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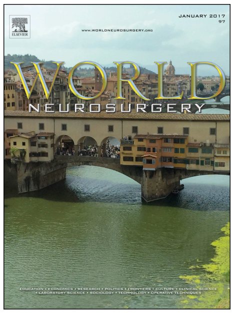

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Risk factors for postoperative cerebrospinal fluid leakage after intradural spine surgery

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Abstract

Objective

Well-defined risk factors for cerebrospinal fluid leakage (CSFL) following intradural spine surgery are scarce in the literature. The aim of this study was to identify patient and surgery related risk factors and the incidence of CSFL.

Methods

For this retrospective cohort study, we identified consecutive patients who underwent intradural spine surgery between 2009 and 2021 at our department. Primary endpoint was the incidence of clinically or radiologically proven CSFL. The impact of clinical and surgical factors on occurrence of CSFL was analyzed.

Results

In total, 375 patients (60.3% female, mean age 54 ± 16.5 years) were included. Thirty patients (8%) had postoperative CSFL and thereby a significantly higher risk for wound healing disorders (OR 24.9, CI 9.3-66.7) and surgical site infections (SSIs; OR 8.4, CI 2.6-27.7) ($p<0.01$ for each).

No patient-related factors were associated with CSFL. Previous surgery at the index level correlated significantly with postoperative CSFL (OR 2.76, CI 1.1-6.8, p=0.03) in multivariate analysis. Furthermore, patients with intradural tumors tended to have a higher risk for CSFL (OR 2.3, CI 0.9-5.8, p=0.07). Surgery related factors did not influence occurrence of CSFL. Surgery on the thoracic spine had a significantly lower postoperative CSFL rate than surgery on the cervical or lumbar spine (OR -2.5, CI 1.3-4.9, p=0.02).

Conclusions

Our study found no modifiable risk factors for preventing CSFL after intradural spine surgery. Patients with previous surgery at the index level were at higher risk for CSFL. CSFL resulted in significantly more wound healing disorders and SSIs necessitating further therapy.

Introduction

Cerebrospinal fluid leakage (CSFL), defined as an open communication between the subarachnoid and epidural space by a meningeal defect,[1] is a well-recognized complication after neurosurgical interventions.[1-6] This complication may occur after brain or spine surgery, in particular following intradural spine surgery, where opening of the dura is required.

While a variety of publications have reported on CSFL following skull-base surgery, literature describing risk factors, preventive measures and treatment for this complication after intradural spine surgery is scarce. Most studies have analyzed extradural spine surgery with incidental durotomy or did not distinguish between intentional and unintended durotomy.[4, 5, 7-12]

The reported incidence of CSFL after intradural spine surgery ranges between 2 and 34%.[2-7, 13] It tends to be higher than the incidence of persistent CSF leakage after incidental durotomies during extradural spine surgeries, which ranges between 0.24 and 9%.[2-7, 13] Furthermore, the available literature is mostly based on small study populations with predefined surgery indications, mainly for spinal tumors. In contrast, literature about risk factors and spine surgery with intended durotomy is rare.[2, 3, 6, 10, 13, 14]

CSFL can cause a multitude of complications such as meningitis, surgical site infections, spinocutaneous fistulas, back pain, and intracranial hypotension with potentially severe consequences for patients.[1-5, 10, 12, 14, 15] Therefore, it is essential to identify risk factors for its occurrence. Treatment of these complications often requires revision surgery and prolonged hospitalization, resulting in higher costs.[2, 3, 13, 14] About one-third of patients with radiographic signs of CSFL are symptomatic.[13] Depending on its extent, CSFL can be treated conservatively by bed rest, more invasively by inserting a lumbar drain, or surgically. However, there is no consensus on the optimal management for patients with CSFL and treatment regimens proposed in the literature differ widely.[1-5, 10, 12, 14, 15]

For unintended durotomy, risk factors such as surgery for degenerative pathologies, older age, longer duration of surgery, resident involvement,[5] obesity and hypertension[9] have been described. For patients undergoing craniotomy, diabetes and systemic inflammation were found to increase the risk for CSFL.[16] In cerebral tumor surgery, a higher BMI has been associated with CSFL.[17] Previous surgery was found to increase the risk for CSFL in patients undergoing extra- and intradural spine surgery.[4, 10, 14]

Watertight suture of the dura is critical in the prevention of postoperative CSFL as the dura is a fragile membrane.[2, 7, 8, 18, 19] Different types of sealants, patches and grafts are used with the aim of reducing CSFL.[18] There is controversy about whether primary dural closure or additive use of sealants influences occurrence of CSFL.[2, 13, 16, 20, 21] Furthermore it is controversial whether postoperative bed rest decreases CSF pressure and thereby decreases the incidence of CSFL.[20]

To the best of our knowledge, there is so far no literature widely reflecting on patient and surgery related risk factors for the occurrence CSFL after intradural spine surgery with intended durotomy. The aim of this study was to determine the incidence of postoperative CSFL, and to identify potential risk factors for this complication in patients undergoing intradural spine surgery.

Material and Methods

Study design and patient selection

We conducted a retrospective single center cohort study. Patients who had had spine surgery between January 2009 and April 2021 at our institution were screened for eligibility. We included adult patients (age >18 years) that underwent intradural spine surgery and in whom a general consent was available. Patients with missing surgical records were excluded. The study was approved by the local ethics committee of the canton of Bern, Switzerland (2021-01144).

Data acquisition

Patient related, surgical and perioperative data obtained from our electronic patient and clinical information system were collected and converted to a database.

Basic demographic data (age, sex, comorbidities, therapeutic agents, pathology and indication for surgery) were assessed. Information on type of procedure and approach, region of spine operated on, extent of operated vertebral segments, use of and number of sealants and use of neuromonitoring, duration of surgery and blood loss was gathered. The spinal column was divided into cervical, thoracic, lumbar and sacral regions. If a pathology (or surgical approach) extended over more than one region, it was described as located on the cervicothoracic, thoracolumbar or lumbosacral junction. Length of hospital stay, discharge management, bed rest and occurrence of postoperative complications were analyzed. Postoperative bed rest was defined as bed rest for longer than 24 hours, as most patients stayed in bed on the day of surgery and were mobilized on the first postoperative day according to the standard practice in our clinic.

As standard care, all patients were followed up clinically 6 to 8 weeks after surgery. After tumor-surgery follow-up included a spinal MRI. For other pathologies, postoperative imaging was at the surgeon's discretion.

The primary endpoint, occurrence of postoperative CSFL, was confirmed by spinal MRI or clinically by subcutaneous CSF collection or leakage out of the wound.

Surgical technique

Surgery was performed under general anesthesia. After intraoperative localization of the segment of interest, a posterior or anterior approach was performed. Depending on the lateralization, size and expected consistency of the pathology a hemi- or complete laminectomy was carried out on one or more segments. In cases of purely anterior pathologies with compression of the spinal cord, an anterior corpectomy was performed. The dura was incised in the midline or paramedian. Surgery for spontaneous intracranial hypotension (SIH) was performed as described previously.[22] As standard operating procedure in our institution, the dura was closed with watertight 6-0 monofilament running sutures. The additional use of sealants was at the discretion of the surgeon. The term "sealant" refers to all types of additive repair adjuncts (fibrin, sealants, grafts, patches).

Statistics

Descriptive statistics were obtained for all data points using mean and standard deviation for metric variables and proportions for nominal variables. Associations of nominal variables with the frequency of CSFL were analyzed using chi-square tests/Fisher's exact test for each factor. Additionally, logistic regression analysis was performed for all nominal and metric variables, including calculation of odds ratios (ORs) to show the relationship between those variables and occurrence of CSFL. Multivariate regression was calculated for those parameters that showed significant results or a tendency towards significance in univariate logistic regression. A two-sided p-value of < 0.05 was set for test significance. Missing values were excluded by pairwise deletion. Statistical analysis was conducted using IBM SPSS Statistics (Version 25.0, IBM Corporation).

Results

Between 01/01/2009 and 04/30/2021, 6010 patients had surgery for a spinal pathology. Of these, 375 underwent intradural spine surgery and were included in the study.

Patient related data

Of the study population, 226 (60.3%) were female. Mean age was 54 (SD ± 17) years. Mean BMI was 25.5 (SD ± 4.6) kg/m². Most patients were classified as American Society of Anesthesiologists (ASA) classification 2 (245/375, 65.3%) or ASA 3 (92/375, 24.5%). Overall, 62 (16.5%) were current smokers. Most patients, 243 of 375 (64.8%), had a tumor. The second leading pathology was SIH, which affected 95 patients (25.3%), 14 (3.7%) had cavernoma, 12 (3.2%) arteriovenous malformation and 11 (2.9%) idiopathic spinal cord herniation.

Of the tumors, 218 (89.7%) were extramedullary and 25 (10.3%) intramedullary. Meningioma and schwannoma were the main tumor entities, affecting 84 (34.6%) and 62 (25.5%) of patients with tumors. Sixty-four patients (17.1%) had previous surgery on the index level of spine. Baseline characteristics are displayed in Table 1.

Surgical technique and perioperative management

A total of 259 patients (69.1%) had a hemilaminectomy with a paramedian approach. Two hundred two patients (53.9%) had surgery on the thoracic spine; the second most frequent regions were cervical (66/375, 17.6%) and lumbar spine (59/375, 15.7%). Extent of surgery involved a mean of 2 (SD ± 1) vertebral segments. Only 19 patients (5.1%) had additional instrumentation. In 282 patients (75.2%) sealants were used in addition to watertight suturing for dural closure. Almost all patients, 352 of 375 (93.6%), had neuromonitoring during surgery. Mean blood loss was 387 (SD ± 473) ml. Mean duration of surgery was 218 (SD ± 109.5) minutes. About one-quarter of patients (88/375, 23.5%) were on postoperative bed rest for longer than one day. Mean duration of hospitalization was 9 (SD ± 5.6) days. Most patients (222/375, 59.2%) were discharged home (see Table 2).

Incidences of postoperative cerebrospinal fluid leakage and other complications

In 30 patients (8.0%), postoperative CSFL was diagnosed. In 11 of 30 patients (36.7%), diagnosis was made during the same hospitalization period as the index surgery, while 19 patients (63.3%) were diagnosed afterwards. CSFL was confirmed clinically in 7 out of 30 patients and with additional MRI in 23 patients. CSFL was significantly associated with wound healing disorders (OR 24.9, CI 9.3-66.7, p<0.001) and need for revision surgery (OR 61.6, 95%-CI 17.9-311.5, p<0.001). Five patients (16.7%) with CSFL had a SSI (four associated with meningitis, one associated with an abscess) (OR 8.4, CI 2.6-27.7, p 0.002). Wound infection was differentiated from wound healing disorders by microbiological tests. Twelve patients (40%) had a wound healing disorder and 27 of 30 patients (90%) with CSFL underwent revision surgery to treat it. Three patients were managed successfully with a lumbar drain, but only 4 of 30 patients had a lumbar drain inserted as a therapeutic option for CSFL. CSFL did not result in longer hospitalization (12.3 days versus 9 days; OR 1.49, CI 0.7-3.2, p 0.31). Occurrence of CSFL had no impact on discharge management. Two of 375 patients died during hospitalization – one because of progressive neurofibromatosis, the other due to cancer that had metastasized. Data on postoperative complications are shown in Tables 3 and 4.

Patient related risk factors for CSFL

Sex, age, ASA classification and BMI had no impact on CSFL. Furthermore, there was no association between occurrence of CSFL and smoking, underlying diabetes, arterial hypertension, renal insufficiency, intake of steroids or anticoagulation therapy. A tendency towards a higher incidence of CSFL was found in spinal tumor patients in whom the risk was doubled (OR 2.3, CI 0.9-5.8, p 0.07). Patients who had undergone previous surgery had incidences of CSFL about twice as high (14.1% versus 6.8%) as those who had not had surgery on the same segment of spine before (OR 2.3, CI 0.98-5.2, p=0.05) (Table 5).

Surgery related risk factors for CSFL

Approach, type of surgery and additional instrumentation did not differ between patients with and without CSFL, as shown in Table 6. In general, use of sealants per se had no effect on occurrence of CSFL (OR 1.4, CI 0.5-3.4, p 0.53), but use of two or more sealants (i.e. patch and fibrin glue for example) was associated with significantly more CSFLs (OR 4.0, CI 1.8-8.8, $p < 0.001$). Extension of surgery over more vertebral segments tended to result in higher CSFL rates (2.3 versus 2.0 segments; OR 1.28, CI 0.96-1.7, p 0.09). Duration of surgery and blood loss had no impact on occurrence of CSFL. Overall incidence of CSFL did not differ between the different treated spine regions. When testing each spine region individually against the others, surgery on the thoracic spine resulted in significantly lower risk for CSFL (OR −2.51, CI 1.3-4.9, p 0.02). Surgery on the cervicothoracic junction showed barely insignificant higher rates of CSFL (OR 2.97, CI 0.9-9.5, p 0.08). Bed rest had no influence on likelihood of developing CSFL (OR 0.6, CI 0.23-1.7, p 0.36) (Table 6 and Figure 1).

Multivariate analysis was performed additionnaly, including factors showing a significant or a tendency towards a significant relationship with CSFL. This condition was applicable for tumor, previous surgery, cervicothoracic spine and thoracic spine. Age was included as constant variable. Previous surgery now was significantly correlated with occurrence of CSFL (OR 2.8, CI 1.1–6.8, p 0.03) whereas surgery on the thoracic spine was no longer significant, as shown in Table 7.

Discussion

In this single center study with retrospective analysis of data on intradural spine surgery in adults, 8.0% (30/375) were diagnosed with postoperative CSFL. Previous surgery was identified as a risk factor for the occurrence of CSFL in multivariate analysis. No modifiable risk factors were found to have an impact on CSFL.

Incidence of postoperative cerebrospinal fluid leakage

Incidence of 8.0% is within the range of incidences reported in the literature of 2 to 34% after intradural spine surgery.[2, 3, 5-7, 13, 14, 20]

Our findings are in line with the results of Lee et al., who found an incidence of CSFL of 8.39% among 311 patients undergoing intradural spine surgery. In a study of 115 patients with intradural spinal tumors, Jenkinson et al. reported a similar rate of 10% CSFL postoperatively.[6,20] In a large series of 638 cases of intradural spine surgery in children, Liu et al. reported an incidence of CSFL of 7.1%.[14] Although this study included only pediatric patients, the rate of CSFL is similar to that in our study. This supports our finding that age had no impact on the rate of CSFL.

In contrast, Koechlin et al. reported a higher incidence of CSFL of 34% among 91 tumor patients after intradural spine surgery. However, these were diagnosed by radiographic signs of CSFL with MRI within 72 hours after surgery, thus potentially overestimating the incidence of clinically relevant CSFL. Furthermore, only 13% of these patients were symptomatic for CSFL with need of therapy.[13] In our study we found a three times lower incidence of CSFL, whereby most patients (80.3%) also had postoperative MRI, performed directly after surgery for those with complications, or 6 to 8 weeks after surgery at the follow-up. The high rate of CSFL that Koechlin et al. reported might be an overestimate as early postoperative MRI might show fluid collections that are difficult to differentiate. Furthermore, we cannot exclude asymptomatic pseudomeningoceles in those cases without postoperative MRI. Since the rate of postoperative MRIs is quiet high in our cohort and the rest of patients were asymptomatic, this fact might not have a substantial impact on the results of our study.

In contrast to our findings, Sellin et al. found a lower incidence of CSFL of 2.8% of 460 cases. However, there was no information about how CSFL was diagnosed.[2] Only one experienced surgeon operated on those patients, which could indicate that more experience might lead to lower incidences of CSFL. In contrast, more than 30 different surgeons, including residents, performed surgeries in our study.

Complications and effects of CSFL

As expected, CSFL is associated with a higher risk of wound healing disorders, and thus often requires re-operation. Hoover et al. observed that complications after intradural spine surgery are most commonly CSF related.[3] In our population, 40% of patients with CSFL had a wound healing disorder. In addition, 27 of 30 patients had revision surgery to treat the CSFL. We tended to be more aggressive in treating postoperative CSFL surgically compared to other groups, who describe a lower rate of revision surgery for CSFL. Sellin et al. and Koechlin et al. reported that two-thirds (9/13) and 50% (6/12) of patients needed re-operation. Complications of CSFL were not described.[2, 13] In children with CSFL after intradural spine surgery a rate of 13.3% for wound infections and 15.6% for neurological worsening was reported and a third were treated by re-operation.[14] Occurrence of postoperative wound infections due to CSFL differs widely between studies. For example, incidence of meningitis due to CSFL ranges between 0.1% and 41%.[1, 5, 6] In our study, 16.7% (5/30) patients developed wound infection, whereas four had meningitis and one an abscess.

Patient related fisk factors for CSFL

In line with previous studies, age and sex did not influence the occurrence of CSFL after spine surgery.[2, 4, 13, 17, 20] There was no significant relationship between health status assessed by ASA classification and CSFL occurrence. This hypothesis is supported by the lack of a correlation between CSFL and other comorbidities. As only a few patients had those comorbidities, our results might not be representative. However, Lee et al. also found no relationship between CSFL and those comorbidities.[20]

Previous surgery at the same level leads to a higher risk for CSFL as shown by multivariate analysis (p 0.03). However, the results of previous studies are equivocal and the relationship thus remains uncertain.[4, 10, 14, 3, 7, 17] Challenging anatomic conditions, missing or altered soft tissue with cicatrisation might explain this circumstance.

We found that patients with intradural tumor tended to have a higher risk for CSFL compared to those with other indications for surgery – 9.9% of tumor patients had CSFL, although this result was not significant (p 0.07). The literature also suggests that different indications have no impact on occurrence of CSFL, although tumor is the most studied pathology.[2, 5, 6, 13, 17, 20] Liu et al. described an association between CSFL and tumor excision.[14] In contrast, the study by Eser et al. suggested that non-tumoral indications might be risk factors for CSFL after spine and posterior fossa surgery.[10]

Surgery related risk factors for CSFL

The type of approach (hemilaminectomy, laminectomy or anterior approach) had no impact on occurrence of CSFL, which supports the findings of Lee et al.[20] and Koechlin et al..[13] When comparing surgery on different spinal regions, we found that surgery on thoracic spine significantly lowered the risk of CSFL, whereas surgery on the cervicothoracic junction tended to increase the risk. Lee et al. found a significant correlation for this condition.[20] The increase in CSFL in the junctional zone/ cervicothoracic junction might be due to the greater motion in these segments whereas the thoracic spine is quite rigid and might be less prone to CSFL.

We expected that surgery in the lumbar spine would be associated with a higher incidence of CSFL as a result of the greater hydrostatic pressure. Contrary to this expectation, our data and existing literature showed no relationship between lumbar durotomy and risk for CSFL.[2, 3, 10, 13, 14, 20] So maybe, in this regard, the higher range of motion at the cervicothoracic junction is a more important risk factor than the hydrostatic pressure in the lumbar spine. Furthermore, we found no association between the occurrence of CSFL and increasing number of vertebral segments operated on. Similarly Koechlin et al.[13] and Lee et al.,[20] found no association between extent of surgery and CSFL.

Watertight suture of the dura is critical in preventing postoperative CSFL.[2, 7, 8, 18, 19] Use of sealants in addition to watertight dura closure is controversial. In our department, we use sealants regularly and they were used in 75.2% of our study population. TachoSil, a fibrinogen/collagen combined seal and DuraSeal, a hydrogel, which are both widely used (including in our study population), combined with a running 6-0 monofilament polypropylene suture achieved high burst pressure in vitro and are therefore thought to reduce CSFL in vivo.[19] Use of sealant per se had no impact on occurrence of CSFL in our study, in line with the existing analyses of use of sealants in spine surgery.[2, 4, 10, 13, 14, 16, 18, 20] Use of two or more sealants was highly correlated with the occurrence of CSFL in our population, which supports this hypothesis. Interestingly, Koechlin et al. reported similar findings.[13] However, the retrospective nature of our data precludes a definitive conclusion, since failure to achieve a watertight dural closure might prompt the surgeon to apply more sealants. Microsurgical technique and experience of the surgeon might have a major impact on success of achieving a watertight suture. Our analysis did not consider this possible confounding factor. Additionally, it would have been interesting to compare different types of sealants, but due to the retrospective study design this data was not available.

One might argue that postoperative bed rest should decrease CSF pressure and thereby decreases risk of CSFL. However, in our study, duration of bed rest had no impact on occurrence of CSFL, and most patients (76.5%) were mobilized on the first postoperative day. There are conflicting reports in the literature; some data suggest longer bed rest for treatment of CSFL, but other studies did not show reduced rates of CSFL with longer bed rest.[5] Lee et al. recently attempted to resolve this question. They analyzed postoperative occurrence of CSFL and other complications after intradural spine surgery in patients who were mobilized on the first postoperative day compared to those who started ambulation after at least 3 days of bed rest. Contrary to the primary hypothesis, longer bed rest was significantly associated with increasing incidence of CSFL resulting in longer hospital stay and higher rates of re-operation.[20] In general, our study confirms that there is no benefit in longer postoperative bed rest after intradural spine surgery. As our study and those of Lee et al. had retrospective character[20], reasons for prolonged bed rest remain unclear.

Limitations

Our study has several limitations. First, the retrospective study design has inherent limitations and a potential for biases. Although, our study was one of the largest on this topic and we screened for a wide range of risk factors, a few conditions and comorbidities were underrepresented. Most patients had either tumorous pathology or SIH, and only a few suffered from other pathologies, which limits the generalizability of our results. Furthermore, surgical technique together with surgical experience might have a major impact on quality of dural closure. We did not adjust for this confounder. Finally, due to the study design we could not analyze the quality of the dura itself, which could also influence the incidence of postoperative CSFL.

Conclusion

Our study found no modifiable risk factor for preventing CSFL after intradural spine surgery. Previous surgery was associated with a higher risk of CSFL. Surgery for spinal tumor and surgery on cervicothoracic spine tended to be associated with a higher risk, while surgery on the thoracic region conferred a lower risk for postoperative CSFL. As a CSFL results in significantly more wound healing disorders, SSIs and need for further therapy, expeditious management is crucial.

Disclosures

All authors declare that they have no conflict of interest.

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Figure legends

Fig. 1: Proportion of CSFL by spinal region

Table 1: Patient related baseline characteristics

Variable	**Total (n = 375)**
Sex, n (%)	
Female	226 (60.3)
Male	149 (39.7)
Age in years, mean (± SD)	54.1 (16.5)
BMI in kg/m², mean (± SD)	25.5 (4.6)
ASA, n (%)*	
1	26 (6.9)
2	245 (65.3)
3	92 (24.5)
4	12 (3.2)
Current smoking, n (%)	62 (16.5)
Pathology, n (%)	
Tumor	243 (64.8)
Extramedullary, n (% of tumor)	218 (89.7)
Meningioma	84 (34.6)
Schwannoma/neurofibroma	62 (25.5)
Ependymoma	29 (11.9)
Others†	28 (11.5)
Intramedullary, n (% of tumor)	25 (10.3)
Astrocytoma	4 (1.6)
Glioblastoma	5 (2.1)
Ependymoma	8 (3.2)
Others†	8 (3.2)
Cavernoma	14 (3.7)
SIH ‡	95 (25.3)
AVM ‡	12 (3.2)
ISCH ‡	11 (2.9)
Previous surgery, n (%)	64 (17.1)
Diabetes, n (%)	22 (5.9)
Insulin dependent	6 (1.6)
Renal insufficiency, n (%)	25 (6.7)
Arterial hypertension, n (%)	101 (26.9)

Steroids, n (%)	52 (13.9)
Anticoagulation/antiplatelet therapy, n (%)	32 (8.5)

*ASA = American Society of Anesthesiologists classification (I = normal healthy patient, II = mild systemic disease, III = severe systemic disease, IV = life threatening disease)

† Others = oligodendroglioma, plexus tumor, ganglioglioma, lymphoma, plasma cell tumor, lipoma, hemangioblastoma/glioma, epidermoid tumor

‡ SIH = Spontaneous intracranial hypotension, AVM = arteriovenous malformation, ISCH = idiopathic spinal cord herniation

Table 2: Surgical technique and perioperative management

Variable	**Total (n = 375)**
Procedure – approach, n (%)	
Hemilaminectomy – paramedian	259 (69.1)
Laminectomy – median posterior	109 (29.1)
Other – anterior	7 (1.9)
Additional instrumentation, n (%)	19 (5.1)
Region, n (%)	
Cervical	66 (17.6)
Cervicothoracic	21 (5.6)
Thoracic	202 (53.9)
Thoracolumbar	24 (6.4)
Lumbar	59 (15.7)
Lumbosacral	3 (0.8)
Sacral	0 (0.0)
Number of segments, mean (± SD)	1.99 (1.01)
Sealant, n (%)*	282 (75.2)
Neuromonitoring, n (%)	351 (93.6)
Duration of surgery in minutes, mean (± SD)	218 (109.5)
Blood loss in ml, mean (± SD)	387 (473)
Bedrest, n (%)	88 (23.5)
Postoperative MRI, n (%)	301 (80.3)
Duration of hospitalization in days, mean (± SD)	9.2 (5.6)
Destination on discharge from clinic, n (%)	
Home	222 (59.2)
Rehabilitation	117 (31.2)
Transfer to other clinic	34 (9.1)
Death	2 (0.5)

* Two or more types of sealants in 21.6% (61/282); dura graft in 5.9% (22/375)

Table 3: Incidence of postoperative cerebrospinal fluid leakage and other complications

Variable	**Total (n = 375)**	**Patients with CSFL (n = 30)***
CSF leakage, n (%)*†	30 (8.0)	
Surgical Site Infection, n (%)	13 (3.5)	5 (16.7)
Healing disorder, n (%)	19 (5.1)	12 (40)
Re-surgery, n (%)‡	72 (19.2)	28 (93.3), 27/30 (90) as therapy for CSFL

*66.7% (20/30) of CSFL manifested and were diagnosed within 14 days postoperatively, 23.3% (7/30) within the 2 first postoperative months, 10% (3/30) after 2 months: 36.7% (11/30) were diagnosed during hospitalization for the index surgery.

† 76.7% (23/30) of CSFLs were diagnosed by magnetic resonance imaging and clinically, 23.3% (7/30) only clinically.

‡ 33.3% (10/27) revision surgeries were performed during hospitalization for the index surgery. Three patients with CSFL were managed successfully by lumbar drainage. One patient with CSFL had revision surgery for recurrence of the tumor, not for CSFL treatment.

Table 4: Complications and effects of CSFL

Variable	CSFL*	No CSFL	p-value	OR CSFL (95% CI)
Surgical Site Infection, n (%)				
Yes	5/30 (16.7)	8/345 (2.3)	**0.002**	**8.43 (2.57–27.66)**
No	25/30 (83.3)	337/345 (97.7)		
Healing disorder, n (%)				
Yes	12/30 (40)	9/345 (2.6)	**< 0.001**	**24.89 (9.29–66.7)**
No	20/30 (66.7)	336/345 (97.4)		
Re-surgery, n (%)†				
Yes	28/30 (93.3)	44/345 (12.8)	**< 0.001**	**95.77 (22.04–416.13)**
No	2/30 (6.7)	301/345 (87.2)		
Duration of hospitalization in days, mean (± SD)	12.27 (8.66)	8.98 (5.24)	0.31‡	1.49 (0.69–3.23)
Discharge, n (%)				
Home	16/30 (53.3)	206/345 (59.7)	0.68	1.3 (0.61–2.74)
Rehabilitation or transfer	14/30 (46.7)	137/345 (39.7)		
Death	0/2 (0)	2/345 (0.6)		

Table 4–showing p-value and odds ratio with 95% confidence interval of logistic regression and chi-square tests calculating association between CSFL and postoperative factors.

*10% (3/30) pseudomeningocele, 16.7% (5/30) only orthostatic symptoms, 26.7% (8/30) healing disorder without infection, 16.7% (5/30) infection, 30% (9/30) symptoms due to displacement effect of liquorrhoe

† Re-surgery as therapy for CSFL (without revision surgery for other reasons): 27/30 (90%) with CSFL vs. 44/345 (12.8%) without CSFL; OR 61.57, 95%-CI 17.92 – 311.49, p<0.001)

‡ p-value and OR for correlation between CSFL and need for hospital stay > 7 days

Table 5: Patient related risk factors for CSFL

Variable	**CSFL**	**No CSFL**	**p-value**	**OR CSFL (95% CI)**
Sex, n (%)				
Female	11/149 (7.4)	138/149 (92.6)	0.72	1.15 (0.53–2.5)
Male	19/226 (8.4)	207/226 (91.6)		
Age, mean (± SD)	51.5 (15.4)	54.4 (16.6)	0.36	0.99 (0.97–1.01)
BMI, mean (± SD)	26.0 (5.1)	25.5 (4.6)	0.6	1.02 (0.94–1.10)
ASA, n (%)*				
I	2/26 (7.7)	24/26 (92.3)	0.95	0.96 (0.22–4.25)
II	18/245 (7.3)	227/245 (92.7)	0.52	0.78 (0.36–1.67)
III	9/92 (9.8)	83/92 (90.2)	0.47	1.35 (0.6–3.07)
IV	1/12 (8.3)	11/12 (91.7)	1.0	1.047 (0.13–8.4)
Current smoking, n (%)				
Yes	4/62 (6.5)	58/62 (93.5)	0.8	0.76 (0.26–2.26)
No	26/313 (8.3)	287/313 (91.7)		
Pathology, n (%)				
Tumor	24/243 (9.9)	219/243 (90.1)	**0.07**	**2.30 (0.92–5.78)**
Cavernoma	0/14 (0.0)	14/14 (100)	0.62	0.92 (0.89–0.95)
SIH †	5/95 (5.3)	90/95 (94.7)	0.26	0.57 (0.21–1.53)
AVM †	0/12 (0.0)	12/12 (100)	0.61	0.92 (0.89–0.95)
ISCH †	1/11 (9.1)	10/11 (90.9)	0.61	1.16 (0.14–9.34)
Tumor, n (%)				
Extramedullary	23/218 (10.6)	195/218 (89.4)	0.48	2.8 (0.33–21.91)
Intramedullary	1/25 (4.0)	24/25 (96.0)		
Previous surgery n (%)				
Yes	9/64 (14.1)	55/64 (85.9)	**0.05**	**2.26 (0.98–5.2)**
No	21/311 (6.8)	290/311 (93.2)		
Diabetes, n (%)				
Yes	3/22 (13.6)	19/22 (86.4)	0.4	1.91 (0.530–6.852)
No	27/353 (7.6)	326/353 (92.4)		
Renal insufficiency, n (%)				
Yes	1/25 (4.0)	24/25 (96)	0.71	0.46 (0.06–3.5)
No	29/350 (8.3)	321/350 (91.7)		

Arterial hypertension, n (%) Yes No	5/101 (5.0) 25/274 (9.1)	96/101 (95.0) 249/274 (90.9)	0.19	0.52 (0.19–1.39)
Steroids, n (%) Yes No	3/52 (5.8) 27/323 (8.4)	49/52 (94.2) 296/323 (91.6)	0.78	0.67 (0.2–2.3)
Anticoagulation, n (%) Yes No	3/32 (9.4) 27/343 (7.9)	29/32 (90.6) 316/343 (91.6)	0.73	1.21 (0.35–4.23)

Table 5–showing p-value and odds ratio with 95% confidence interval of logistic regression and chi-square tests calculating association between CSFL and patient related factors.

*ASA = American Society of Anesthesiologists classification (I = normal healthy patient, II = mild systemic disease, III = severe systemic disease, IV = life threatening disease)

† SIH = spontaneous intracranial hypotension, AVM = arteriovenous malformation, ISCH = idiopathic spinal cord herniation

Table 6: Surgery related risk factors

Variable	CSFL	No CSFL	p-value	OR CSFL (95%-CI)
Procedure n (%)				
Hemilaminectomy	19/259 (7.3)	240/259 (92.7)	0.48	0.76 (0.35–1.64)
Laminectomy	10/109 (9.2)	99/109 (90.8)	0.59	1.24 (0.56–2.75)
Other	1/7 (14.3)	6/7 (85.7)	0.45	1.95 (0.23–16.74)
Additional instrumentation, n (%)				
Yes	2/19 (10.5)	17/19 (89.5)	0.66	1.38 (0.30–6.27)
No	28/356 (7.9)	328/356 (92.1)		
Number of segments in numbers, mean (± SD)	2.3 (1.86)	1.96 (0.9)	0.09	1.28 (0.96–1.70)
Region, n (%)*				
Cervical	6/66 (9.1)	60/66 (90.9)	0.72	1.19 (0.47–3.03)
Cervicothoracic	4/21 (19.0)	17/21 (81)	**0.08**	**2.97 (0.93–9.47)**
Thoracic	10/202 (5.0)	192/202 (95.0)	**0.02**	**−2.51 (1.29–4.9)**
Thoracolumbar	3/24 (12.5)	21/24 (87.5)	0.43	1.714 (0.48–6.12)
Lumbar	7/59 (11.9)	52/59 (88.1)	0.29	1.72 (0.7–4.2)
Lumbosacral	0/3 (0.0)	3/3 (100)	1.0	0.92 (0.9–0.95)
Sealant, n (%) †				
Yes	24/282 (8.5)	258/282 (91.5)	0.53	1.35 (0.53–3.41)
No	6/93 (6.5)	87/93 (93.5)		
Duration of surgery in minutes, mean (± SD)	248.4 (137.46)	214.8 (106.5)	0.11	1.00 (0.99–1.00)
Blood loss in ml, mean (± SD)	528.5 (950.8)	375.4 (408.5)	0.13	1.0 (0.99–1.00)
Bed rest, n (%)				
Yes	5/88 (5.7)	83/88 (94.3)	0.36	0.63 (0.23–1.7)
No	25/287 (8.7)	262/287 (91.3)		

Discharge, n (%)				
Home	16/222 (7.2)	206/222 (92.8)	0.5	0.77 (0.37–1.63)
Rehabilitation	11/117 (9.4)	106/117 (90.6)	0.54	1.31 (0.6–2.84)
Transfer	3/34 (8.8)	31/34 (91.2)	0.75	1.13 (0.32–3.92)
Death	0/2 (0.0)	2/2 (100)	1.0	0.92 (0.89–0.95)

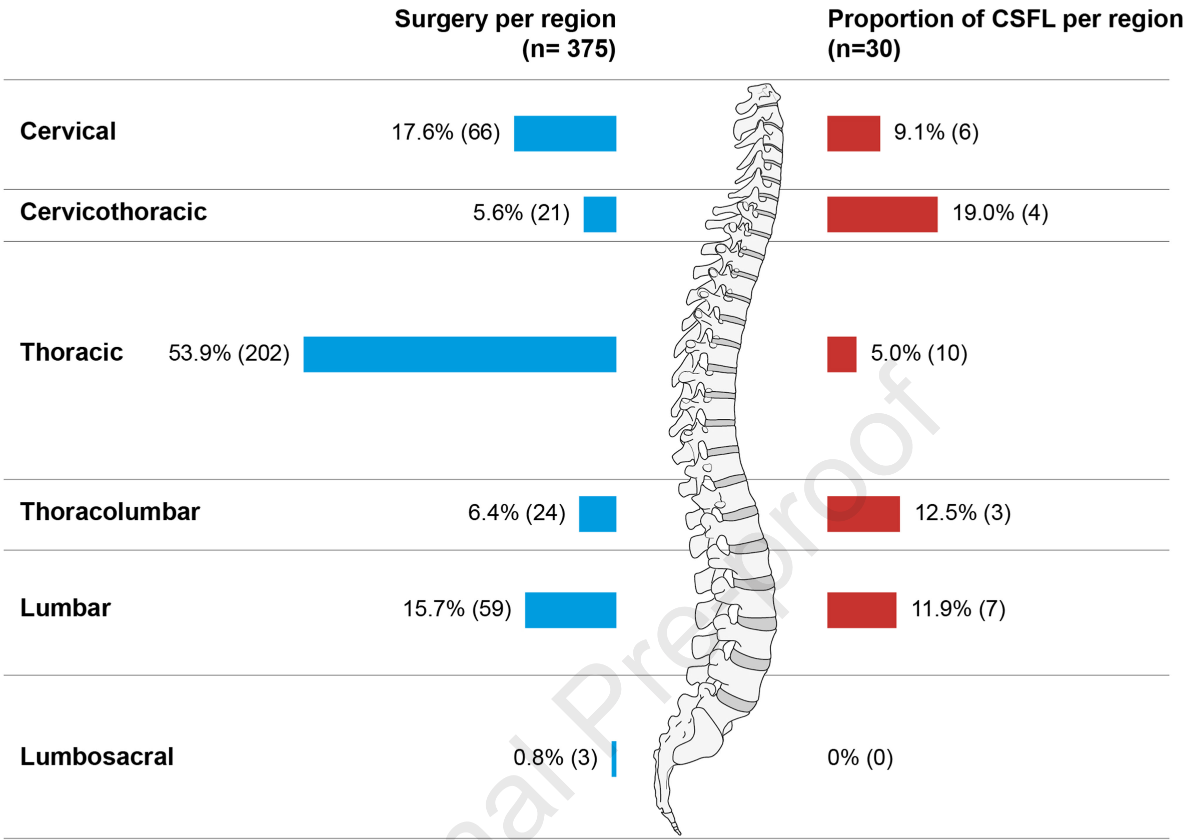
Table 6–showing p-value and odds ratio with 95% confidence interval of logistic regression and chi-square tests calculating association between CSFL and factors concerning perioperative phase.

* thoracolumbar, lumbar, lumbosacral, sacral (10/86, 11.6% versus 20/289, 6.9%, p 0.18)

† Use of two or more sealants resulted in significantly more CSFL (12/61, 19.7% versus 18/312, 5.8%) compared to use of no sealant or one sealant (OR CSFL 4.00, 95% CI 1.81–8.82, $p < 0.001$)

Table 7: Multivariate analysis of factors showing a significant or a tendency towards a significant relationship with CSFL

Variable	**p-value**	**OR CSFL (95% CI)**
Age	0.31	0.99 (0.96–1.01)
Tumor	0.1	2.39 (0.85–6.69)
Previous surgery	**0.03**	**2.76 (1.12–6.84)**
Cervicothoracic spine	0.26	2.18 (0.56–8.48)
Thoracic spine	0.26	0.6 (0.25–1.46)
Number of segments	0.77	1.05 (0.76–1.44)


Surgery per region
(n= 375)
Proportion of CSFL per region
(n=30)
Cervical
17.6% (66)
9.1% (6)
Cervicothoracic
5.6% (21)
19.0% (4)
Thoracic
53.9% (202)
5.0% (10)
Thoracolumbar
6.4% (24)
12.5% (3)
Lumbar
15.7% (59)
11.9% (7)
Lumbosacral
0.8% (3)
0% (0)

Abbreviations

ACDF = anterior cervical discectomy and fusion; AHT = arterial hypertension; ASA = American Society of Anesthesiologists; AVM = arteriovenous malformation; BMI = body mass index; CSFL = cerebrospinal fluid leakage; ISCH = idiopathic spinal cord herniation; MRI = magnetic resonance imaging; OR = odds ratio; SD = standard deviation; SIH = spontaneous intracranial hypotension; SSI = surgical site infection

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Christopher M Jesse: Conceptualization, Methodology, Writing - Review & Editing, Data Curation.

Helena Schermann: Data Curation, Formal analysis, Writing – Original Draft.

Johannes Goldberg: Formal analysis, Writing- Reviewing and Editing

Marco Gallus: Data curation

Levin Häni: Methodology, Writing- Reviewing and Editing

Andreas Raabe: Supervision

Ralph T Schär: Supervision, Writing- Reviewing and Editing