

## Closure Methods for the Prevention of CSF Fistula in Transsphenoidal Surgery: A Large Study

### Transfenoidal Cerrahide BOS Fistülünün Önlenmesine Yönelik Kapatma Yöntemleri: Geniş Kapsamlı Bir Çalışma

Hidayet Şafak Çine<sup>1</sup>, Ece Uysal<sup>2</sup>

1 İstanbul Medeniyet University, Prof. Dr. Suleyman Yalcin City Hospital, Neurosurgery, Turkey, <https://orcid.org/0000-0002-0808-5921>

2 University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital, Neurosurgery, Turkey, <https://orcid.org/0000-0002-2355-8395>

#### Abstract

**Aim and Background:** Aim and Background: The primary objective of this extensive series is to conduct a comparative analysis of microscopes and endoscopes and investigate the extent of variability in CSF leakage based on the surgical approach employed, the occurrence of complications during the procedure, the techniques employed for closure, and any postoperative interventions.

**Method:** A retrospective analysis was conducted on lesions in the sellar region that were surgically treated via the transsphenoidal approach in the Department of Neurosurgery. Microscope, endoscope, or both were used during the approach. The access route used in this study was the transnasal transsphenoidal (TNTS), sublabial, or transcranial+TNTS approach. The repair procedure involved the use of a Surgicel-coated nasal flap, fat graft, or fascia graft and fibrin glue.

**Results:** The cohort of individuals experiencing CSF leaks exhibited a notably elevated use of endoscopic procedures, while the use of microscopic techniques was relatively few. The incidence of fat graft, nothing, fat+fascia, and the presence of surgicel was rather low in patients presenting with CSF leakage. There was no statistically significant disparity observed in the frequencies of lumbar puncture among patients who did not exhibit cerebrospinal fluid leakage. The rates of lumbar drainage and meningitis were found to be considerably greater in patients with CSF leak compared to those without ( $p<0.001$  for both variables).

**Conclusion:** It has been suggested that selecting an appropriate closure approach should be based on the intraoperative complications observed during the surgical procedure, to prevent CSF leakage.

**Keywords:** Transsphenoidal Surgery, Endoscope, Cerebrospinal Fluid.

#### Özet

**Giriş ve Amaç:** Bu kapsamlı serinin birincil amacı, mikroskop ve endoskopların karşılaştırmalı bir analizini yapmak ve kullanılan cerrahi yaklaşıma dayalı olarak BOS sızıntısındaki değişkenliğin derecesini, prosedür sırasında komplikasyonların ortaya çıkışını, kapama için kullanılan teknikleri araştırmaktır. ve ameliyat sonrası müdahaleler.

**Yöntem:** Nöroşirürji Anabilim Dalı'nda transsfenoidal yaklaşımla cerrahi olarak tedavi edilen sellar bölgedeki lezyonlar retrospektif olarak incelendi. Yaklaşım sırasında mikroskop, endoskop veya her ikisi birden kullanıldı. Bu çalışmada kullanılan erişim yolu, transnazal transsfenoidal (TNTS), sublabial veya transkranyal+TNTS yaklaşımıydı. Onarım prosedürü, surgicel kaplı nasal grefti, yağ grefti ve/veya fasya grefti ve fibrin yapıştırıcı kullanımını içeriyordu.

**Corresponding Author:** Hidayet Şafak Çine, e-mail: [cinesafak@gmail.com](mailto:cinesafak@gmail.com)

**Received:** 18.07.2023, **Accepted:** 23.08.2023, **Published Online:** 30.09.2023

**Cite:** Çine HŞ, et al. Closure Methods for the Prevention of CSF Fistula in Transsphenoidal Surgery: A Large Study. Acta Medica Ruha. 2023;1(3):356-362. <https://doi.org/10.5281/zenodo.8267504>



**Bulgular:** Endoskopik prosedürlerde BOS sızıntısı yaşayan bireyler kayda değer bir artış sergilerken, mikroskopik tekniklerin kullanımında nispeten azdı. BOS kaçağı olan hastalarda yağ grefti, hiçbir şey, yağ+fasya ve cerrahi varlığı insidansı oldukça düşüktü. Beyin omurilik sıvısı kaçağı göstermeyen hastalar arasında lomber ponksiyon sıklıklarında istatistiksel olarak anlamlı bir eşitsizlik gözlenmedi. BOS kaçağı olan hastalarda olmayanlara göre lomber drenajı ve menenjit oranları anlamlı olarak yüksek bulundu (her iki değişken için  $p<0,001$ ).

**Sonuç:** Uygun bir kapatma yaklaşımının seçilmesinin, BOS sızıntısını önlemek için cerrahi prosedür sırasında gözlenen intraoperatif komplikasyonlara dayanması gerektiği öne sürülmüştür.

**Anahtar Kelimeler:** Transsphenoidal Cerrahi, Endoskop, Beyin Omurilik Sıvısı.

---

## **INTRODUCTION**

The adoption of reconstruction techniques is crucial in minimizing the occurrence of cerebrospinal fluid (CSF) leakage subsequent to endoscopic and microscopic transsphenoidal endonasal procedures performed on the skull base. In more than 60% of cases, the surgical intervention of intrasellar lesions might result in significant intraoperative CSF leakage (1). The literature has documented a range of postoperative leak rates for endoscopic pituitary surgery, varying from 1.9% to 10% (2). To reduce this issue, fat grafts may be employed, either with or without the inclusion of fascia or a vascularized septal flap. The implementation of the nasoseptal flap has notably diminished the occurrence of CSF leakage. Various studies have demonstrated that the incidence of CSF leakage following pituitary surgery can be significantly reduced to a range of 0-2.9% with the implementation of a nasoseptal flap for sella reconstruction (3). Nevertheless, it is important to acknowledge that the situation presents certain complications, including nasal pain, severe crusting, and anosmia. The detection or oversight of CSF leakage is possible during the surgical procedure. Following the surgical procedure, the manifestation of any occurrence may arise as a consequence (4). The primary objective of this extensive series is to conduct a comparative analysis of microscopes and endoscopes in their application to the sellar region. Additionally, the study aims to investigate the extent of variability in CSF leakage based on the surgical approach employed, the occurrence of complications during the procedure, the techniques employed for closure, and any postoperative interventions implemented.

## **METHODS**

### **Patients**

A retrospective analysis was conducted on lesions in the sellar region that were surgically treated via the transsphenoidal approach in the Department of Neurosurgery. The study investigated many factors including patient demographics, tumor pathology, type of operation, method of surgical opening, utilization of microscope or endoscope, occurrence of complications during the operation, surgical closure method, and efforts to prevent CSF leaks post-surgery. The analysis focused on examining potential risk factors and preventative approaches associated with postoperative CSF rhinorrhea.

### **The Identification and Assessment of CSF Fistula**

In individuals presenting with suspected postoperative CSF fistula, a positive CSF fistula was determined based on the observation of a noticeable excess of fluid coming from the nasal cavity. The  $\beta$ -2-transferrin test was conducted for diagnostic purposes in cases where suspicion of the condition was present.

## **The Operation Technique**

Microscope, endoscope, or both were used during the approach. The access route used in this study was the transnasal transsphenoidal (TNTS), sublabial, or transcranial+TNTS approach. In the context of opening, otolaryngologists used a septal flap, or the standard opening procedure was conducted.

## **Techniques for Repairing CSF Leaks**

The Valsalva maneuver was executed to ascertain an intraoperative leak's presence. In the case that a CSF leak was identified during the surgical procedure, various solutions were employed to rectify the issue. The repair procedure involved the use of a Surgicel-coated nasal flap, fat graft, or fascia graft. Fibrin glue was added to a subset of the cases. During the post-operative follow-up, external lumbar drainage was maintained for a duration of 2-4 days, or CSF was extracted with lumbar puncture over a period of 2-4 days.

## **Statistical Analysis**

The statistical analysis was conducted using the SPSS 15.0 for Windows software application. The analysis includes descriptive statistics for both categorical and numerical variables. For category variables, the number and percentage are reported. The mean, standard deviation, median, minimum, and maximum values are provided for numerical variables. The rates within the categories were subjected to statistical analysis using the Chi-Square Test. The alpha significance level was deemed statistically significant at a p-value of less than 0.05.

## **RESULTS**

Out of the total sample size of 54 patients, 30 individuals (55.5%) were women, whereas 24 individuals (44.4%) were men. The age distribution of the patients in the study spanned from 5 to 85 years, with a calculated average age of 48. The surgical procedure known as TNTS surgery was conducted on 47 patients, accounting for 87.0% of the sample. Among the remaining patients, 5 individuals (9.2%) underwent a second opening of the TNTS procedure, while 2 patients (3.7%) received a sublabial intervention. The prevalence of apoplexy was 5.5%. Most instances, specifically 51 out of 54 (94.4%), were initiated using a standard opening technique. However, in a minority of cases, precisely 3 out of 54 (5.6%), an alternative approach, including creating a nasal flap, was employed. A microscope was used in 75.9% of the cases, but in 22.2% of the cases, both an endoscope and a microscope were employed simultaneously. In the remaining 1 cases, only the endoscope was employed. Most of the pathological samples consisted of pituitary adenomas, specifically 33 cases (61.1%). During the surgical procedure, 40.7% of CSF was not visually detected, whereas 7.4% of thin arachnoid membranes were detected (Table 1).

The nasal flap rate in individuals with CSF leak was considerably higher than those without CSF leak ( $p < 0.001$ ). Statistically significant differences were seen in the frequencies of microscope/endoscope utilization, problems during surgery, and closure of patients without CSF leak ( $p < 0.001$ ,  $p = 0.009$ ,  $p < 0.001$ , respectively). The cohort of individuals experiencing CSF leaks exhibited a notably elevated use of endoscopic procedures, while the use of microscopic techniques was relatively few. There was no statistically significant disparity observed in the frequencies of lumbar puncture among patients who did not exhibit cerebrospinal fluid leakage (Table 2).

**Table 1.** Summary of clinical characteristics

Age Mean±SD (Min-Max)		48,9±18,4 (5-85)	
		n	%
<b>Gender</b>	Female	30	55,5
	Male	24	44,4
<b>Operation</b>	TNTS	47	87,0
	Repeat TNTS	5	9,2
	Sublabial	2	3,7
<b>Apoplexy</b>	No	49	94,5
	Yes	3	5,5
<b>Opening</b>	Standart	51	94,4
	Nasal Flap	3	5,6
<b>Microscope/ Endoscope</b>	Microscope	41	75,9
	Microscope + Endoscope	12	22,2
	Endoscope	1	1,8
<b>Pathology</b>	Pituitary adenoma	33	61,1
	Atypical Pituitary adenoma	7	12,9
	Ratke Cleft Cyst	4	7,4
	Craniopharyngioma	3	5,5
	Meningioma	2	3,7
	Chordoma	1	1,8
	Pituitary Hyperplasia	1	1,8
	Adenocarcinoma	1	1,8
	Chondrosarcoma	1	1,8
	Diffuse B- cell Lenfoma	1	1,8
<b>Complications During Surgery</b>	No CSF	22	40,7
	Yes CSF- open suprasellar	16	29,6
	Yes CSF- small	10	18,5
	No CSF- thin arachnoid	4	7,4

*TNTS: Transnasal transsphenoidal, CSF: Cerebrospinal Fluid*

**Table 2.** Comparison of the data according to the CSF leak seen or not seen

		CSF leak				p
		No		Yes		
		n	%	n	%	
<b>Opening</b>	Nasal Flap	2	3,9	1	33,3	<0,001
	Standart	49	96,0	2	66,6	
<b>Microscope/ Endoscope</b>	Endoscope	1	1,9	0	0	<0,001
	Microscope	39	76,4	1	50,0	
	Microscope + Endoscope	11	21,5	1	50,0	
<b>Complications During Surgery</b>	No CSF	7	13,7	1	50,0	0,009
	Yes CSF	15	29,4	1	50,0	
<b>Closure</b>	Fat and Facia + Surgicel	13	25,4	0	0	<0,001
	Fat and Facia + Surgicel + Fibrin glue	2	3,9	0	0	
	Fat and Facia + Surgicel + Fibrin glue + Septal Flap	1	1,9	0	0	
	Fat and Facia + Surgicel + Septal Flap	1	1,9	0	0	
	Fat and Fascia	1	1,9	0	0	
	Fat Graft	16	31,3	1	50,0	
	Fat Graft + Fibrin Glue	1	1,9	0	0	
	Septal Flap + Fibrin Glue	1	1,9	1	50,0	
	Nothing	15	29,4	0	0	
<b>Lumber puncture</b>	No	40	78,4	1	50,0	1,000
	Yes	11	21,5	1	50,0	
<b>Lumber drenaige</b>	No	42	82,3	1	50,0	<0,001
	Yes	9	17,6	1	50,0	

*CSF: Cerebrospinal Fluid*

## **DISCUSSION**

Transsphenoidal (TNTS) surgery has become a standard procedure for different kind of sellar and parasellar lesions in the last two decades. Since Schloffer, who described the TNTS with the transnasal approach in 1907, TNTS has experienced improvements over time and every neurosurgeon has introduced their own special interventions (5). Halstead and Cushing used the sublabial approach until the current pituitary approach was converted to the transcranial surgery by the Dandy and Krause (6). Although the TNTS is known as a simple and practical procedure, because of the mortal complications such as CSF leaks, meningitis, hypothalamic and vascular injuries, it had been abandoned at that time. Afterward, this procedure was popularized by Hardy with the involvement of the microscope in surgery (7). Also, transsphenoidal surgery has become more performable with the use of further technological advancements like endoscope by Jho and Carrau in 1997 (8).

TNTS is an effective and safe procedure for most of the sellar and parasellar lesions that can be reached from the sphenoid sinus. This procedure is not only used for pituitary adenomas but also for other kinds of skull base tumors such as craniopharyngiomas, Rathke cleft cysts, meningiomas, chordomas, chondrosarcomas, and metastases. The mortality rates are reported between 0 and 1.4% recently. Although the complications are extremely rare and treatable, are still possible. These include diabetes insipidus, anterior pituitary gland injury, intracranial hematoma, nasal septum perforation, carotid artery injury, sinusitis, central nervous system injury, CSF fistula, and meningitis (9).

In contemporary medical practice, the endoscopic endonasal transsphenoidal approach allows the visualization of more possible cavities inside a confined space. This technique overcomes traditional microscopic procedures' limitations by accessing previously inaccessible structures. Consequently, patients benefit from improved eyesight, improved tumor resection outcomes, and reduced hospitalization durations (10). Furthermore, difficulties related to CSF fistulas can persist, leading to prolonged hospitalization, heightened reliance on antibiotics for the treatment of meningitis, and increased morbidity. Our study aimed to investigate the etiology of CSF fistula in the context of surgical approaches to the sellar area. We also aimed to evaluate the outcomes associated with different closure and post-operative procedures.

Furthermore, CSF leakage was identified in a 76.4% patients using a microscope alone. Similarly, when a microscope and an endoscope were utilized in tandem, CSF leakage was observed in only 5 out of 72 patients. This finding suggests that using a microscope may be more effective in identifying and treating a CSF fistula. The meta-analysis findings indicate a greater incidence of CSF leakage following endoscopic surgery (11). This finding aligns with the outcomes observed in our surgical procedures.

CSF fistula is a common intraoperative complication, particularly in cases involving malignancies requiring access to the suprasellar region. In order to access the suprasellar space, it is necessary to go through the arachnoid membrane, which creates contact with the CSF. The outcome is expected. Preserving the integrity of the arachnoid membrane during surgical procedures is paramount, unless deemed essential. In situations of this type, autologous materials have been suggested as potential solutions, including mucosal grafts sourced from the middle turbinate, fat grafts obtained from the abdomen region, muscle grafts derived from the lateral thigh, and fascia grafts harvested from the fascia lata, lateral thigh, or temporal muscle (12).

When unexpected access or opening of the suprasellar area occurs, a combination of fat and fascia grafts is employed. To secure the grafts, surgicel is utilized, followed by the application of fibrin glue (13). In instances when noCSF leakage was detected, our approach often involved either choosing not the graft usage or only employing a fat graft. In addition, our preference was mostly towards utilizing fat grafting in cases where a thin arachnoid membrane was observed, even without visualization of CSF. In situations when a minor CSF fistula was observed, the usual approach involves the insertion of surgicel with the fat and fascia graft as a means of repair (14).

Additionally, our findings indicate that the utilization of continuous lumbar drainage is a more efficacious approach for managing CSF compared to intermittent lumbar puncture. The reason for this phenomenon is that continuous drainage has a greater efficacy in reducing CSF pressure and facilitating the healing process of the membrane. Despite the performance of lumbar puncture, unregulated fluctuations in CSF pressure continue to result in the occurrence of CSF leakage.

## **CONCLUSION**

Cerebrospinal fluid (CSF) leakage is a commonly seen complication in both endoscopic and microscopic transsphenoidal surgeries. It has been suggested that selecting an appropriate closure approach should be based on the intraoperative complications observed during the surgical procedure, to prevent CSF leakage.

**Funding:** There is no specific funding related to this research.

**Competing interests:** The authors declare that they have no competing interests.

**Ethical Declaration:** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent has been obtained from all participants.

**Study Concept / Design** : HSC, EU

**Data collecting** : EU

**Data Analysis / Interpretation** : HSC

**Text Draft** : HSC

**Technical Support / Material Support** : EU

**Critical Review of Content** : EU

**Literature Review** : HSC

## **REFERENCES**

1. Fraser S, Gardner PA, Koutourousiou M, et al. Risk factors associated with postoperative cerebrospinal fluid leak after endoscopic endonasal skull base surgery. *J Neurosurg.* 2018;128(4):1066-1071. doi:10.3171/2016.12.JNS1694



2. Almeida JP, Marigil-Sanchez M, Karekezi C, Witterick I, Gentili F. Different Approaches in Skull Base Surgery Carry Risks for Different Types of Complications. *Acta Neurochir Suppl.* 2023;130:13-18. doi:10.1007/978-3-030-12887-6\_2
3. Strickland BA, Lucas J, Harris B, et al. Identification and repair of intraoperative cerebrospinal fluid leaks in endonasal transsphenoidal pituitary surgery: surgical experience in a series of 1002 patients. *J Neurosurg.* 2018;129(2):425-429. doi:10.3171/2017.4.JNS162451
4. Sanders-Taylor C, Anaizi A, Kosty J, Zimmer LA, Theodosopoulos PV. Sellar Reconstruction and Rates of Delayed Cerebrospinal Fluid Leak after Endoscopic Pituitary Surgery. *J Neurol Surg B Skull Base.* 2015;76(4):281-5. doi:10.1055/s-0034-1544118
5. Pait GT, Arnautovic KI. The pituitary: historical notes. In: Krisht AF, Tindall GT, eds. *Pituitary Disorders: Comprehensive Management.* 1st ed. Baltimore, Md: Lippincott Williams & Wilkins; 1999:3-23.
6. Cushing H. *The Pituitary Body and its Disorders. Clinical States Produced by Disorders of the Hypophysis Cerebri.* Philadelphia, Pa/London: JB Lippincott; 1912.
7. Hardy J. Transsphenoidal hypophysectomy. *J Neurosurg.* 1971;34:582-594.
8. Jho HD, Carrau RL. Endoscopy-assisted transsphenoidal surgery for pituitary adenoma. *Acta Neurochir (Wein).* 1996;138: 1416-1425.) (Jho HD, Carrau RL, Ko Y, et al. Endoscopic pituitary surgery: an early experience. *Surg Neurol.* 1997;47:213-223.
9. Barzaghi LR, Losa M, Giovanelli M, Mortini P: Complications of transsphenoidal surgery in patients with pituitary adenoma: experience at a single center. *Acta Neurochir (Wien)* 149: 877-885, discussion 885-876, 2007.) (Black PM, Zervas NT, Candia GL: Incidence and management of complications of transsphenoidal operation for pituitary adenomas. *Neurosurgery* 20:920-924, 1987.
10. Li A, Liu W, Cao P, Zheng Y, Bu Z, Zhou T. Endoscopic Versus Microscopic Transsphenoidal Surgery in the Treatment of Pituitary Adenoma: A Systematic Review and Meta-Analysis. *World Neurosurg.* 2017;101:236-246. doi:10.1016/j.wneu.2017.01.022
11. Esquenazi Y, Essayed WI, Singh H, et al. Endoscopic Endonasal Versus Microscopic Transsphenoidal Surgery for Recurrent and/or Residual Pituitary Adenomas. *World Neurosurg.* 2017;101:186-195. doi:10.1016/j.wneu.2017.01.110
12. Di Perna G, Penner F, Cofano F, et al. Skull base reconstruction: A question of flow? A critical analysis of 521 endoscopic endonasal surgeries. *PLoS One.* 2021;16(3):e0245119. doi:10.1371/journal.pone.0245119
13. Dusick JR, Mattozo CA, Esposito F, Kelly DF. BioGlue for prevention of postoperative cerebrospinal fluid leaks in transsphenoidal surgery: A case series. *Surg Neurol.* 2006;66(4):371-376. doi:10.1016/j.surneu.2006.06.043
14. Conger A, Zhao F, Wang X, et al. Evolution of the graded repair of CSF leaks and skull base defects in endonasal endoscopic tumor surgery: trends in repair failure and meningitis rates in 509 patients. *J Neurosurg.* 2018;130(3):861-875. doi:10.3171/2017.11.JNS172141