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# Incidence and risk factors of cerebrospinal fluid leakage related complications after spinal intradural tumor resection

Hiroaki Nakashima[1], Kyotaro Ota[2], Sadayuki Ito[1], Naoki Segi[1], Jun Ouchida[1], Ippei Yamauchi[1], Yukihito Ode[1] and Shiro Imagama[1]

*[1]Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan*
*[2]Department of Orthopedic Surgery, Toyota Kosei Hospital, Toyota, Japan*

## ABSTRACT

Cerebrospinal fluid (CSF) leakage is a common and serious complication of spinal surgery, particularly after intradural tumor resection. CSF leakage can lead to debilitating headaches, neurological deficits, and other symptoms, with an incidence rate of 0.3%–16%. This study aimed to investigate the incidence, risk factors, and outcomes of CSF-related complications in patients who underwent spinal intradural tumor surgery. This was a retrospective cohort study including 102 patients who underwent resection of intradural tumors, including ependymomas, astrocytomas, and meningiomas. Data were collected, including patient demographics, surgical details, and postoperative outcomes. The extent of CSF accumulation was evaluated using magnetic resonance imaging (MRI) findings. Statistical analyses were performed to identify risk factors for symptomatic CSF leakage. Postoperative CSF accumulation was observed in 94.1% of patients. Among them, 28.1% experienced symptomatic complications, such as severe headache (20.8%), unexplained fever (6.3%), and CSF leakage (3.1%). Patients with larger CSF accumulation, particularly subcutaneous accumulation, had a significantly higher incidence of symptomatic complications, with the highest rate observed in subfascial accumulation cases ($P = 0.0002$). Symptomatic patients did not show significant differences in age, sex, surgical level, drainage duration, or blood loss compared to asymptomatic patients. Additionally, the use of artificial dura mater did not significantly affect symptomatic outcomes. Predicting the occurrence of symptoms based on preoperative and surgical factors remains challenging. However, patients with subfascial CSF accumulation were more likely to develop symptoms, highlighting the necessity of confirming CSF accumulation using MRI for appropriate postoperative management.

Keywords: cerebrospinal fluid leakage, intradural tumor, postoperative complications, MRI evaluation, risk factors

Abbreviations:
CSF: cerebrospinal fluid
MRI: magnetic resonance imaging



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Corresponding Author: Hiroaki Nakashima, MD, PhD
Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan
Tel: +81-52-741-2111, Fax: +81-52-744-2260, E-mail: nakashima.hiroaki.s8@f.mail.nagoya-u.ac.jp

## INTRODUCTION

Cerebrospinal fluid (CSF) leakage is a significant and challenging complication of spinal surgery, with an incidence rate of 0.3%–16%.[1,2] It often induces substantial discomfort and potentially leads to severe complications, such as neurological deficits and prolonged hospital stays. Despite advancements in surgical techniques, the incidence of CSF leakage highlights a substantial risk that warrants deeper investigation, especially in intradural spinal tumor surgeries where dural incisions are unavoidable. With symptomatic manifestations such as debilitating headaches and, less commonly, compromised neurological function, understanding the epidemiology and risk factors of CSF leakage is crucial for improving surgical outcomes and patient recovery.[1,2] Dural tears are often the source of CSF leakage, occurring in approximately 1%–17% of spinal surgeries.[1,2] These dural injuries can lead to persistent CSF leakage, resulting in complications such as headache, pseudomeningoceles, and, in severe cases, neurological deficits.[3]

Headaches are the most common symptom associated with CSF leakage and can be debilitating. The typical presentation includes orthostatic headaches, which worsen when the patient is upright and improve when lying down.[3,4] Additionally, CSF leaks can lead to more serious neurological symptoms, such as radiculopathy, myelopathy, or cranial nerve palsies due to the mass effect of the accumulating fluid or pseudomeningoceles formation.

Previous studies have highlighted several risk factors for CSF leaks, including reoperation, extensive laminectomy, and revision surgery.[5] However, these studies often focused on general spinal surgeries and did not provide a detailed analysis of intradural tumor resection cases specifically. Furthermore, information on the incidence and detailed characteristics of CSF-related complications in patients undergoing spinal tumor surgery, especially when performing dural incision, is limited. Most studies have not comprehensively addressed the outcomes related to different extents of CSF accumulation and their symptomatic manifestations. Therefore, this study aimed to investigate the incidence and details of CSF-related complications in patients who underwent intradural tumor resection.

## MATERIALS AND METHODS

### *Study design*

This retrospective cohort study was conducted at Nagoya University Hospital, with approval from the Institutional Review Board. The study adhered to the Declaration of Helsinki and the guidelines set forth by the Institutional Review Board. All cases of intradural tumor resection performed during the study period were included. Informed consent was obtained through an opt-out process, ensuring that participants retained the right to refuse the use of their data.

### *Participants*

A total of 108 patients who underwent spinal surgery were enrolled in this study. The inclusion criteria were patients who had intradural tumors requiring resection, and those who had undergone postoperative magnetic resonance imaging (MRI) to assess CSF accumulation.

### *Pathological diagnosis*

The pathological diagnoses of all 108 cases were reviewed and categorized based on histopathological findings. Schwannoma was the most common diagnosis, accounting for 55 cases, followed by meningioma (16 cases) and ependymoma (12 cases). Other diagnoses included astrocytoma (6 cases), cavernous hemangioma (6 cases), hemangioblastoma (4 cases), neurofibroma (4 cases), and glioma (3 cases, including suspected cases). Less frequent diagnoses were epidermoid cyst (2 cases), myxopapillary ependymoma (2 cases), and spinal arachnoid cyst (2 cases). Rare pathological findings included hemangioma (1 case), intramedullary aneurysm (1 case), malignant lymphoma (1 case), multiple sclerosis (1 case), syringomyelia (1 case), intramedullary lipoma (1 case), and hemangiopericytoma/solitary fibrous tumor (1 case).

*Data collection and outcome measures*

Data were collected from medical records, including patient demographics (age and sex), surgical details (tumor type, surgical duration, and blood loss), and postoperative outcomes (CSF accumulation and complications). Body mass index (BMI) of 25 kg/m$^2$ or higher was defined as obesity.

All patients underwent standardized surgical techniques, including meticulous dural suturing with the use of a fibrin sealant (fibrin glue) in all cases to enhance dural closure and minimize CSF leakage. Artificial dura mater was used in 46.1% of cases, primarily when direct closure without tension was not feasible. Autologous fascia (harvested from the lumbar fascia) was not used in this case series. CSF drainage was performed in 21.6% of cases. The extent of CSF retention was assessed based on MRI findings at 2 weeks postoperatively and classified as subcutaneous, subfascial, intra-arch, or none.

In this study, "symptomatic" cases were defined as those in which patients exhibited any symptoms potentially related to CSF leakage, excluding cases with clear signs of infection. Unexplained fever was defined as body temperature >37 °C for more than 10 days without an identifiable source of infection. CSF leakage was confirmed by clinical signs and imaging.

The primary outcome was the incidence of CSF-related complications. The secondary outcome was defined as the extent of CSF accumulation, evaluated using MRI findings, which was classified into subcutaneous, subfascial, sublaminar, or none. Comparisons between symptomatic and asymptomatic patients were conducted for explanatory variables such as age, surgical duration, blood loss, drain output on day 1, duration until drain removal, and C-reactive protein (CRP) levels on postoperative days 1 and 7.

*Statistical analysis*

Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as percentages. The normality of continuous variables was assessed using the Shapiro-Wilk test. As the results indicated that the data did not follow a normal distribution, the Mann-Whitney U test was used for comparisons between groups. Fisher's exact test was applied for categorical variables. Statistical analysis was performed using SPSS software (version 28.0; IBM Corp, Armonk, NY, USA). A $P$-value < 0.05 indicated statistical significance.

## RESULTS

Of the 108 patients initially enrolled in this study, 102 were included in the final analysis. Six patients were excluded due to postoperative complications, including one case of surgical site infection, one case of postoperative pneumonia, and four cases of postoperative urinary tract infection. Among the 102 analyzed patients, 51 were male and 51 were female, with a mean age of 49.8 ± 18.4 years. Postoperative MRI findings revealed CSF accumulation in 96 patients (94.1%), of whom 27 (28.1%) developed CSF-related complications. The most common complication was headache, occurring in 20 patients (20.8%). Additionally, 6 patients (6.3%) experienced unexplained fever, and 3 (3.1%) had CSF leakage. These complications often overlapped, with some patients experiencing multiple symptoms.

A comparison between symptomatic and asymptomatic patients with CSF accumulation showed that symptomatic patients tended to be younger (mean age 42.3 ± 16.7 years) than asymptomatic patients (mean age 52.6 ± 18.2 years), although the difference was not statistically significant ($P = 0.40$). Sex also had no significant impact on the incidence of symptoms, with symptomatic rates of 19.6% in males and 33.3% in females ($P = 0.18$). Moreover, the duration until drain removal was similar between symptomatic (mean 3.22 ± 1.03 days) and asymptomatic patients (mean 2.72 ± 0.93 days), with no significant difference ($P > 0.99$; Table). Furthermore, there was no significant difference in the prevalence of diabetes mellitus (DM) and obesity ($P > 0.99$; Table).

**Table** Comparison of symptomatic and asymptomatic groups

| Variable | Symptomatic (n = 27) | Asymptomatic (n = 75) | *P*-value |
|---|---|---|---|
| **Demographics** | | | |
| Age (years) | 42.3 ± 16.7 | 52.6 ± 18.2 | 0.40 |
| Sex (Male:female) | 10:17 | 41:34 | 0.18 |
| DM (n) | 0 | 7 | 0.19 |
| Obesity (n) | 1 | 2 | >0.99 |
| **Surgical Details** | | | |
| Surgical duration (min) | 321.3 ± 130.3 | 277.7 ± 117.8 | >0.99 |
| Blood loss (mL) | 220.1 ± 300.0 | 213.4 ± 228.5 | >0.99 |
| Drain output on day 1 (mL) | 265.2 ± 164.4 | 254.4 ± 177.3 | >0.99 |
| Duration until drain removal (days) | 3.22 ± 1.03 | 2.72 ± 0.93 | >0.99 |
| **Extent of CSF Accumulation and Symptomatic Rates** | | | |
| Subcutaneous (n) | 4 | 19 | 0.0002 |
| Subfascial (n) | 22 | 25 | |
| Sublaminar (n) | 1 | 20 | |
| None (n) | 0 | 9 | |
| **Surgical site** | | | |
| Cervical spine (n) | 10 | 16 | 0.28 |
| Thoracic spine (n) | 9 | 33 | |
| Lumbar spine (n) | 8 | 26 | |
| **Surgery-related factors** | | | |
| Use of implants (n) | 5 | 7 | 0.29 |
| Use of artificial dura mater (n) | 15 | 33 | 0.37 |
| Presence of CSF drainage (n) | 9 | 13 | 0.10 |
| Postoperative steroid use (n) | 5 | 15 | 0.51 |

n: number of cases
CSF: cerebrospinal fluid
DM: diabetes mellitus

No significant differences were observed between symptomatic and asymptomatic patients in terms of surgical duration (mean 321.3 ± 130.3 min vs 277.7 ± 117.8 min, $P > 0.99$) or blood loss (mean 220.1 ± 300.0 mL vs 213.4 ± 228.5 mL, $P > 0.99$; Table). Similarly, drain output on postoperative day 1 did not differ significantly between symptomatic and asymptomatic patients (265.2 ± 164.4 mL vs 254.4 ± 177.3 mL, $P > 0.99$; Table). Additionally, CRP levels on postoperative days 1 and 7 showed no significant differences between symptomatic and asymptomatic patients (mean 3.80 ± 3.51 mg/dL vs 3.17 ± 2.42 mg/dL, $P = 0.32$ on day 1; 2.04 ± 3.16 mg/dL vs 1.80 ± 1.69 mg/dL, $P > 0.99$ on day 7).

Further analysis revealed that the extent of CSF accumulation significantly influenced symptom incidence. Patients with subfascial CSF accumulation had the highest symptomatic rate, followed by those with subcutaneous and sublaminar accumulation ($P = 0.0002$; Table). Notably, none of the patients without CSF accumulation exhibited symptoms.

Additionally, the potential influence of various patient and surgical factors on the incidence of CSF-related complications was assessed. The surgical site had no significant impact on symptom incidence, with symptomatic rates of 38.5% for cervical spine surgeries, 21.4% for thoracic spine surgeries, and 23.5% for lumbar spine surgeries ($P = 0.28$; Table). The use of implants or artificial dura mater did not significantly affect symptomatic rates. Furthermore, the presence of CSF drainage did not significantly influence symptom development (33.3% in patients with drainage vs 17.3% in those without, $P = 0.10$). Postoperative steroid use also showed no significant association with symptomatic rates ($P = 0.51$; Table).

## DISCUSSION

The present study investigated the incidence and details of CSF-related complications in patients who underwent intradural tumor resection. We found that the overall incidence of CSF-related complications was 28.1%, with headache being the most common symptom. However, there were no significant differences between patients with and without CSF-related complications in terms of age, sex, surgical duration, blood loss, drain output, duration until drain removal, CRP levels, and use of artificial dura mater or CSF drainage.

Interestingly, the postoperative CSF accumulation rate observed in this study (94.1%) was higher than previously reported rates, which typically range from 50% to 80%.[5-9] Several factors may explain this discrepancy. First, we adopted a broad definition of CSF accumulation, encompassing even minor subcutaneous collections identified on MRI, which may not have been classified as clinically significant in prior studies. Second, the timing of MRI evaluations likely influenced the observed rates. In the present study, MRIs were performed within two weeks post-surgery, a period when transient CSF retention is common. Earlier studies with lower reported rates often assessed CSF accumulation at later intervals, by which time minor collections may have resolved. Third, surgical techniques and closure methods may have contributed to the differences. All cases in the present study involved meticulous dural suturing with fibrin glue application, which may have altered CSF distribution, leading to localized accumulation rather than free leakage. Despite the high rate of MRI-detected CSF accumulation, the incidence of symptomatic complications remained at 28.1%, indicating that not all fluid collections were clinically significant. Further studies are needed to investigate whether early MRI findings correlate with long-term symptomatic outcomes and to establish standardized imaging criteria for clinically relevant CSF accumulation.

Contrary to prior reports suggesting that younger patients are more susceptible to post-lumbar puncture headaches, our study found no significant age-related differences in CSF-related complications following intradural tumor resection.[10] This discrepancy may reflect fundamental differences between lumbar puncture procedures and intradural tumor surgeries. While both involve CSF manipulation, the mechanisms underlying CSF dynamics and dural healing differ substantially. Post-lumbar puncture headaches primarily arise from CSF depletion through a single dural defect, whereas intradural tumor resection involves complex factors, including dural manipulation, intracranial pressure fluctuations, and varied healing responses. These complexities may account for the absence of a clear age-related susceptibility pattern in our findings.

Additionally, our analysis of surgical variables—including drain duration, artificial dura mater usage, and intraoperative blood loss—revealed no significant correlation with symptomatic CSF accumulation. These findings align with recent studies that similarly reported no associations between surgical parameters and postoperative CSF-related complications in intradural procedures.[6] This suggests that symptomatic CSF-related complications may be more influenced by individual patient factors or postoperative CSF dynamics than specific surgical techniques.

The higher prevalence of symptoms in patients with subfascial CSF accumulation, compared to other locations, may be attributable to physiological mechanisms. The subfascial space, enclosed by dense fascia, may create elevated local pressure when filled with CSF. This increased pressure could irritate adjacent neural structures and pain receptors, leading to more frequent symptomatic presentations. Furthermore, the confined nature of the subfascial space may impede the natural reabsorption of CSF, prolonging its presence and contributing to sustained pressure effects and chemical irritation of surrounding tissues.

This study has several limitations. First, the retrospective design inherently risks selection bias and relies on the accuracy of medical records. Second, the study was conducted at a single center, which may limit the generalizability of the findings to other settings. Third, while the sample size was sufficient for primary analyses, it may have been underpowered to detect smaller differences or associations. Future studies involving larger, multicenter cohorts are warranted to validate these findings and enhance their applicability.

In conclusion, this study underscores the complexity of CSF-related complications following intradural tumor resection. While the overall incidence of symptomatic complications remains significant, the anticipated age-related differences observed in lumbar puncture contexts do not appear as pronounced. These findings emphasize the need for multifactorial analyses to elucidate the intricate interplay between surgical techniques, patient characteristics, and CSF retention. Prospective studies with larger cohorts and standardized imaging criteria will be essential to further refine surgical approaches and adjunctive therapies aimed at minimizing CSF-related risks.

## AUTHOR CONTRIBUTION

HN and KO served as co-first authors and contributed equally to the work.

## CONFLICT OF INTEREST

There are no conflicts of interest, and we have not received any funding for this work.

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