allowing relief from back pain and claudication. A large portion of flat-back deformities is postural and thus reversible, although long periods of altered posture may lead to degenerative atrophy and the hyposthenia of the paraspinal muscles. Fujii et al. showed a reactive sagittal alignment change after spinous process splitting, especially in patients with poor preoperative alignment [14], probably related to the resolution of a compensatory posture. In Hikata et al.'s study, preoperative sagittal imbalance improved after surgery, suggesting the reversibility of degenerative changes in extensor muscles [15]. Jeon et al. showed that decompressive laminectomy caused the posterior migration of C7PL, an increase in the LL and the restoration of upright posture thanks to improvements in pain and function [16]. However, we believe that the restoration of sagittal balance (SB) is not an essential parameter in the evaluation of short-term clinical outcomes after surgery. Similarly, Bayerl et al. demonstrated that imbalanced patients benefit from decompression to the same degree as patients with normal balance at 1-year follow-ups [17]. The average SS in asymptomatic adult subjects has been reported to be 41° ± 8° [8]; this parameter is affected by a patient's position. In our series, SS significantly decreased after surgery ($p = 0.03$) (39.58° ± 10.40° vs 36.81° ± 10.39°). Pelvic tilt (PT) is also a dynamic parameter, changing through the rotation of the pelvis near the hip axis. Positive values of PT denote an posterior rotation of the pelvis (retroversion) and negative values an anterior rotation (antiversion) [9]. PT increases during childhood, being smaller in children than in adolescents (4° in 7-year-old and 8° in 13-year-old subjects); PT in asymptomatic adults has been reported to be 13° ± 6° [18]. We observed a significantly increased PT after surgery ($p = 0.002$) (13.5° ± 7.27° vs 16.73° ± 7.84°), whereas no modification in the LL and the general alignment was noticed (postoperative PI-LL = 6.54°). The morphology and orientation of the lumbar spine and the pelvis are usually strictly related: In an asymptomatic adult, a high correlation has been demonstrated between LL and SS (R: [0.65;0.86]), while that between LL and PI is slightly weaker (R: [0.60;0.69]). No correlation between the LL and the PT has been reported [8]. Unlike the data in the literature [16], we observed a slight, though not statistically significant, reduction in LL after laminectomy, but it did not cause a global misalignment (postoperative PI-LL = 6.54°), probably because of the weakness and degenerative atrophy of the paraspinal muscle, secondary to patient age and long periods of forward-bending postures. The EOS device and sterEOS 3D reconstruction software brought a strikingly new possibility in the study of degenerative spine pathology, completing data obtained from computed tomography (CT) scans acquired in the supine position with coronal and sagittal curves relative to the upright position [19, 20]. The EOS system allows for the simultaneous capture of the upright full body, at low radiation doses, in a spatially calibrated way, thus avoiding the positioning problems that can distort a proper 3D reconstruction. Image quality is optimized, providing clear anatomical landmarks for proper 3D reconstruction. The vertebral vector is a mathematical entity that is characterized by its length and spatial direction and that projects onto each of the planes with its specific angle [9]. The pre- and postoperative AVRs of each vertebra are calculated by the sterEOS 3D software on the basis of reconstructed 3D models; we did not obtain statistically significant differences after surgery. Only a limited number of studies have investigated the effects of surgical decompression on adjacent levels. According to Zander et al., laminectomy has only a negligible effect on the intersegmental forces in the facet joints of the segments above [21]. Similarly, Bisschop et al. found that a single-level laminectomy alters segmental biomechanical behaviour without affecting adjacent segments [22]. Delank et al. found that adjacent levels were not substantially affected, even after facetectomy [23]. On the contrary, Cardoso et al. found that adjacent instability occurs after a more extensive decompressive surgery [24]. In our experience, a significant improvement in clinical outcomes was noticed, more than so than that in the restoration of the spino-pelvic alignment. In fact, the VAS and ODI values significantly decreased after surgery ($p < 0.05$ for both), while the mJOA values significantly increased ($p < 0.05$). Such evaluation scores are currently applied in clinical practice because they offer immediate and easily comparable numeric values. The mJOA score gives an immediate overview of a patient's neurological status; it needs to be assessed by a physician because it includes objective parameters. VAS and ODI evaluations provide complementary information about subjective perceptions of pain and their impact on daily activities and quality of life. In our experience, a combination of objective and subjective evaluations offers a better comprehension of clinical outcomes.

5 Conclusion

In our opinion, the facet-preserving laminectomy has an effect on AVR and an insignificant repercussion on SB. Furthermore, a standard SB does not exist among the normal population [25], while congruence between the pelvic and spinal parameters is crucial to achieve an economic posture, placing the axis of gravity in a physiological position [8]. This is only a preliminary study on a small number of patients and therefore requires further studies correlating the level and number of laminae removed. The short follow-up time could be a limitation; a longer time of observation could probably detect the progression of the degenerative cascade, expecially when considering that most of the affected patients included in the study were over 65 years old.

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Ethics Approval Approval was obtained from the ethics committee of IRCCS Neuromed. The procedures used in this study adhered to the tenets of the 1964 Declaration of Helsinki.

Consent to Participate Informed consent was obtained from all individual participants included in the study.

Consent to Publish Patients signed informed consent regarding publishing their data and images.

References

1. Overdevest G, Vleggeert-Lankamp C, Jacobs W, Thomé C, Gunzburg R, Peul W. Effectiveness of posterior decompression techniques compared with conventional laminectomy for lumbar stenosis. Eur Spine J. 2015;24(10):2244–63.
2. Dubousset J, Charpak G, Dorion I, Skalli W, Lavaste F, Deguise J, Kalifa G, Ferey S. A new 2D and 3D imaging approach to musculoskeletal physiology and pathology with low-dose radiation and the standing position: the EOS system. Bull Acad Natl Med. 2005;189(2):287–97; discussion 297–300.
3. Melhem E, Assi A, El Rachkidi R, Ghanem I. EOS biplanar X-ray imaging: concept, developments, benefits, and limitations. J Child Orthop. 2016;10(1):1–14.
4. Schizas C, Heumann N, Burn A, Tansey R, Wardlaw D, Smith FW, Kulik G. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. Spine. 2010;35:1919–24.
5. Fairbank JC, Pynsent PB. The oswestry disability index. Spine. 2000;25:2940–52.
6. Reips UD, Funke F. Interval-level measurement with visual analogue scales in internet-based research: VAS generator. Behav Res Methods. 2008;40:699–704.
7. Sato N, Sekiguchi M, Kikuchi S, Shishido H, Sato K, Konno S. Effects of long-term corset wearing on chronic low back pain. Fukushima J Med Sci. 2012;58:60–5.
8. Roussouly P, Gollogly S, Berthonnaud E, Dimnet J. Classification of the normal variation in the sagittal alignment of the human lumbar spine and pelvis in the standing position. Spine. 2005;30:346–53.
9. Illés T, Somoskeöy S. Comparison of scoliosis measurements based on three-dimensional vertebra vectors and conventional two-dimensional measurements: advantages in evaluation of prognosis and surgical results. Eur Spine J. 2013;22:1255–63.
10. Mayer TG, Vanharanta H, Gatchel RJ, Mooney V, Barnes D, Judge L, Smith S, Terry A. Comparison of CT scan muscle measurements

and isokinetic trunk strength in postoperative patients. Spine. 1989;14(1):33–6.
11. Bresnahan L, Ogden AT, Natarajan RN, et al. A biomechanical evaluation of graded posterior element removal for treatment of lumbar stenosis: comparison of a minimally invasive approach with two standard laminectomy techniques. Spine. 2009;34(1):17–23.
12. Hindle RJ, Pearcy MJ, Cross A. Mechanical function of the human lumbar interspinous and supraspinous ligaments. J Biomed Eng. 1990;12(4):340–4.
13. Suzuki H, Endo K, Kobayashi H, Tanaka H, Yamamoto K. Total sagittal spinal alignment in patients with lumbar canal stenosis accompanied by intermittent claudication. Spine. 2010;35:E344–6.
14. Fujii K, Kawamura N, Ikegami M, Niitsuma G, Kunogi J. Radiological improvements in global sagittal alignment after lumbar decompression without fusion. Spine. 2015;40(10):703–9.
15. Hikata T, Watanabe K, Fujita N, Iwanami A, Hosogane N, Ishii K, Nakamura M, Toyama Y, Matsumoto M. Impact of sagittal spinopelvic alignment on clinical outcomes after decompression surgery for lumbar spinal canal stenosis without coronal imbalance. J Neurosurg Spine. 2015;23:451–8.
16. Jeon CH, Lee HD, Lee YS, Seo HS, Chung NS. Change in sagittal profiles after decompressive laminectomy in patients with lumbar spinal canal stenosis. A 2-years preliminary report. Spine. 2015;40(5):E279–85.
17. Bayerl SH, Pöhlmann F, Finger T, Onken J, Franke J, Czabanka M, Woitzik J, Vajkoczy P. The sagittal balance does not influence the 1-year clinical outcome of patients with lumbar spinal stenosis without obvious instability after microsurgical decompression. Spine. 2015;40(13):1014–21.
18. Mac-Thiong JM, Berthonnaud E, Dimar JR, Betz RR, Labelle H. Sagittal alignment of the spine and pelvis during growth. Spine. 2004;29:1642–7.
19. Aaro S, Dahlborn M. Estimation of vertebral rotation and spine rib cage deformity in scoliosis by computer tomography. Spine. 1981;6(5):460–7.
20. Yazici M, Acaroglu ER, Alanay A, Deviren V, Cila A, Surat A. Measurement of vertebral rotation in standing versus supine position in adolescent idiopathic scoliosis. J Pediatr Orthop. 2001;21(2):252–6.
21. Zander T, Rohlmann A, Klockner A, Bergmann G. Influence of graded facetectomy and laminectomy on spinal biomechanics. Eur Spine J. 2003;12(4):427–34.
22. Bisschop A, van Engelen SJPM, Kingma I, Holewijn RM, Stadhouder A, van der Veen AJ, van Dieën JH, van Royen BJ. Single level lumbar laminectomy alters segmental biomechanical behavior without affecting adjacent segments. Clin Biomech (Bristol, Avon). 2014;29(8):912–7.
23. Delank KS, Gercek E, Kuhn S, Hartmann F, Hely H, Röllinghoff M, Rothschild MA, Stützer H, Sobottke R, Eysel P. How does spinal canal decompression and dorsal stabilization affect segmental mobility? A biomechanical study. Arch Orthop Trauma Surg. 2010;130(2):285–92.
24. Cardoso MJ, Dmitriev AE, Helgeson M, Lehman RA, Kuklo TR, Rosner MK. Does superior-segment facet violation or laminectomy destabilize the adjacent level in lumbar transpedicular fixation? An in vitro human cadaveric assessment. Spine (Phila Pa 1976). 2008;33(26):2868–73.
25. Stagnara P, De Mauroy JC, Dran G, Gonon GP, Costanzo G, Dimnet J, Pasquet A. Reciprocal angulation of vertebral bodies in a sagittal plane: approach to references for the evaluation of kyphosis and lordosis. Spine. 1982;7(4):335–42.

Transtubular Endoscopic Neuronavigation–Assisted Approach for Extraforaminal Lumbar Disk Herniations: A New Trend for a Common Neurosurgical Disease

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1 Introduction

Extraforaminal lumbar disk herniations (ELDHs) are rare entities, accounting for 1–12% of all lumbar disk herniations [1]. Diagnosis is still challenging because they often compress the dorsal root ganglion around the axilla of the exiting nerve, mostly causing unilateral superior radiculopathy [2]. The diagnostic pathway is based on magnetic resonance imaging (MRI) scans, noncontrast computed tomography (CT) scans, and dynamic X-rays. Dynamic X-rays show the presence of instability (suggesting an instrumented approach), the combination of MRI scans and CT scans helps the surgeon find a better localization of the rootlet compression [3]. First, a conservative approach based on Non-steroidal anti-inflammatory drugs (NSAIDs) and steroids is commonly used thanks to its favorable natural history [4]. Surgery is used only in restricted cases; in patients with severe symptoms, no response to pharmacotherapy within 6–8 weeks or in the presence of neurologic deficits has been reported [2]. In the literature, several surgical approaches have been mentioned for ELDH treatment. The transmuscular paramedian approach to the extraforaminal space, first described by Wiltse and Spencer, is widely considered the standard surgical approach. In fact, no muscle detachment or facet joint removal is needed, reducing the incidence of postoperative instability at the same segment [3, 5]. Medial approaches (complete facetectomy or laminotomy with medial facetectomy) are used to achieve nerve decompression, by sacrificing a significant part of the facet joint [5]. No superiority of one approach over the others has been shown, so surgeons should tailor one approach to their patients' needs [3]. On considering the tiny dimensions of the extruded disk fragment, the application of spinal navigation and spinal endoscopy in implementing minimally invasive techniques seems to offer great advantages.

2 Materials and Methods

This is a retrospective study, performed at the Villa Azzurra private hospital in Syracuse, Italy. Nine patients were treated between August 2015 and June 2016, six men and three women, with a mean age of 57.89 years (range: 47–73 years). The lumbar vertebral levels affected were L2-L3 in one patient, L3-L4 in four patients, and L4-L5 in four patients. Each one reported experiencing radicular pain, paresthesia, and dysesthesias, and six of them presented both lower-back pain. No sensorimotor deficits were present. The side affected by radiculopathy was the left one in three patients and the right one in six patients. The mean time of pain was 10 weeks (range: 6–17 weeks). Each patient underwent preoperative lumbar MRI and CT scans (thin slices, neuronavigation protocol) (Fig. 1).

All surgical procedures were performed by using the Brainlab Quick Spinal Neuronavigation system and a Storz endoscope. After the induction under general anesthesia, patients were in the prone position on the operating table with decubitus cushions. The spinous process of the overlying vertebra and the transverse processes of both vertebrae were first identified with fluoroscopic assistance. A median skin incision was made, and the spinous processes and laminae were detached from the soft tissue. The reference frame was placed in the spinal process, and pointer-guided record-

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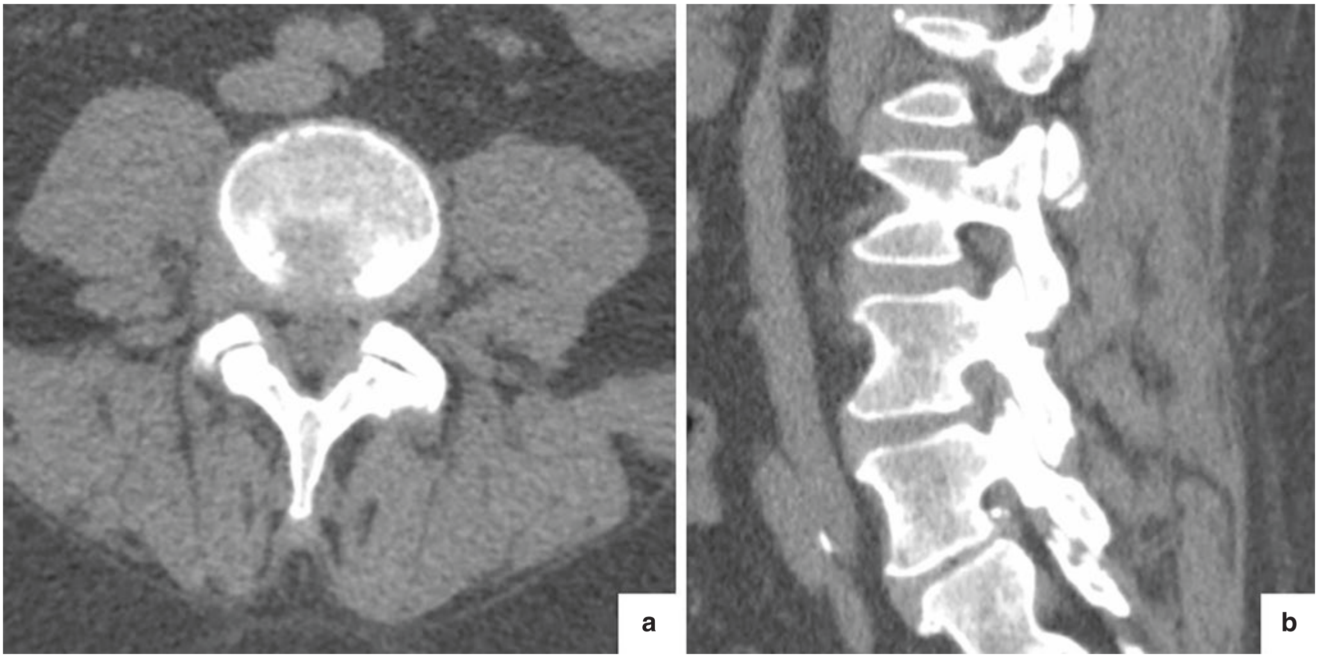

Fig. 1 Thin slices of CT scan showing Right L4-L5 extraforaminal disk herniation: (**a**) axial section; (**b**) sagittal section

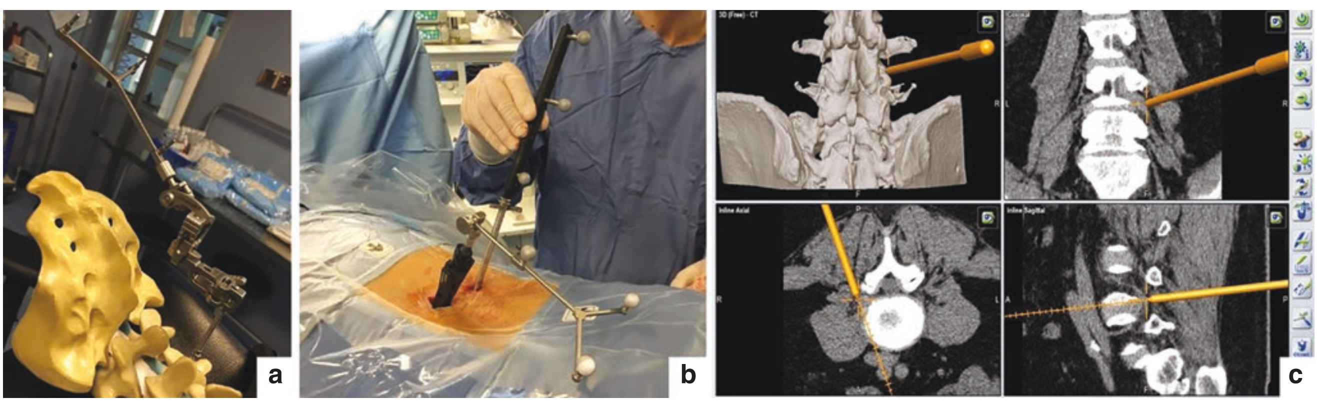

Fig. 2 An illustrative layout of the registration phase: (**a**) The reference frame is placed in the spinal process of the superior vertebra via a median incision (e.g., in the case of an L3-L4 ELDH, the reference frame is placed into the L3 spinal process); (**b**) a pointer-guided paramedian skin incision; (**c**) a neuronavigation view

ings of the vertebra were carried out. Next, a pointer-guided paramedian 1.5 cm skin incision was made. A special custom-made prototype of a percutaneous reference array was used during the endoscopic transtubular approach to the ELDHs (Fig. 2).

First, the initial dilator was registered and advanced to create a safe muscle-splitting way to introduce the tubular retractor system. After sequential dilatation, the final dilatator was introduced, and the endoscope was registered. We Took a purely endoscopic, transmuscular intertransverse approach to the extraforaminal space. The extraforaminal lumbar disk herniations were successfully removed from all the patients. At the end of surgery, no drainage was used, and the wound was closed in the standard fashion (Fig. 3).

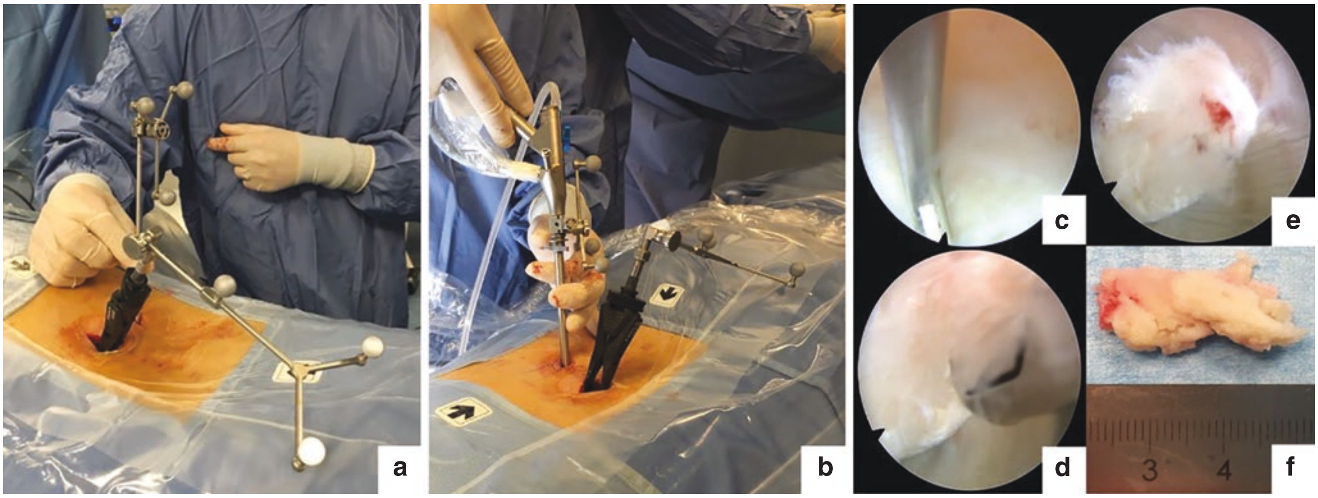

Fig. 3 An illustrative framework of our custom-made prototype: (**a**) placement of dilator; (**b**) neuronavigated endoscope; (**c**, **d**, **e**) microscopic view of extraforaminal herniation; (**f**) complete removal of extraforaminal disk fragment

3 Results

Each patient underwent a day-1 postoperative CT scan. No surgical complications were recorded. Patients were mobilized on the first postoperative day, and they were discharged on postoperative day 1, in the afternoon. The surgical time was measured from skin incision to wound closure. The mean operation time was 47.05 min (range: 42.7–50.1). Patients presented a mean preoperative VAS score of 8.56 (range: 7–10).

We considered the procedure successful if patients showed a >3-point reduction in their respective VAS scores. This reduction was achieved by eight patients at 1 week after surgery and by all of them at 2 months after surgery. We recorded a notable improvement in VAS scores both at the 1-week (3.56, range 1–5) and at the 2-month (1.89; range: 1–4) postoperative examinations. All patients were discharged on postoperative day 1.

4 Discussion

In choosing the best surgical approach for ELDHs, no superiority of one approach over another has been shown. Medial approaches imply the subtotal or total removal of the overlying facet joint, and they aim to achieve an optimal nerve rootlet decompression, which can lead to the destabilization of the motion segment and consequent postoperative back pain. While there is a risk of introducing instability, medial anatomy is well known and familiar to neurosurgeons [3, 5]. The paramedian surgical approach implies a splitting of the paramedian muscles and no bone removal but with direct access to the neural foramen. This does not introduce instability, but the exposed anatomy is not commonly practiced. The safety of performing this approach depends on the surgeons' understanding of the anatomy, and there is a risk of inadequate decompression or causing nerve damage [1, 3, 4, 6].

The most challenging phase during ELDH surgery is finding the exact location of the disk herniation [7]. Surgeons' training limits could be overcome by using an intraoperative neuronavigation system. The device helps in finding the best trajectory to achieve total disk herniation removal without causing neurological deficits on the nerve rootlet. It's a useful tool to help surgeons' orientation and to ensure the safe removal of herniation without causing neurological deficits. The use of neuronavigation when combined with an endoscope helps surgeons in amplifying the operative field without extending the surgical wound [8]. Moreover, the use of progressive dilatators and endoscopes allows a less bloody detachment so that the extraforaminal space can be reached, which achieves a better visualization of the nerve rootlet.

Our data are supported by a recent case series by Yoshikane et al. [9]. A recent work by Liu et al. retrospectively compared patients undergoing surgery via the paramedian approach by using a microscope or an endoscope, which showed the superiority of the endoscopic approach [10]. This new technique enables surgeons to reduce hospital intraoperative timing and thus hospitalization and bed rest after surgery. The preservation of bone structures and surrounding soft tissues, the muscle detachment by using finger as a soft dissector, and the lack of using monopolar cautery also imply less postoperative pain from the muscle detachment [1, 11]. In contrast, in the literature, a higher incidence of postoperative paresthesia or postoperative dysesthesia has been reported, possibly caused by the nerve traction to reach the underlying disk [5]. In our case series, no sensorimotor deficits were shown.

In the literature, the paramedian muscle-splitting approach has been used in several recent case series [1, 2, 12]. The results are promising, but the surgeons' training levels in minimally invasive spine surgery (MISS) to access the extraforaminal discal space are strongly correlated with levels of surgical success [13].

5 Conclusion

Extraforaminal lumbar disk herniations (ELDHs) are rare entities, and their treatment is still challenging. The paramedian muscle-splitting approach should be preferred to avoid the iatrogenic destabilization of vertebral segments. We present a simple and fast technique to perform this approach. In our experience the combination of endoscopy and neuronavigation provide a safe and effective guide in approaching the extreme lateral disk prolaps through the extraforaminal space reducing the risk of intraoperative nerve damage.

Conflicts of Interest The authors declare that they have no conflicts of interest.

References

1. Pirris SM, Dhall S, Mummaneni PV, Kanter AS. Minimally invasive approach to extraforaminal disc herniations at the lumbosacral junction using an operating microscope: case series and review of the literature. Neurosurg Focus. 2008;25(2):E10. https://doi.org/10.3171/FOC/2008/25/8/E10.
2. D'Ercole M, Innocenzi G, Ricciardi F, Bistazzoni S. Prognostic value of Michigan State University (MSU) classification for lumbar disc herniation: is it suitable for surgical selection? Int J Spine Surg. 2021;15:466. https://doi.org/10.14444/8068.
3. Epstein NE. Case presentation and short perspective on management of foraminal/far lateral discs and stenosis. Surg Neurol Int. 2018;9:87. https://doi.org/10.4103/sni.sni_66_18.
4. Evran S, Katar S. Evaluation of the effectiveness of transforaminal epidural steroid injection in far lateral lumbar disc herniations. Ideggyogy Sz. 2021;74:27. https://doi.org/10.18071/isz.74.0027.
5. Viswanathan R, Swamy NK, Tobler WD, Greiner AL, Keller JT, Dunsker SB. Extraforaminal lumbar disc herniations: microsurgical anatomy and surgical approach. J Neurosurg. 2002;96(2 Suppl):206–11. https://doi.org/10.3171/spi.2002.96.2.0206.
6. Al-Khawaja DO, Mahasneh T, Li JC. Surgical treatment of far lateral lumbar disc herniation: a safe and simple approach. J Spine Surg. 2016;2:21. https://doi.org/10.21037/jss.2016.01.05.
7. Ünsal Ü, Senturk S. Minimally invasive far-lateral microdiscectomy: a new retractor for far-lateral lumbar disc surgery. Cureus. 2021;13:e12625. https://doi.org/10.7759/cureus.12625.
8. Nicoletti GF, Umana GE, Chaurasia B, Ponzo G, Giuffrida M, Vasta G, Tomasi SO, Graziano F, Cicero S, Scalia G. Navigation-assisted extraforaminal lumbar disc microdiscectomy: technical note. J Craniovertebr Junction Spine. 2020;11(4):316–20. https://doi.org/10.4103/jcvjs.JCVJS_146_20.
9. Yoshikane K, Kikuchi K, Okazaki K. Posterolateral transforaminal full-endoscopic lumbar discectomy for foraminal or extraforaminal lumbar disc herniations. World Neurosurg. 2020;146:e1278–86. https://doi.org/10.1016/j.wneu.2020.11.141.
10. Liu L, Xue H, Jiang L, Chen H, Chen L, Xie S, Wang D, Zhao M. Comparison of percutaneous transforaminal endoscopic discectomy and microscope-assisted tubular discectomy for lumbar disc herniation. Orthop Surg. 2021;13(5):1587–95. https://doi.org/10.1111/os.12909.
11. Miller JW, Sasso RC. Lumbar extraforaminal decompression: a technical note and retrospective study looking at potential complications as an outpatient procedure. SAS J. 2018;5(1):4–8. https://doi.org/10.1016/j.esas.2010.11.002.
12. O'Toole JE, Eichholz KM, Fessler RG. Minimally invasive far lateral microendoscopic discectomy for extraforaminal disc herniation at the lumbosacral junction: cadaveric dissection and technical case report. Spine J. 2007;7:414. https://doi.org/10.1016/j.spinee.2006.07.008.
13. Wang H, Huang B, Li C, Zhang Z, Wang J, Zheng W, Zhou Y. Learning curve for percutaneous endoscopic lumbar discectomy depending on the surgeon's training level of minimally invasive spine surgery. Clin Neurol Neurosurg. 2013;115:1987. https://doi.org/10.1016/j.clineuro.2013.06.008.

Long-Term Clinical and Radiological Evaluation of Low-Grade Lumbar Spondylolisthesis Stabilization with Rigid Percutaneous Pedicle Screws

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1 Introduction

Decompression with or without instrumented fusion has been advocated for in the treatment of lumbar spondylolisthesis (LS). However, both strategies come with their own drawbacks. Decompression alone is associated with a substantial number of long-term failures and needing reoperations [1], whereas reports of pseudarthrosis showing patients' self-rated excellent clinical outcomes should question the need for fusion, either posterior or interbody [2]. Furthermore, decompression alone was noninferior to decompression with instrumented fusion over a period of 2 years [3]. Instrumented fusions are also associated with important morbidity and excessive costs [4].

The restriction of lumbar spine motion and decrease in intradiscal pressure offered by external immobilization has been shown to control the axial symptoms resulting from LS [5]. This may indicate that the role of spinal instability is a major pathophysiological cause of symptoms. LS internal stabilization with percutaneous pedicles screw (PPS) instrumentation without fusion or decompression may arise as a suitable option. Moreover, PPSs share many of the virtues of minimally invasive spine surgery (MISS) insofar as both limit approach-related morbidity. These concepts enabled us to study the long-term efficacy, including clinical and radiological outcomes, of PPSs on a cohort of 24 patients experiencing LS.

2 Materials and Methods

We performed a retrospective study from prospectively collected data, enrolling 24 consecutive patients with LS presenting with lower-back pain (LBP) and radiculopathy refractory to reasonable conservative treatment. Patients were submitted to PPS stabilization by the same surgeon between 2012 and 2020. Patients with neurogenic claudication, radiculopathy as the only symptom, severe lumbar canal stenosis or disk herniation, or >10° of angular motion lumbar scoliosis (Cobb angle >25°) were excluded from the study.

All patients answered self-completed pre- and postoperative follow-up clinical questionnaires, such as for the Oswestry Disability Index (ODI) and the visual analog scale (VAS). A detailed analgesic medication intake before and at the last follow-up after surgery was also collected. Index-level slippage correction, foraminal and disk height changes, lumbar lordosis (LL), pelvic incidence (PI), pelvic tilt (PT), and sacral slope (SS) were measured on standing neutral plain radiographies of the spine before and after surgery. Segmental range of motion (ROM) measurements of the lumbar spine were derived from full flexion/extension films. Radiological data were obtained by using Sectra Medical Imaging software.

Continuous variables were expressed as the mean (M), median (Mdn), standard deviation (SD), minimum (Min), and maximum (Max), whereas categorical variables are reported as frequencies and percentages. A dependent *t*-test or Wilcoxon test was performed after checking whether the dependent variable showed a normal distribution or not. The difference between a dichotomous dependent variable between two related groups was assessed by using the

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McNemar test. A p-value <0.05 was considered statistically significant.

The Statistical Package for the Social Sciences (IBM-SPSS), version 23, was used for statistical analyses.

3 Results

In total, 24 patients with LS were submitted to only PPSs between 2012 and 2020 by the same neurosurgeon. The mean follow-up was 5.5 ± 2.25 years (range: 1.3–9.7 years). The mean age at the time of surgery was 51.5 ± 10.6. Of the 24 patients, 17 (70.8%) were women and 7 (29.2%) were men. All 24 patients presented with LBP and seven (20.2%) patients also experienced radiculopathy. All the patients presented as either stable or unstable with grade I spondylolisthesis. Furthermore, 21 patients underwent percutaneous fixation at one level (87.5%), two patients at two levels (8.3%), and one patient at three levels (4.1%), which amounts to a total of 28 operated levels (Table 1). The mean operative time was 43.2 ± 12.4 min. The average estimated blood loss was less than 50 mL. There were no intraoperative complications. The mean in-hospital stay time was 1.5 days. The average cost of the procedure was EUR 7085.91.

Table 1 The lumbar levels submitted to percutaneous pedicle screw fixation

Levels	Patient (n/%)
3 levels	
L2-L3; L3-L4; L4-L5	1 (4.2%)
2 levels	
L3-L4; L4-L5	2 (8.3%)
1 level	
L3-L4	1 (4.2%)
L4-L5	8 (33.3%)
L5-S1	12 (50.0%)

A statistically significant decrease in VAS back scores from a mean preoperative score of 8.75 ± 0.94 to a postoperative one of 3.13 ± 1.99 ($p < 0.001$) and in ODI scores from a mean preoperative score of 41.54 ± 8.74 to a postoperative one of 17.33 ± 12.61 ($p < 0.001$) were observed (Table 2). Regarding the intake of analgesic medication, a reduction after surgery was found to have statistical significance for acetaminophen ($p = 0.022$) and statistical nonsignificance for opioids ($p = 0.063$) and for nonsteroidal anti-inflammatory drugs (NSAIDs) ($p = 0.063$). A description of the intake of analgesic medications before and after surgery is shown in Table 3.

On standing dynamic lumbar radiographs, after surgery, the index-level ROM reduced from 5.82 ± 4.54 to 3.62 ± 3.29 ($p = 0.009$). On neutral radiographs, the mean of slippage in the index-level vertebral bodies before surgery was 7.92 ± 3.78 versus 6.22 ± 2.91 after surgery ($p < 0.003$). No change at the index-level foramen height was disclosed (16.32 ± 4.33 versus 16.27 ± 4.36, $p = 0.955$). Postoperatively, a decrease in the mean disk height was shown—from 10.38 ± 5.82 to 9.40 ± 2.80 ($p = 0.026$)—at the expense of anterior disk height reduction ($p < 0.001$) (Table 4).

Regarding spinopelvic parameters, pelvic incidence angle (PI), sacral slope (SS), and pelvic tilt angle (PT) did not improve with the PPS stabilization of LS, as described in Table 4. Segmental lordosis decreased from 9.3 ± 3.97 to 5.40 ± 2.89 ($p < 0.001$), but the PI-LL index changed from 9.97 ± 14.11 to 4.30 ± 9.98 ($p < 0.028$), as shown in Table 5. An illustrative example is shown on Fig. 1.

Table 2 Clinical outcome variations after surgery

Variables	Preoperative	Postoperative	p-Value
VAS score (mean)	8.75 ± 0.94	3.13 ± 1.99	<0.001
ODI score (mean)	41.54 ± 8.74	17.33 ± 12.61	<0.001
Minimal disability (0–20%)	1 (4.2%)	18 (75%)	
Moderate disability (20–40%)	13 (54.2%)	3 (12.5%)	
Severe disability (40–60%)	10 (41.7%)	3 (12.5%)	

Table 3 The intake of analgesic medications before and after surgery

	Acetaminophen		Opioid		NSAID	
	Yes	No	Yes	No	Yes	No
Before surgery	12 (50%)	12 (50%)	5 (20.8%)	19 (79.2%)	10 (41.7%)	14 (58.3%)
After surgery	3 (12.5%)	21 (87.5%)	–	24 (100%)	5 (20.8%)	19 (79.2%)
McNemar test	$p = 0.022$		$p = 0.063$		$p = 0.063$	

Table 4 Radiological outcomes measured before and after surgery

	Preoperative	Postoperative	*p*-Value
Slippage (mm)	7.92 ± 3.78	6.22 ± 2.91	0.003
Anterior disk height (mm)	12.66 ± 3.88	10.62 ± 3.44	0.001
Posterior disk height (mm)	7.61 ± 2.49	8.18 ± 2.66	0.209
Mean disk height (mm)	10.38 ± 2.85	9.40 ± 2.80	0.026
Foramen height (mm)	16.32 ± 4.33	16.27 ± 4.36	0.955
Segmental angle (°)	9.3 ± 3.97	5.40 ± 2.89	< 0.001
Segmental ROM (°)	5.82 ± 4.54	3.46 ± 3.22	0.009

ROM range of motion

Table 5 Spinopelvic parameter variations induced by percutaneous pedicle screw stabilization

	Before surgery	After surgery		Literature reference values [6]
	Mean; [Min–Max]	Mean; [Min–Max]	*p*-Value	Mean; [Min–Max]
Lumbar lordosis (LL) (°)	67.04 ± 7.46; [50.4–75.5]	62.31 ± 5.57; [50.8–72.3]	0.069	–; [30° –79°]
Pelvic incidence (PI) (°)	57.07 ± 9.55; [44.8–77.9]	56.98 ± 13.72; [26.0–78.5]	0.468	52°; [34°–84°]
Pelvic tilt (PT) (°)	14.94 ± 6.47; [3.4–28.5]	16.43 ± 7.18; [5.3–30.9]	0.434	12°; [5°–30°]
Sacral slope (SS) (°)	42.13 ± 6.69; [32.1–53.5]	42.18 ± 6.87; [25.7–53.4]	0.964	40°; [20°–65°]
Difference in PI-LL (°)	−9.97 ± 14.11	−4.30 ± 9.98	0.028	LL = PI +9°

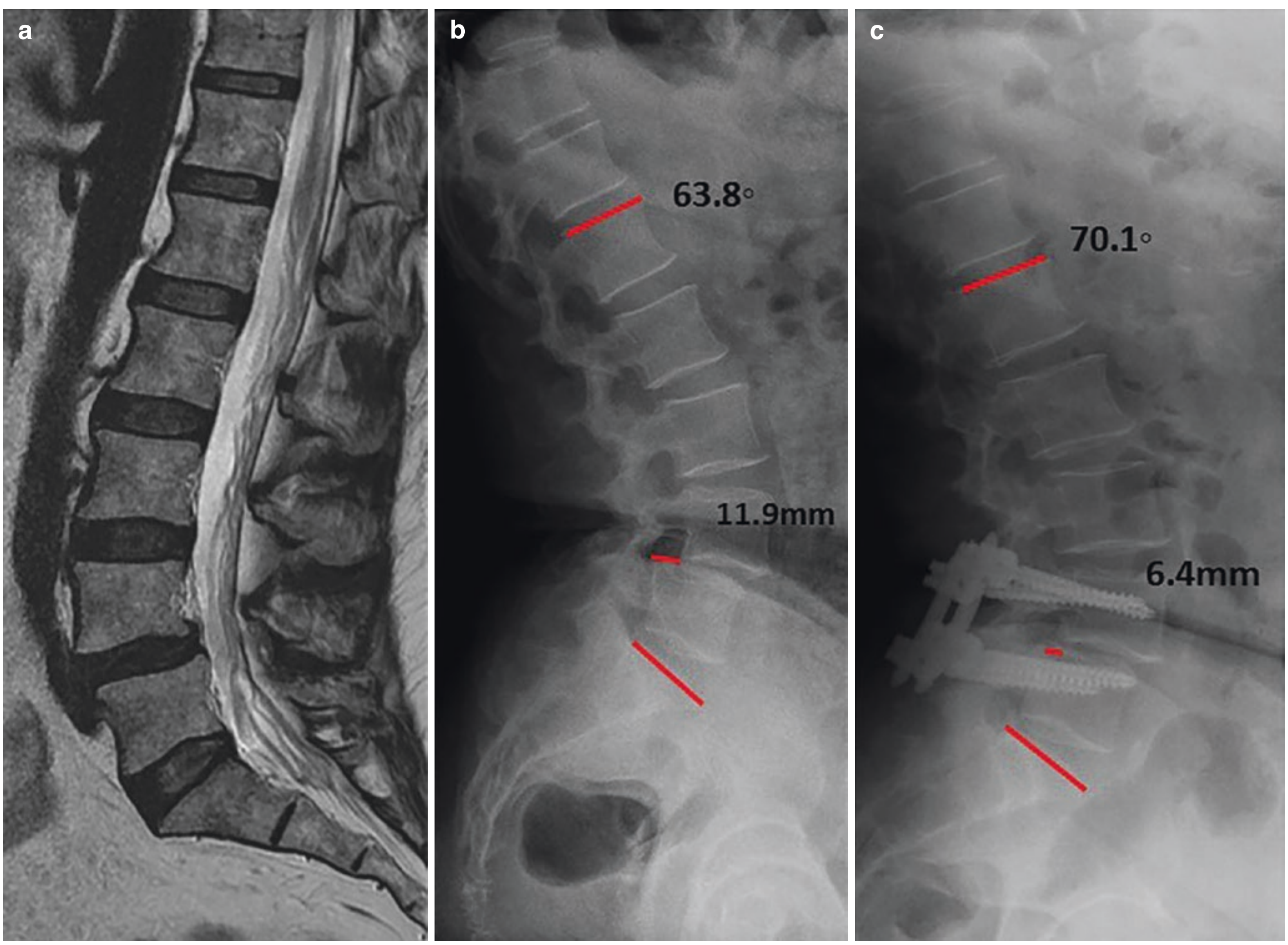

Fig. 1 (**a**) T2 sagittal MRI from a 68-year-old woman presenting with a L4–5 grade I degenerative spondylolisthesis causing long-standing refractory LBP (VAS 9; 50% ODI scale) that improved postoperatively (VAS: 4; ODI: 24%); (**b**, **c**) standing lumbar spine radiographs on lateral view showing an increase in preoperative LL from 63.8° to 70.1° and a reduction in L4–5 slippage from 11.9 to 6.4 mm; 6-year follow-up showing foraminal height preservation. *VAS* visual analog scale, *ODI* Oswestry Disability Index

4 Discussion

There is controversy about the gold-standard technique for the surgical treatment of lumbar spondylolisthesis. In LS, symptoms arise from a varying combination of canal and/or foraminal stenosis and mechanical instability. Decompression can be obtained by either the direct release of neural compression or by the indirect distraction of the neural foramen through interbody devices or pedicle screws. Instrumentation also serves to increase the fusion rate to prevent or abolish mechanical instability, to tackle LBP of the facet joint or disk origin, restore sagittal alignment, and correct the slippage.

However, several reports have questioned the need for fusion in all LS patients [3, 5]. The SPORT trial reported that clinical outcomes (short-form-36 (SF-36) bodily pain and physical function scales and the modified ODI (AAOS/Modems version)) are not always better with solid fusion compared with pseudarthrosis groups at 4-year follow-ups [7]. A fibrous union appears to provide sufficient stabilization and to provide pain relief of the back and lower extremities [8]. Although pseudarthrosis developed in 55% of patients in the noninstrumented group, the clinical outcome was still noted to be excellent or good in 15 of 18 patients (83%), reflecting a lack of understanding on the exact mechanism of pain relief [9]. According to Goel et al., the reduction or elimination in segmental range of motion results in the alleviation of lumbar pain, and consequently, stabilization can shape the cornerstone of treatment without the need for any kind of decompression [10]. When treating patients who have degenerative LS by using dynamic stabilization only, at 4-year follow-ups, Schaeren et al. found that VAS and walking distance significantly improved ($p < 0.001$), spondylolisthesis did not progress, and motion segments remained stable, leading to 95% rate of patient satisfaction [11]. Furthermore, complex fusion is associated with hospital and 5-year overall costs, owing to subsequent reoperation rates at index or adjacent levels and to the 90-day complication rates that are significantly higher (64% versus 5.52%) than decompression alone [12]. On the decompression alone side, Fox et al. found a 25% rate of new postoperative slippage in patients without prior spondylolisthesis and an increase in slippage in 57% of patients with prior spondylolisthesis after laminectomy without partial or total facetectomy [1], in accordance with the biomechanical work that has demonstrated an increase in segmental mobility following a disruption in the posterior osseoligamentous structures in bilateral laminectomy [13]. Finally, stabilization with interlaminar devices, which are less rigid than pedicle screws are, significantly outperformed fusion controls in several clinical outcomes [14].

These findings encouraged us to evaluate the effects of lumbar stabilization with rigid PPSs on the treatment of LS as an intermediate option between decompression alone and solid fusion. Zhao et al., reporting on 781 patients, established the PPS as a safe and reliable technology with a spurious rate of screw-related complications [15]. Similar safety can be derived from our study, which counted only one case (one of 106 screws) of screw breakage, without any screw malpositioning, screw pullout, vascular or visceral injury, or infection. PPSs share the merits of minimally invasive surgery (MIS) techniques in reducing approach-related morbidity. In this study, we report a vestigial loss of blood, a mean operation time of 43.2 ± 12.4 min, and a mean in-hospital stay of 1.5 days, which is notably less than that observed in other types of open or MIS fusion techniques. A significant reduction in analgesic intake was reached, revealing less long-term postoperative pain as a result of paraspinal muscle preservation from an iatrogenic injury, positively influencing patients' satisfaction. Furthermore, using a percutaneous technique for pedicle screw insertion significantly reduces the risk of injury to the medial branch nerve that innervates the multifidus muscle, when compared to open approach (205% versus 84%, respectively) [16].

In parallel to analgesic intake reduction, we report the effective control of LBP and radicular pain, as well as a significant improvement in ODI values, consistent with the elimination of chronic pain from the iliac crest bone graft harvest site; nerve root manipulation or retraction and broad dissection beyond the facet joint; and, above all, segment immobilization afforded by the PPSs. This result is even more relevant if we take into account that most of our patients showed a mean preoperative slippage of 7.92 mm and an angular motion of 5.82°, denoting unstable cases of LS. Cadaveric studies have shown that pedicle screws outperform interbody cages in treating spondylolisthesis [17]. Pedicle screws significantly limit all ranges of motion (ROMs) in the lumbar spine (72% flexion/extension; 68.5% lateral bending; and 39% axial rotation) [18]. This is relevant to avoiding pain-generating stimuli, such as an increase in intradiscal pressure and foraminal compression in the extremes of ROM, especially in cases of borderline foraminal compression. Bilateral pedicle screws are superior to interlaminar devices in controlling range of motion in all directions, especially in lateral bending. The key role of PPSs in primary stability can be understood in posterolateral fusion cohorts who showed significant improvements in clinical results, as early as 1-month after surgery, when fusion had not yet been achieved [19]. In our series, a clear drop in ROM at the index level, from 5.82° ± 4.54° to 3.46° ± 3.22° ($p = 0.009$), was demonstrated, where the immediate stability effect was amplified because the percutaneous technique spared all the posterior band tension elements (Fig. 2). A similar phenomenon was detailed at multiple early postoperative time points with interlaminar device (ILD) cohorts

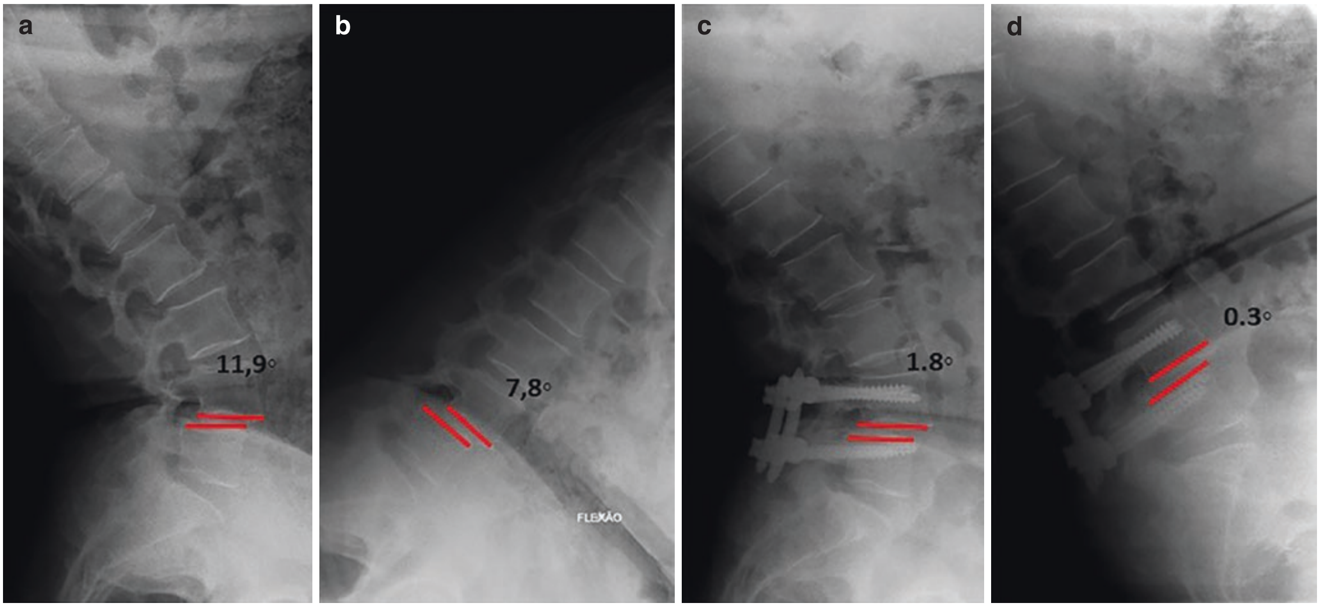

Fig. 2 Preoperative (**a**, **b**) and postoperative (**c**, **d**) standing lumbar spine radiographs on lateral view demonstrating at L4–5 a postoperative decrease in ROM from 4.1° to 1.5°

whose patients experienced improved outcomes, even though ILDs perform less well than pedicle screws in controlling spondylolisthesis, which is a rotary deformity and not a simple forward (or backward) displacement.

Contributing factors to positive clinical outcomes included the significant reduction in spondylolisthesis slippage ($p < 0.003$) and the maintenance of foramen height ($p = 0.955$) at the last follow-up. Reducing spondylolisthesis may improve sagittal alignment by moving the C7 plumb line more posterior to the anterior sacrum, and it may also indirectly decompress the nerve root by increasing the cross-sectional area in the foramen and lateral recess. Pedicle screws are as effective as interbody cages in reducing listhesis and restoring disk height [20]. The mean index segment disk height was reduced ($p = 0.026$) at the expense of a loss in anterior disk height ($p = 0.001$). The mean posterior disk height increased, though not significantly, reflecting a distractive force applied to the final construct; this result is in opposition to other reports that have found a significant decrease compared to the baseline, as a result of compression. Nevertheless, the vertebral disk height results were achieved as early as 1 week after surgery and maintained at the last follow-up, a phenomenon that is not fusion dependent but rather related to pedicle screw biomechanics, according to Kuraishi et al. [19].

Our results were in accordance with the findings of Ferrero et al. for LS patients in that spondylolisthesis was characterized by an abnormal sacropelvic morphology, disturbing the global sagittal balance of the spine. LS patients presented greater PI angles (58.8° vs. 53.2°, $p < 0.001$) and smaller lumbar lordosis values than asymptomatic subjects did [21]. By applying a leverage distractive force in the final tightening of the construct, in order to obtain a foraminal height increase, a kyphotic effect was obtained at the index level (the segmental angle decreased from 9.3° ± 3.97° to 5.40° ± 2.89°, $p < 0.001$). Opposite variations in anterior disk height and posterior disk height confirm this effect. Despite the occurrence of segmental kyphosis, only one case (4.1%) of screw breakage was detected, but it did not need reoperation. There were no significant changes in PI, PT, or SS. Although a nonsignificant loss of LL was identified, the PI-LL index values varied significantly, from −9.97 ± 14.11 to −4.3 ± 9.98 ($p = 0.028$). This corrected the mismatch between LL and PI, which we identify as a contributing factor of the superior clinical outcomes. Duval-Beaupere et al. proposed a formula for predicting lumbar lordosis: LL = PI +9° (± 9°) [22]. A mismatch between PI and LL reflects an inadequate amount of LL and a global malalignment.

In our study, the mean slippage was 7.92 mm with less than 10° of angulation, as assessed by dynamic standing radiographs. Nevertheless, the long-term incidence of reoperation was lower than the incidence reported by Blumenthal et al. in their study on patients with no instability: 4% at a mean follow-up of 5 years versus 37.5% at a mean follow-up of 3 years in a well-designed prospective study on open laminectomies in 58 patents with preoperative slippage [23]. Our reoperation rate also ranked as inferior to cohorts of patients treated with decompression and fusion that required secondary surgeries [24]. Our PPS constructs exhibited much less stiffness than fusion ones, resulting in less excessive load on adjacent segments. Despite a significant rise in the proportion of fusion surgeries for LS (31.13% in the 2003 versus 91.54% in the 2008 cohort), it failed to reduce the reoperation probability in the 2008 cohort (8.1%) compared with that in the 2003 cohort (6.2%) [25]. Early reoperation owing to adjacent segment pathology was most common in the laminectomy/fusion group (13.3%), whereas same-level recurrence was significantly higher in the interlaminar device group (33.3%) ($p < 0.0001$) [26]. In Grob et al.'s study ($n = 50$) on dynamic pedicle screw fixation with and without decompression, back and leg pain improved in 67% of patients, but their functional capacities improved only 40%, with a high rate of reoperation (19%) [2]. Unequivocally, our results, with a more rigid construct without any direct decompression, showed far better clinical results. This suggests that more-rigid constructs should be selected if open decompression is performed, adapting the surgical option to patient selection.

Our study has a limitation insofar as it is not a comparative study featuring decompression and different fusion techniques.

5 Conclusions

To the best of our knowledge, this is the first study in the literature to provide evidence that rigid percutaneous pedicle screws alone in the treatment of low-grade LS are associated with LBP control and favorable radiological outcomes. The effective mechanical stabilization provided by PPSs may challenge the relevance of routine fusion for all LS patients. This quick, safe, and less technically demanding technique, being replicable by a larger number of surgeons, may fill the gap between decompression alone and solid fusion procedures. In the decision-making process, variables that can be used to assist in identifying the most appropriate therapeutic pathway need to be identified. Accordingly, further randomized controlled studies are needed to achieve more-robust conclusions.

Conflict of Interest The authors declare that they have no conflicts of interest to disclose.

References

1. Fox MW, Onofrio BM, Onofrio BM, Hanssen AD. Clinical outcomes and radiological instability following decompressive lumbar laminectomy for degenerative spinal stenosis: a comparison of patients undergoing concomitant arthrodesis versus decompression alone. J Neurosurg. 1996;85(5):793–802.
2. Grob D, Benini A, Junge A, Mannion AF. Clinical experience with the Dynesys semirigid fixation system for the lumbar spine: surgical and patient-oriented outcome in 50 cases after an average of 2 years. Spine. 2005;30(3):324–31.
3. Austevoll IM, Hermansen E, Fagerland MW, Storheim K, Brox JI, Solberg T, Rekeland F, Franssen E, Weber C, Brisby H, Grundnes O, Algaard K, Böker T, Banitalebi H, Indrekvam K, Hellum C, NORDSTEN-DS Investigators. Decompression with or without fusion in degenerative lumbar spondylolisthesis. N Engl J Med. 2021;385(6):526–38.
4. Deyo RA, Mirza SK, Martin BI, Kreuter W, Goodman DC, Jarvik JG. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. JAMA. 2010;303(13):1259–65.
5. Newcomer K, Laskowski ER, Yu B, Johnson JC, An KN. The effects of a lumbar support on repositioning error in subjects with low back pain. Arch Phys Med Rehabil. 2001;82(7):906–10.
6. Savarese LG, Menezes-Reis R, Bonugli GP, Herrero C, Defino H, Nogueira-Barbosa MH. Spinopelvic sagittal balance: what does the radiologist need to know? Radiol Bras. 2020;53(3):175–84.
7. Abdu WA, Lurie JD, Spratt KF, Tosteson AN, Zhao W, Tosteson TD, Herkowitz H, Longely M, Boden SD, Emery S, Weinstein JN. Degenerative spondylolisthesis: does fusion method influence outcome? Four-year results of the spine patient outcomes research trial. Spine. 2009;34(21):2351–60.
8. Mardjetko SM, Connolly PJ, Shott S. Degenerative lumbar spondylolisthesis. A meta-analysis of literature 1970–1993. Spine. 1994;19(20 Suppl):2256S–65S.
9. Fischgrund JS, Mackay M, Herkowitz HN, Brower R, Montgomery DM, Kurz LT. 1997 Volvo Award winner in clinical studies. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. Spine. 1997;22(24):2807–12.
10. Goel A, Ranjan S, Shah A, Patil A, Vutha R. Lumbar canal stenosis: analyzing the role of stabilization and the futility of decompression as treatment. Neurosurg Focus. 2019;46(5):E7.
11. Schaeren S, Broger I, Jeanneret B. Minimum four-year follow-up of spinal stenosis with degenerative spondylolisthesis treated with decompression and dynamic stabilization. Spine. 2008;33(18):E636–42.
12. Lad SP, Babu R, Baker AA, Ugiliweneza B, Kong M, Bagley CA, Gottfried ON, Isaacs RE, Patil CG, Boakye M. Complications, reoperation rates, and health-care cost following surgical treatment of lumbar spondylolisthesis. J Bone Joint Surg Am. 2013;95(21):e162.
13. Gillespie KA, Dickey JP. Biomechanical role of lumbar spine ligaments in flexion and extension: determination using a parallel linkage robot and a porcine model. Spine. 2004;29(11):1208–16.
14. Davis R, Auerbach JD, Bae H, Errico TJ. Can low-grade spondylolisthesis be effectively treated by either coflex interlaminar stabilization or laminectomy and posterior spinal fusion? Two-year clinical and radiographic results from the randomized, prospective, multicenter US investigational device exemption trial: clinical article. J Neurosurg Spine. 2013;19(2):174–84.
15. Zhao Q, Zhang H, Hao D, Guo H, Wang B, He B. Complications of percutaneous pedicle screw fixation in treating thoracolumbar and lumbar fracture. Medicine. 2018;97(29):e11560.
16. Regev GJ, Lee YP, Taylor WR, Garfin SR, Kim CW. Nerve injury to the posterior rami medial branch during the insertion of pedicle screws: comparison of mini-open versus percutaneous pedicle screw insertion techniques. Spine. 2009;34(11):1239–42.
17. Cagli S, Crawford NR, Sonntag VK, Dickman CA. Biomechanics of grade I degenerative lumbar spondylolisthesis. Part 2: treatment with threaded interbody cages/dowels and pedicle screws. J Neurosurg. 2001;94(1 Suppl):51–60.
18. Pradhan BB, Turner AW, Zatushevsky MA, Cornwall GB, Rajaee SS, Bae HW. Biomechanical analysis in a human cadaveric model of spinous process fixation with an interlaminar allograft spacer for lumbar spinal stenosis: laboratory investigation. J Neurosurg Spine. 2012;16(6):585–93.
19. Kuraishi S, Takahashi J, Mukaiyama K, Shimizu M, Ikegami S, Futatsugi T, Hirabayashi H, Ogihara N, Hashidate H, Tateiwa Y,

Kinoshita H, Kato H. Comparison of clinical and radiological results of posterolateral fusion and posterior lumbar interbody fusion in the treatment of L4 degenerative lumbar spondylolisthesis. Asian Spine J. 2016;10(1):143–52.
20. Fujimori T, Le H, Schairer WW, Berven SH, Qamirani E, Hu SS. Does transforaminal lumbar interbody fusion have advantages over posterolateral lumbar fusion for degenerative spondylolisthesis? Global Spine J. 2015;5(2):102–9.
21. Ferrero E, Ould-Slimane M, Gille O, Guigui P, French Spine Society (SFCR). Sagittal spinopelvic alignment in 654 degenerative spondylolisthesis. Eur Spine J. 2015;24(6):1219–27.
22. Schwab F, Lafage V, Patel A, Farcy JP. Sagittal plane considerations and the pelvis in the adult patient. Spine. 2009;34(17):1828–33.
23. Blumenthal C, Curran J, Benzel EC, Potter R, Magge SN, Harrington JF Jr, Coumans JV, Ghogawala Z. Radiographic predictors of delayed instability following decompression without fusion for degenerative grade I lumbar spondylolisthesis. J Neurosurg Spine. 2013;18(4):340–6.
24. Wang T, Ding W. Risk factors for adjacent segment degeneration after posterior lumbar fusion surgery in treatment for degenerative lumbar disorders: a meta-analysis. J Orthop Surg Res. 2020;15(1):582.
25. Kim CH, Chung CK, Choi Y, Kim MJ, Kim MJ, Shin S, Yang SH, Hwang SH, Kim DH, Park SB, Lee JH. Increased proportion of fusion surgery for degenerative lumbar spondylolisthesis and changes in reoperation rate: a nationwide cohort study with a minimum 5-year follow-up. Spine. 2019;44(5):346–54.
26. Brodke DS, Annis P, Lawrence BD, Woodbury AM, Daubs MD. Reoperation and revision rates of 3 surgical treatment methods for lumbar stenosis associated with degenerative scoliosis and spondylolisthesis. Spine. 2013;38(26):2287–94.

Fluoroscopy-Assisted Freehand Versus 3D-Navigated Imaging-Assisted Pedicle Screw Insertion: A Multicenter Study

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1 Introduction

Vertebral fusion performed by segmented pedicle screw fixation is a globally well-established method to restore spine stability, preserve neurological function, and relieve pain and neurological symptoms. Pedicle screw fixation improves and restores the stability of spine biomechanics in patients with traumatic vertebral fractures, degenerative disease (stenosis/spondylolisthesis), neoplastic disease (primary or secondary), infective disease (spondylodiscitis), or spine deformities [1]. Potential errors in screw placement implies muscular, bone, vascular, or neuronal lesions, resulting in major or minor complications, from postoperative pain or neurological deficits up to life-threatening conditions, such as vascular complications [2].

The intraoperative control provided by using a C-arm fluoroscope was one of the first techniques to assess screw trajectory, obtaining 2D image projections. However, a high rate of misplacement, from 14% to 40%, has been reported [3–5].

One of the latest techniques developed to further lower the misplacement rate is the three-dimensional (3D) cone-beam computed tomography (CT) O-arm (Medtronic Navigation, Louisville, CO, USA), which allows for the intraoperative 3D acquisition of vertebral images. The 3D images can be used by the neuronavigation system, StealthStation (Medtronic Navigation, Louisville, CO, USA), which provides direct 3D path control for screw placement.

This is a retrospective, multicenter study evaluating the mispositioning rate of 1288 peduncular screws in a population of 222 patients, screws that were placed with the freehand technique thanks to C-arm assistance and the O-arm II Complete Multidimensional Surgical Imaging System (Medtronic Navigation, Louisville, CO, USA), coupled with the StealthStation navigation system (Medtronic Navigation, Louisville, CO, USA).

2 Materials and Methods

From January 2018 to January 2020, 222 patients in total from two neurosurgical complex units were enrolled in this study. Patients were divided into group A and group B. Group A included 107 patients (59 women, 55.14%; 48 men, 44.86%), whose mean age was 57 years and 6 months. Patients in this group underwent spinal fusion with peduncular screws placed with the freehand technique with the help of C-arm assistance at the Neurosurgical Unit of the University Hospital of Palermo. Group B included 115 patients (62 women, 53.91% and 53 men, 46.09%), whose mean age was 62 years and 7 months. Patients in this group underwent pedicular screws placed with the O-arm II

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Complete Multidimensional Surgical Imaging System (Medtronic Navigation, Louisville, CO, USA), coupled with the StealthStation navigation system (Medtronic Navigation, Louisville, CO, USA) at the Neurosurgical Unit of the ARNAS Garibaldi in Catania.

Clinical inclusion criteria incorporated both clinical and radiological aspects, comparatively lower back pain with or without radiculopathy, claudicatio spinalis or motor or sensory neurological impairment, and the presence of a herniated disk, spinal stenosis, a traumatic fracture, or degenerative lystesis. In this study, patients with previous spinal surgery, patients with any neoplastic or infective spinal deformity, and patients affected by severe osteoporosis or any comorbidities compromising their eligibility for the surgery were excluded. In group A, proper peduncular screw placement was checked day 1 after surgery with a 3D spine CT. In group B, at the end of the surgical treatment, the 3D acquisition of images was carried out with the O-arm system, and these images were obtained to evaluate proper screw placement. In all cases, polyaxial screws with a diameter from 5.5 to 6.5 mm and a length from 45 to 75 mm were inserted.

On the radiological CT images, the screw trajectory and potential screw misplacement were estimated by using the Gertzbein–Robbins classification (Fig. 1) [6]. Clinical and demographic data, including age, sex, and operative time, are reported in Table 1. In Fig. 2, the screws' surgical placements in the different levels are documented.

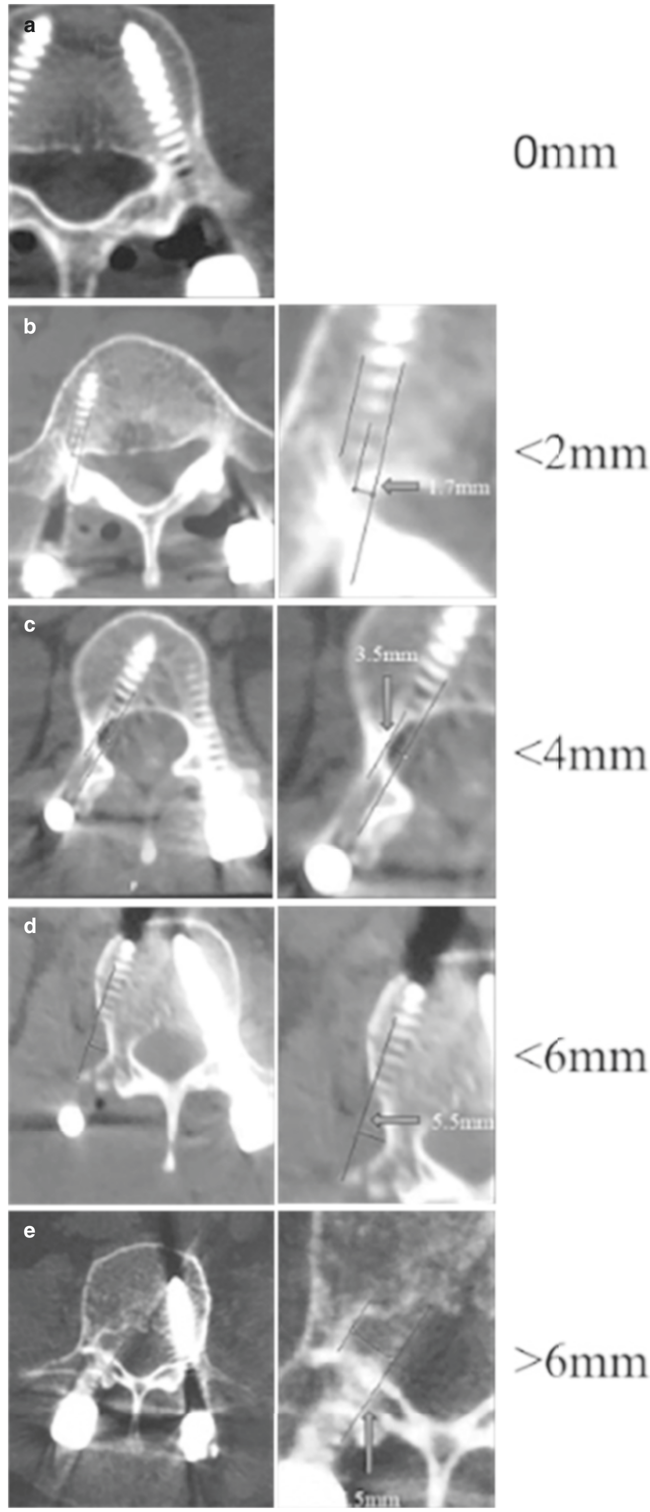

Fig. 1 The Gertzbein–Robbins classification: Transpedicular screw position is graded from (**a**) to (**e**) according to breaches in the pedicle cortex, where Grade (**a**) refers to a fully intrapedicular position without a breach in the pedicle cortex; Grade (**b**) refers to a pedicle cortical breach <2 mm; Grade (**c**) refers to a pedicle cortical breach between 2 and 4 mm; Grade (**d**) refers to a pedicle cortical breach between 4 and 6 mm; and Grade (**e**) refers to a pedicle cortical breach >6 mm or one outside of the pedicle

Table 1 Clinical and demographic data

	Freehand	O-Arm	Total
No. of patients	107	115	222
Male (%)	48 (44.9)	53 (46.1)	101 (45.5)
Female (%)	59 (55.1)	62 (53.9)	121 (54.5)
Age, years (range)	57.5 (21–76)	62.6 (21–78)	
No. of screws	665	643	1288
Average no. of screws per patient (range)	6.21 ± 2.1 (4–14)	5.59 ± 1.6	
Surgical time	3 h 57 min ± 1 h 07 min	4 h 21 min ± 1 h 41 min	

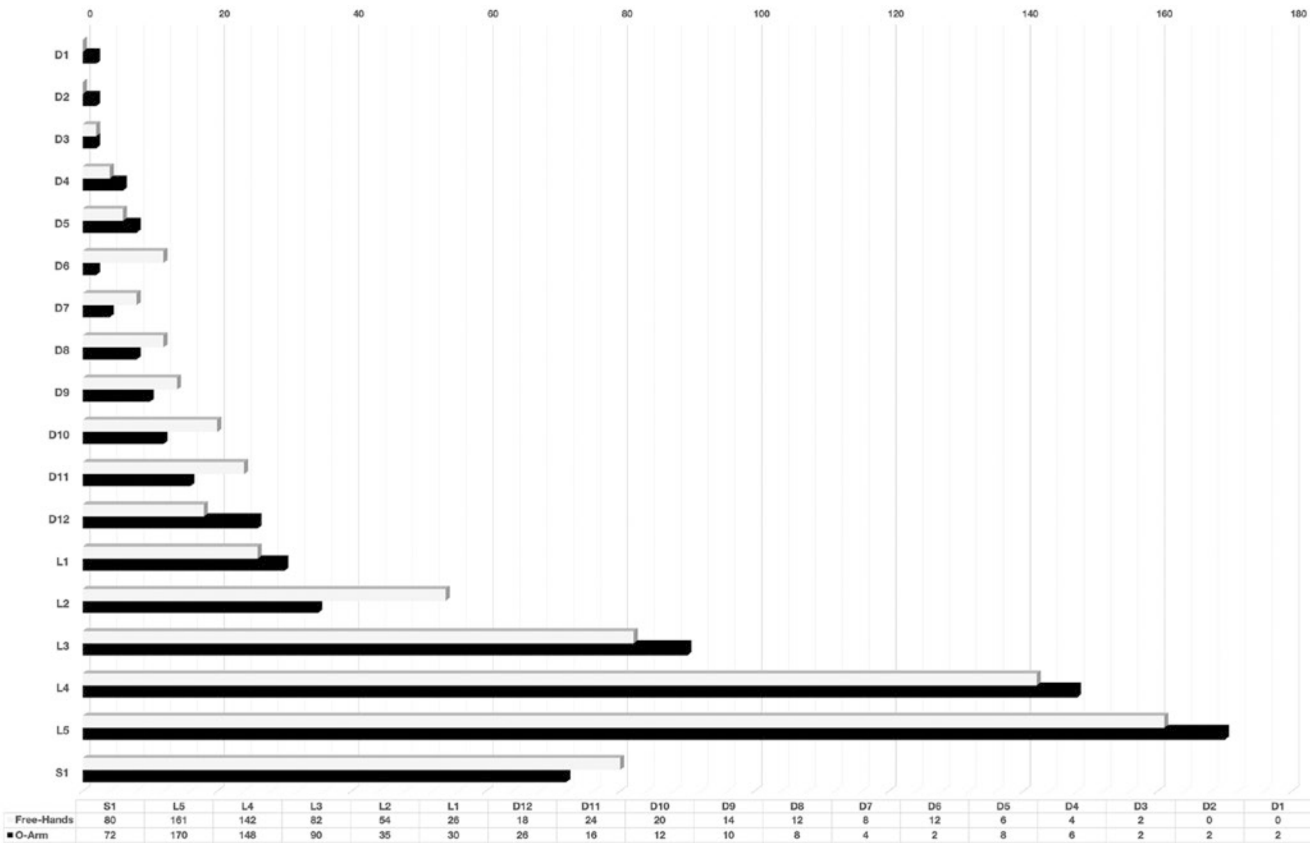

Fig. 2 Levels of screw positioning

3 Results

The study included 222 patients for a total of 1288 implanted pedicular screws. Group A included 107 patients (59 women, 55.14% and 48 men, 44.86%), whose mean age was 57 years and 6 months. Patients in this group underwent spinal fusion with peduncular screws placed with the freehand technique thanks to C-arm assistance. The median operative time was 3 h and 57 min (standard deviation: 1 h and 7 min). Group B included 115 patients (62 women, 53.91% and 53 men, 46.09%), whose mean age was 62 years and 7 months. Patients in this group underwent spinal fusion with pedicular screws placed with the O-arm II Complete Multidimensional Surgical Imaging System (Medtronic Navigation, Louisville, CO, USA), coupled with the StealthStation navigation system (Medtronic Navigation, Louisville, CO, USA). The median operative time was 4 h and 21 min (standard deviation: 1 h and 41 min).

Table 2 Grade of pedicular screws' misplacement according to the Gertzbein-Robbins classification respectively in Freehand and O-Arm group of patients

Gertzbein–Robbins classification	Freehand no. (%)	O-Arm no. (%)
Grade A (complete)	617 (92.78%)	631 (98.13%)
Grade B (0–2 mm)	13 (1.95%)	11 (1.71%)
Grade C (2–4 mm)	19 (2.86%)	1 (0.16%)
Grade D (4–6 mm)	14 (2.11%)	–
Grade E (> 6 mm)	2 (0.3%)	–
Anterior cortical perforation	8 (1.2%)	4 (0.6%)
Lateralization	10 (1.5%)	8 (1.2%)
Revision surgery	5 pz	2 pz

In group A, 665 screw were positioned. Cortical peduncular rupture occurred in 43 patients (40.19%), for a total of 56 misplaced screws (8.42%). In detail, according to the Gertzbein–Robbins classification, 13 screws were Grade B, 19 Grade C, 14 Grade D, and two Grade E. The placement of eight screws (1.2%) implied cortical anterior vertebral body rupture, and in ten cases, the screws were lateralized (Table 1). In four cases, a revision surgery for pedicular screws was required because of neurological compromise.

In group B, 643 pedicular screws were placed. In 12 patients, cortical pedicular rupture occurred (10.43%), for a total of 12 misplaced screws (1.87%). In detail, according to the Gertzbein–Robbins classification, 11 screws were Grade B and one was Grade C. No Grade D or Grade E screws were reported. Among those cases, only in two cases was a revision surgery required. Four screws (0.62%) ruptured the vertebral cortical anterior body, and in eight cases, the screws were lateralized (Table 2).

4 Discussion

Spinal arthrodesis is a well-known surgical procedure that aims to restore functional spine unit (FSU) integrity. Spinal arthrodesis stability is related to proper peduncular screw placement. The use of C-arm fluoroscopy in the freehand technique has improved surgical outcomes, decreasing the mispositioning rate to around 10–40% [7, 8].

Technological advancement in the surgical field has favored the development of intraoperative neuroimaging that has aimed to provide live radiological images of surgical instrumentation to improve performance accuracy. The intraoperative imaging guidance system was developed to prevent complications related to instrumented spine surgery [9–11]. In 1982, Shalit and Lunsford first introduced the use of CT imaging in operating theaters, applying it mainly to brain surgery [12, 13]. A computer-assisted navigation system was used for pedicle screw fixation for the first time in 1995, and since then, various kinds of equipment have been developed, including 3D intraoperative imaging systems [14]. Among these, the O-arm (Medtronic Surgical Navigation Technologies, Louisville, CO, USA) represents an effective device that acts as a platform for image-guided procedures when connected to a navigation system [15]. In this way, it was possible to improve the accuracy of transpedicular screw positioning, lowering the mispositioning rate to around 5% [16, 17].

Our study compared the accuracy rate of screw placement, showing that the freehand group had a mispositioning rate of 8.42% and that the O-arm group had a rate of 1.87%, corroborating the fact that the real-time vision of the screw trajectory can reduce the risk of incorrect positioning and therefore of surgical complications. In Grade A, the screw is perfectly positioned inside the pedicle, without interrupting the vertebral cortex; in Grade B, the screw violates the pedicle cortex by less than 2 mm; in Grade C, the violation of the pedicle cortex is between 2 and 4 mm; in Grade D, the violation of the pedicle cortex is between 4 and 6 mm; and in Grade E, the violation of the pedicle cortex is greater than 6 mm. The data reported in the study show that the need for surgical revision was essentially halved. The study also made it possible to show the existence of a safety zone near the medial portion of the pedicle, consisting of the subarachnoid and epidural spaces with a size between 1 and 4 mm, which suggests that the pedicle cortex is smaller than 2 mm, so Grade B screw placements are to be considered acceptable because they are silent according to a clinical and biomechanical point of view [18]. Given that Grade B screws are adequately positioned, our data highlight the greater ability of the O-arm neuronavigation system to reduce the mispositioning that is truly responsible for postoperative complications.

Regarding the risk of perforating the anterior cortex of the vertebral body—attributable to the placement of an excessive number of transpedicular screws, excessive when compared to the anatomical dimensions of the vertebral body—it has been shown that this event occurred in four cases in the O-arm group (0.64%) versus in eight cases (1.2%) in the freehand group. This result is attributable to the use of neuronavigation system software programs, which allow the simulation of the screws in such a way as to be able to determine their correct dimensions for thickness and length, a determination that in the freehand group entirely depends on the experience level of the surgeon and on careful preoperative planning. On the other hand, the rates of lateral malposition are comparable, where ten cases of violating the lateral cortex of the pedicle were found in the freehand group and eight in the O-arm group.

This phenomenon seems to be attributable to the difference between the median longitudinal axis of the pedicle (the ideal trajectory of the screw) and the anatomically feasible axis in clinical practice. In these cases, the surgeon therefore accepts the possibility of a cortical perforation that is compatible with the reduced number of neurological complications attributable to it [19].

Although this technological advancement has yielded important advantages in spinal surgery, it is still possible to detect a series of problems capable of justifying the persistence of errors, albeit only a few, in the calibration of intraoperative navigation with an O-arm. These errors can be divided into the following:

1. Irremediable errors are attributable in part to inevitable manufacturing errors that involve a nonabsolute correspondence to the neuronavigation recording technique, owing to on one hand distortions in the radiation cone used for the reconstruction of the image and on the other hand the use of polyaxial screws that, although they guarantee great advantages from the surgical point of view, could lead to slight changes in the trajectory [20, 21].
2. Reversible errors may result from the inadequate positioning of the detection devices, which should be placed at a distance that is as close as possible to the surgical field and at the same time constantly within the visual field of the navigation system optics. This proximity to the surgical field increases the risk of accidental contact by surgeons during the procedure and decreases navigation accuracy [22–26].

The introduction of the reference device, used in our study, where this device is not subject to any type of movement, because it is firmly screwed to the spinous process, allows for an early recognition of the loss of accuracy in the calibration of the neuronavigation system and allows for a further reduction in the degree of mispositioning the transpedicular screws, lowering the mispositioning rate to 1%.

As highlighted in this study, CT-guided intraoperative navigation involves a slight increase, about 20 min, in the operative times, which can be attributed to the learning curve necessary to obtain a correct visual-spatial orientation with the navigation instruments. An inversely proportional relationship was found between the progressive reduction in operative times and the number of screws placed by the first operator [27]. Regarding radiation exposure, considerations are needed for both methods. During procedures performed with C-arm fluoroscopy, the surgeon is exposed to a massive dose of radiation—estimated for an average of about 120 procedures at around 12 mSv/year; in contrast, during O-arm procedures, the radiation dose is practically unidentifiable [28]. There is therefore an important advantage in terms of reduced radiation exposure for all subjects in the surgical procedure. Procedures that use intraoperative 3D imaging increase the radiation dose to which the patient is exposed by 40% compared to those that use C-arm fluoroscopy [29]. However, given the radiation dose to which the patient must expose themself during the necessary postoperative CT scan, the difference between the two procedures is negligible.

5 Conclusions

CT-guided intraoperative imaging navigation systems are proven surgical tools for implementing the accurate placement of transpedicular screws, making the procedure safer and reducing the risk of complications.

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References

1. Cummins J, Lurie JD, Tosteson TD, Hanscom B, Abdu WA, Birkmeyer NJO, et al. Descriptive epidemiology and prior healthcare utilization of patients in the Spine Patient Outcomes Research Trial's (SPORT) three observational cohorts: disc herniation, spinal stenosis and degenerative spondylolisthesis. Spine. 2006;31(7):806–14. https://doi.org/10.1097/01.brs.0000207473.09030.0d.
2. Wang JC, Dailey AT, Mummaneni PV, Ghogawala Z, Resnick DK, Watters WC, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 8: lumbar fusion for disc herniation and radiculopathy. J Neurosurg Spine. 2014;21(1):48–53. https://doi.org/10.3171/2014.4.SPINE14271.
3. Hsieh PC, Wienecke RJ, O'Shaughnessy BA, Koski TR, Ondra SL. Surgical strategies for vertebral osteomyelitis and epidural abscess. Neurosurg Focus. 2004;17(6):E4. https://doi.org/10.3171/foc.2004.17.6.4.
4. Vialle LR, Bellabarba C, Kandziora F. AOSpine masters series. Thoracolumbar spine trauma, vol. 6. New York: Thieme Medical Publishers; 2016. ISBN 978-1-62623-225-9.
5. Jónsson B, Sjöström L, Olerud C, Andréasson I, Bring J, Rauschning W. Outcome after limited posterior surgery for thoracic and lumbar spine metastases. Eur Spine J. 1996;5(1):36–44.
6. Gertzbein SE, Robbins SD. Accuracy of pedicular screw placement in vivo. Spine. 1990;15(1):11–4. https://doi.org/10.1097/00007632-199001000-00004.
7. Gelalis ID, Nikolaos K, Paschos NK, Paschos EE, Politis AN, Arnaoutoglou CM, et al. Accuracy of pedicle screw placement: a systematic review of prospective in vivo studies comparing free hand, fluoroscopy guidance and navigation techniques. Eur Spine J. 2012;21:247–55. https://doi.org/10.1007/s00586-011-2011-3.
8. Castro WH, Halm H, Jerosch J, Malms J, Steiinbeck J, Blasius S. Accuracy of pedicle screw placement in lumbar vertebrae. Spine. 1996;21:1320–4.
9. Foley KT, Smith MM. Image-guided spine surgery. Neurosurg Clin N Am. 1996;7(2):171–86.
10. Holly LT, Foley KT. Intraoperative spinal navigation. Spine. 2003;28:S54–61.
11. Mattei TA, Fassett DR. The O-arm revolution in spine surgery (Letter). J Neurosurg Spine. 2013;19:644–7. https://doi.org/10.3171/2013.6.SPINE13577.
12. Shalit MN, Israeli Y, Matz S, Cohen ML. Experience with intraoperative CT scanning in brain tumors. Surg Neurol. 1982;17:376–82.
13. Lunsford LD. A dedicated CT system for the stereotactic operating room. Appl Neurophysiol. 1982;45(4–5):374–8. https://doi.org/10.1159/000101625.

14. Amiot LP, Labelle H, DeGuise JA, Sati M, Brodeur P, Rivard CH. Computer-assisted pedicle screw fixation. A feasibility study. Spine. 1995;20(10):1208–12.
15. Lin EL, Park DK, Whang PG, An HS, Phillips FM. O-arm surgical imaging system. Semin Spine Surg. 2018;20:209–13.
16. Van de Kelft E, Costa F, Van der Planken D, Schils F. A prospective multicenter registry on the accuracy of pedicle screw placement in the thoracic, lumbar, and sacral levels with the use of the O-arm imaging system and StealthStation Navigation. Spine. 2012;37:E1580–7.
17. Oertel MF, Hobart J, Stein M, Schreiber V, Scharbrodt W. Clinical and methodological precision of spinal navigation assisted by 3D intraoperative O-arm radiographic imaging. J Neurosurg Spine. 2011;14(4):532–6. https://doi.org/10.3171/2010.10.SPINE091032.
18. Santos ERG, Ledonia CG, Castro CA, Truong WH, Sembrano JN. The accuracy of intraoperative O-arm images for the assessment of pedicle screw position. Spine. 2012;37(2):E119–25. https://doi.org/10.1097/BRS.0b013e3182257cae.
19. Gelalis ID, Paschos NK, Pakos EE, et al. Accuracy of pedicle screw placement: a systematic review of prospective in vivo studies comparing free hand, fluoroscopy guidance and navigation techniques, Eur Spine J. 2012;21(2):247–55. https://doi.org/10.1007/s00586-011-2011-3.
20. Miller CA, Ledonio CG, Humt MA, Siddiq F, Polly DW Jr. Reliability of the planned pedicle screw trajectory versus the actual pedicle screw trajectory using intra-operative 3D CT and image guidance. Int J Spine Surg. 2016;10:38. https://doi.org/10.14444/303.
21. Kleck CJ, Cullilmore I, LaFleur M, Lindley E, Rentschler ME, Burger EL. A new 3-dimensional method for measuring precision in surgical navigation and methods to optimize navigation accuracy. Eur Spine J. 2016;25(6):1764–74. https://doi.org/10.1007/s00586-015-4235-0.
22. Stieglitz LH, Fichtner J, Andres R, et al. The silent loss of neuronavigation accuracy: a systematic retrospective analysis of factors influencing the mismatch of frameless stereotactic systems in cranial neurosurgery. Neurosurgery. 2013;72(5):796–807. https://doi.org/10.1227/NEU.0b013e318287072d.
23. Van de Kelft E, Costa F, Van der Planken D, Schils F. A prospective multicenter registry on the accuracy of pedicle screw placement in the thoracic, lumbar, and sacral levels with the use of the O-arm imaging system and StealthStation Navigation. Spine. 2012;37(25):E1580–7. https://doi.org/10.1097/BRS.0b013e318271b1fa.
24. Scalia G, Umana GE, Graziano F, Tomasi SO, Furnari M, Giuffrida M, Ponzo G, Nicoletti GF. Letter: image-guided navigation and robotics in spine surgery. Neurosurgery. 2020;87(6):E720–1. https://doi.org/10.1093/neuros/nyaa404.
25. Umana GE, Scalia G, Perrone C, Garaci F, Pagano A, De Luna A, Cicero S, Visocchi M, Nicoletti GF, Germanò A, Lunardi P. Safety and efficacy of navigated trocarless pedicle screw placement: technical note, 100771. Interdiscip Neurosurg. 2020;21 https://doi.org/10.1016/j.inat.2020.100771. ISSN 2214-7519.
26. Nicoletti G, Furnari M, Giuffrida M, Ponzo G, Iacopino DG, Cammarata G, Scalia G, Graziano F. A new tool to improve pedicle screw placement accuracy in navigated spine surgery: a monocentric study. J Neurosurg Sci. 2020;65(3):348–53. https://doi.org/10.23736/S0390-5616.20.04957-7.
27. Sclafani JA, Regev GJ, Webb J, Garfin SR, Kim CW. Use of a quantitative pedicle screw accuracy system to assess new technology: initial studies on O-arm navigation and its effect on the learning curve of percutaneous pedicle screw insertion. SAS J. 2011;5(3):57–62. https://doi.org/10.1016/j.esas.2011.04.001.
28. Tabaraee E, Gibson AG, Karahalios DG, Potts EA, Mobasser JP, Burch S. Intraoperative cone beam-computed tomography with navigation (O-ARM) versus conventional fluoroscopy (C-ARM): a cadaveric study comparing accuracy, efficiency, and safety for spinal instrumentation. Spine. 2013;38(22):1953–8. https://doi.org/10.1097/BRS.0b013e3182a51d1e.
29. Nakagawa H, Kamimura M, Uchiyama S, Takahara K, Itsubo T, Miyasaka T. The accuracy and safety of image-guidance system using intraoperative fluoroscopic images: an in vitro feasibility study. J Clin Neurosci. 2003;10(2):226–30. https://doi.org/10.1016/s0967-5868(02).

Extreme Lateral Interbody Fusion (XLIF) with Lateral Modular Plate Fixation: Preliminary Report on Clinical and Radiological Outcomes

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Abbreviations

ALIF	Anterior lumbar interbody fusions
MISS	Minimally invasive spine surgery
PLF	Posterolateral lumbar fusion
PLIF	Posterior lumbar interbody fusion
TLIF	Transforaminal lumbar interbody fusion
XLIF	Extreme lateral interbody fusion

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1 Introduction

Minimally invasive spine surgery (MISS) is nowadays considered worldwide as an effective, low-risk, and safe treatment modality for degenerative spine disorders [1–3]. MISS has garnered interest as a feasible alternative to open surgery with some advantages, including reduced soft tissue manipulation, decreased blood loss, lower surgical site infection rates, improved cosmesis, and functional recovery [4].

The lateral approach to the lumbar spine has been growing in popularity because it has been adapted for a variety of indications, including neuroforaminal stenosis, spondylolisthesis, spinal stenosis with instability, and adult degenerative scoliosis [1, 4, 5].

Specifically, the lateral transpsoas approach, known as extreme lateral interbody fusion (XLIF), was devised to reduce the vascular injuries due to anterior lumbar interbody

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fusions (ALIFs) and limit the muscular/soft tissue trauma due to transforaminal lumbar interbody fusions (TLIFs) and posterior lumbar interbody fusions (PLIFs).

The use of a lateral transpsoas approach allows surgeons to use nonlordotic and lordotic cage sizes to help restore intervertebral disk height, correct sagittal alignment, and improve fusion rates [1, 6].

The lateral access preserves the anterior and posterior stabilizing structures while affording liberal disk removal and the placement of a wide cage spanning the apophyseal ring. Given such inherent structural benefits, it has been proposed that extensive and/or invasive posterior fixation could be unnecessary with lateral approaches [7].

However, the use of standalone MISS devices has consistently raised doubts in the medical-scientific community because of the high risk of complications, including a reduced fusion rate and inadequate functional recovery that a circumferential arthrodesis can support.

The recent introduction of a novel XLIF cage possessing integrated lateral modular plate fixation (XLPF) may further enhance the structural rigidity. XLPF, which consolidates the cage and the plate into a single modular entity, creating a continuous rigid body at an index level capable of promoting an effective and durable arthrodesis of the segment without needing posterior instrumented surgery. However, the extent to which this device facilitates segmental rigidity is not yet understood, according to the literature [8], and its effectiveness is limited to a few cadaveric studies and case reports.

This study illustrates our multicenter experience in the use of XLPF in XLIF using standalone devices for selected cases of lumbar spine pathologies.

2 Material and Methods

2.1 Patient Selection and Demographics.

Between January 2020 and February 2021, nine patients underwent a procedure of 1-level extreme lateral interbody fusion using an XLIF cage with lateral modular plate fixation in the neurosurgical centers of the Sapienza University of Rome (Hospital Sant'Andrea and Policlinico Umberto I, Rome, Italy), the Cattolica University of Rome (Hospital Gemelli, Rome, Italy), and the University of Turin (Molinette Hospital, Turin, Italy).

The diagnosis prompting fusion was junctional stenosis following previous multilevel posterior stabilization with disk collapse and with up-down foraminal stenosis in six patients and was adult degenerative scoliosis with sagittal imbalance and adjacent-level (juxtafusion) degeneration in three patients. The cohort included six women and three men, with an average age of 60.1 years (range: 47–73.8 years; the assumed data appear in Table 1). Exclusion criteria for the procedure were primarily multisegment limited pathology and the presence of osteoporosis or the oncologic pathology of the bone.

Clinical information was obtained for all patients from office charts, operative notes, and radiographic images. The information obtained from medical records included patient demographics, medical comorbidities, preoperative and postoperative clinical assessments, intraoperative findings, operative times, implant information, and postoperative complications. Visual analog scale (VAS) scores for pain were obtained before surgery and at each postoperative office visit

Table 1 Patients' demographics

No	Patients	Age	Surgical center	Date of intervention	Diagnosis	Pre-operative VAS	Level	Procedure time (min)	Outcome	Post-operative VAS
1	QM	47	Sapienza, Rome	14/12/2020	Junctional Stenosis	8	L2-L3	54	Good	2
2	BP	54	Sapienza, Rome	07/01/2021	Junctional Stenosis	9	L2-L3	45	Good	2
3	ME	54	Sapienza, Rome	19/02/2021	Junctional Stenosis	9	L3-L4	45	Good	2
4	MS	66	Sapienza, Rome	21/02/2021	Junctional Stenosis	8	L3-L4	65	Good	2
5	FA	67	Cattolica, Rome	13/01/2021	Adult Scoliosis with sagittal imbalance	8	L3-L4	34	Good	3
6	RJ	59	Cattolica, Rome	08/06/2016	Adult Scoliosis with sagittal imbalance	9	L3-L4	27	Good	4
7	PV	73	Cattolica, Rome	16/03/2016	Adult Scoliosis with sagittal imbalance	8	L3-L4	24	Good	3
8	GG	\	Università degli studi di Torino	16/03/2021	Junctional Stenosis	8	L2-L3	62	Good	2
9	TR	\	Università degli studi di Torino	07/02/2020	Junctional Stenosis	9	L3-L4	68	Good	3

(6 weeks, 3 months, 6 months, 1 year). Standing preoperative, immediate postoperative, and most-recent radiographs at a minimum of 1 year after surgery were measured for end plate angulation in the operated discal space in both the coronal (scoliotic angle) and sagittal (lordotic angle) planes. The interbody cage position was measured in the coronal and sagittal planes with reference to adjacent vertebral borders on immediate postoperative and final follow-up radiographs. Fusion was routinely assessed at 1 year after surgery by using computed tomography (CT) scans. CT images were also used to measure the amount of subsidence in the interbody cage that is imparted into the superior and inferior end plates (Fig. 1).

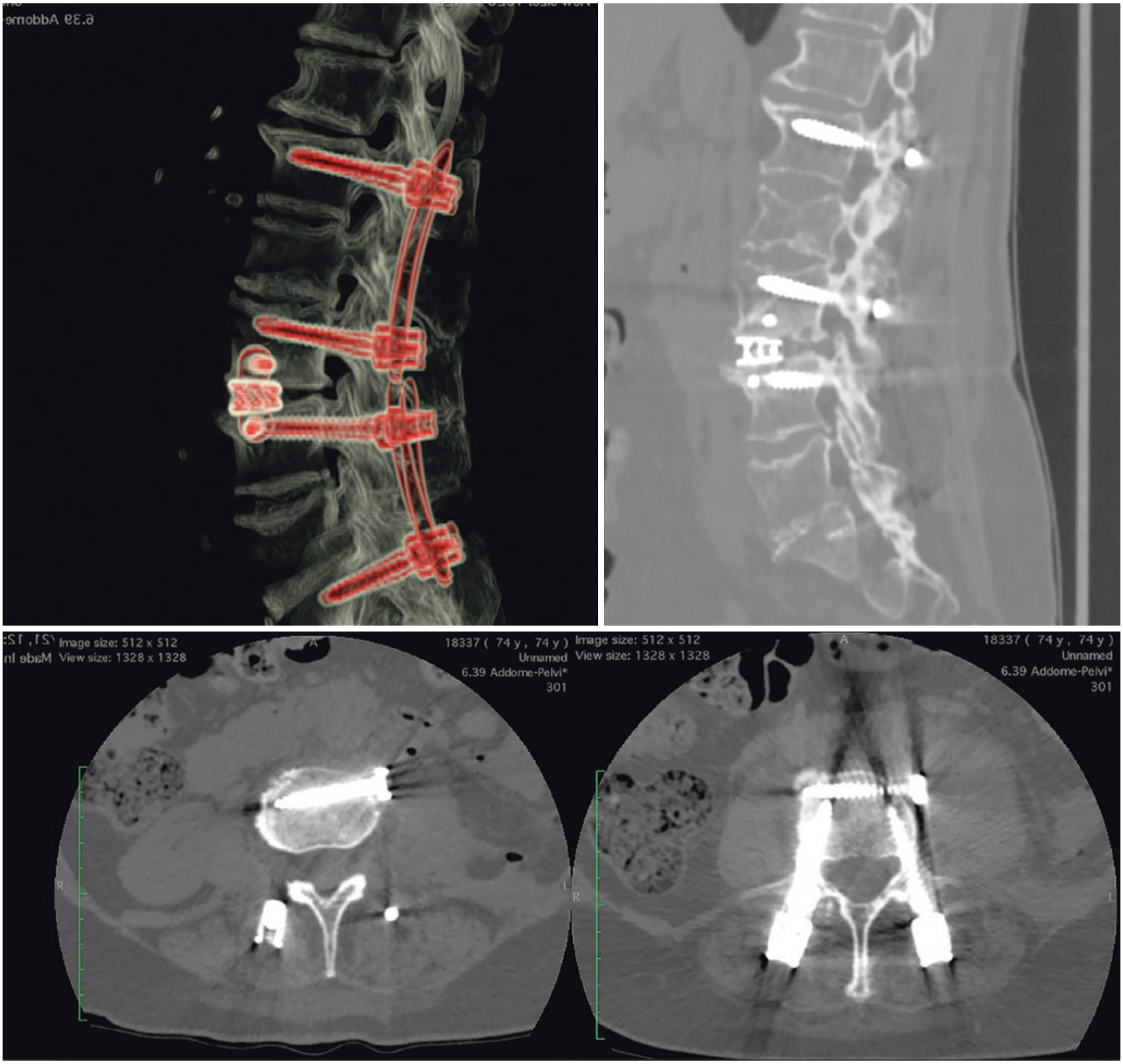

Fig. 1 A 66-year-old woman presenting with bilateral leg pain, neurogenic claudication, and lower-back pain for whom medical treatment failed; preoperative radiographs and magnetic resonance imaging demonstrating a previous stabilization on L1-S1 for lumbar stenosis and a debut of the severe monosegmental stenosis of the L2-L3 segment within the context of junctional syndrome

2.2 Operations and Technical Note

Lateral interbody fusion was performed by using the technique described by Ozgur et al. [9].

The side for the procedure was chosen on the basis of which side of the column had the greater concavity, the presence of large vessels, and the level of any osteophytes in the affected soma. Each procedure was performed with the aid of the level of neurophysiological monitoring necessary to detect any stretch damage caused to the adjacent nerve plexus. XLIF cages were filled with Grafton demineralized bone matrix.

In cases of reported degenerative scoliosis, the anterior longitudinal ligament section was performed to allow the insertion of a 30° lordotic cage; in all other cases, the cage had a 15° lordosis.

After the interbody cage was placed, anterior instrumentation (Nuvasive XLP plate) was placed via the same incision. The XLPF system uses a 5.5 mm fixed-angle screw placed into the vertebral bodies above and below the cage. Before cage insertion, any possible reduction in the number of somatic lateral osteophytes was performed to allow the placement of the plate adjacent to the somatic bodies.

3 Results

The mean operative time was 47.11 min, starting from the time when the positioning of the patient in the lateral decubitus position began until the posterior wound was closed. The estimated blood loss averaged 125 mL. No patient received a transfusion during the procedure or the postoperative period. The average length of postoperative hospital stay was 3.6 days.

VAS scores improved from a preoperative average of 8.4 to a postoperative average of 2.5, a statistically significant improvement of 5.9 points ($p < 0.001$).

3.1 Radiographic Findings

The mean radiographic follow-up time was 13 months. Four patients had sufficient clinical follow-ups to be included in the study but were excluded from the radiographic portion of the study because their available radiographic follow-up times were <1 year. It was radiographically demonstrated that there was no cage migration in either the coronal plate or the sagittal plane at the final follow-up. There were no end plate fractures or signs of subsidence on either immediately postoperative radiographs or final follow-up radiographs.

4 Discussion

Since its introduction, the XLIF technique has undergone constant technical evolution, in which a powerful light system, new retractors, and electromyography combined in a minimally invasive procedure have allowed for the insertion of a large interbody implant through the lateral aspect of the intervertebral discal space. Thus, these techniques may minimize interbody cage subsidence and preserve intervertebral disk height and alignment correction depending on appropriate cage size selection [5].

The interbody cages developed for XLIF are biomechanically distinct from cages used for anterior or posterior lumbar interbody fusion. The cage used with XLIF, placed from the lateral aspect of the vertebral body, is wide enough to span the entire width of the vertebra so that it rests on apophyseal bone on either side. This could provide a biomechanical advantage in that the peripheral apophyseal bone is significantly stronger than the central cancellous bone, which is used to provide support for interbody fusion devices used in posterior approaches [10].

In general, the benefits of this lateral approach include the preservation of back muscle and of bony and ligamentous structures, and it also allows for the placement of an intervertebral cage. In addition, the current procedure results in the correction of spondylolisthesis and rotatory deformity and in indirect nerve decompression thanks to ligamentotaxis force. These advantages may result in less surgical pain and quicker recovery than those achieved in traditional approaches.

Because of the XLIF implant's inherent stability, many surgeons use the cage with alternative forms of fixation, including anterior plate fixation or unilateral posterior pedicle screw fixation, or they use it as a standalone implant. Although the effectiveness of minimally invasive lumbar interbody fusions with percutaneous pedicle screws has been described and well noted, a comparatively high complication rate of standalone XLIF, including postoperative thigh symptoms, not has been reported [11]. In contrast, relatively few biomechanical studies have evaluated the stability of an interbody fusion construct with and without additional anterior or posterior instrumentation inserted while using this approach [8, 12].

The XLPF plate (NuVasive, Inc., San Diego, CA, USA) is an anterolateral instrumentation system developed for use with the XLIF system for lateral approaches. The XLPF lateral plate is made of titanium and is fixed to the lateral vertebral bodies by using two screws that lock into the plate, creating a fixed-angle construct. Biomechanical data demonstrate that the XLPF plate increases construct stiffness when used in conjunction with the XLIF interbody cage compared

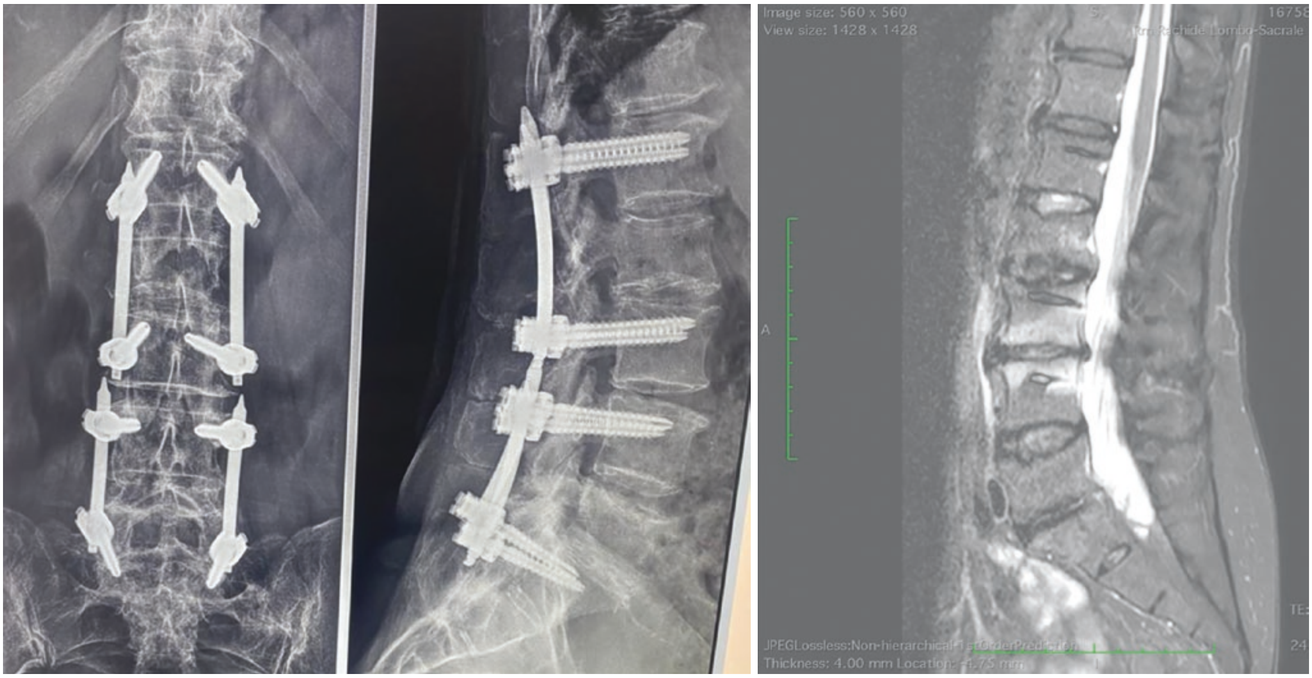

Fig. 2 Postoperative CT scan and radiograph: The patient was submitted to L2-L3 XLIF with anterolateral instrumentation and with lateral plating and minimally invasive decompression; her initial postoperative course was unremarkable, and she mobilized well with resolution of leg pain and mild lower-back pain; the patient showed improvement in lower-back and pelvic pain and mobilized gradually; at her 3-month follow-up, her lower-back pain and pelvic pain were mild; at her 1-year follow-up, her leg pain has resolved without lower-back pain; the patient recently underwent a CT scan, which demonstrated the solid fusion of the system

with a standalone interbody cage [5]. Other studies have produced data on the efficacy and complications associated with anterolateral lumbar instrumentation [6, 7, 11, 13, 14], but the clinical performance of plating systems used in association with LTIF has not been reported, because of the recency of its introduction (Fig. 2).

By providing comparable rigidity in patients who have previously undergone an arthrodesis procedure or in patients with extensive degeneration of the spine, the XLPF iterations could significantly diminished the need for posterior fixation in those respective planes. Whether assembled before insertion or in situ, the integrated design of the XLPF construct may also support the intraoperative ease of plate placement and plate alignment optimization not achieved with traditional independent plates [13, 14]. DenHaese et al. [8] reported the operative time, fluoroscopy time, and blood loss data from XLPF, and they did not differ from the data on those variables from placing a traditional cage alone [15].

Lateral plating does not extend the intraoperative footprint, because the plate is placed through the same surgical corridor as that for the interbody cage, and it provides immediate rigidity to the anterior column in the axial and coronal planes [8] without any additional surgical risk. In our cases, the standalone XLIF cage implantation procedure may require more time than the simple procedure does, mainly because the lateral osteophytes need to be osteo-reduced to allow the correct application of the cage. It is further important to not violate the end plates with the plates and to exercise extreme caution when reducing the lateral osteophytosis necessary for proper plate placement, avoiding the possibility of impairing the cortical of the vertebral soma or impairing the oversized interbody implants with XLPF because it may exacerbate any stress-rising effects. This step is to be considered the most delicate for this procedure because the reduction must be performed without encouraging the excessive demolition of compact bone. The selection of the cage must also be carefully evaluated, favoring in some cases a slightly narrower size, always to avoid the imperfect lateral alignment of the plate. It is important to sequentially unbreak the table before tightening the XLPF bolts until the plate is locked into a physiological position. The position of the iliac crest in the extreme lateral interbody fusion approach can prohibit a true lateral trajectory to the spine at L4-L5, thus making plates difficult if not impossible to place in an orientation orthogonal to the long axis of the spine [16]. Finally, in cases of advanced osteoporosis, bilateral posterior supplementation may be appropriate and standalone plating should be avoided in osteoporotic patients because of the risk of vertebral body fracture [17].

Most studies on standalone XLIF using lateral plates have evaluated the outcome measure only indirectly, through cadaveric studies. In fact, most studies have positively evaluated range of motion (ROM) as a variable affecting the safety and efficacy of a treatment. Biomechanically, the XLIF construct significantly reduced ROM in all directions of loading compared with an intact spine, indicating an inherent measure of stability in the standalone approach.

The addition of an XLPF did not increase the stability of the LLIF construct during flexion or extension [10, 18]. In addition, posterior screws are harder to place on the plated side because of the potential for interference with the screws and the screw trajectory of the lateral plate fixation. When using XLPF, the screws are placed in proximity directly above and below the cage. This places a stress riser in an area of stress concentration, possibly resulting in fracture. Some authors advocate for the use of additional unilateral posterior fixation in single-level lumbar fusion. Unilateral posterior fixation could be used in patients undergoing a single-level lumbar fusion, which was amenable to LTIF, depending on the level (above L5-S1) and in the absence of spondylolisthesis. It was used on the nonplated side to provide additional contralateral stabilization [15].

XLIF constructs with posterior bilateral pedicle screw fixation or facet screw fixation, or combined anterior-posterior lateral-spinous process plate fixation, provided the most stability in the three principal planes of motion, and in our opinion, it is still fundamental in the treatment of some degenerative forms of spondylolisthesis with isthmic lysis and in the treatment of advanced forms of degenerative scoliosis.

5 Limitations and Further Studies

The main limitation of this preliminary report is the limited number of cases examined and the retrospective nature of the study. In addition to increasing the series, it is necessary to evaluate sagittal and coronal imbalance changes by comparing them with the more traditional XLIF technique. Clinical studies are essential to support the validity of this instrumented surgical strategy in order to evaluate its complications, clinical stability, risk of subsidence, quality-of-life outcomes, and fusion rates and to compare them with those of traditional implantation with posterior stabilization.

6 Conclusion

A large number of clinical studies involving XLIF have been reported in the medical literature, with good outcomes and low complication rates. Although it has been shown that the use of interbody fusion cages with supplemental posterior fixation improves stabilization in all directions, the technique of standalone lateral cages may also have a place in spine surgery because the stability may be sufficient in selected cases, such as in junctional syndrome in patients who have already undergone posterior arthrodesis surgery and in some forms of degenerative scoliosis instead of traditional osteotomies. The use of the standalone XLIF approach with the use of XLPF is a valid and effective technique, but at the moment, it can be implemented only in a few selected cases and is not applicable to the whole range of degenerative pathologies of the lumbar spine for which the technique with posterior screw fixation remains more indicated.

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Conflict of Interest We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We wish to draw the attention of the editor to the following facts, which may be considered as potential conflicts of interest, and to the significant financial contributions to this work.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study. The patients consented to the submission of this review chapter.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing, we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the corresponding author is the sole contact for the editorial process (including editorial manager and direct communications with the office). They are responsible for communicating with the other authors about progress, the submissions of revisions, and the final approval of proofs. We confirm that we have provided a current, correct email address that is accessible by the corresponding author and that has been configured to accept email.

References

1. Armocida D, Pesce A, Cimatti M, Proietti L, Santoro A, Frati A. Minimally invasive transforaminal lumbar interbody fusion using expandable cages: increased risk of late postoperative subsidence without a real improvement of perioperative outcomes: a

clinical monocentric study. World Neurosurg. 2021;156:e57–63. https://doi.org/10.1016/j.wneu.2021.08.127. Epub 2021 Sep 4. PMID: 34492389.

2. Barone G, Scaramuzzo L, Zagra A, Giudici F, Perna A, Proietti L. Adult spinal deformity: effectiveness of interbody lordotic cages to restore disc angle and spino-pelvic parameters through completely mini-invasive trans-psoas and hybrid approach. Eur Spine J. 2017;26(Suppl 4):457–63. https://doi.org/10.1007/s00586-017-5136-1. Epub 2017 May 18. PMID: 28523382.
3. Proietti L, Perna A, Ricciardi L, Fumo C, Santagada DA, Giannelli I, Tamburrelli FC, Leone A. Radiological evaluation of fusion patterns after lateral lumbar interbody fusion: institutional case series. Radiol Med. 2021;126(2):250–7. https://doi.org/10.1007/s11547-020-01252-5. Epub 2020 Jul 11. PMID: 32654029.
4. Sharif S, Shaikh Y, Peev N. Minimally invasive spinal surgery: how to keep out of trouble. World Neurosurg. 2018;119:517–26.
5. Chen E, et al. Cage subsidence and fusion rate in extreme lateral interbody fusion with and without fixation. World Neurosurg. 2019;122:e969–77.
6. Patel PD, Canseco JA, Houlihan N, Gabay A, Grasso G, Vaccaro AR. Overview of minimally invasive spine surgery. World Neurosurg. 2020;142:43–56. https://doi.org/10.1016/j.wneu.2020.06.043.
7. Basra S, Bucklen B, Muzumdar A, Khalil S, Gudipally M. A novel lateral lumbar integrated plate-spacer interbody implant: in vitro biomechanical analysis. Spine J. 2015;15:322–8.
8. DenHaese R, Gandhi A, Ferry C, Farmer S, Porter R. An in vitro biomechanical evaluation of a lateral lumbar interbody fusion device with integrated lateral modular plate fixation. Global Spine J. 2021;11(3):351–8. https://doi.org/10.1177/2192568220905611. Epub 2020 Feb 20. PMID: 32875868; PMCID: PMC8013934.
9. Ozgur BM, Aryan HE, Pimenta L, et al. Extreme lateral interbody fusion (XLIF): a novel surgical technique for anterior lumbar interbody fusion. Spine J. 2006;6:435–43.
10. Fogel GR, Turner AW, Dooley ZA, Cornwall GB. Biomechanical stability of lateral interbody implants and supplemental fixation in a cadaveric degenerative spondylolisthesis model. Spine (Phila Pa 1976). 2014;39(19):E1138–46. https://doi.org/10.1097/BRS.0000000000000485. PMID: 24979274.
11. Youssef JA, McAfee PC, Patty CA, Raley E, DeBauche S, Shucosky E, Chotikul L. Minimally invasive surgery: lateral approach interbody fusion: results and review. Spine (Phila Pa 1976). 2010;35(26 Suppl):S302–11.
12. Bess RS, Cornwall GB, Vance RE, Bachus KN, Brodke DS. Biomechanics of lateral arthrodesis. In: Goodrich JA, Volcan IJ, editors. Extreme lateral interbody fusion (XLIF). St. Louis: Quality Medical Publishing; 2008. p. 31–40.
13. Barbagallo GM, Albanese V, Raich AL, Dettori JR, Sherry N, Balsano M. Lumbar lateral interbody fusion (LLIF): comparative effectiveness and safety versus PLIF/TLIF and predictive factors affecting LLIF outcome. Evid Based Spine Care J. 2014;5(1):28–37.
14. Joseph JR, Smith BW, La Marca F, Park P. Comparison of complication rates of minimally invasive transforaminal lumbar interbody fusion and lateral lumbar interbody fusion: a systematic review of the literature. Neurosurg Focus. 2015;39(4):E4.
15. DenHaese R, Hill C, Strenge B, et al. Lateral lumbar interbody fusion with modular plate fixation: initial experience with a novel technology. Intra-op and 1-year outcomes. Paper presented at: Society of Minimally Invasive Spine Surgery (SMISS) Global Forum, Las Vegas, NV; 5–7 Nov 2015.
16. Smith WD, Huntington CF. Letter to the editor regarding: Dua K, Kepler CK, Huang RC, Marchenko A. Vertebral body fracture after anterolateral instrumentation and interbody fusion in two osteoporotic patients. Spine J 2010;10:e11–5. Spine J. 2011;11(2):166–7; author reply 167. https://doi.org/10.1016/j.spinee.2010.12.008. PMID: 21296303.
17. Dua K, Kepler CK, Huang RC, Marchenko A. Vertebral body fracture after anterolateral instrumentation and interbody fusion in two osteoporotic patients. Spine J. 2010;10(9):e11–5. https://doi.org/10.1016/j.spinee.2010.07.007. PMID: 20797649.
18. Reis MT, Reyes PM, Bse, Altun I, Newcomb AG, Singh V, Chang SW, Kelly BP, Crawford NR. Biomechanical evaluation of lateral lumbar interbody fusion with secondary augmentation. J Neurosurg Spine. 2016;25(6):720–6. https://doi.org/10.3171/2016.4.SPINE151386. Epub 2016 Jul 8. PMID: 27391398.
19. Ge T, Ao J, Li G, Lang Z, Sun Y. Additional lateral plate fixation has no effect to prevent cage subsidence in oblique lumbar interbody fusion. J Orthop Surg Res. 2021;16(1):584. https://doi.org/10.1186/s13018-021-02725-7. PMID: 34635143; PMCID: PMC8507130.
20. Kaneda K, Taneichi H, Abumi K, et al. Anterior decompression and stabilization with the Kaneda device for thoracolumbar burst fractures associated with neurological deficits. J Bone Joint Surg Am. 1997;79:69–83.

A New Interlaminar/Interspinous and Facet-Joint Stabilization System in Lumbar Degenerative Disk Disease: 2 Years of Results

Giulia Guizzardi, Carlo Antonio Todaro, and Gualtiero Innocenzi

Abbreviations

ASD	Adjacent segment degeneration
BDUA	Bilateral decompression via the unilateral approach
BMD	Bilateral microdecompression
DDD	Degenerative disk disease
DS	Degenerative spondylolisthesis
ILIF	Interspinous/interlaminar lumbar instrumented fusion
VAS	Visual analog scale

1 Introduction

In lumbar degenerative disk diseases (DDDs), we include a wide range of lumbar pathologies. Even though there are different pathological and radiological patterns, they all determine back and/or leg pain. Lumbar spinal stenosis with or without spondylolisthesis is a common cause for lower-limb pain in elderly patients. The same problems can occur, especially in middle-aged patients, with degenerative spondylolisthesis. Lumbar fusion is nowadays one of the most performed treatments for symptomatic lumbar DDD, after conservative treatment has failed [1]. The surgical treatment of lumbar DDD consists of the decompression of the neural structures or the decompression and fusion of the involved motion segment. The latter procedure is performed mostly in the presence of leg symptoms and significant back pain, particularly when there is evidence of an unstable slipped vertebra [2, 3]. Surgically treated patients have significantly better long-term outcomes compared to conservatively treated patients [4]. The most performed surgical procedures are conventional laminectomy, unilateral laminotomy with bilateral decompression, and bilateral laminotomy: All these procedures allow for obtaining a good grade of bilateral decompression and are comparable in terms of clinical outcomes [5]. Nevertheless, about 22% of patients who underwent lumbar surgery postoperatively reported dissatisfaction [6].

Unfortunately, rigid spinal implants followed by fusion cause increased stresses on the neighboring spinal segments, often leading to adjacent segment degeneration (ASD) [7, 8]. The current methods of vertebral fusion are posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), oblique lateral interbody fusion (OLIF), and extreme lateral interbody fusion (XLIF) in combination with pedicle screw instrumentation. Each of these, however, poses certain risks to the patient, because while pedicle screw instruments and implants are being placed, they pass close to nerve roots and vascular structures [9, 10]. Furthermore, C-arm fluoroscopy is required to ensure proper screw placement, exposing the patients and the surgical team to high levels of radiation. Depending on the patient's condition, anatomy, age, and activity level, the implantation of a combination of an interspinous-interlaminar and facet-joint fixation system has shown construct stability comparable to that of pedicle screw fixation, but with lower risks [11–13]. The aim of this paper is to present a new system for interlaminar/interspinous and facet-joint stabilization and fusion (ILIF: ISCHIA and FILICUDI implants from Tsunami Medical, Italy). Furthermore, we report and discuss the surgical results of a group of patients treated with these devices between 2018 and 2021.

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We subscribe to the following biomechanical concept: In the "normal" lumbar spine motion segment, 80% of the load is carried in the anterior column [14]. With the disk and facet-joint degeneration (the evolution of the degenerative cascade), almost the same percentage of the load is transferred into the posterior column.

2 Material and Methods

2.1 Device Characteristics

The devices are designed to promote a better and more efficient intervertebral fusion, and they are completely different from other available fusion systems on the market for the following reasons:

- The device's combination of systems (interspinous/interlaminar and facet-joint fixation) confers stability.
- Bone-to-bone contact and not bone-to-titanium or bone-to-polyetheretherketone (PEEK) contact obtain a kind of biological fusion.

Bone Ingrowth technology allows the system to achieve the best response from the bone tissue by facilitating bone growth and tissue vascularization. The main function of the fins of the ISCHIA implant is to induce osteogenesis by keeping the laminae continually stressed, which improves the vascularization of the newly created bone tissue, which promotes rapid fusion (Fig. 1). The system has a dedicated instrumentation, which facilitates its sizing and positioning. Furthermore, this surgical procedure can be used in conjunction with multiple fusion procedures, such as PLIF, TLIF, ALIF, OLIF, and XLIF.

2.2 Patient Selection

From March 2018 to June 2021, 175 patients with severe lumbar back and/or leg pain were operated on with this device (EC certificate no. 1826/MDD on 11 April 2017) after the failure of conservative treatment for a minimum of 6 months. For the study, we considered 75 available patients with a minimum follow-up time of 24 months (from 24 to 36 months, with a median follow-up time of 28 months; see Table 1). Diagnostic imaging studies—namely magnetic resonance imaging (MRI) scans, computed tomography (CT) scans, and flexion/extension radiograms—were obtained preoperatively to confirm the diagnosis. Patients rated their back pain and leg pain on a visual analog scale (VAS) before surgery and at the last follow-up; also, the postoperative consumption of analgesic drugs was investigated. Finally, patients were asked whether they would undergo this kind of surgery again or recommend it (Table 2).

The median age was 68 years (42–89 years), and the study featured 36 women and 39 men. The average preoperative VAS score for back pain was 7.5 and that for leg pain was 7.8. All patients experienced lumbar stenosis and/or initial instability, accompanied by degenerative spondylolisthesis Meyerding Grade 1, and required single- or double-level decompression [15, 16]. In the flexion/extension X-rays, the cases with spondylolisthesis showed a translation equal to or less than 6 mm.

2.3 Surgical Intervention and Technique

Patients were in the prone position, under general anesthesia, and in mild kyphosis. X-rays control the right level. We prepared the location for the position of the implant, cleaning and gently removing the superficial part of the cortical bone where it was in contact with the implant to increase the contact surface area. We prepared the facet joint by opening the capsule and searching the right interarticular line. Mobilizing the segment can be very helpful to properly identify the entrance. Use recurved curettes and rasps to enter in the joint space, and while making the articulating surfaces of the facet joint, bleed and prepare the location for the facet fusion cages. Use trial instruments to choose the right size of the interspinous/interlaminar implant; next, fill the inner space with biological materials, and press. At this point, recuperate the right lordosis of the lumbar spine, fill the facet fusion cages in the same way, and press in the prepared facet joint. Control the stability of the implants.

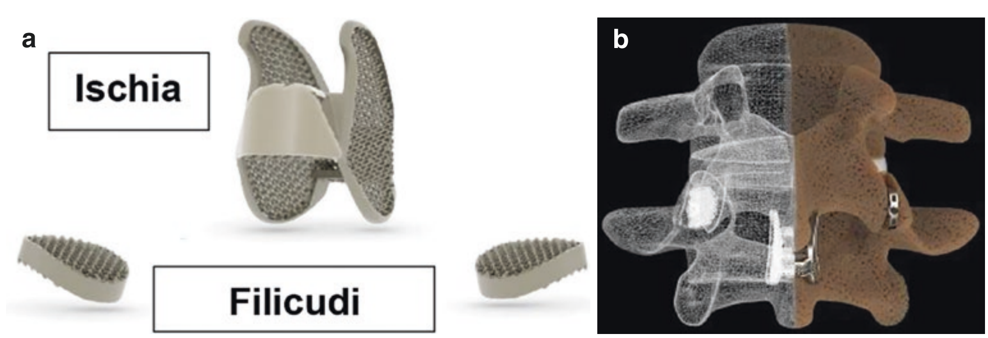
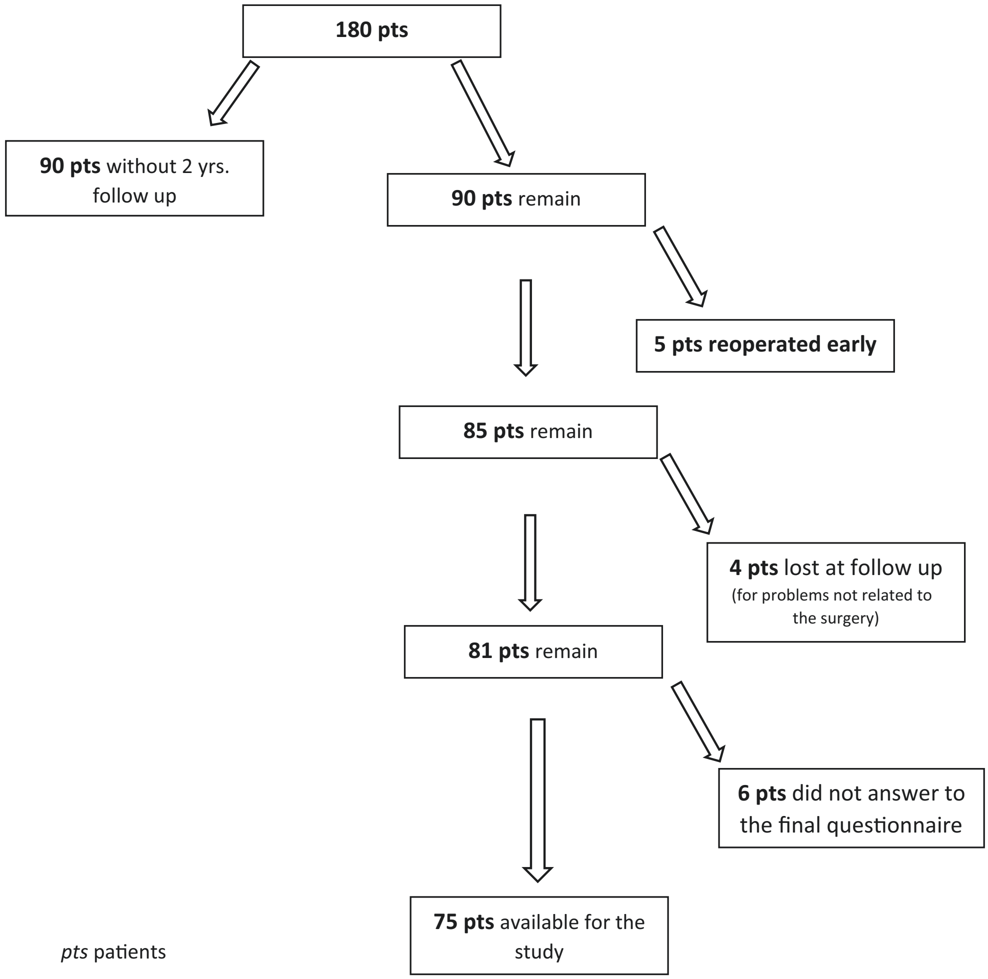


Fig. 1 Interlaminar/interspinous and facet-joint cages (**a**) and didactic rendering (**b**)

Table 1 Patient flowchart



pts patients

Table 2 Implant failures

Patient	Age	Pathology	Dispositives implanted	Complication	Second surgery	Third surgery	Dispositive removal
A.A.	79	L3-L4 and L4-L5 foraminal stenosis	ISCHIA + FILICUDI + intra	Subcutaneous ISCHIA pullout	Yes	No	Yes
G.R.	55	L4-L5 spondylolisthesis	ISCHIA + FILICUDI + intra	Subcutaneous ISCHIA pullout (bilateral)	Yes	No	Yes
P.A.	70	L3-L4 stenosis with L4-L5 instability	ISCHIA + FILICUDI + intra	Subcutaneous ISCHIA pullout	Yes	No	Yes
M.M.	89	L3-L5 stenosis	ISCHIA	Fracture of L3 spinous process and articular process L3-L4	Yes (screws and PLIF)	No	Yes
V.V.	74	L4-L5 stenosis	ISCHIA + FILICUDI	Subcutaneous ISCHIA pullout	Yes (screws and PLIF)	No	Yes

Decompression of stenotic levels was performed in 54 patients (72%). Only soft tissue removal (Senegas "recalibrage" [17]) or partial bone asportation were performed, accurately preserving the facet joints. In the other cases, only the fusion system was implanted.

2.4 ISCHIA and FILICUDI Implantation

Patients underwent general anesthesia and were prepared in a prone position with a moderate kyphosis. After exposing the laminae and articular processes, a dedicated instrumenta-

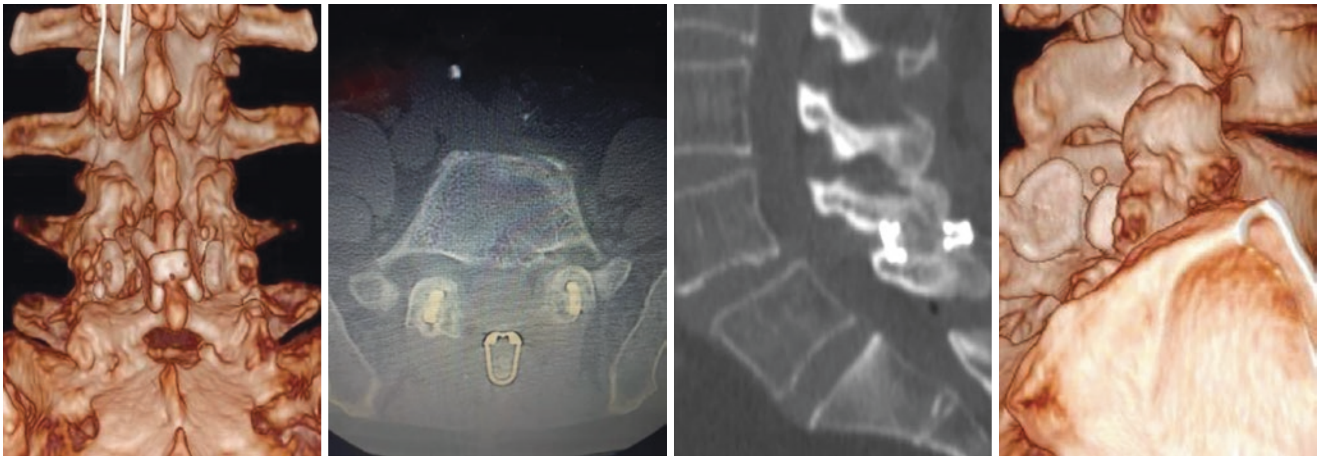


Fig. 2 Interspinous and solid facet-joint arthrodesis 6 months after surgery

tion was used to distract and freshen the spinous processes' border and the facet joints' surfaces. One special instrument, the implant trial instrument, was used to determine the correct size of the implants (8, 10, 12, and 14 mm were the available heights for the ISCHIA device, and 5 and 7 mm were the available sizes for the facet fusion cages in the FILICUDI device). Next, both implants were filled with bone chips and positioned.

In our series, 71 patients received the complete system (ISCHIA +2 FILICUDI). In four cases, the interlaminar/interspinous device ISCHIA was implanted alone. Moreover, in 32 patients, a single- or double-level interlaminar soft shock absorber device with a ligament (IntraSPINE, Cousin Biotech, France) was also positioned in order to assist in cranial and caudal disk implantation and to prevent ASD (Fig. 2).

The size of the ILIF used was 8 mm in 25 patients (33.3%), 10 mm in 29 patients (38.6%), 12 mm in 18 patients (24%), and 14 mm in three patients (4%).

3 Results

3.1 Surgical Results

All procedures were performed without any complications, with an average operative time of 93 min. During each procedure, the correct position of the implants was confirmed via X-rays.

During the postoperative period, surgical wound dehiscence was reported in five patients (6.7%).

3.2 Reoperation Data (Patients Removed from the Study)

The need of surgical reintervention with removal of the implants or the requirement of transpeduncular screw fixation within early postoperative period (4 months), was considered as implant failure. In one case, a spinous process and unilateral articular process fracture occurred. In four cases, a subcutaneous ISCHIA (one case) or FILICUDI (three cases) pullout was observed. These patients underwent reoperation within a few months of the initial procedure (2–4 months): In all cases, the implants were easily removed, and a transpedicular screw fixation with interbody cage placement was performed in only one. In the other three cases of facet-joint cage displacement, the patients required the surgical removal of this part of the device without also needing transpedicular screw fixation (Table 2).

Four patients died during the follow-up: two because of respective heart attacks, one because of cancer, and one because of a car accident.

3.3 Statistical Analyses

P-values were used to assess the differences between pre- and postoperative back and leg pain scores. The level of significance was set at 0.05 for all assessed variables.

3.4 Clinical Outcomes

Significant improvements following lumbar surgery were observed. These improvements were documented by using VAS scores. The average preoperative score dropped from an average VAS score of 7.5 for back pain and an average VAS score of 7.8 for leg pain to an average postoperative VAS score of 2.8 for back pain ($p = 0.01$) and that of 2.4 for leg pain ($p = 0.01$). Only six patients (8.1%) were not satisfied and would not recommend the surgery. On drug consumption at follow-up, 36 patients reported any level of drug use (48%), 27 reported occasional drug use (36%), nine reported regular drug use (12%), and three reported worse drug use (4%).

3.5 Radiological Outcomes

We evaluated the rate of evident fusion with CT scans at 6-month follow-ups (Fig. 2). Fusion was evident in 58 of 75 patients (77.3%); moreover, in the cases without fusion, the clinical results seemed to not be influenced by the absence of evident fusion. A satisfactory segment realignment was seen in most patients with spondylolisthesis (Figs. 2 and 3).

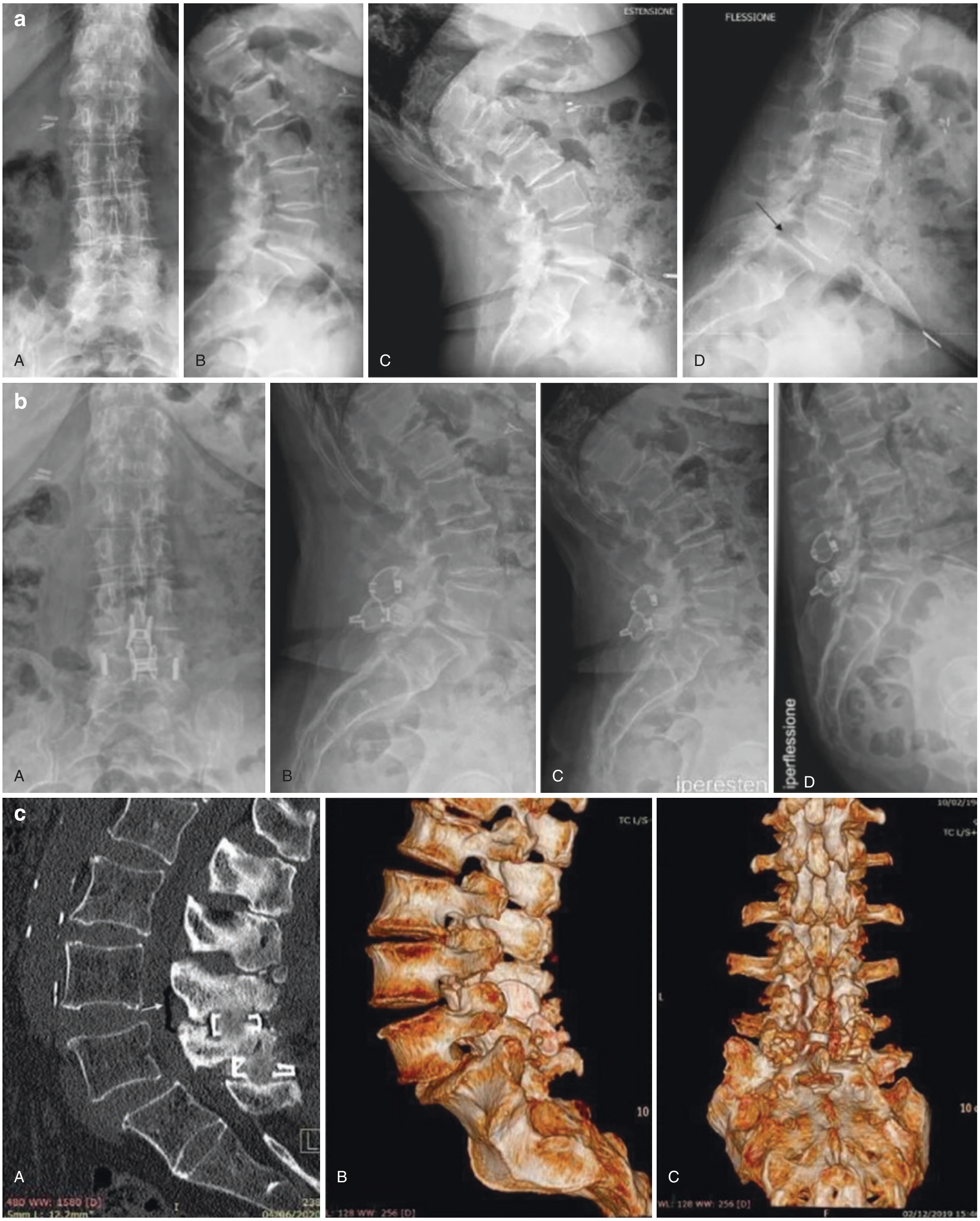


Fig. 3 (**a**) Preopeartive dynamic X-ray with mild instability in the L4-L5 level (S1 lumbarization); (**b**) the same dynamic postoperative X-ray with good stability in the L4-L5 level after the decompression; (**c**) CT scan control at 2 years showing a very good arthrodesis (the arrow indicates an increase in epidural fat after the decompression)

4 Discussion

In recent decades, BMD or BDUA has become an alternative to laminectomy, whether associated with spinal fusion or not, in lumbar stenosis with or without DS [16, 17]. In patients with DS, BMD or BDUA was typically performed in Grade I olisthesis with mild or no instability in the slipped vertebra. However, stenotic patients with or without DS undergoing decompression were found to be at a higher risk of vertebral slipping and dynamic translational instability after surgery [17]. However, three studies [18–20] showed a main increase in vertebral slipping of 1.7–8.4% after surgery, and in another study [21], 6.5% of patients required subsequent fusion at the decompressed level. In other studies [22, 23], in which BDUA was performed in patients with Grade I DS who had no or certain preoperative instability, the average slip increased by 0.7% and 5.4%, respectively. It thus appears that both BMD and BDUA may expose patients to a higher risk of vertebral slipping after surgery. This risk is particularly applicable to patients with dynamic translational motion in the listhetic vertebra, in whom symptoms related to instability may worsen after surgery. The final clinical results in our series were excellent in 41 patients (54.6%), good in 25 (33.3%), and unchanged or bad in nine (12%). In our series, the rate of solid fusion was 77.3% (58 of 75 patients). Of the results, 87.9% were excellent or good, which compare well with the 87% found by Wang et al. [24] in 16 patients with no DS. None of our patients with solid fusion plain radiographs showed increased vertebral slipping or instability in the slipped vertebra. Conversely, of the 27 patients with no evident fusion on their imaging, none had an increase in slipping and the slipping remained unchanged on postoperative dynamic radiographs. However, a systematic review of the literature [25] and a multicenter study [26], revealed that satisfactory clinical outcomes are more likely to occur with fusion. This observation and the results of our study show that bony fusion, although not as obvious as when using pedicle screw instrumentation, may be sufficient to improve the clinical results and avoid a postoperative increase in olisthesis. The advantages of the ILIF are that it is a minimally invasive procedure, requiring a short operative time, little blood loss, and minor complications if any. Thus, it is a procedure to be taken into account for Grade I DS with instability in the slipped vertebra because it ensures sufficient vertebral stability in a high percentage of cases, as this study has shown, and because it avoids the drawbacks of both the sole decompression and the major types of fusion. Our retrospective study confirmed the results of a previous paper, by Postacchini et al. [27]. A limitation of this study is that there was no control group undergoing similar types of decompression without an ILIF implant.

5 Conclusions

Our interspinous/interlaminar and facet-joint implant solution, associated with bone grafting, provided vertebral fusion in most stenotic patients with Grade I DS undergoing BMD or BDUA. At the 2-year follow-up, all patients with fusion who preoperatively had chronic back pain showed highly significant improvements on all outcome measures, indicating a satisfactory clinical result, and none had an increase in olisthesis or showed an increase in the instability in the slipped vertebra. A higher number of patients and a longer follow-up time will certainly be required to completely validate these new devices, but this MIS is currently very encouraging and satisfactory. We are strongly motivated to continue this experience, especially because of the very low patient morbidity rates, because it is a minimally invasive surgical procedure, and because of the high grade of patient satisfaction.

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Conflicts of Interest All the authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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References

1. Gibson JN, Waddell G. Surgery for degenerative lumbar spondylosis: updated Cochrane review. Spine (Phila Pa 1976). 2005;30:2312–20.
2. Postacchini F. Management of lumbar spinal stenosis. J Bone Joint Surg Br. 1996;78:154–64.
3. Andersson GB. Epidemiological features of chronic lowback pain. Lancet. 1999;354:581–5.
4. Weinstein JN, Lurie JD, Tosteson TD, Zhao W, Blood EA, et al. Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis. Four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts. J Bone Joint Surg Am. 2009;91:1295–304.
5. Thome C, Zevgaridis D, Leheta O, Bazner H, Pockler-Schoniger C, et al. Outcome after less-invasive decompression of lumbar spinal stenosis: a randomized comparison of unilateral laminotomy, bilateral laminotomy, and laminectomy. J Neurosurg Spine. 2005;3:129–41.
6. Macki M, Alvi MA, Kerezoudis P, et al. Predictors of patient dissatisfaction at 1 and 2 years after lumbar surgery [published online ahead of print, 2019 Nov 22]. J Neurosurg Spine. 2019:1–10. https://doi.org/10.3171/2019.8.SPINE19260.

7. Okuda S, Iwasaki M, Miyauchi A, Aono H, Morita M, Yamamoto T. Risk factors for adjacent segment degeneration after PLIF. Spine (Phila Pa 1976). 2004;29:1535–40.
8. Kim TH, Lee BH, Moon SH, Lee SH, Lee HM. Comparison of adjacent segment degeneration after successful posterolateral fusion with unilateral or bilateral pedicle screw instrumentation: a minimum 10year follow-up. Spine J. 2013;13:1208–16.
9. Amato V, Giannachi L, Irace C, Corona C. Accuracy of pedicle screw placement in the lumbosacral spine using conventional technique: computed tomography postoperative assessment in 102 consecutive patients. J Neurosurg Spine. 2010;12:306–13.
10. Raley DA, Mobbs RJ. Retrospective computed tomography scan analysis of percutaneously inserted pedicle screws for posterior transpedicular stabilization of the thoracic and lumbar spine: accuracy and complication rates. Spine (Phila Pa 1976). 2012;37:1092–100.
11. Lee SH, Lee JH, Hong SW, Chung SE, Yoo SH, et al. Spinopelvic alignment after interspinous soft stabilization with a tension band system in grade 1 degenerative lumbar spondylolisthesis. Spine (Phila Pa 1976). 2010;35:E691–701.
12. Gibson JN, Depreitere B, Pflugmacher R, Schnake KJ, Fielding LC, et al. Decompression and paraspinous tension band: a novel treatment method for patients with lumbar spinal stenosis and degenerative spondylolisthesis. Spine J. 2015;15:S23–32.
13. Mulconrey DS. Fluoroscopic radiation exposure in spinal surgery: in vivo evaluation for operating room personnel. Clin Spine Surg. 2016;29(7):E331–5.
14. Ghezelbash F, Schmidt H, Shirazi-Adl A, El-Rich M. Internal load shering in the human passive lumbar spine: review of in virto an finite element model studies. J Biomech. 2020;102:109441.
15. Natarajan RN, Watanabe K, Hasegawa K. Posterior bone graft in lumbar spine surgery reduces the stress in the screw-rod system—a finite element study. J Mech Behav Biomed Mater. 2020;104:103628.
16. Meyerding HW. Spondyloptosis. Surg Gynaecol Obstet. 1932;54:371–7.
17. Senegas J, Etchevers JP, Vital JM, et al. Le recalibrage du canal lombaire, alternative à la laminectomie dans le traitement des sténoses du canal lombaire. Rev Chir Orthop Reparatrice Appar Mot. 1988;74(Suppl. 2):15–22.
18. Aryanpur J, Ducker T. Multilevel lumbar laminotomies: an alternative to laminectomy in the treatment of lumbar stenosis. Neurosurgery. 1990;26:429–32.
19. Hong SW, Choi KY, Ahn Y, et al. A comparison of unilateral and bilateral laminotomies for decompression of L4-L5 spinal stenosis. Spine (Phila Pa 1976). 2011;36:E172–8.
20. Sasai K, Umeda M, Maruyama T, Wakabayashi E, Iida H. Microsurgical bilateral decompression via a unilateral approach for lumbar spinal canal stenosis including degenerative spondylolisthesis. J Neurosurg Spine. 2008;9:554–9.
21. Kelleher MO, Timlin M, Persaud O, Rampersaud YR. Success and failure of minimally invasive decompression for focal lumbar spinal stenosis in patients with and without deformity. Spine (Phila Pa 1976). 2010;35:E981–7.
22. Park JH, Hyun SJ, Roh SW, Rhim SC. A comparison of unilateral laminectomy with bilateral decompression and fusion surgery in the treatment of grade I lumbar degenerative spondylolisthesis. Acta Neurochir. 2012;154:1205–12.
23. Jang JW, Park JH, Hyun SJ, Rhim SC. Clinical outcomes and radiologic changes following microsurgical bilateral decompression via a unilateral approach in patients with lumbar canal stenosis and grade I degenerative spondylolisthesis with a minimum 3-year follow-up. J Spinal Disord Tech 2012 [Epub].
24. Wang S, Chao J, Wei J, Diaz FG. Short-term effectiveness of interlaminar lumbar instrumented fusion through a small incision for lumbar spinal stenosis. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2012;26:703–7.
25. Martin CR, Gruszczynski AT, Braunsfurth HA, Fallatah SM, O'Neil J, Wai EK. The surgical management of degenerative lumbar spondylolisthesis: a systematic review. Spine (Phila Pa 1976). 2007;32:1791–8.
26. Rampersaud YR, Fisher C, Yee A, et al. Health-related quality of life following decompression compared to decompression and fusion for degenerative lumbar spondylolisthesis: a Canadian multicentre study. Can J Surg. 2014;57:E126–33.
27. Postacchini F, Postacchini R, Menchetti PP, Sessa P, Paolino M, Cinotti G. Lumbar interspinous process fixation and fusion with stand-alone interlaminar lumbar instrumented fusion implant in patients with degenerative spondylolisthesis undergoing decompression for spinal stenosis. Asian Spine J. 2016;10(1):27–37.

Posterior Surgical Ligation and Cyst Decompression -via Needle Puncture- of a Large Anterior Sacral Pelvic Meningocele Through Posterior Sacral Laminectomy

Luis Azmitia, Giampiero Tamburrini, and Massimiliano Visocchi

1 Introduction

In order to understand the anterior sacral meningocele pathophysiology, we must first refer to the development of the spinal cord, which can be divided into three general phases: (1) gastrulation, (2) primary neurulation, and (3) secondary neurulation [1–5]. Immediately after the closing of the caudal neuropore—i.e., during the secondary neurulation—the development of the lower sacral segments of the spinal cord continues through day 26 (stage 12 of neurulation). During this phase, there is a nondirect involvement of the ectoderm (explaining the observed clinical closed dysraphism), and in parallel, the retrogressive differentiation—or necrosis—of the previously formed tail structures will develop into the filum terminale, the coccygeal ligament, and the ventriculus terminalis of the conus [2, 3]. Any related event during this stage will result in a structural deviation, thus leading to congenital malformations, such as an abnormally long spinal cord, a persisting ventriculus terminalis, a tight filum terminale, a terminal myelocistocele, or an intra−/anterosacral meningocele, among others.

This last one, the anterosacral meningocele, was first described by Bryant in 1837 [1] as a cystic mass that protrudes as an anterior sacral—unilocular or multilocular—defect into the pelvic retroperitoneal space. This structural malformation is mostly congenital (like Currarino syndrome, a rare autosomal dominant disorder of embryonic development characterized by a triad of anorectal malformations, presacral masses—most commonly an anterior sacral meningocele—and sacral bony defects) but sometimes acquired (always as consequence of an ectasia related to Marfan syndrome or Ehlers–Danlos syndromes, neurofibromatosis, or trauma sustained in the sacrum) [6]. Furthermore, thanks to its inner clinical evolution, typical clinical flags to consider are cutaneous manifestations (in 50–80% of the patients since birth), neurological deficits (e.g., gait disturbances), uterus duplications, lipomas, sacrococcygeal teratomas, dermoid cysts, and epidermoid tumors, thus leading the clinician to suspect a hidden dysraphism [6, 7]. A clinical history of the mother and other clinical manifestations (e.g., anorectal defects) or asymptomatic/nonspecific symptoms, such as constipation, dysmenorrhea, dyspareunia, urinary retention, incontinence, dysuria, polyuria, radicular pain, and paresthesia (related to colorectal, reproductive, genitourinary, and neurological dysfunctions), will help us to consider more-complex clinical syndromes, such as Currarino syndrome, and other associated congenital disabilities [6, 8, 9]. Radiological exams are needed to complete the diagnosis and plan the clinical approach: X-rays show a pathognomonic scimitar-shaped sacrum (mostly caudal and always present), which are followed by a 3D computed tomography (CT) scan and complemented with MRI/myelography of the area (the gold standard), thus not only showing the circumscribing of the neck of the meningocele—its narrow communication through the defect—but also showing other concomitant pathologies while describing the pelvic anatomy prior to determining the therapeutical approach [10]. Ultrasound is usually the first diagnostic tool, and it will help us in cases where the patient require surgery and follow-up.

2 Case Presentation

A young (24-year-old) female Mediterranean patient came to our neurosurgical department with a subjective sensation of a pelvic mass, along with a lazy bladder syndrome with urinary retention (400 mL rest urine) but without fur-

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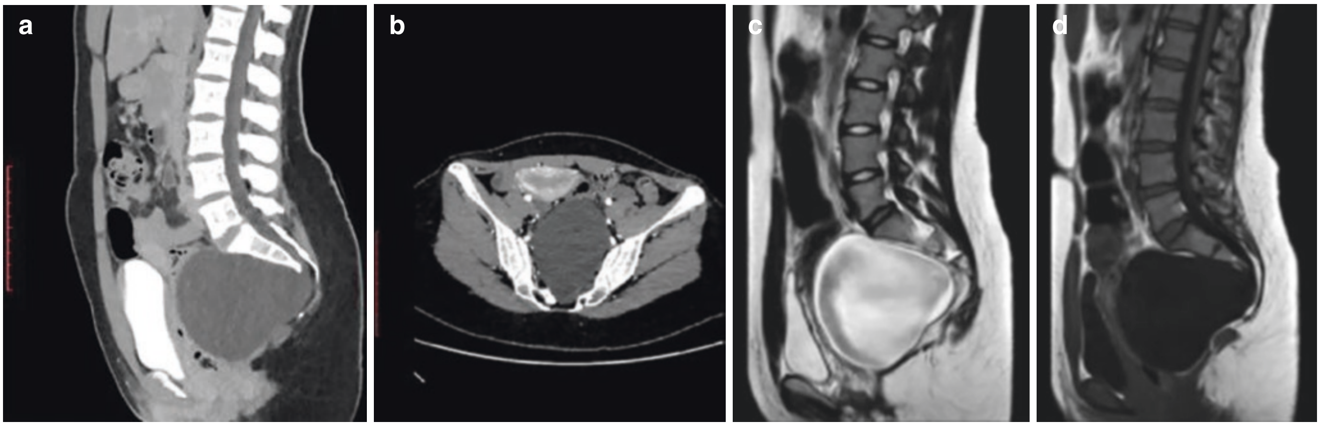

Fig. 1 (**a**) Sagittal CT scan showing the cyst entering the pelvic region; (**b**) contrast-enhanced CT of the anterior sacral meningocele; (**c**) and (**d**) MR of T2 and T1 sagittal lumbosacral reconstruction; CSF turbulence (hypointensity inside hyperintensity in the meningocele) is evident in the meningocele caudal to S3 (**c**) and a hypertrophic fat layer in the sacrum

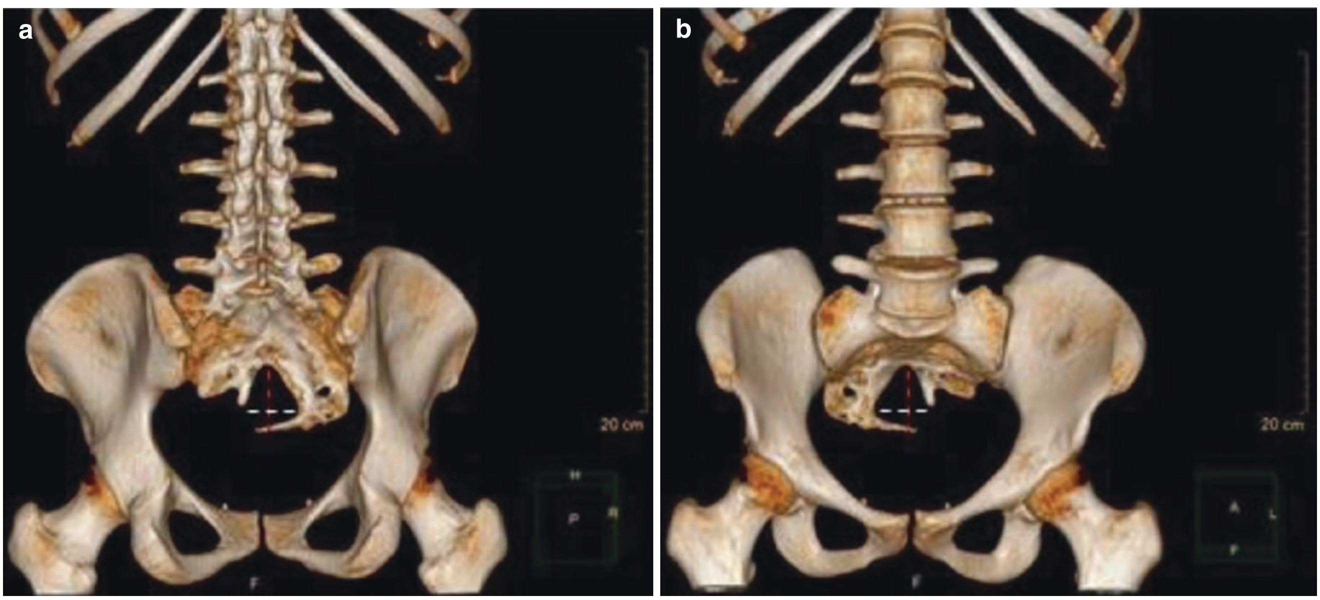

Fig. 2 CT scan of the lumbosacral, pelvic, and spine areas: (**a**) posterior aspect of the sacral defect; (**b**) anterior aspect of the sacral defect; in both cases, the defects were measured, showing a vertical diameter of approximately 4 cm (dotted red line) and a horizontal diameter of 3 cm (scale right, in yellow)

ther relevant deficits, symptoms, or diagnoses (in particular, defecation remained intact). Further clinical history was also negative. An initial CT scan was performed, followed by MRI (Fig. 1), specifically the myelographic sequences, which showed a hyperintense cystic lesion at the anterosacral level with no evidence of further masses. A CT scan with 3D reconstruction (Fig. 2) was performed, and it better defined the anterosacral defect under S2. Owing to the size of the meningocele, we decided to operate, aiming to completely interrupt the communication between the meningocele and the spinal subarachnoidal space [6].

3 Surgery

Under general anesthesia, the patient was put into a prone position (Fig. 3a). Electrophysiological monitoring was performed during the whole operation (Fig. 3c). A medial incision from the sacrum to last lumbar vertebra (including the L5 spinous process; see Fig. 3b) was performed. During the careful dissection in the planes, no lipoma but local fat hypertrophy was observed along the surgical corridor, so it was resected in order to simplify the surgery. An antenna for neuronavigation was placed at L5, and intraoperative 3D reconstruction was performed. Minimal laminectomy—cranial to the bone defect—was performed after the identification of the S2 roots and after confirmation through electrophysiological monitoring. The sparing of S2 and exposition down from S3 were carried out. The further careful dissection of the nerve roots from S3 to the filum terminale allowed the delimitation of the anterior sacral defect.

The S2 nerve root was repeatedly stimulated, which was confirmed under electrophysiological testing. The dissection of the anterior epidural space at the level of S3-S4, just before the neck of the meningocele, was conducted with curved Kelly forceps. The Kelly forceps were passed toward the contralateral side (left to right) and through the dissected epidural space in order to pass a switch and to ligate all the nerve roots down to S3 with a nonabsorbable thread. In addition, two more threads were placed in the same fashion and at the same level. The further dissection of the neck of the meningocele under neuronavigation (Fig. 3d) was carried out, along with needle punction (Fig. 3e) and aspiration with approximately 400 mL of CSF from the dorsal. Finally, direct microsurgical exploration via enlarging the aspiration

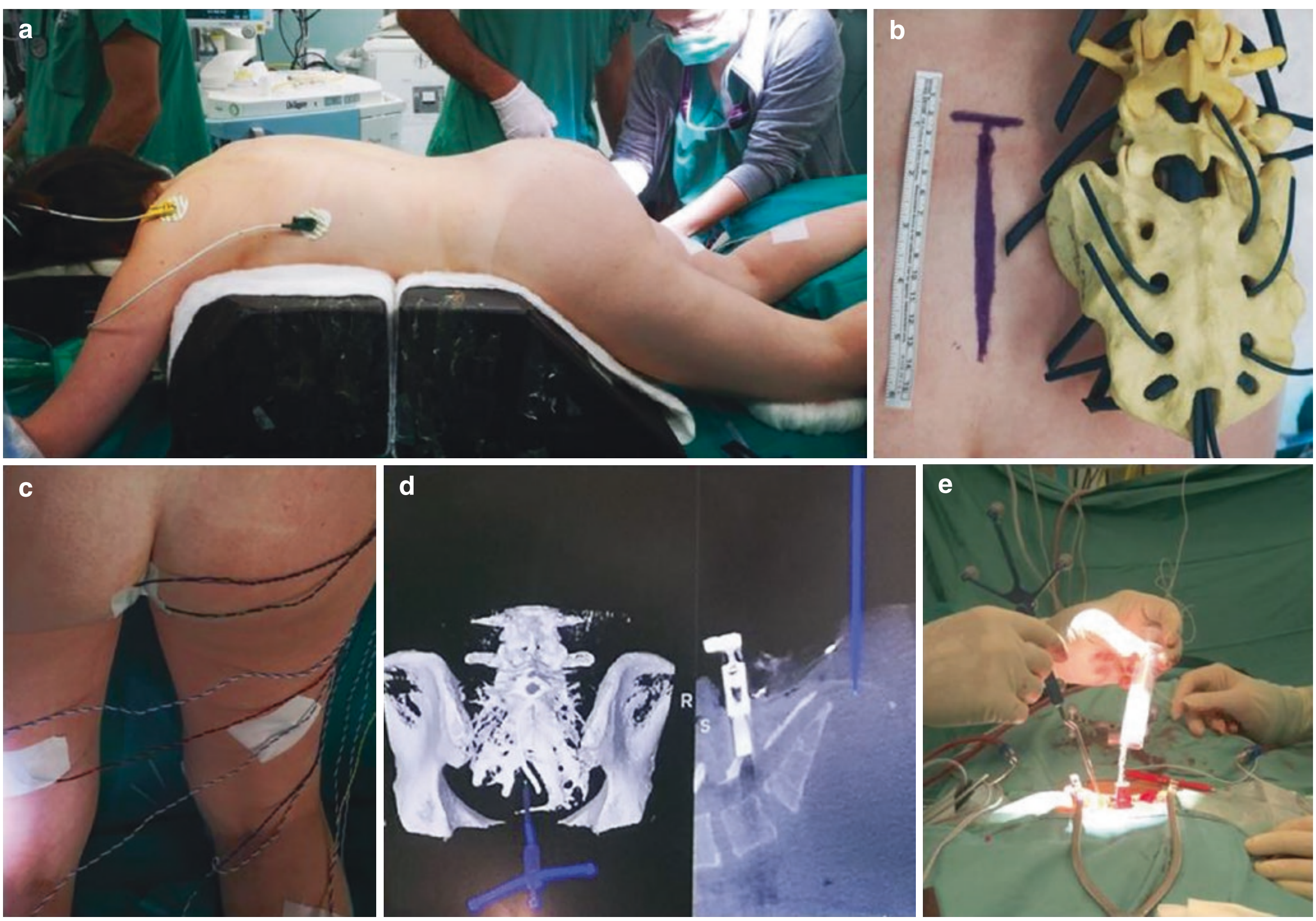

Fig. 3 Operational procedure: (**a**) prone position of the patient; (**b**) incision and comparison with an anatomical model; (**c**) electrophysiological placement of sensors for control over nerve roots S1 and S2; (**d**) confirmation of puncture's trajectory through neuronavigation; (**e**) needle aspiration of the cyst

Fig. 4 Postoperative MR of T2 sagittal reconstruction showing the disappearance of the meningocele dorsal to the distended bladder

point was performed, and intraoperative control was done through ultrasound, confirming a succesful decompression of the cyst in situ. No intradural dissection was needed because no intradural elements were confirmed during diagnosis. The puncture site was closed with three knots and Dura plastic with TachoSil. The Valsalva maneuver evidenced no residual CSF fistulas. No further exploration or drainage was needed. Closure was completed in layers. The patient was mobilized day 1 after surgery and released during the first week after procedure without any complications. A postoperative MRI scan conducted shortly after surgery showed complete regression (Fig. 4). The patient had no new postoperative-related symptoms, and their bladder dysfunction progressively recovered. At the latest, 3-month follow-up, the patient had completely recovered.

4 Discussion

Because the majority of the symptoms are due to mechanical compression from the meningocele pushing into the pelvic cavity and because the pelvic meningocele is fed through the neck of the meningocele (from the subarachnoidal space), the goal of surgery is to achieve a complete occlusion of the linkage between the pelvic meningocele and the normal subarachnoidal space [10].

Although conservative treatment for small and uncomplicated defects has been reported, no spontaneous regression has been documented [10, 11]. The previous goals of achieving minimal invasiveness have been described, such as decompression through the rectum or vagina, but with the risk of lethal consequences like meningitis, therefore not recommended [1]. Similarly, other, more-invasive alternatives have been described, such as abdominal cyst shunts [10]. Nevertheless, such cases were approached after evaluating the individuals' specific particularities. When facing anterior sacral defects, the clinician has to exclude any other rare disorder (e.g., Currarino syndrome), principally because of the risk of other masses with a malignant tendency (e.g., teratomas) but also because of the risk of life-threatening complications (e.g., rupture). Thus, the multifaced architecture of such pathology, reaffirms the importance of surgical planning and therapy, while highlighting the safety of posteriour approaches [10, 12].

Similarly to that discussed in the previous paragraph, the symptoms will be also a result of obvious direct mechanical stress, therefore careful surgical planning/execution is recomended [12]. Some reports have confirmed that patients who did not undergo surgical decompression had a 30% mortality after a pelvic obstruction (e.g., during labor) or after having developed an erosion near the rectum with subsequent meningitis [1]. Although ultrasound is the first step of diagnosis, further radiological imaging before surgery should include X-rays, CT scans with 3D reconstruction, and MRI scans of the pelvic region with myelography in order to plan the surgery and exclude any other malformations. During this diagnostic stage, we encourage considering Currarino syndrome by excluding any hemiagenesis/agenesis, partial sacral agenesis with the presence of S1, hemisacrum, or coccygeal agenesis [8]. Furthermore, if the anterior sacral meningocele has been confirmed, principally in bigger defects, and if the stalk is too wide or/and superior to S2, an anterior approach might again be considered. Nevertheless, "bigger" is defined after the individual has become symptomatic; by the experience of the clinician or a multidisciplinary team; and mostly by the presence of any neural elements in the cyst [1].

If a surgical approach is indicated, planning is important to clarify the level of the lesion because the plan has to preserve the S1 and S2 functional roots, whereas the caudal levels can be sacrificed without any clinical consequences. Although the S3 roots are involved in bladder innervation in 100% of cases, they are exclusively involved in only 20% of cases. Other sacral nerve roots are involved, namely S3 + S4 (in 30% of cases), followed by S2 + S3 (in 15% of cases), S2 + S3 + S4 (in 15% of cases), and S3 + S4 + S5 (in 5% cases) [13]. Hence, a posterior approach (cyst decompression with a needle) will help us to minimize the invasiveness and thus save S1 and S2.

To help guide the strategy, Cheng et al. has suggested, on the basis of their experience of 11 cases a three-class grading system that is in accordance with anatomy and the relationship between the nerve root and the meningocele: namely caudal, paraverval and nerve root types. There is still no neurosurgical consensus and more experience might be needed [6].

Even though a patient with an anterior sacral meningocele may not develop hydrocephalus (in contrast with posterior dysraphism) from the risk of a theoretical recurrence and its concomitants (e.g., fistula via constant CSF pulsation, meningitis, and postoperative pelvic contamination after punction), we suggest regular neurosurgical counseling [10].

5 Conclusion

The posterior approach to an anterior meningocele appears to be feasible when dealing with a meningocele neck located down to S3. In this circumstance, cyst decompression with a needle after dural sac ligation down to S3 via the sparing of the upper sacral roots (i.e., S1 and S2) appears to be a safe and minimally invasive procedure. Otherwise, an anterior approach has to be studied on the basis of the specific symptoms of the patient and the experience of the surgeon when dealing with a meningocele neck located up to S3. Finally, the goals have to be (1) the interruption of the communication defect between the cyst and the intraspinal subarachnoidal space and (2) the effective drainage of CSF from the meningocele.

Conflicts of Interest The authors declare no conflicts of interest.

References

1. Villarejo F, Scavone C, Blazquez MG, Pascual-Castroviejo I, Perez-Higueras A, Fernandez-Sanchez A. Anterior sacral meningocele: review of the literature. Surg Neurol. 1983;19(1):57–71.
2. Back SA, Plawner LL. Chapter 60: Congenital malformations of the central nervous system. In: Gleason CA, Devaskar SU, editors. Avery's diseases of the newborn. 9th ed. Philadelphia: W.B. Saunders; 2012. p. 844–68. https://www.sciencedirect.com/science/article/pii/B9781437701340100605. [zitiert 30 Aug 2021].
3. O'Rahilly R, Müller F. Neurulation in the normal human embryo. In: Bock G, Marsh J, editors. Novartis Foundation Symposia. Chichester: Wiley; 2007. p. 70–89. https://onlinelibrary.wiley.com/doi/10.1002/9780470514559.ch5. [zitiert 28 Aug 2021].
4. Stone JG, Bergmann LL, Takamori R, Donovan DJ. Giant pseudomeningocele causing urinary obstruction in a patient with Marfan syndrome. J Neurosurg Spine. 2015;23(1):77–80.
5. Mühl-Benninghaus R. [Spina bifida]. Radiologe. 2018;58(7):659–63.
6. Cheng C, Tao B, Bai S, Gao G, Li S, Shang A. Anterior sacral meningocele: a new classification and treatment using the dorsal transsacral approach. Spine. 2020;45(7):444–51.
7. Acharya UV, Pendharkar H, Varma DR, Pruthi N, Varadarajan S. Spinal dysraphism illustrated; Embroyology revisited. Indian J Radiol Imaging. 2017;27(4):417–26.
8. Serratrice N, Fievet L, Albader F, Scavarda D, Dufour H, Fuentes S. Multiple neurosurgical treatments for different members of the same family with Currarino syndrome. Neurochirurgie. 2018;64(3):211–5.
9. Vinod MS, Chandra Shaw S, Devgan A, Mukherjee S. The Currarino triad. Med J Armed Forces India. 2018;74(4):374–6.
10. Wang Y, He B, Yang J, Xu J, Liu J, Huang S. Individualized management of giant anterior meningoceles-case series. Medicine (Baltimore). 2020;99(14):e19631.
11. Manson F, Comalli-Dillon K, Moriaux A. Anterior sacral meningocele: management in gynecological practice. Ultrasound Obstet Gynecol. 2007;30(6):893–6.
12. Tucker AM, Morgenstern P, Diaz D, Sedighim S, Shaul D, Sydorak R, et al. Neurosurgical management of Currarino syndrome: a case series and review of literature. Surg Neurol Int. 2019;10:70.
13. Carlucci L, Wavasseur T, Bénard A, Sesay M, Delleci C, Goossens D, Vignes J-R. Functional variability of sacral roots in bladder control. J Neurosurg Spine. 2014;21(6):961–5. https://doi.org/10.3171/2014.9.SPINE13667. Epub 2014 Oct 17. PMID: 25325171.