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REVIEW

The incidence of postoperative cerebrospinal fluid leakage after elective cranial surgery: a systematic review

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Abstract

Cerebrospinal fluid (CSF) leakage is a major complication after elective neurosurgical procedures. The aim of this systematic literature review is to summarize the incidence rates of postoperative cerebrospinal fluid leakage for neurosurgical procedures, classified by surgical approach. The Pubmed, Cochrane, Embase, and Web of Science databases were searched for studies reporting the outcome of patients undergoing elective neurosurgical procedures. The number of patients, surgical approach, and indication for surgery were recorded for each study. Outcomes related to CSF leakage such as clinical manifestation and treatment were reported as well. One hundred and thirteen studies were included, reporting 94,695 cases. Overall, CSF leaks were present in 3.8% of cases. Skull base surgery had the highest rate of CSF leakage with 6.2%. CSF leakage occurred in 5.9% of anterior skull base procedures, 6.4% of middle fossa, and 5.2% of transpetrosal surgeries. 5.8% of reported infratentorial procedures were complicated by CSF leakage versus 2.9% of supratentorial surgeries. CSF leakage remains a common serious adverse event after cranial surgery. There exists a need for standardized procedures to reduce the incidence of postoperative CSF leakage, as this serious adverse event may lead to increased health care costs.

Keywords Cerebrospinal fluid leakage · Complication · Cranial surgery · Skull base surgery

Introduction

Cerebrospinal fluid (CSF) acts as an important protector for the central nervous system. Apart from mechanical protection as shock absorber, it provides nutrients to the brain and disposes of waste products. The CSF in the subarachnoid space is surrounded externally by tough dura mater which is formed by a double layer of connective tissue consisting of collagen fibers, elastin filaments, and fibroblasts. The dura mater protects the brain from invasion by infectious agents and supports blood vessels nourishing the central nervous system.

Various neurosurgical procedures require opening of the dura. Postoperative CSF leakage represents a major and challenging complication in skull base surgery and neurosurgery in general. It can manifest as rhinorrhea, otorrhea, or leakage through the operation wound, i.e. incisional leakage. When a subcutaneous fluid collection does not exit the wound, it is referred to as pseudomeningocele. CSF leakage often results in secondary complications including surgical site infection, meningitis, delayed wound healing, or cranial hypotension. A postoperative CSF leak can be treated conservatively, using bed rest and/or pressure dressings. Lumbar punctures or placement of a lumbar drain may resolve the leak, but in about 3% of surgeries, reoperation is needed [23]. The accompanying increased healthcare needs, including prolonged hospitalization or redo surgeries, result in increased healthcare costs, both to the patient and the healthcare system.

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Incidence rates of postoperative CSF leakage have been reported in up to 13% of elective neurosurgical procedures [28]. However, no systematic reporting nor definition of CSF leakage exists. Some studies only reported leaks requiring reoperation, while others included spontaneously resolving leaks as well. The incidence of CSF leakage also depends on the surgical approach, location, and size of the lesion as well as patient characteristics as shown in previous studies where a correlation between the incidence of CSF leaks and the age of the patient, comorbidities, and patient-specific risk factors was observed [68, 90].

Given the major consequences of CSF leakage, it is clear that adequate dural closure is of paramount importance. A large variety of methods and techniques for optimization of dural closure has been described. These include the use of grafts or augmentation techniques, based on both autologous as well as synthetic products [13]. However, controversy exists about which method is the most effective.

To our knowledge, no extensive review nor meta-analysis has been performed on postoperative CSF leakage, taking into account the surgical approach, regardless of closure technique. The current review aims to describe the incidence rates of postoperative CSF leakage for neurosurgical procedures, classified per surgical approach.

Methods

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Ethical approval was not required to perform this study.

Information sources and search method

The literature search was performed in PubMed, Embase, Cochrane, and Web Of Science Core Collection (WOS) databases. The strategy was based on the population, intervention, control and outcomes (PICO) principle and constructed using MeSH-terms for PubMed and Emtree terms in the Embase search. The 22 documents the search strategy used for all databases.

Study selection

Title and abstract were used to select for relevant publications. Potentially suitable publications for this review were screened for eligibility based on their full text by BC. Additional publications were included by “snowballing” the references in the selected studies.

Articles written in English, Dutch, and French were screened. Case reports, literature reviews, and meta-analyses were excluded. Spinal and maxillofacial procedures were not included in this review. Studies including trauma cases were excluded as well because these cases are generally approached and treated in a distinct way due to diverse pathophysiology. An adult study population (excluding articles with a specific focus on an elderly or pediatric population) with at least 100 subjects per surgical approach or per treatment group was required for inclusion. Studies describing a specific technique or material for dural closure were included unless the aim of the study was to demonstrate efficacy of these products or techniques. Studies were included only if the rate of CSF leakage could be determined. The final decision for inclusion was based on the full text manuscript. An overview of the inclusion and exclusion criteria is summarized in Table 1.

Outcome definition

The primary outcome was the rate of CSF leakage for a specific surgical approach in elective cranial surgery. Secondary outcome was defined as the clinical presentation such as incisional wound leakage, CSF rhinorrhea, CSF otorrhea, middle ear effusion, or pseudomeningocele. In addition, data on the treatment of CSF leaks (conservative, pressure dressing, puncture, lumbar drainage, redo surgery …) were included. A formal meta-analysis was not possible because of the large clinical heterogeneity in the articles regarding surgical indication, surgical approach, and closure techniques.

Table.1 Inclusion and exclusion criteria

Criteria for inclusion	Criteria for exclusion
Cranial procedures	Spinal and maxillofacial procedures
Specification of surgical approach	Surgery for trauma
Studies published in English, French, or Dutch	Case reports
Adult population	Systematic reviews, meta-analyses
At least 100 patients per group/approach	Studies on a pediatric or elderly population
	Uncontrolled studies on dural closure to show efficacy of a specific technique or material
	Less than 100 patients included per group/approach

Studies were subdivided in three groups according to surgical approach: supratentorial, infratentorial, and skull base surgery. Skull base surgeries were further classified into open and endoscopic approaches. Open skull base procedures involved anterior fossa, middle fossa, and transpetrosal procedures. Endoscopic skull base procedures included transsphenoidal and extended endonasal procedures (transcribriform, transplanum, transclival approaches).

Results

A literature search through the PubMed, Embase, Cochrane Central, and Web of Science databases was performed on May 10, 2021 (search strategies, see 22). The search yielded 10,176 results (Pubmed 4422, Embase 688, Cochrane 306, WOS 2760) of which 2893 duplicates were resolved resulting in 7383 unique hits (Fig. 1). Based on title, 5822 articles were excluded. Abstracts of 782 publications were screened leading to 233 articles eligible for full-text screening. Based on the reference lists of included studies (snowballing), another 15 articles were added. Eventually, 113 publications were included in this review. The majority of included studies were retrospective analyses of single-center or multicenter surgical data. Main reasons for exclusion based on full-text articles included surgical approach not specified (10 studies); less than 100 patients per group or surgical approach (20 studies); CSF leak rate not mentioned (14 studies); other language (13 studies); trauma cases (5 studies); description of a specific surgical technique without comparison (18 studies), or extradural procedures (2 studies).

Level of evidence

This systematic review summarizes data from 94,695 patients in 113 studies. For this analysis, no reviews or meta-analyses were included. Two randomized controlled trials were included, accounting for 562 patients (level I evidence). Nine prospective studies were included with a total of 5267 patients (level II). Eight retrospective reviews of prospectively collected data (level III) and 8 retrospective cohort studies (level IV) accounted for a total of 10,465 and 30,993 patients, respectively. All 86 other included studies were mainly case series, including 47,408 subjects (Table 2).

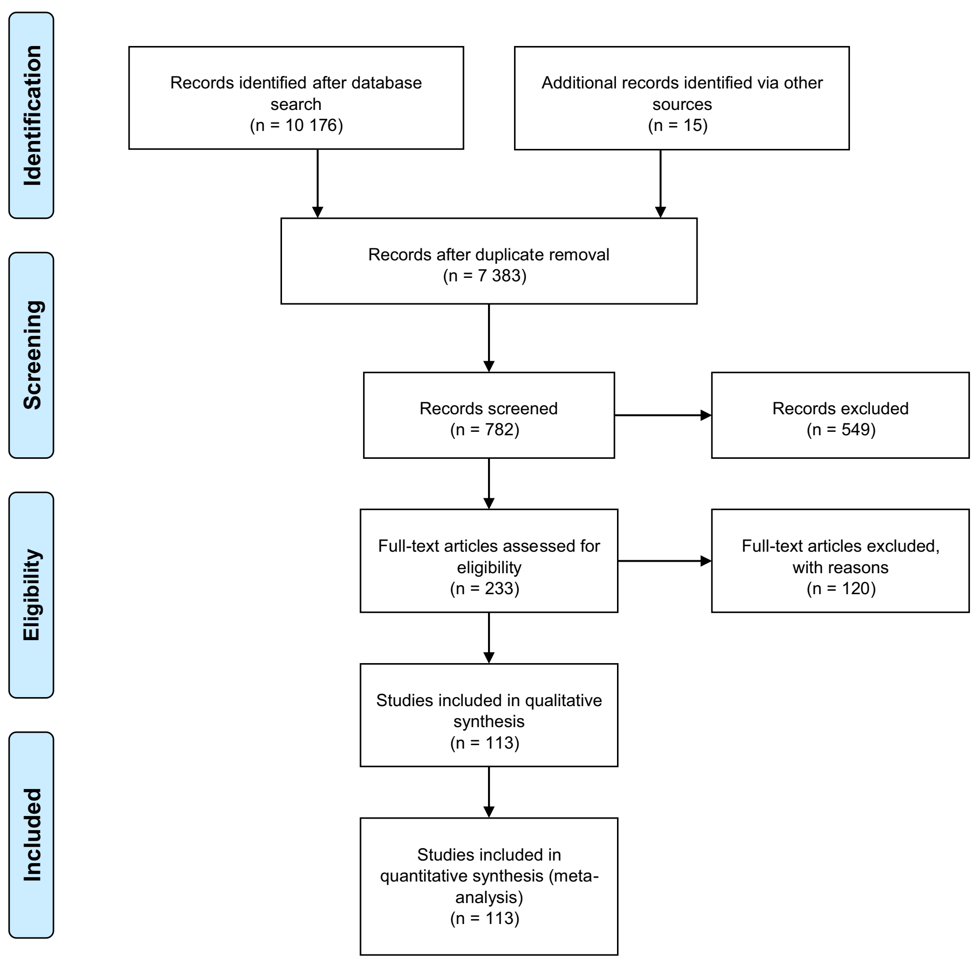

Fig. 1 PRISMA flow diagram for systematic reviews

Table.2 Level of evidence of included studies

Level of evidence	Trial type	Number of studies included	Number of patients
I	Randomized controlled trials	2	562
II	Prospective studies	9	5267
III	Retrospective review of prospective databases	8	10,465
IV	Retrospective cohort studies	8	30,993
V	Other (case series)	86	47,408
Total	-	113	94,695

Supratentorial surgery

Postoperative CSF leakage after elective supratentorial surgery was reported in 16 studies, representing data from 12,803 patients (Table 3) [5, 9, 32, 35, 37, 38, 41, 58, 59, 67, 84, 86, 87, 99, 108]. A total of 376 leaks were reported, corresponding to 2.9% of patients. The incidence rate of CSF leakage in these 16 studies ranged from 1.2% [35] to 10.9% [9], with a calculated mean of 4.1%.

The included studies did not always mention the indication for surgery. Tumors were mentioned in 2321 cases (18.1%), including 1682 meningioma resections. Other indications were epilepsy surgery (1253 cases, 9.8%) and

Table.3 Supratentorial approach

Reference	Surgical approach/ lesion type	N (supratentorial procedures)	N (CSF leaks)	% CSF leak	Definition of CSF leak	Treatment
Reddy et al. [84]	Tumor (meningioma (60), glioma (61), metastasis (27)), vascular (21), other (19)	188	9	4.7%	NS	Revision (5) CSF shunt (2)
Grotenhuis et al. [37]	Tumor (glioma (89), meningioma (30), other (62)), vascular (79), other (9)	269	17	6.3%	NS	NS
Korinek et al. [58]	NS	2284	101	3.4%	NS	NS
Korinek et al. [59]	NS	6234	120	1.9%	NS	NS
Barth et al. [9]	Tumor (glioma (43), meningioma (40), metastasis (25)),vascular (13), other (16)	137	15	10.9%	Incisional (2), subcutaneous collection (13)	Revision (2), conservative (13)
Guangming et al. [38]	Epilepsy surgery	342	21	6.1%	Subcutaneous collection (21)	Puncture + pressure dressing (21)
Litvack et al. [67]	NS	325	15	4.6%	NS	Revision (11), CSF shunt (18)
Sanai et al. [87]	Tumor (meningioma): convexity	141	2	1.4%	NS	NS
Sade et al. [86]	Tumor (meningioma (326))	326	9	2.8%	Incisional (1), collection (8)	NS
Giovanni et al. [32]	Tumor (glioma (115), meningioma (72)), vascular (89)	276	9	3.2%	Subcutaneous collection (9)	NS
Walcott et al. [108]	NS	399	12	3%	NS	NS
Gooneratne et al. [35]	Epilepsy surgery	911	11	1.2%	NS	Resuture (11)
Sicking et al. [99]	Tumor (meningioma): Convexity (297), parasagittal (109)	965	17	2%	NS	Revision
Alwadei et al. [5]	Tumor (glioma (39), meningioma (48), other (66)), vascular (39), other (24)	216	8	4%	NS	CSF shunt
Hamou et al. 2020 [41]	Tumor (112), vascular (20), other (18)	150	10	6.7%	NS	Revision

NS not stated, *CSF* cerebrospinal fluid vascular surgery (261 cases, 2.0%). Meningiomas [86, 87, 99] had an average postop CSF leakage rate of 1.9%. In other studies, no CSF leakage rate per indication was mentioned.

The surgical approach was determined as frontal in 378 cases (3.0%), pterional in 152 cases (1.2%), temporal in 821 (6.4%), and parietal in 60 cases (0.5%). For all other cases (88.9%), the surgical approach was not mentioned.

As a consequence of CSF leakage, seventy-three patients needed to return to the operation room. Of these 73, revision surgery was necessary in 45 cases and 28 patients needed CSF shunting. In another 11 reported cases, the wound was resutured with good results [35]. Puncture and/or pressure dressing resolved a CSF collection in 21 patients [109]. Conservative treatment was sufficient in 13 cases [9].

Several risk factors related to CSF leakage were studied. Recurrent surgery and tumor volume were also reported as risk factors for CSF leakage [110]. Another study however [67] found no difference in CSF leak rate between patients with and without previous surgeries. Additionally, Korinek et al. showed that CSF leakage could be a significant risk factor for infection (up to 36.8% leakage rate in infected patients versus 1.4% in noninfected patients) [58, 59].

Skull base surgery

Open anterior fossa approach

Five studies reported postoperative leakage rates after anterior skull base surgery (Table 4) [44, 81, 92, 102, 110]. 5.9% (49 of 827 patients) manifested with a postoperative CSF leak. Incidence rates ranged between 2.2% [44] and 9.5% [102]. While certain authors [44, 81, 92] reported CSF leakage as cases that required surgical revision or CSF shunting, others [102] [110] did not specify the treatment for CSF leakage. Schneider et al. [92] assessed the correlation with extent of tumor resection and found a significantly higher CSF leakage rate (10.1%) in case of radical resection with excision of the dural tail (Simpson grade I) compared to less aggressive Simpson grade II resections (2.3% CSF leakage).

Open middle fossa approach

Six studies described a total of 1616 patients who underwent middle fossa skull base approaches [10, 50, 72, 81, 91, 100] and reported an average of 6.4% postoperative CSF leakage rate (1.3% [81]–20.4% [51]) (Table 4). Of the patients with reported CSF leaks, 5 were specified as incisional leak and 24 presented with rhinorrhea. Conservative or noninvasive treatment was sufficient in 90 cases, of which pressure dressing was exerted for 77 patients. Surgical wound revision was required in 55 cases. CSF diversion with a lumbar drain was performed in 38 patients. The highest reported incidence of CSF leakage was 20.4% [51]. In this study, eight of 32 patients diagnosed with postoperative CSF leakage needed surgical revision representing 5% of the total study population.

Open transpetrosal approach

Eleven distinct publications including 4831 patients discussed the transpetrosal approach (Table 4) [6, 10, 20, 30, 55, 63, 74, 77, 93, 100, 101]. Postoperative CSF leakage was reported in 5.2% of cases (0.85% [6]–20% [101]). Out of the 252 leaks, 58 represented incisional leaks and 90 patients suffered from oto- or rhinorrhea. Reoperation was required in 71 cases (28%), while a lumbar drain was placed in 52 cases (21%). Subcutaneous wound collections occurred in 26 patients (10%). Conservative treatment, including pressure dressing or bed rest sufficed in 22 cases (9%). Other cases of CSF leakage and their treatment were not specified.

Endonasal surgery

The total reported incidence rate of postoperative CSF leakage after transsphenoidal surgery was 2.8% (1136 out of 41,028 subjects), based on 45 studies [1, 2, 7, 8, 11, 14, 17, 18, 24, 26, 29, 34, 40, 42, 43, 48, 52, 53, 56, 60, 66, 69, 76, 78, 80, 83, 85, 88, 94, 96–98, 104, 106, 111–115, 117]. Incidence rates ranged between 0.17 and 15.9% (Table 5).

Transsphenoidal surgery using the microscopic endonasal technique was reported in 9 studies, while 24 studies reported results of the endoscopic endonasal transsphenoidal approach. An additional 10 publications did not mention the approach (microscopic/endoscopic). The largest retrospective study [83] mentioned 13,070 patients undergoing transsphenoidal surgery for pituitary neoplasms and found an overall rate of 1.7% (230 of 13,070 patients).

The highest rate of postoperative CSF leakage was reported by Kassam et al. [53], which represents the first large retrospective study on endoscopic endonasal skull base surgery. Of the 800 patients, 127 needed endoscopic repair or lumbar drain placement due to postoperative CSF leakage after endoscopic transsphenoidal surgery. Younus et al. [114] only reported one case in 584 that needed readmission due to CSF leakage (0.17%) after endoscopic transsphenoidal pituitary surgery. However, other interventions related to CSF leakage such as treatment during the initial hospital stay and interventions that did not require readmission were not mentioned here.

Overall, endoscopic procedures (4.1%) tended to have higher leakage rates than microscopic surgery (1.7%). On

Table.4 Open skull base approach

Reference	Surgical approach/ lesion type	N (procedures)	N (CSF leaks)	% CSF leak	Definition of CSF leak	Treatment
Anterior fossa approach						
Solero et al. [102]	Combined craniofacial resection	168	16	9.5%	NS	NS
Horowitz et al. [44]	Subcranial resection	135	3	2.2%	NS	Revision
Wang et al. [110]	Lateral open approach to skull base chordoma	238	9	3.8%	NS	NS
Perry et al. [81]	NS	119	11	8.5%	NS	Revision
Schneider et al. [92]	Frontobasal meningioma	167	10	6.0%	NS	CSF shunt
Middle fossa approach						
Kanzaki et al. [51]	Acoustic neuroma (extended middle fossa approach)	160	32	20.4%	NS	Revision (8)
Slattery et al. [100]	NS	432	25	5.7%	NS	Reoperation (36), CSF shunt (25), pressure dressing (76), or combination (NS)
Becker et al. [10]	Acoustic neuroma	100	10	10%	Incisional (6), rhinorrhea (4)	Revision, CSF shunt, conservative
Meyer et al. [72]	NS	162	9	5.6%	NS	Revision (1), CSF shunt (8)
Scheich et al. [91]	Acoustic neuroma	148	19	13%	Rhinorrhea (18), incisional (1)	Revision (2), pressure dressing (1), conservative (13), CSF shunt (5)
Perry et al. [81]	NS	614	8	1.3%	NS	Readmission, revision (8)
Transpetrosal approach						
Leonetti et al. [63]	Translabyrinthine	209	8	3.8%	NS	Revision
Slattery et al. [100]	Translabyrinthine	1225	135	11%	NS	Reoperation (36), CSF shunt (25), pressure dressing (76), or combination (11)
Sluyter et al. [101]	Translabyrinthine-transtentorial: acoustic neuroma	120	24	20%	Rhinorrhea (8), incisional(16)	Revision surgery (6), CSF shunt (18)
Becker et al. [10]	Translabyrinthine: acoustic neuroma	100	13	13%	Rhinorrhea (6), incisional (6), combination (1)	Revision, CSF shunt, conservative (NS)
Fishman et al. [30]	Acoustic neuroma	101	5	5%	Incisional (3), nasal (2)	Reoperation, CSF shunt
Khrais et al. [55]	Enlarged translabyrinthine: acoustic neuroma	709	10	1.4%	Rhinorrhea (7), incisional (2), combination (1)	NS
Ben Ammar et al. [6]	Translabyrinthine: acoustic neuroma	1865	16	0.85%	Rhinorrhea (9), otorrhea (1), incisional (NS), pseudomeningocele (5)	Revision (10), CSF shunt (2), pressure dressing (6)
Nonaka et al. [77]	Translabyrinthine: acoustic neuroma	103	8	7.8%	Rhinorrhea (8), otorrhea (3), incisional (20)	Revision, CSF shunt, pressure dressing
Moffat et al. [74]	Translabyrinthine: acoustic neuroma	128	3	2.5%	NS	Revision (1), CSF shunt (2)

Table.4 (continued)

Reference	Surgical approach/lesion type	N (procedures)	N (CSF leaks)	% CSF leak	Definition of CSF leak	Treatment
Copeland et al. [20]	Translabyrinthine: acoustic neuroma	164	25	15.2%	Incisional (12), otorhinorrhea (33)	NS
Schwartz et al. [93]	Translabyrinthine: acoustic neuroma	107	5	4.6%	NS	CSF shunt, resuture (5)

NS not stated, *CSF* cerebrospinal fluid

the other hand, endoscopic surgery has been more extensively described in the literature.

Endonasal extended approach

Four studies described the expanded endonasal approach [31, 61, 70, 118]. Twenty-seven of 506 (5.3%) patients presented with postoperative CSF leak, which resolved with CSF shunting in 16 cases. Other cases of postoperative CSF leakage and their treatment were not specified. An extensive variety of closure material and multilayer reconstructions were used for dural closure and reconstruction of the skull base, including fat, pericranium, or fascia lata grafts; bone fragments; fibrin sealants or glues; gelatin sponges; and nasoseptal flaps. Mascarenhas et al. [70] reported lower CSF leakage rates when introducing gasket sealing (4.2% with fascia lata and fibrin glue gasket seal versus 11% with fat graft and fibrin glue alone), even more so after the additional introduction of the nasoseptal flap (1.8% leakage). Preventive lumbar CSF drainage was not consistently applied, and its effect on postoperative CSF leakage was not assessed.

Infratentorial surgeries

A total of 47 studies reported surgical and postoperative data in infratentorial surgeries [3, 4, 10, 12, 15, 20, 21, 25, 27, 33, 45–47, 49, 54, 62, 64, 65, 67, 71, 73, 75, 77, 79, 81, 89, 103, 105, 107, 116, 119, 120] (Table 6). Of 28,078 patients, 1625 were diagnosed with postoperative CSF leakage, which accounts for 5.8%. The most common indications here were microvascular decompression (MVD) and acoustic neuroma resection. Not all studies specified the surgical approach. CSF shunting with a VP shunt or lumbar drainage was performed in 30 patients.

Retrosigmoid approach

The retrosigmoid approach was the most frequently described approach to the posterior fossa. In total, 18,607 patients were included in 20 studies, with a total leak rate of 7.4% (1382 out of 18,607 patients). The largest study [3] describing complications of acoustic neuroma resections discussed 6820 included patients with CSF leakage in 14% of patients. Hospital readmission was required for 3.5% of patients. The lowest leakage rate (0.2%) was reported in a recent series on MVD for hemifacial spasm [49].

Evolution of postoperative CSF leakage over time

In order to establish the evolution of postoperative CSF leakage, studies published during the last 2 years (2019–2020) were compared to studies published before 2005 (Table 7). Before 2005, the reported incidences were systematically higher than those reported since 2019. All publications (before 2005, as well as more recent ones) mention the highest incidence of postoperative CSF leakage after anterior skull base procedures. This incidence was also high for transpetrosal surgeries, where 7.9% of patients had symptoms of CSF leakage before 2005. This approach was not documented in articles published after 2018. The endoscopic approach for transsphenoidal surgeries was not reported before 2005. However, the incidence of postoperative CSF leakage is lower in recent studies for both the microscopic and endoscopic approach compared to older studies, partially due to the introduction of advanced preventive surgical tools and techniques, e.g., the vascularized nasoseptal flap.

Discussion

Cerebrospinal fluid leakage represents a major complication after elective neurosurgical procedures. Specific risk factors for postoperative CSF leakage include recurrent surgery, the condition of the dura, the duration of the surgery, the size of the dural defect, or comorbidities such as arterial hypertension or obesity. Common complications associated with CSF leakage include surgical site infection, meningitis, and hydrocephalus, the latter being important because of the risk for persistent CSF leakage due to a pressure gradient. As CSF leakage can be defined in several ways, there are no accurate numbers on its incidence. This review summarizes the reported incidences of postoperative CSF leakage, by surgical approach.

Overall, CSF leakage was present in 3.8% of cranial surgeries and the incidence of postoperative CSF leakage

Table.5 Endonasal approach

Reference	Surgical approach	N (procedures)	N (CSF leaks)	% CSF leaks	Definition of CSF leak	Treatment
Woollons et al. [111]	Sublabial (80), transnasal (105)	185	8	4.3%	NS	Revision (4), CSF shunt (1), conservative (3)
Shiley et al. [97]	NS	217	13	6.0%	NS	Revision (9), CSF shunt (2), conservative (2)
Nishioka et al. [76]	NS	200	5	2.5%	Rhinorrhea (5)	Revision (2), CSF shunt (3)
Abbassioun et al. [1]	Adenoma	151	12	7.9%	NS	Revision (2), CSF shunt (10)
Han et al. [42]	Macroadenoma	592	26	4.4%	Rhinorrhea	Revision (14), CSF shunt (NS), combination (8)
Raikundalia et al. [83]	Benign pituitary neoplasms	13,070	230	1.7%	NS	NS
Koutourousiou et al. [60]	Sellar lesions with cavernous sinus invasion	234	18	7.7%	NS	NS
Strickland et al. [104]	Microadenoma (462), macroadenoma (491), NS (49)	1002	26	2.59%	Rhinorrhea	Revision
Microscopic						
Fatemi et al. [29]	NS	881	19	2%	NS	NS
Sharma et al. [96]	NS	224	17	7.6%	NS	CSF shunt
Halvorsen et al. [40]	NS	268	12	4.7%	NS	Revision, CSF shunt
Kim et al. [56]	NS	1352	44	3.3%	Rhinorrhea	NS
Asemota et al. [7]	NS	3207	244	7.61%	Rhinorrhea (84), dura tear (35), other (165)	NS
Azad et al. [8]	NS	6049	54	0.9%	NS	NS
Zhang et al. [117]	NS	474	13	2.7%	NS	Revision (5), CSF shunt (8)
Agam et al. [2]	NS	983	20	2.0%	NS	NS
Riesgo et al. [85]	NS	302	7	2.3%	NS	Revision (6), CSF shunt (1)
Endoscopic						
Agam et al. [2]	Pituitary surgery	160	4	2.5%	NS	NS
Dehdashti et al. [24]	Adenomas	200	7	3.5%	NS	Revision (3), CSF shunt (4)
Senior et al. [94]	Pituitary surgery	193	20	10.3%	Rhinorrhea	Revision (6), CSF shunt (14)
Yano et al. [113]	NS	213	9	4.2%	NS	Revision (1), CSF shunt (8)
Gondim et al. [34]	Adenomas	301	8	2.6%	NS	Revision (3), CSF shunt (5)
Kassam et al. [53]	NS	800	127	15.9%	NS	Revision (44), CSF shunt (30), combination (53)
Berker et al. [11]	NS	570	8	1.3%	NS	Revision (6)
Duntze et al. [26]	NS	337	11	3.1%	NS	Revision (10), CSF shunt (1)
Cavallo et al. [17]	Craniopharyngioma	103	15	14.6%	NS	NS
Halvorsen et al. [40]	NS	238	12	5.6%	NS	Revision, CSF shunt
Paluzzi et al. [78]	Adenomas (expanded 55.9%)	555	28	5%	NS	NS

Table.5 (continued)

Reference	Surgical approach	N (procedures)	N (CSF leaks)	% CSF leaks	Definition of CSF leak	Treatment
Sanders-Taylor et al. [88]	Abdominal fat reconstruction	289	5	1.9%	Rhinorrhea	Revision (1), CSF shunt (5)
Boling et al. [14]	Adenomas	982	54	5.5%	NS	NS
Jang et al. [48]	NS	331	6	1.8%	NS	NS
Karnezis et al. [52]	Sellar surgery	1161	68	5.9%	NS	NS
Magro et al. [69]	Adenomas; nonfunctioning	300	8	2.7%	NS	Revision
Asemota et al. [7]	Pituitary surgery	2679	365	13.62%	Rhinorrhea (167), dura tear (46), other (219)	NS
Azad et al. [8]	Sellar lesions	3621	62	1.7%	NS	NS
Cheng et al. [18]	Pituitary neoplasms	129	9	6.9%	Rhinorrhea	Revision (2), CSF shunt (6), conservative (1)
Patel et al. [80]	Sellar surgery	806	38	4.7%	NS	NS
Shkarubo et al. [98]	Transclival approach to clivus and anterior region of posterior fossa	136	9	6.62%	NS	Revision
Younus et al. [114]	Pituitary surgery	584	1	0.17%	NS	Readmission
Hannan et al. [43]	NS	270	24	9%	Rhinorrhea	Revision, CSF shunt
Little et al. [66]	Nonfunctioning adenomas	177	6	3.4%		Revision
Vengerovich et al. [106]	NS	833	17	2.0%	Rhinorrhea	Readmission
Xue et al. [112]	Adenomas	216	13	6.0%	NS	Revision (9), CSF shunt (4)
Younus et al. [115]	NS	1000	20	2%	NS	NS
Extended endonasal endoscopic						
Laedrach et al. [61]	NS	122	4	3.3%	NS	CSF shunt
Zhao et al. [118]	NS	126	7	5.6%	NS	NS
Mascarenhas et al. [70]	Transplanum transtuberculum	126	4	3.2%	NS	NS
Fomichev et al. [31]	Suprasellar craniopharyngiomas	136	12	8.8%	NS	CSF shunt

NS not stated, *CSF* cerebrospinal fluid

is higher in infratentorial surgery, namely in 5.8%, compared to 2.9% in supratentorial surgery. Open skull base surgery generally led to the highest complication rates, with CSF leakage in 6.2% of cases (5.9% for anterior skull base, 6.4% for middle fossa, and 5.2% for transpetrosal approaches). Endonasal skull base surgery resulted in an average postoperative CSF leakage rate of 2.8%, with rates of 4.1% for endoscopic procedures, 1.7% for microscopic procedures, and 5.3% for extended procedures. The main indications for supratentorial surgery were tumors. Resection of intracerebral tumors often require large dural openings, which can be associated with a higher risk of reconstruction failure with associated CSF leakage, compared to more limited defects. In meningiomas (more particularly in Simson grade I resections), part of the dura mater is resected and replaced by grafts, which can also lead to CSF leakage. The use of a graft is often as well advocated after long-lasting surgeries: exposure of the dura to air and illumination may dry out the dural edges, which can result in shrinkage. One of the highest incidences of CSF leakage after supratentorial procedures (6.3%) was reported in a study to evaluate the costs associated with postoperative CSF leakage [37]. This high incidence could result from the fact that all events associated with postoperative CSF leakage were reported including spontaneously resolving minor subcutaneous CSF collections, asymptomatic CSF collections observed on postoperative imaging, pseudomeningoceles, subcutaneous collections with a need for puncture, or overt surgical site leakage as well as otorrhea and rhinorrhea. Infratentorial and skull base surgery

Table.6 Infratentorial approach

Reference	Surgical approach/indication	N (infratentorial procedures)	N (leak)	% leak	Leak definition	Treatment
McLaughlin et al. [71]	MVD	4415	96	2.17%	NS	Revision, CSF shunt
Duong et al. [27]	Meningioma	140	21	15%	Incisional, pseudomeningocele	Revision, CSF shunt
Sanna et al. [89]	Acoustic neuroma	707	21	3.0%	Incisional (20), pseudomeningocele (1)	Revision (15), conservative (5)
Dubey et al. [25]	Cerebellopontine angle lesions (220), MVD (110)	330	39	11.8%	NS	NS
Litvack et al. [67]	NS	150	17	11.3%	NS	Revision (11), CSF shunt (18)
Zuev et al. [120]	Chiari malformation; Suboccipital craniectomy	125	4	3.2%	Incisional (1), pseudomeningocele (3)	NS
Kher et al. [54]	MVD; endoscopic procedure	178	5	2.8%	NS	NS
Bhimani et al. [12]	Medulla and spinal cord decompression; suboccipital craniectomy	672	27	4%	NS	Revision, CSF shunt, puncture
Zeng et al. [116]	MVD	220	9	4%	NS	NS
Cote et al. [21]	MVD	1005	17	1.7%	NS	Reoperation (10), readmission (7)
De Vlieger et al. [107]	MVD	105	8	7.6%	Incisonal (4), pseudomeningocele (4)	Revision (3), CSF shunt (2), conservative (3)
Perry et al. [81]	NS	1421	36	2.5%	NS	Readmission (36), revision
Retrosigmoid-retromastoid						
Leonetti et al. [63]	NS	191	15	7.8%	NS	Revision, CSF shunt, pressure dressing
Becker et al. [10]	Acoustic neuroma	100	10	10%	Incisional (1), rhinorrhea (8), combination (1)	Resuture, CSF shunt
Jain et al. [47]	Suboccipital	250	10	4%	Rhinorrhea (6), otorrhea (2)	Revision (3), Lumbar puncture (NS), CSF shunt (NS)
Miyazaki et al. [73]	Tumor (355), vestibular neurotomy (345), MVD (477)	1177	36	3.1%	NS	Reoperation (26)
Park et al. [79]	Lateral RS suboccipital approach (MVD) with muscle plug	678	2	0.29%	Rhinorrhea (1), incisional (1)	CSF shunt
Mostafa et al. [75]	NS	121	18	15%	NS	NS
Li et al. [65]	Cranial nerve surgery	516	29	5.6%	Pseudomeningocele (17), middle ear effusion (8), combination (4)	Revision (7), puncture (NS), pressure dressing (22)
Stieglitz et al. [103]	Acoustic neuroma	420	19	4.52%	Rhinorrhea	Reoperation (1), CSF shunt (18)
Jagannath et al. [46]	Retromastoid suboccipital	137	9	6.6%	Incisional (4), rhinorrhea (1), otorrhea (2), pseudomeningocele (2)	NS
Nonaka et al. [77]	Acoustic neuroma	290	23	7.9%	Rhinorrhea (8), otorrhea (3), incisional (20)	Revision (13), CSF shunt (NS), pressure dressing (16)
Copeland et al. [20]	Acoustic neuroma	256	18	7.0%	Incisional (12), otorhinorrhea (33)	NS
Lee et al. [62]	MVD	2263	111	4.90%	Middle ear effusion (13), rhinorrhea (119)	CSF shunt (8)
Theodros et al. [105]	NS	482	4	0.8%	NS	NS

Table.6 (continued)

Reference	Surgical approach/indication	N (infratentorial procedures)	N (leak)	% leak	Leak definition	Treatment
Zhao et al. [119]	MVD	1548	34	1.55%	Incisional (27), rhinorrhea (7)	Resuture (NS), CSF shunt (7)
Alattar et al. [3]	Acoustic neuroma	6820	960	14.06%	Rhinorrhea (152), otorrhea (29), NS (779)	Readmission (37)
Breun et al. [15]	NS	502	46	9.2%	NS	Revision (11), CSF shunt (46)
Hyun et al. [45]	NS	1174	3	0.25%	NS	CSF shunt
Go et al. [33]	NS	360	10	2.8%	Middle ear effusion (5), rhinorrhea (5)	Conservative
Alford et al. [4]	MVD	197	22	11.2%	Incisional (12), pseudomeningocele (10)	Revision (2), CSF shunt (NS)
Jiang et al. [49]	MVD	1152	3	0.2%	NS	NS

NS not stated, *CSF* cerebrospinal fluid, *MVD* microvascular decompression

Table.7 Comparison of reported incidence of postoperative CSF leakage before 2005 and after 2019

Procedure	CSF leak rate (%)	
	Before 2005	After 2019
Supratentorial	4.6	4.9
Skull base surgery	8.4	2.6
Anterior fossa	9.5	7.3
Middle fossa	9.7	1.3
Transpetrosal	7.9	NS
Endonasal	4.3	3.3
Posterior fossa	2.6	2.4
Retrosigmoid	4.1	2.5

were associated with higher rates of CSF leakage. The infratentorial approach was found to represent a univariate predictor for CSF leakage ($p = 0.015$) [108]. This was explained by increased stress on the suture line because of high hydrostatic pressure associated with posterior fossa lesions. Due to the challenging accessibility of the region, skull base surgery resulted in the highest incidence of postoperative CSF leakage. The open approach to the skull base, including anterior fossa and transpetrosal surgeries has high complication rates in general. Endoscopic approaches to the skull base are less invasive and could result in lower complication rates; however, controversy exists between the endoscopic and microscopic approach. Regarding efficacy, for sellar lesions, the endoscopic approach is currently preferred according to a growing amount of evidence, for example, a higher rate of gross total resection in case of pituitary tumors and lower rates of complications [22]. On the other hand, CSF leakage was more common after endoscopic surgery. Additionally, Broersen et al. [16] reviewed the literature on microscopic versus endoscopic transsphenoidal surgery for Cushing's disease and also found a higher incidence of CSF leakage after endoscopic surgery (12.9%) compared to microscopic surgery (4.0%). According to the authors, this might be explained by the more challenging nature of the cases and the attempt to achieve complete tumor resection. Dural repair after extended endoscopic endonasal skull base procedures remains most challenging and suprasellar extension of the lesion can cause arachnoidal defects with a high chance of intraoperative CSF leak. Intraoperative CSF leakage was found to be a risk factor for postoperative CSF leakage. Shahangian et al. [95] reported an overall CSF leak repair failure in 5.3% of cases. In case of an intraoperative leak, the leak repair failure rate increased to 19.9%. Therefore, the reconstruction of intraoperative leaks needs to be performed adequately, for instance by application of grafts such as fascia lata, the Hadad nasoseptal flap [39], or other closure techniques, e.g., in combination with fibrin glues. The efficacy of the Hadad nasoseptal flap for intraoperative leak reconstruction or as a preventive measure was demonstrated, with decrease in leakage rates from 11 to 2.7% [78]. Additionally, in case of intraoperative CSF leakage, other preventive measures could be taken to minimize the risk for postoperative leakage, including lumbar drain placement or compulsory bed rest. Finally, surgical experience can furthermore influence postoperative CSF leakage. In a survey study among 3172 neurosurgeons across the USA, the CSF leak rate was estimated to be 3.9% [19].

Higher age is often considered a risk factor for surgical and postsurgical complications; in the geriatric population, the dura is prone to tears and adherent to the bone [121]. However, studies comparing elderly versus younger patients are at present limited to underpowered retrospective studies. Phan et al. [82] conducted a systematic review comparing outcomes of microvascular decompression in elderly and younger patients. The results suggested that some complications may be significantly higher in the elderly (such as stroke or death); however, no difference was found in the incidence of CSF leakage between both groups (14 out of 439 elderly cases, i.e., 3.2% versus 28 out of 897 (3.1%) in the younger population).

Dural reinforcement

As primary dural closure is not always sufficient to provide adequate sealing, dural reinforcement is often performed. This can be accomplished with autologous material such as pericranium, fat or muscle grafts, or fascia lata. Commercially available fibrin sealants can also be used for dural reinforcement. While numerous studies assessed the use of augmentation material for dural closure, no clear advantage of these sealants could be found. A systematic review on this topic reported no significant advantage of fibrin sealants, with a postoperative CSF leakage rate of 8.2% when no sealant was used, compared to 8.4% in the sealant group. [57]

Limitations of the study

For this review, we assessed the CSF leakage rate taking into account the type of surgery and approach. A major limitation is that few prospective studies exist on this topic which leads to important gaps and missing data. Most importantly, details on the surgical approach and indication were not always provided. Additionally, most manuscripts did not mention a general description or definition of outcome. Most studies reported postoperative CSF leaks only if reoperation, CSF shunting, or readmission were necessary. Subcutaneous fluid collections, imaging suggestive of CSF leak, or other nonclinically relevant CSF leaks requiring interventions, e.g., bed rest, pressure dressing, or puncture, were rarely considered even though these might alter the duration of hospital admission, patient quality of life, and healthcare costs.

In order to diminish the risk of bias due to large discrepancies in CSF leakage rates described by small studies, we decided to only include studies if at least 100 cases were reported. In case several approaches or surgical techniques were described in the same study, a minimum of 100 patients per group were required for inclusion. It is crucial to emphasize the importance of the learning curve because results and adverse events in surgery are influenced by the surgeon's experience. It has been reported that the experience of both the surgeon and the institution play a role in the incidence of complications, including CSF leak. However, more experienced surgeons may be involved in more challenging cases, which can have opposite effects [16, 19, 53, 69].

Another limitation is the role of the use of commercial sealants or dural substitutes for obtaining watertight dural closure. In order to minimize bias, we did not include commercial studies aiming to show efficacy of a specific commercial product. However, some of the included studies did use commercially available sealants as part of their standard practice. The use of commercial sealants was already reviewed by Esposito et al. in 2016 [28], who concluded that there was no decrease in incidence of postoperative CSF leakage when commercial fibrin sealants were used. However, these findings were based on only one randomized controlled trial in 139 subjects [36]. Such findings emphasize the importance of further research regarding the safety and efficacy of commercial fibrin sealants, and optimal techniques for dura closure in a more extensive way.

Conclusion

Since postoperative CSF leakage remains a widely reported complication of elective neurosurgical procedures, there is a need for a standardized procedure for meticulous dural closure in order to reduce the incidence of this serious adverse event, especially when taking into account the many secondary complications and their additional costs. These include local infection and meningitis, and all associated risks related to hospital readmission, reoperations or other clinically invasive procedures. Powered large-numbered randomized controlled trials are necessary to determine the optimal treatment for dural closure, minimizing the risk of postoperative complications, and CSF leakage in particular.

Appendix. Search strategy

PUBMED

Concept 1: cranial surgery.

((“surgery” [Subheading] OR “Surgical Procedures, Operative”[Mesh:NoExp] OR surgery[tiab] OR surgeries[tiab] OR surgical[tiab] OR operati*[tiab] OR resect*[tiab]) AND (“Skull”[Mesh] OR skull[tiab] OR ‘head skeleton’[tiab] OR Skulls[tiab] OR crania[tiab] OR cranial[tiab] OR cranium[tiab] OR cranii[tiab] OR frontal-bone*[tiab] OR os-frontale [tiab] OR occipital-bone*[tiab] OR os-occipitale[tiab] OR parietal-bone*[tiab] OR os-parietale[tiab] OR temporal-bone*[tiab] OR os-temporale[tiab] OR sphenoid* [tiab] OR sella*[tiab])).

OR “Neurosurgical Procedures”[Mesh:NoExp] OR neurosurg*[tiab] OR skull-surg*[tiab] OR brain-surg*[tiab] OR Craniotomy[Mesh] OR craniotom*[tiab] OR Trephin*[tiab] OR Trepanation*[tiab] OR Trepanning*[tiab]

OR "Decompression, Surgical"[Mesh:NoExp] OR decompressi*[tiab] OR decompression-surg*[tiab] OR decompressive-surg*[tiab] OR "Microvascular Decompression Surgery"[Mesh] OR "Dura Mater"[Mesh] OR Dura-Mater[tiab] OR duratom*[tiab] OR Dura-repair[tiab] OR Duraplast*[tiab].

Concept 2: postoperative complication.

'wound healing'[tiab] OR 'wound regeneration'[tiab] OR 'Wound repair'[tiab] OR "Postoperative complications"[Mesh:NoExp] OR "Postoperative Period"[Mesh:NoExp] OR postop*[tiab] OR post-operat*[tiab] OR after-surgery[tiab] OR postsurgery[tiab] OR after-surgical[tiab] OR post-surgical[tiab] OR postsurgery OR complication*[tiab] OR adverse-event*[tiab] OR "adverse effects" [Subheading] OR adverse-effect*[tiab].

Concept 3: CSF leak.

"Cerebrospinal Fluid Leak"[Mesh] OR cerebro-spinal [tiab] OR cerebrospinal[tiab] OR CSF[tiab] OR Liquorrhea[tiab] OR Liquorhea[tiab] OR Liquorrea[tiab] OR Liquorea[tiab] OR Liquorrhoea[tiab] OR Pseudomeningocele*[tiab] OR Pseudomeningocoele*[tiab] OR "Intracranial Hypotension"[Mesh] OR intracranial-hypotension[tiab] OR meningocele*[tiab] OR meningocoele*[tiab].

Concept: study type.

"Clinical Trial" [Publication Type] OR randomized[tiab] OR randomised[tiab] OR 'RCT'[tiab] OR review*[tiab] OR "case–control"[tiab] OR retrospective[tiab].

OR prospective[tiab] OR clinical-trial*[tiab] OR intervention-stud*[tiab].

OR "Observational Study"[Publication Type] OR observational-stud*[tiab] OR "epidemiologic studies"[Mesh] OR epidemiolog*[tiab] OR "cohort studies"[Mesh] OR cohort*[tiab] OR incidence[tiab] OR epidemiology [subheading] OR etiology [subheading] OR etiolog*[tiab] OR pathogenesis [tiab].

Cochrane Library (CENTRAL)

Concept 1

#1: ([mh ^ "Surgical Procedures, Operative"] OR [mh "General Surgery"] OR [mh /SU]).

#2: (surgery OR surgeries OR surgical OR operati* OR resect*):ti,ab,kw.

#3: #1 OR #2

#4: [mh "Skull"].

#5: (Skull OR skulls OR cranium OR crania OR cranial OR cranii OR "head skeleton" (frontal NEXT bone*) OR (os frontale) OR (occipital NEXT bone*) OR (os occipitale) OR (parietal NEXT bone*) OR (os parietale) OR sphenoid* OR sella* OR (temporal NEXT bone*) OR (os temporale) OR sella*):ti,ab,kw.

#6: #4 OR #5

#7: #3 AND #6

#8: [mh ^ "Neurosurgical Procedures"] OR [mh "Craniotomy"] OR [mh ^ "Decompression, Surgical"] OR [mh "Microvascular Decompression Surgery"] OR [mh "Dura Mater"].

#9: (neurosurg* OR (skull NEXT surg*) OR (brain NEXT surg*) OR craniotom* OR Trephin* OR Trepanation* OR Trepanning* OR decompressi* OR (decompression NEXT surg*) OR (decompressive NEXT surg*) OR (Microvascular NEXT Decompression*) OR "Dura Mater" OR duratom* OR "Dura repair" OR Duraplast*):ti,ab,kw.

#10: #8 OR #9 OR #7

Concept 2

#11: [mh ^ "Postoperative complications"] OR [mh "Postoperative Period"] OR [mh /AE].

#12: ("wound healing" OR "wound regeneration" OR "wound repair" OR postop* OR (post NEXT operat*) OR "after surgery" OR "after surgical" OR complication* OR (adverse NEXT event*) OR (adverse NEXT effect*)):ti,ab,kw.

#13: #11 OR #12

Concept 3

#14: [mh "Cerebrospinal Fluid Leak"] OR [mh "Intracranial Hypotension"].

#15: ((cerebro NEXT spinal) OR cerebrospinal OR CSF OR Liquorrhea OR Liquorhea OR Liquorrea OR Liquorea OR Liquorrhoea OR Pseudomeningocele* OR Pseudomeningocoele* OR "intracranial hypotension" OR meningocele* OR meningocoele*):ti,ab,kw.

#16: #14 OR #15

#17: #10 AND #13 AND #16

EMBASE

Concept 1: cranial surgery.

(('surgery' OR 'surgeries' OR 'surgical' OR 'operati*' OR 'resect*') NEAR/6 ('skull' OR 'skulls' OR 'crania' OR 'cranial' OR 'cranium' OR 'cranii' OR 'head skeleton' OR 'frontal bone' OR 'os frontale' OR 'occipital bone' OR 'os occipitale' OR 'parietal bone' OR 'os parietale' OR 'temporal bone' OR 'os temporale' OR 'sphenoid*' OR 'sella*')):ti,ab,kw.

OR 'skull surgery'/exp OR 'neurosurgery'/exp OR 'neurosurg*':ti,ab,kw OR 'brain surg*':ti,ab,kw OR 'craniotomy'/exp OR 'craniotom*':ti,ab,kw OR 'Trephin*':ti,ab,kw OR 'Trepanation*':ti,ab,kw OR 'Trepanning*':ti,ab,kw OR 'decompression surgery'/de OR decompressi*: ti,ab,kw OR 'microvascular decompression'/exp OR 'dura mater'/exp OR 'dura mater':ti,ab,kw OR 'duratom*':ti,ab,kw OR 'dura repair':ti,ab,kw OR 'duraplast*':ti,ab,kw OR 'duraplasty'/exp.

Concept 2: postoperative complication.

'wound healing':ti,ab,kw OR 'wound regeneration':ti,ab,kw OR 'Wound repair':ti,ab,kw OR 'postoperative complication'/de OR 'postoperative period'/de OR 'postop*':ti,ab,kw OR 'post-operat*':ti,ab,kw OR 'after-surgery':ti,ab,kw OR 'postsurgery':ti,ab,kw OR 'after-surgical':ti,ab,kw OR 'post-surgical':ti,ab,kw OR 'complication*':ti,ab,kw OR 'adverse effect*':ti,ab,kw OR 'adverse-event*':ti,ab,kw OR 'adverse event'/de.

Concept 3: CSF leak.

'liquorrhea'/exp OR 'cerebro-spinal':ti,ab,kw OR 'Cerebrospinal':ti,ab,kw OR 'CSF':ti,ab,kw OR 'Liquorhea':ti,ab,kw OR 'Liquorrea':ti,ab,kw OR 'liquorrhea':ti,ab,kw OR 'Liquorrhoea':ti,ab,kw OR 'Pseudomeningocele*':ti,ab,kw OR 'Pseudomeningocoele*':ti,ab,kw OR 'Intracranial Hypotension':ti,ab,kw OR 'intracranial hypotension'/exp OR 'meningocele'/exp OR 'meningocele*':ti,ab,kw OR 'meningocoele*':ti,ab,kw.

Concept study design.

'randomi?ed':ti,ab,kw OR 'clinical trial*':ti,ab,kw OR 'clinical trial'/de OR 'RCT':ti,ab,kw OR 'review*':ti,ab,kw OR 'case–control':ti,ab,kw OR 'controlled clinical trial'/exp OR 'case control study'/exp OR 'case–control':ti,ab,kw OR 'retrospective':ti,ab,kw OR 'prospective':ti,ab,kw OR 'observational study'/exp OR 'intervention$stud*':ti,ab,kw.

WOS core collection

Concept 1: cranial surgery.

(("surgery" OR "surgeries" OR "surgical" OR "operati*" OR "resect*") NEAR/6 ("skull" OR "skulls" OR "crania" OR "cranial" OR "cranium" OR "cranii" OR "head skeleton" OR "frontal bone" OR "os frontale" OR "occipital bone" OR "os occipitale" OR "parietal bone" OR "os parietale" OR "temporal bone" OR "os temporale" OR "sphenoid*" OR "sella*")).

OR "neurosurg*" OR "brain surg*" OR "craniotom*" OR "Trephin*" OR "Trepanation*" OR "Trepanning*" OR "decompressi*" OR "dura mater" OR "duratom*" OR "dura repair" OR "duraplast*".

Concept 2: postoperative complication.

"wound healing" OR "wound regeneration" OR "Wound repair" OR "postop*" OR "post-operat*" OR "after-surgery" OR "postsurgery" OR "after-surgical" OR "post-surgical" OR "complication*" OR "adverse effect*" OR "adverse-event*"

Concept 3: CSF leak.

"cerebro-spinal" OR "Cerebrospinal" OR "CSF" OR "Liquorhea" OR "Liquorrea" OR "liquorrhea" OR "Liquorrhoea" OR "Pseudomeningocele*" OR "Pseudomeningocoele*" OR "Intracranial Hypotension" OR "meningocele*" OR "meningocoele*"

Concept study design.

"clinical trial*" OR "randomi?ed" OR "RCT" OR "review*" OR "case control study" OR "case-control" OR "retrospective" OR "prospective" OR "observational stud*" OR "intervention stud*" OR "cohort*" OR "incidence*" OR "epidemiolog*" OR "etiolog*" OR "pathogenesis"

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Declarations

Competing interests The authors declare no competing interests.

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