A Journey from the Past to the Future

60

Muharrem Yazici, Behrooz A. Akbarnia,
George H. Thompson, Ron El-Hawary, and John B. Emans

Contents

60.1 Yesterday

Although first attempts at treating spinal deformities date as far back as many years before Christ, those groundbreaking changes that define our contemporary practice of spinal surgery were accomplished by senior spine surgeons many of whom are still actively practicing today. If we recall that the history of the first universal implant, pedicle screw, multisegmentary instrumentation, and the development of intraoperative neuromonitoring was only 40–45 years ago, we can better grasp the amount of distance that has been traversed in such a short period of time.

Harrington does not only hold historical significance because he invented a type of spinal implant that would improve the problems of innumerable patients, but more importantly, because he took the first and most crucial step in making instrumented surgery possible for young children with scoliosis. Harrington's implant today may be only a curiosity of the past. However, the inspiration and courage it kindled endowed contemporary spine surgeons with the resolve to go beyond the acceptable and aim for better, the best results. With the demonstration of this kind of resolve, a wide range of patients from children and adolescents to octogenarians have been able to benefit from the rewards of corrective spinal surgery.

Despite these rapid developments in spinal deformity surgery, early-onset scoliosis (EOS) remained an orphan area that did not receive the attention it deserved for a long time. The causes for this paucity of interest can be traced back to the rarity of this condition, the lack of sufficient infrastructure and superstructure in many clinics to handle this complicated patient group, and a lack of knowledge regarding the natural history, availability, and effective management of the pathology. Historically, earlier EOS treatment focused on controlling the spinal deformity, often with early spinal fusion. The attitude that "short and straight" is better than curved led to many short spines after early fusion for EOS. Moe and Harrington attempted the first growing rods that were plagued with technical failures.

Fortunately, today the field of EOS has changed drastically, becoming an area of passionate discussion, generation of tremendous evidence, and rapid discovery of knowledge. The incendiary effect of two factors that serve to accelerate and facilitate this striking change cannot be denied. The first is the definition of the thoracic insufficiency syndrome by Dr. Robert Campbell and the subsequent development of his

M. Yazici
Department of Orthopaedics and Traumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

B. A. Akbarnia
Department of Orthopaedic Surgery, University of California, San Diego, San Diego, CA, USA

G. H. Thompson
Department of Orthopaedic Surgery, Rainbow Babies and Children's Hospital, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH, USA

R. El-Hawary (✉)
Paediatric Orthopaedics, School of Biomedical Engineering, IWK Health Centre, Dalhousie University, Halifax, NS, Canada
e-mail: ron.el-hawary@iwk.nshealth.ca

J. B. Emans
Department of Orthopedic Surgery, Harvard Medical School, Boston Children's Hospital, Boston, MA, USA

B. A. Akbarnia et al. (eds.), *The Growing Spine*, https://doi.org/10.1007/978-3-030-84393-9_60

implant to correct the problem. The second is the establishment of new standards for a well-known technique that had fallen into disfavor due to its previously disappointing results: the growing rod. Akbarnia and Thompson's use of dual growing rods, as well as Campbell's VEPTR device, and the recognition that chest and spine growth are connected fueled the contemporary advances in EOS discovery and treatment.

Many other advances have contributed to the invention of new treatment techniques, the design of new implants, and, more importantly, a better understanding of the disease and the conception of more realistic solutions. Among these are the formation of a committee on growing spine problems within the Scoliosis Research Society (SRS) that inspired new research and contributed to its coordination; the International Congress on Early Onset Scoliosis (ICEOS), the first of which convened in Madrid in 2007, bringing together all interested parties (surgeons, nurses, pulmonologists, basic scientists, and others) and providing a consistent scientific platform for the exchange of ideas; the founding of the Growing Spine Study Group (GSSG) and Children's Spine Study Group (CSSG), the collection of multicenter data with eventual merger of these two groups into the Pediatric Spine Study Group (PSSG); and, last but not the least, the publication of this book in three successively larger editions, dedicated exclusively to spinal disorders in young children.

60.2 Today

Early-onset spine deformities are no longer orphan diseases. In the last few years, a number of high-evidence-level studies have been completed, addressing a multitude of topics in EOS, from classification to the definition of risk factors, from the development of patient-specific outcome analysis instruments to how the natural history affects the spine and nonspine organs, and from sophisticated and objective clinical and radiographic evaluation methods to efficient and safe treatment options. EOS treatment is evolving with data-driven knowledge, such as the realization that early surgical treatment of spine-based distraction may lead to early cessation of lengthening, that serial casting is more successful than initially expected, and that EOS surgical treatment works well for previously untreatable neuromuscular and syndromic patients (i.e., spinal muscular atrophy). The EOS literature has proven itself to possess a trend for exponential expansion. A search of the term "early onset scoliosis" on the National Institute of Health's PubMed.gov site demonstrates the impressive growth in the number of articles published per year from 6 published in the year 2000, to 25 published in the year 2010, to 152 published in the year 2020 for a total of 1023 total publications as of June 2021.

Through all these developments, surgeons who find themselves facing a young child with a deformed spine and a distorted chest cage can now feel more knowledgeable regarding treatment and are able to assist these children's families in looking more hopefully upon a brighter future. However, although we know we are on the right path, it is obvious to us that the road is long and beset with many obstacles. It undoubtedly remains important to achieve sufficiently long, functionally, and cosmetically aligned spines for these children, comparable to those of their peers. However, the questions that loom before us are these: what is the price to be paid for the attainment of this goal, and how close can we get, at the end of the road, to achieving as close to normalcy, regarding the spine in particular and the patient's physical and mental well-being in general?

With the increase of the variety of treatments available for EOS, obtaining a spine with normal length and alignment in all three planes during adolescence – at least in idiopathic EOS patients without comorbidity – is no longer a long shot, but rather a routine outcome. Unfortunately, these groundbreaking developments have not been proven yet to be efficient in eliminating the ambiguity in what the future holds for the surgically treated patients in terms of mental well-being and pulmonary function in adulthood. Future studies in this area should definitely be prioritized, as should the promotion of actions that can be taken in childhood to avoid potential detrimental impacts.

60.3 Tomorrow

After emphasizing the significance of the juncture at which we have arrived, and highlighting the greatness of the distance traversed, we can summarize the points that are still in requirement of intense research as such.

Today, spinal deformity surgeons can perform operations that as short a time as 10 years ago appeared to be no more than figments of the imagination. The safe three-dimensional reconstruction of the spine, regardless of severity of the deformity or etiology, is now a realistic expectation, and fortunately, thousands of children around the world can now look forward to better health due to its availability. Despite these truly remarkable advances, two significant abilities still elude us: recognize early those patients with a predisposition to deformity, and reliably predict and prevent progression of, or even reverse, existing deformity.

The SRS Growing Spine Committee has published the following goals of treatment for patients with EOS: minimize spinal deformity over the life of the patient, maximize thoracic volume and function over the life of the patient; minimize the extent of any final spinal fusion; maximize motion of chest and spine; minimize complications, procedures, hospitalizations, and burden for the family; and to

consider the overall development of the child. These goals are aspirational and should be viewed as the current standard for the future treatment of EOS.

The first step in effective treatment is the prevention of the disease. Preventative medicine is the successful resolution of conflict between disease and physician without the spillage of blood. However, spinal surgeons can only enter the picture at the conclusion of the process, and the treatment they apply cannot bring back what has been lost up until that point or prevent damage before it occurs. Although the genetic background of spinal deformities has been on the forefront of scientists' agendas for many years, it is impossible to say that great strides have been made regarding this subject. Genetic research regarding EOS is at the time almost nonexistent. However, the necessary knowledge for early recognition of individuals under risk, perhaps during the intrauterine period or even before pregnancy, would provide a unique opportunity for the development and institution of preventative measures. An Orthopaedic Research and Education Fund (OREF) sponsored effort by the PSSG and Texas Scottish Rite Hospital for Children (TRSH) led by Dr. Wise is currently evaluating the frequency of diagnostic genetic mutations in patients with idiopathic EOS. The project aims to identify patients with atypical presentations that confound the clinical diagnosis as well as to identify new idiopathic EOS candidate genes. Another important initiative on genomics research for EOS is The Nathan Project for Rare Diseases, led by Garcia's team in Perth, Australia. The goal of this project is to collaborate with the PSSG registry and link it to existing biobank infrastructure. This will provide the appropriate resources required for the effective translation of basic research into clinical practice, ultimately improving patient outcomes and quality of life.

> Studies on the genetic background of EOS are required, which would command intensive effort and determination, especially as this is not an area where short-term projects and quick results abound.

The possible relationship between melatonin and adolescent idiopathic scoliosis (AIS) discovered during the late 1990s and early 2000s caused much excitement among spinal surgeons. The possibility of medically controlling adolescent curves resounded with many. Since then, the lack of progress that was hoped for in this area may have caused disappointment. However, persistent research into the mechanisms that create deformity will undoubtedly result, one day, in the discovery of methods that enable us to reverse them. Through this kind of advances, it will become possible to engage these curves in a more humane manner, without the bloodshed, and to be proactive by nipping the deformity in the bud before it gains a hold of the spine.

> Studies regarding the etiology of deformity and the management/modulation of these etiological factors utilizing medical, biological, and other such methods are the most critical advances expected in the near future.

Contemporary techniques utilized in the treatment of EOS such as surgery and casting expose young children to the potentially detrimental effects of repetitive anesthesia. Strong evidence exists regarding these negative effects on the immature brain, indicating that children undergoing repetitive general anesthesia sessions grow up to suffer from learning disabilities and abnormal behavior. Understanding this matter will continue to grow with the conclusion of some large-scale, prospective, multicenter trials. If these concerns are legitimate, the recent popularity of cast treatment, which has reemerged as an alternative to growth-friendly surgical methods because of its ability of controlling curve progression without affecting spinal growth and mobility, will need to be reexamined.

> There exists a great need for data on the effects of undergoing anesthesia during childhood on growth and development. Detailed studies examining the effects of the various types of anesthetic agents and number of applications on the same should be conceived.

Patients with EOS are evaluated routinely with diagnostic imaging modalities that are associated with high doses of radiation with upward of 60 mSv exposure. Extrapolating from data on adolescent idiopathic scoliosis patients, who have a 4.8 relative risk of developing cancer as compared to the population, EOS patients will also likely have an increased risk of developing cancer in adulthood. Currently, low-radiation biplanar slot scanning radiographs are able to be performed in older EOS patients; however, further research is required to be able to use this modality in younger children. Future innovation is also required for intraoperative imaging and navigation in order to lessen the radiation burden.

Childhood is a period of life that should be experienced without anxiety or worry about the future. However, the existence of a condition that precludes a profoundly joyful experience of this life chapter, one that brings with itself a necessity for serious medical and surgical intervention, creates a massive stress generator for the child and parents regardless of the innate effects of this condition on the body. This stress will be greatly magnified if, during the treatment of this condition, the child is forced to leave their social circle for extended periods of time, to be imprisoned in cold and desolate hospital environments full of frightful strangers, and, more importantly, to undergo multiple painful procedures and bouts of immobilization afterward.

Treatments such as the traditional growing rods (TGR), vertical expandable titanium ribs (VEPTRs), and cast applications under anesthesia require long-term, repetitive dependency on hospitals and doctors, causing children to spend

many birthdays and holidays in the hospital. Should complications occur, the process becomes even more difficult on the children and they must endure greater stress. This shifts the focus from problems in the present to possible, but not certain, implications of the disease in the future. The recent use of magnetically controlled growing rods (MCGRs) has addressed, at least partially, some of these issues.

Although the psychological effects of other childhood disorders have been the subject of many previous studies, a paucity of information exists regarding health problems specific to EOS, the treatments intending to decrease these problems, their effects on the psychologies of the individual and the family, or the variation in such effects as pertains to the severity of disease and success of treatment.

> It is entirely insufficient to evaluate the long-term effects of EOS and their treatments on the individual child, solely by clinical and radiographic methods. Ability to see the complete picture will emerge only if psychological aspects of the situation are also considered and included within the study design. Evaluation with instruments specifically developed for this disease with inclusion of the special situations that may arise during its treatment is essential.

Historically, the measurement of the success of treatment for spinal deformities was based on radiological parameters alone. Improvements in major curve angles were considered evidence of treatment success. Once it was recognized that clinical improvement and radiology did not always correlate with true clinical outcomes, the necessity arose to include other parameters such as cosmetic determinants (shoulder balance, rib hump, waistline asymmetry, etc.) and those of functional capacity as well. The introduction into our daily practice of health-related quality of life tools, such as PROMIS scores and EOS Questionnaire (EOSQ) scores, that aim to determine objectively the perception of the patient of the clinical and radiological improvements imparted upon their body with or without treatment is relatively new. Studies have been performed on the pediatric age group aiming to determine the impact on quality of life of some disorders both in childhood and later in adulthood and the outcomes of treatment. The parent is relied upon for the acquisition of data during childhood that can, in adolescence and adulthood, be obtained from the patient themselves. The reliability of this secondhand information is subject to controversy. Again, evaluations performed at the beginning and at the end of the process when the child is able to communicate will be obtained from two different people, who, even though sharing a common living space, are still two different people with different experiences, making an objective and reliable comparison impossible. Having never experienced the normal, the expectations of children with chronic disease are shaped by their afflictions, introducing new and fundamental difficulties for the comparison of the data obtained from them to that obtained from healthy individuals.

Furthermore, EOS includes a fairly heterogeneous group of patients, ranging in etiology from congenital deformities with serious pulmonary comorbidities to serious muscular dystrophies with a life expectancy of only one or two decades and from spastics with profound developmental delay to spina bifida patients burdened to go through life with immobile, insensate lower extremities. Even though it may be a good start, it will soon be obvious that combining these children afflicted with this huge spectrum of problems together, into the subject heading of "early-onset spine deformity" and hoping to evaluate them effectively, utilizing a single questionnaire, is insufficient.

> The development of new, detailed questionnaires specific to EOS that take into account the child's comorbidities that are sensitive enough to distinguish the negative effects of disease from those of treatment complications and show high compatibility between information collected from child and/or parents and caregivers is required. Studies utilizing such questionnaires will profoundly affect the future direction of treatment. This should also include an evaluation of the burden of care on the mental and physical well-being of the child's caregiver.

The concept of MCGR that aim to halt the progression of young children's spinal deformities while protecting them from repeated surgical procedures and possible complications, and preserving their growth potential is undoubtedly going to become a new keystone in EOS treatment. It is remarkable progress that this concept has become reality today, when very recently it was only a dream for pediatric spinal deformity surgeons. This ability to adjust an implanted device painlessly and bloodlessly with a mechanism outside the body will enable us to reach our treatment goals more easily than with the often-problematic traditional methods. This advance is significant not only for our current patients treated with this treatment today, but the great group of future patients not even born yet who will benefit from yet newer, perhaps even less invasive, methods inspired by the magnetic rod itself.

While the concept of MCGR is groundbreaking and hopefully inspiring, the treatment is far from being ideal from technological and design points of view. This subject is virgin territory, with a great need for the conception and completion of many research projects. Further innovation with self-lengthening growth-friendly rods is included in this edition of our textbook. A new chapter entitled "Other Growth-Friendly Instrumentation" describes three novel self-lengthening growth-friendly devices from around the world. The Modern Luqué Trolley (MLT) was developed in Canada and utilizes low-friction materials such as polyethylene, PEEK, and low-friction titanium to allow for growing rods to lengthen along unique anchors as the child grows. The One-Way Self-Expanding Rod (OWSER) was developed in France and takes advantage of permanent tension between the two ends of a bipolar construct to allow for

elongation secondary to patient growth and from activities of daily living. The Spring Distraction System (SDS) was created and evaluated in the Netherlands. This system imparts permanent internal distraction forces through a pre-tensioned longitudinal helical spring that is able to deliver a continuous distraction force. At early follow-up, these three guided growth systems appear to be a safe alternative option with a low complication and particularly low-revision surgery rates.

> The noninvasive ability of adjusting implanted devices from outside of the body, which aims to control spinal deformity, investigations on the feasibility of yet more different technologies other than magnetism such as smart metals, the creation of technologies that will in addition to pure distraction, allow correction based on translation and derotation, and the design of new surgical techniques, more friendly to physiological spinal alignment are topics awaiting those researchers equipped with curiosity and drive.

Anterior vertebral body tethering is also proving to be a feasible treatment for the older child with EOS. The goal of this treatment is to control the patient's remaining spinal growth to prevent further progression and to achieve curve correction by exploiting the Heuter–Volkman principle. The determination of ideal candidates and indications for VBT continues to evolve. Very young, immature patients can be at risk of overcorrection, and patients with very large curves may experience insufficient correction. Further research and development will be required to enhance the reliable utilization of this fusionless solution for progressive juvenile idiopathic scoliosis.

60.4 Conclusion

In summary, judging by developments in the field of EOS that have taken place in the last decade and today give rise to the most passionate discussions, we can expect even more fascinating, thought-provoking, and powerful advances in the near future. Under the light of healthy and objective analysis of the past, walking to a brighter future ceases to be a dream. Evidence-based guidance engendered by study groups, scientific associations, and discussion platforms such as the ICEOS will create a more productive and efficient work environment for surgeons dedicated to EOS, allowing us to come together and, for our young children afflicted with spinal deformities, provide a better and brighter future. The recent merger of the two major EOS registries, the GSSG and the CSSG, into the PSSG has created the largest pediatric spine database in the world. With close to 10,000 patients enrolled in this registry, the international EOS community is now in a position to achieve our group's simply stated, yet lofty, mission of helping children with spine problems live longer, better lives.