

Original Article

Risk factors associated with postoperative cerebrospinal fluid leak after endoscopic endonasal skull base surgery: A single-center retrospective cohort study

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ABSTRACT

Background: Over the past two decades, endoscopic endonasal skull base surgery (EESBS) has revolutionized the treatment of skull base tumors by enabling minimal access to resect significant pathologies such as meningiomas, pituitary adenomas, and chordomas. Despite its efficacy, complications such as cerebrospinal fluid (CSF) leak pose significant challenges, with an average incidence of 8.9% following EESBS. Therefore, our study aims to investigate the risk factors associated with postoperative CSF leak after employing an endoscopic endonasal approach for skull base surgery, focusing on patients treated at King Abdul-Aziz Medical City in Jeddah and King Abdullah Medical City in Makkah, Saudi Arabia.

Methods: A retrospective review of patients who underwent an endoscopic endonasal approach for the resection of intradural skull base pathology between January 2016 and December 2022 was performed with a total of 51 patients. Basic demographic data were collected, along with patient comorbidities, presenting symptoms, tumor pathology, tumor site, the extent of resection, and outcomes.

Results: 51 participants were analyzed, with a mean age of 43.41. Male participants comprised (58.8%), while headaches were the most common symptom (74.5%), followed by visual disturbances (51.0%). Nonsecretory tumors predominated, primarily located in the sellar and suprasellar regions (58.8%). Gross total resection was performed in the majority (56.9%), with a 9.8% incidence of postoperative CSF leak. Notably, all four patients with CSF leak experienced preoperative headaches. Hypertension was prevalent in Cases 1 and 4, with Case 4 having a history of neurological disease and radiation therapy. Anterior skull base tumors were most frequent in Cases 3 and 4.

Conclusion: The incidence of CSF leakage after surgery in this study was similar to that previously reported. It is worth noting that repeated surgeries may increase the risk of postoperative CSF leakage. Therefore, it is important to carefully evaluate the surgical approach for tumor removal and skull base reconstruction, considering the tumor characteristics and the patient's overall condition.

Keywords: Cerebrospinal fluid leak, Endoscopic endonasal skull base surgery, Postoperative outcomes, Risk factors, Saudi Arabia, Skull base tumors

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INTRODUCTION

Endoscopic endonasal skull base surgery (EESBS) has completely changed how skull base tumors are treated over the past two decades. This method has evolved to allow minimal access to the resection of significant skull base tumors, such as meningiomas, pituitary adenomas, and chordomas.^[10] Despite its effectiveness, this technique is occasionally used in more complex and advanced cases, such as recurrent malignancies with or without prior radiation, when the patient is in poor general health and has coexisting illnesses. The use of EESBS in these patients might raise the possibility of complications, including the development of postoperative cerebrospinal fluid (CSF) leaks.^[15] This complication remains the most clinically significant consequence of endoscopic skull base surgery and its principal criticism.^[6]

Few studies have compared the rates of postoperative CSF leakage in different tumor types. The postoperative repair can be affected by a variety of parameters depending on the type of tumor, including tumor size, location, and whether it requires subarachnoid dissection. After reconstruction of dural defects with a nasoseptal flap, endoscopic surgery for tumors located in the central skull base has been shown to have higher rates of CSF leakage than endoscopic surgery for tumors located in the anterior skull base.^[7] Furthermore, several studies have reported an incidence of CSF leakage after EESBS ranging from 1.6% to 40%, with an average CSF leakage rate of 8.9% across different studies.^[3,5] According to a study by Ozawa *et al.*, the incidence of CSF leakage was 4.8%, and the rate of CSF leakage may vary depending on the tumor pathology, degree of intraoperative CSF leak, and repeated surgeries, which have been identified as significant risk factors.^[15] Considering the clinical significance of this topic, it is necessary to identify the incidence of and risk factors associated with local CSF leakage.

According to our knowledge, no studies have been conducted in Saudi Arabia in general or at our facility in particular to explore these issues. Therefore, in this study, we aimed to investigate the risk factors associated with postoperative CSF leakage after an endoscopic endonasal approach for skull base surgery.

MATERIALS AND METHODS

We carried out a retrospective study from January 01, 2016, to December 31, 2022, at King Abdul-Aziz Medical City, Jeddah, and King Abdullah Medical City, Makkah. Fifty-one patient profiles diagnosed with skull base pathology and treated using an endoscopic endonasal approach to resect the tumor, who were followed up for at least 3 months, were reviewed. Meanwhile, incomplete medical records or patients with other causes of CSF leakage, such as skull base trauma, were excluded.

The information obtained included patient demographics such as age, sex, and body mass index (BMI). We also collected comprehensive clinical data for our cases, encompassing the duration of symptoms, presence of co-morbidities, history of skull base trauma, utilization of perioperative lumbar drainage, and the presence of any clinical or radiological indicators of preoperative hydrocephalus. In addition, we ensured that tumor data such as location, surgical indication, size of the dural defect, and tumor pathology were available. For the outcome, we obtained the surgical location and reconstruction technique as well as postoperative complications.

RESULTS

A total of 51 participants were included in the study, with a mean age of 43.41 (standard deviation = 15.404). Most participants were from King Abdul-Aziz Medical City, Jeddah (80.4%), and the rest were from King Abdullah Medical City, Makkah (19.6%). Male participants outnumbered female participants, 58.8% and 41.2%, respectively. The most common symptom among the participants was a headache (74.5%). Visual disturbances were prevalent (51.0%). A smaller percentage of participants reported other symptoms, such as nausea/vomiting (27.5%), disturbed sensation (19.6%), and weakness (11.8%). Seizures, loss of consciousness, and hydrocephalus were relatively rare, experienced by <10% of the participants. A family history of the disease and a history of other tumors were reported by 17.6% of the participants [Table 1].

All cases were of primary origin. The radiological diagnosis varied among participants, with the most common being pituitary microadenoma (49.0%), followed by omphalocele (21.6%) and pituitary macroadenoma (15.7%). Similarly, the tumor histopathology varied, with nonsecretory tumors being the most common (49.0%) [Table 2 and Figure 1].

The sellar and suprasellar regions were the most common sites for tumors (58.8%), followed by the anterior skull base (23.5%) and sellar with extension to cavernous regions (11.8%). Regarding the extent of resection, the majority of the participants underwent gross total resection (56.9%), followed by subtotal resection (41.2%). Finally, regarding postsurgical complications, recurrence was reported in 9.8% of the cases, while a leak was reported in four patients (7.8%) [Table 3].

To provide a thorough summary of the medical profiles and tumor characteristics of the four patients who experienced postoperative CSF leak, all four patients experienced headaches as a symptom before their diagnosis. For cases 1 and 4, hypertension was a common chronic condition. Case 4 had a history of neurological diseases, specifically bilateral

Table 1: Participants demographics, symptoms, and medical history.

Demographic variables	Number of participants	Frequency (%)
Age		
1–20 years	4	7.84
21–40 years	17	33.3
41–60 years	24	47.06
Above 60	5	11.76
Gender		
Male	30	58.8
Female	21	41.2
Location		
King Abdul-Aziz Medical City, Jeddah	41	80.4
King Abdullah Medical City, Makkah	10	19.6
Symptom/Medical History		
Headache	38	74.50
Nausea/vomiting	14	27.50
Seizure	4	7.80
Loss of consciousness	4	7.80
Weakness	6	11.80
Disturb sensation	10	19.60
Visual disturbance	26	51.00
Hydrocephalus	3	5.90
Family history	9	17.60
History of other tumors	9	17.6

Table 2: Radiological, histopathological diagnosis, and source of lesions.

Diagnosis	Number of participants	Percentage
Radiology		
Pituitary microadenoma	25	49
Pituitary macroadenoma	8	15.7
Apoplexy	1	2
Omphalocele	11	21.6
Chordoma	1	2
Craniopharyngioma	1	2
Colloid cyst	1	2
Unknown	3	5.9
Tumor histopathology		
Nonsecretory pituitary adenoma	25	49
Omphalocele	11	21.6
Secretory pituitary adenoma	8	15.7
Chordoma	3	5.9
Rathke cleft cyst	2	3.9
Craniopharyngioma	1	2
Meningioma	1	2

sensorineural hearing loss/chronic suppurative otitis media (SNHL/CSOM), and had undergone radiation therapy. The most common tumor site was the anterior skull base, as identified in cases 3 and 4 [Tables 4 and 5].

Table 3: Operative and postoperative conditions.

Operative and postoperative conditions	Number of participants	Percentage
Tumor site		
Sellar, suprasellar	30	58.8
Sellar+cavernous	6	11.8
Anterior skull base	12	23.5
Clival	2	3.9
3 rd ventricular	1	2
Extent of resection		
Gross total resection≥98%	29	56.9
Subtotal 89–70%	21	41.2
Debulking/biopsy<70%	1	2
Condition		
Recurrence	5	9.8
Regrowth of residual	4	7.8
Leak	4	7.8

DISCUSSION

EESBS is a well-established surgical approach that adds significantly to the neurosurgery field for approaching anterior skull base tumors. However, this approach has been limited by complications such as CSF leaks, and the risk factors for these complications can be divided into pre-, intra, and postoperative risk factors.

Preoperative risk factors in individual patients compared to existing literature

The preoperative phase is pivotal in assessing the risk profiles of patients undergoing EESBS. After reviewing the literature, we identified several preoperative risk factors.

The age range of our patients, from 33 to 57 years, with an equal distribution between males and females, offers a demographic representation that is less discussed in early literature, such as Jho and Carrau,^[10] but has become increasingly relevant in recent studies. The presence of hypertension in half of the patients aligns with Fraser *et al.*,^[6] where systemic conditions are recognized as potential influencers of surgical outcomes owing to their impact on healing and recovery. The fact that all patients are unemployed may reflect socioeconomic factors, which are not traditionally examined in the EESBS literature but can have indirect effects on health outcomes.

The duration of symptoms, ranging from 4 months to 2 years in our patients, may indicate the progressive nature of the underlying pathology. Ozawa *et al.*^[15] suggested that longer symptom duration can correlate with larger or more aggressive lesions, potentially complicating the surgical approach.

In the context of EESBS, obesity is acknowledged as a risk factor for the development of postoperative CSF leaks,

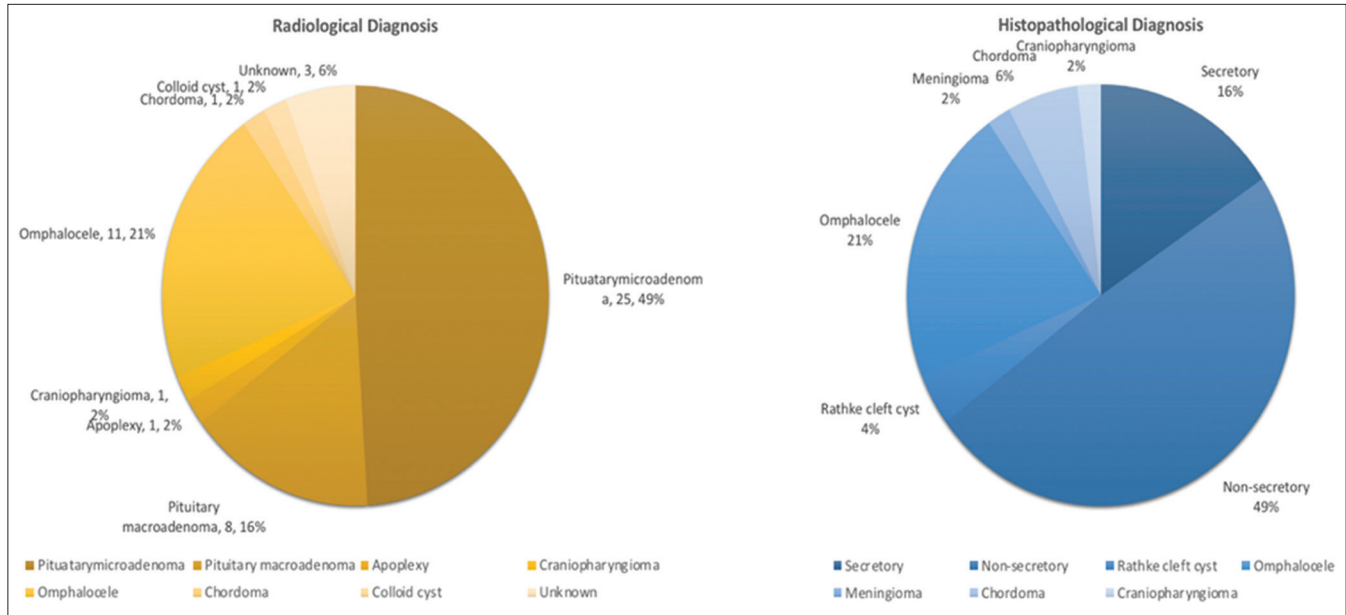


Figure 1: Tumor radiological and histopathological diagnosis.

Table 4: Summary of demographic and medical history.

Case number	Age	Gender	Employment status	Chronic diseases	Neurological diseases	Symptoms duration	Smoking status	Other tumors	Family history
1	57	Male	Unemployed	Hypertension	No	4 months	Yes	No	No
2	33	Male	Unemployed	No	No	6 months	No	No	No
3	56	Female	Unemployed	No	No	2 years	No	No	Yes
4	39	Female	Unemployed	Hypertension	Bilateral SNHL/CSOM	8 months	No	Yes	No

SNHL/CSOM: Sensorineural hearing loss/chronic suppurative otitis media

Table 5: Summary of tumor characteristics and diagnosis.

Case number	Lesion origin	Radiologic diagnosis	Histopathology diagnosis	Tumor site
1	Primary	Pituitary macroadenoma	Nonsecretory pituitary adenoma	Suprasellar
2	Primary	Clivus chordoma	Chordoma	Clival
3	Primary	Frontoethmoidal encephalocele (CSF leak)	Omphalocele	Anterior skull base
4	Primary	CSF rhinorrhea	Omphalocele	Anterior skull base

CSF: Cerebrospinal fluid

which were not directly measured in the current study. The correlation between a higher BMI and increased rates of CSF leak post-surgery is underscored in the findings of Fraser et al.^[6] They reported a significant association between a preoperative BMI exceeding 25 kg/m² and the occurrence of postoperative CSF leaks. This association likely stems from the increased intracranial pressure (ICP) associated with obesity, which may exert additional pressure on the surgical site, leading to a heightened risk of CSF leaks. While this particular risk factor was not within the scope of our investigation, its recognition in the broader surgical literature highlights the

necessity for its inclusion in preoperative evaluations and its potential to be a focus of future studies aimed at enhancing patient outcomes after EESBS. Prior revision surgery is a well-recognized intraoperative risk factor for CSF leak.^[20]

A history of smoking is a critical preoperative factor to consider because of its well-established association with poor healing outcomes. A history of smoking has been linked to an increased risk of surgical site infections, impaired wound healing, and other complications that can adversely affect postoperative recovery.^[17] Evidence suggests that patients who smoke are at a significantly

higher risk of experiencing postsurgical complications, including delayed wound healing, which is particularly relevant to procedures such as EESBS, where the integrity of the surgical site is paramount for preventing CSF leaks.^[17] Therefore, smoking history should be the focus of preoperative assessments, and smoking cessation interventions might be beneficial in the perioperative management of patients undergoing EESBS.

Intraoperative risk factors in individual patients compared to existing literature

Intraoperatively, the location and nature of the lesion are among the most significant factors influencing surgical strategy and associated risks. Primary versus metastatic lesions are crucial, as Patel *et al.*^[16] noted that primary lesions tend to have more predictable outcomes, whereas metastatic lesions can present variable challenges owing to previous treatments and their unpredictable biological behavior.

The radiological diagnosis of pituitary macroadenoma, clivus chordoma, and frontoethmoidal encephalocele, along with the associated histopathological diagnoses of nonsecretory pituitary adenoma, chordoma, and CSF rhinorrhea, presents a spectrum of surgical challenges. Batra *et al.*,^[3] emphasized that the histopathologic and radiologic characteristics of a tumor significantly influence the surgical technique and approach. For instance, resection of a macroadenoma requires careful manipulation to preserve endocrine function, whereas chordomas necessitate a more aggressive resection due to their invasive growth patterns.

The tumor site, particularly in the anterior skull base, as seen in two of our patients, requires a nuanced surgical approach to manage the complex anatomy and achieve effective dural reconstruction. Gruss *et al.*^[7] discussed the importance of tumor location in relation to the risk of CSF leaks.

Factors that increase the risk of CSF leakage following transsphenoidal surgery for pituitary adenomas include tumor size, adenoma consistency, and intraoperative CSF leakage.^[20]

A detailed comparison of preoperative and intraoperative risk factors with established literature underscores the importance of individualized patient assessment. The distinct profiles presented by our patients highlight the necessity of a tailored approach to EESBS to manage the complex interplay between factors that can influence surgical outcomes. This discussion adds to the body of knowledge by clarifying the impact of these risk factors in the context of current surgical practices.

Postoperative risk factors associated with CSF leak

When comparing endoscopic and microscopic approaches in transsphenoidal surgery, the endoscopic method seems to offer a slight advantage in reducing CSF leakage.^[20]

A review was conducted on delayed CSF leaks following the treatment of skull base tumors. Nine patients who experienced CSF leak at least 3 months after treatment were examined. These findings indicate that individuals with delayed CSF leaks were more likely to have a history of radiation exposure and might exhibit symptoms of meningitis. The study recommends maintaining a high level of suspicion for CSF rhinorrhea in patients with a history of skull base tumors even years after treatment^[14] [Figure 2].

Preventive and management strategies for CSF leakage

Placement of a postoperative lumbar drain is commonly employed to address temporary spikes in ICP or to create lower-than-normal pressure during the initial healing period. In this series, not all drains were utilized to prevent leaks during surgery but to deter leaks after surgery, specifically in patients with high-flow leaks where they were placed after the procedure. While lumbar drains can be effective in preventing intraoperative leaks, they are not typically applicable to high-flow leaks stemming from significant dural defects resulting from tumor resection or surgical access to the tumor.^[6]

Analysis of postoperative CSF leakage rates over time has declined in recent years. This reduction in incidence is attributed to several factors, including the introduction of a nasoseptal flap and the increased expertise of surgeons. The latter signifies the learning curve associated with adopting these relatively new approaches and techniques, which is distinct from the vascularized reconstruction in multivariate analysis. This underscores the significance of clinical experience and the concentration of such cases at specialized centers in mitigating complication rates.^[6]

As vascularized flaps in EESBS have progressed, the use of pedicled nasoseptal flaps for skull base reconstruction has also increased. A systematic review revealed that vascularized flaps are associated with a reduced occurrence of postoperative CSF leaks.^[18] In instances of high-flow intraoperative CSF leakage, the pedicled vascularized flap demonstrates a more substantial impact.

Perioperative lumbar drainage is frequently employed to alleviate ICP and prevent postoperative CSF leaks subsequent to EESBS for skull base lesions.^[1,4] A prospective randomized controlled trial demonstrated that perioperative lumbar drainage decreased the incidence of postoperative CSF leaks following EESBS.^[21]

The primary methods used to prevent postoperative CSF leaks include free tissue grafts, vascularized flaps, gasket sealing, and lumbar drains.^[13] A comparative study^[19] compared two methods of sellar closure during EESBS for pituitary adenoma resection. They found that using a fibrin-coated collagen fleece (TachoSil) reduced the rate of postoperative CSF leaks compared to conventional packing with a dural sealant (DuraSeal).

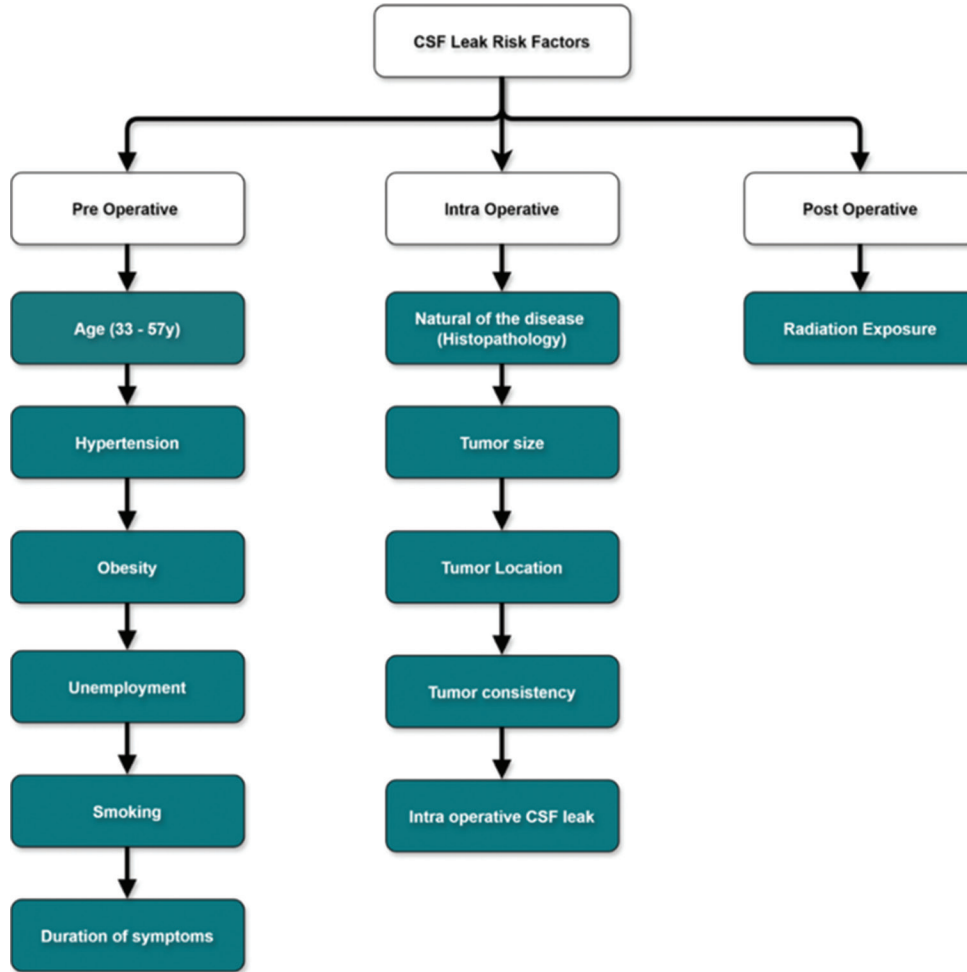


Figure 2: Pre, intra, and postoperative cerebrospinal fluid leak risk factors.

Another study^[12] reviewed a modified temporoparietal myofascial flap for the repair of recurrent CSF leaks. In six cases, this flap technique was successful in preventing CSF leaks during a 6–48-month follow-up period.

A systematic review addressed the prevention of postoperative CSF leakage after the endoscopic endonasal approach. This review included 34 case-control and cohort studies with 9144 patients who underwent transsphenoidal surgery for pituitary adenoma. This review identified several risk factors for postoperative CSF leakage, including tumor size, adenoma consistency, revision surgery, and intraoperative CSF leakage. In addition, the review showed that the endoscopic approach had a slight protective benefit compared to the microscopic approach in preventing CSF leakage. This suggests that screening for these risk factors and considering the endoscopic approach may help reduce complications related to CSF leakage.^[20]

A meta-analysis^[9] found that endoscopic repair of CSF leaks was successful in 90% of the cases after the first attempt. Ultimately, 97% of leaks were repaired using an endoscopic

approach. The success rates of repairs using different techniques and materials were high and were not statistically different. The incidence of major complications such as meningitis, subdural hematoma, and intracranial abscess was <1% for each complication. This study supports the effectiveness and low morbidity of the endoscopic approach for repairing CSF leaks.

The dural flap technique for dural opening and closure during endoscopic pituitary surgery helped restore normal anatomy after tumor removal and provided a better physiological barrier between the sinonasal cavity and intrasellar compartment. A previous study reported no postoperative CSF leakage in cases in which the dural flap technique was used.^[2]

Overall, the literature supports the use of the endoscopic endonasal approach for managing CSF leaks, with high success rates and low morbidity. The dural flap technique and pedicled nasoseptal flap are effective methods for dural opening and closure, providing optimal anatomical reconstruction and preventing postoperative leakage.

A study evaluated a method for preventing postoperative CSF leakage using autologous fascia lata grafts and pressure-controlled spinal drainage in patients with skull base lesions requiring a wide opening of the ventral dura. The researchers retrospectively analyzed data from 50 cases, including recurrent cases, and found that the multilayer closure method with pressure-controlled spinal drainage is simple, safe, and effective for preventing postoperative CSF leakage.^[8]

A study^[11] included a retrospective case series of patients with postoperative CSF leaks after an expanded endonasal approach of the sphenoclivus axis. Of the 326 patients, 10 required therapeutic intervention for closure failure of central skull base defects. The median time to presentation of CSF leak was 25 days, with symptoms including rhinorrhea, meningitis, and pneumocephalus. Most patients were initially managed with lumbar drain placement, and nine of the 10 patients eventually required endoscopic repair. Vascularized mucosal flap repair is the most common technique used to repair CSF leaks. The failure sites were mainly located outside the Sella, reflecting their direct relationship with the intracranial cisterns. The initial operative repair provided definitive treatment in most cases (70%). The correct placement of a vascularized local pedicle-based flap was found to be essential for successful repair.

Based on a systematic review, endoscopic repair techniques can be effective in managing postoperative CSF leaks following an endoscopic endonasal approach. However, the specific management strategy may vary depending on the individual case, with vascularized mucosal flap repair being a commonly used technique.^[11]

CONCLUSION

This study provides a comprehensive analysis of the risk factors that contribute to CSF leakage following EESBS. It assesses preoperative conditions, such as hypertension and neurological disorders, intraoperative challenges, including lesion characteristics and surgical techniques, and postoperative complications, emphasizing the significance of individualized patient assessments. Through a meticulous comparison with global studies, this study enhances our understanding of effective management strategies, advocating the adoption of vascularized flaps, meticulous lumbar drainage practices, and precise endoscopic repair methods. These insights are pivotal for refining surgical protocols to reduce the incidence of CSF leaks and improve patient outcomes. This study plays an important role in advancing patient care standards by bridging the gaps in the existing literature and introducing novel findings.

Ethical approval

The research/study was approved by the Institutional Review Board at King Abdullah International Medical Research Center, number NRJ23J/184/07, dated October 09, 2023.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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