

## INTRODUCTION

Postoperative cerebrospinal fluid (CSF) leak is a significant complication following endoscopic transsphenoidal surgery (ETS) for craniopharyngioma. Several preoperative and intraoperative factors have been suggested to influence the risk of postoperative CSF leak, including tumor size, pattern of suprasellar extension, tumor consistency, prior treatment, and the choice of reconstruction strategy.

A persistent gap in literature concerns the relationship between objective clinical risk factors and surgeon perception. While cohort-based analyses identify statistical predictors of postoperative complications, they do not reflect how surgeons anticipate or manage these risks. Conversely, practice surveys highlight variations in management strategies but lack validation against patient-level outcomes.

Addressing this disconnect is essential for establishing more consistent, evidence-based standards for reconstruction and perioperative care. This study aims to address clinical and statistical gaps by integrating a multicenter retrospective cohort analysis with a complementary survey.

## OBJECTIVES

**Primary objective** - To identify independent risk factors for postoperative CSF leak following ETS for craniopharyngioma.

**Secondary objective** – To evaluate the divergence between objective risk factors and surgeon-reported management practices, thereby elucidating contemporary practice patterns and guiding future efforts toward standardization.

## METHODS

A multicenter retrospective cohort study was conducted across 20 institutions participating in the RAPID Consortium. The cohort was stratified into an Early Epoch (2007-2015) and a late Epoch (2016-2025). The primary outcome was a postoperative CSF leak within 90 days of ETS. Secondary outcomes included postoperative meningitis, need for revision surgery, and the occurrence of new endocrine deficit. To contextualize the findings, a complementary, multi-institutional survey was administered to 19 experienced pituitary and skull base neurosurgeons to capture current practice patterns and management strategies. Surgeons were asked to rank the perceived importance of specific preoperative and intraoperative risk factors and the preference for reconstruction materials. The mean rank for each factor was calculated by averaging the individual rank assigned by each surgeon. The Likert ranking scale ranged from 1 to 5, where 1 indicated 'Extremely Important' or 'Always Used,' and 5 indicated 'Not at all Important' or 'Never Used.'

## RESULTS

The overall postoperative CSF leak rate was 13.5% (56/416 patients). Univariate analysis identified that tumors with a predominantly cystic component (34% vs. 21%,  $p = 0.034$ ), and the intraoperative use of a lumbar drain (LD) ( $p < 0.028$ ) were significantly associated with CSF leak. In the overall multivariable analysis (**Table 1**), LD use was the only independent predictor of a leak (OR 1.91, 95% CI 1.06–3.46;  $p = 0.030$ ). Between the Epochs, the utilization of the nasoseptal flap (NSF) for multilayer reconstruction increased from 70.7% in the Early Epoch (2007-2015) to 87.6% in the Late Epoch (2016-2025) ( $p < 0.001$ ). The use of fascia lata also increased from 22.7% to 35.3% ( $p = 0.035$ ). Epoch specific multivariable analysis revealed that the NSF was significantly protective (OR 0.26, 95% CI 0.07–0.92;  $p = 0.037$ ) in the Early Epoch (**Table 2**). In the Late Epoch, no factors remained statistically significant. Surgeon survey results demonstrated consensus on high-risk factors, including prior surgery (average rank 1.80; 1 to 5 scale) and intraoperative CSF leak (1.74). The NSF was the preferred primary reconstructive material (1.16). Management of a confirmed leak included antibiotic coverage (3rd rank) and LD trial (4th rank) before immediate surgical return of all patients (5th rank).

**Table 1: Bivariate and Multivariable Logistic Regression Analysis of Risk Factors for Postoperative Cerebrospinal Fluid Leak**

Variables	Bivariate		Multivariable	
	p - value	OR (95% CI)	p - value	OR (95% CI)
Primarily Cystic Tumor Consistency	0.035*	1.91 (1.02–3.49)	0.151	1.58 (0.83–2.95)
Nasoseptal Flap Use	0.035*	0.48 (0.25–0.97)	0.143	0.59 (0.30–1.22)
Lumbar Drain Use	0.011*	2.10 (1.19–3.73)	0.030*	1.91 (1.06–3.46)
Age	0.660	1.00 (0.99–1.01)	0.612	1.00 (0.99–1.01)
Gender, male	0.061	0.58 (0.32–1.02)	0.093	0.60 (0.33–1.08)

**Table 2: Multivariate Logistic Regression Analysis of Risk Factors for Postoperative CSF Leak in the Early Epoch (2007-2015) and the Late Epoch (2016-2025).**

Variables	Bivariate		Multivariable	
	p - value	OR (95% CI)	p - value	OR (95% CI)
<b>Early Epoch (2007-2015)</b>				
Nasoseptal Flap Use	0.016*	0.22 (0.06–0.74)	0.045*	0.28 (0.08–0.97)
Lumbar drain Use	0.021*	4.43 (1.31–17.72)	0.055	3.63 (1.02–14.98)
<b>Late Epoch (2016-2025)</b>				
Nasoseptal Flap Use	0.685	0.82 (0.35–2.29)	0.998	0.99 (0.41–2.85)
Fat Graft Use	0.063	1.86 (0.96–3.57)	0.233	1.55 (0.75–3.15)
Fascia Lata Use	0.152	1.61 (0.83–3.09)	0.347	1.39 (0.69–2.74)
Lumbar Drain Use	0.118	1.68 (0.88–3.23)	0.287	1.45 (0.73–2.86)

## DISCUSSION

The transition of the NSF from a potent independent protective factor in the Early Epoch ( $p = 0.045$ ) to a non-significant variable in the Late Epoch ( $p = 0.998$ ) illustrates its evolution from a selective reconstruction material to the foundation of standardized care. While the use of fascia lata also increased significantly from 22.7% to 35.3% ( $p = 0.035$ ), neither fascia lata nor fat graft use emerged as independent predictors of postoperative CSF leak in the Late Epoch. This suggests a hierarchical approach to reconstruction; while the NSF serves as the foundation of standardized care for high-flow defects, the elective addition of secondary adjunctive materials maybe governed more by specific intraoperative findings or individual surgeon preference as found in the survey. In the Early Epoch, the risk of CSF leak persisted despite the concurrent use of LD as demonstrated by a potent bivariate association (OR 4.43, 95% CI 1.31–17.72;  $p = 0.021$ ), however, by the Late Epoch there was no association (Bivariate OR 1.68,  $p = 0.118$ ; Multivariable OR 1.45,  $p = 0.287$ ). Survey responses reflect this complexity; while experts ranked the LD as a preferred management trial for high-risk scenarios, there is a clear trend toward selective rather than routine use. The reported management preference in this survey for a confirmed leak revealed that surgeons often opt for antibiotics and LD trials before reoperation, but this sequence remains controversial as it potentially delays eventual definitive repair. Given that 50%–75% of cases are aseptic, prophylactic antibiotics may need to be used judiciously. **Limitations:** Our data on intraoperative LD use did not distinguish between prophylactic placement at the start of the procedure and reactive placement following the observation of a high-flow leak. This prevents a definitive assessment of whether the observed risk association in the overall cohort is entirely due to confounding by indication.

## CONCLUSIONS

By combining a multicenter retrospective analysis with a detailed survey of experienced skull base surgeons, this study identifies not only objective risk factors but also the "perception-data gap." The standardization of multilayered reconstruction, has successfully mitigated the anatomical and clinical challenges that historically predisposed patients to postoperative CSF leaks. The divergence between expert consensus and clinical outcomes regarding LD use underscores the impact of confounding by indication and the need for more evidence-based protocols for its selective utilization.

\*RAPID Consortium: Anthony P. Heaney, Kyle Wu, Daniel Prevedello, James J Evans, Michael R Chicoine, Albert H Kim, Julie M Silverstein, Michael Karsy, Won Kim, Donato R Pacione, Connor Liu, Debraj Mukherjee, Paul Gardner, Stephanie Cheek, Nathan Zwagerman, Charles Christenson, Spiros Blackburn, Varun R Kshetry, Robert C Rennert, William T Couldwell, Ramin Morshed, Gami Barkhoudarian, Juan C. Fernandez-Miranda, Gabriel Zada, Carolina Benjamin, Michael P Catalino, Adam Mamelak, Andre Beer Furlan, Georgios Zenonos, Michelle M Mendoza, Andrew S Little