

Delayed cerebrospinal fluid leak following endoscopic transnasal skull base surgery

Association between reconstruction method and impact of radiation therapy

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Abstract

- Aggressive skull base tumors such as chordomas and high-grade meningiomas are challenging to manage, requiring endoscopic transnasal surgery (ETS) followed by radiation therapy (RT). However, delayed cerebrospinal fluid (CSF) leaks can occur as a late complication.
- This study retrospectively analyzed 287 patients who underwent ETS, with a focus on the incidence and risk factors for delayed CSF leaks. The results showed a significantly higher incidence in the RT group (7.0% at 10 years) compared to the non-RT group (0% at 10 years). Importantly, no delayed CSF leaks occurred in patients who underwent mucosal flap-based reconstruction.
- Our findings suggest that vascularized mucosal flaps provide greater resilience against radiation-induced complications. For patients requiring multiple surgeries and RT, skull base reconstruction using pedicled mucosal flaps may be a key factor in preventing delayed CSF leaks.

Introduction

- ETS has been widely adopted for resection of midline skull base tumors, including aggressive tumors such as chordomas, meningiomas, and craniopharyngiomas.
- In our institution, **non-vascularized multilayered closure** has been basically utilized for skull base reconstruction. Mucosal flap-based closure is limitedly used avoiding postoperative nasal dysfunction.¹

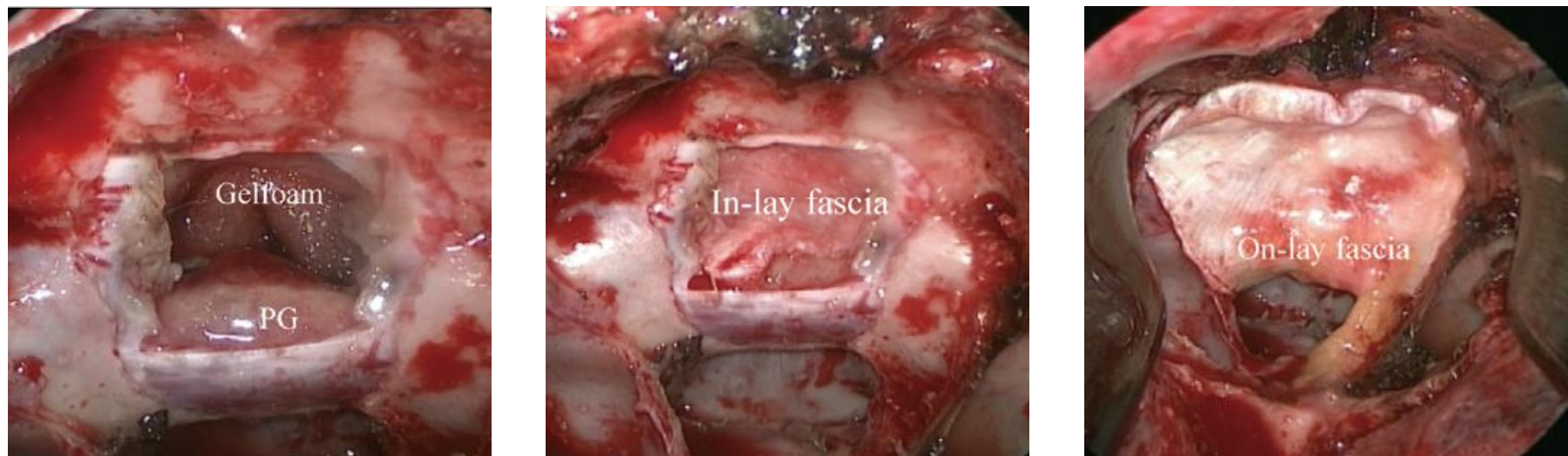


Figure 1. Non-vascularized multilayered closure from Hasegawa et al.¹

- Despite advancements in reconstruction techniques, **delayed CSF leaks remain a rare but serious complication**, particularly in patients undergoing RT.²⁻⁴
- This study investigates the incidence of delayed CSF leaks, the impact of RT, and the efficacy of various reconstruction techniques.

Methods and Materials

Patient Selection: Retrospective study of 287 patients who underwent ETS **Study Period:** Nov 2016 – Oct 2023.
Data Collected: Baseline/Tumor pathology/Number of ETS and RT sessions
Reconstruction Method:
1) Simple closure
2) Non-vascularized multilayered closure
3) Mucosal flap-based multilayered closure
Definition of Delayed CSF Leak: Any CSF leak occurring ≥6 months post-surgery.
Statistical Analysis: Kaplan–Meier survival analysis and Cox proportional hazard models were used to assess risk factors.

Age/ Sex	Pathology	No. ETS	Espo sito	Skull base reconstruction	No. RT	RT	From initial/late t ETS to CSF leak, m	From initial/late t RT to CSF leak, m	Reconstruction for delayed CSF leak	From mucosal flap reconstructi on to last follow-up, m
38 M	Chordoma Figure 4	7	3	Non-vascularized multilayered closure	9	Proton, GK	193/46	129/4	1 st , Non-vascularized multilayered closure (failure at 26 months); 2 nd , Inferior turbinate mucosal flap [†]	31
49 F	Chordoma	2	3	Non-vascularized multilayered closure	6	GK	74/19	73/1	Nasopharyngeal flap	16
69 F	Chordoma	3	3	Non-vascularized multilayered closure	1	GK	68/54	46/46	Nasopharyngeal flap	8
23 F	Chordoma	5	0	Simple closure	2	GK	36/8	35/6	Nasopharyngeal flap	42
75 F	Atypical meningioma	5	3	Non-vascularized multilayered closure	3	GK	38/8	32/5	Middle turbinate mucosal flap	20

Table 1. Summary of delayed cerebrospinal fluid leaks after endoscopic transnasal surgery.

Results

- Incidence of Delayed CSF Leaks**
Overall incidence: 1.7% (5/287 patients).
- Risk Factors for Delayed CSF Leaks**
RT Group (n=102): Higher incidence of delayed CSF leak (7.0%/10 years).
Non-RT Group (n=185): No delayed CSF leaks (0%/10 years, $p=0.030$).
 - Significant risk factors:
 - Chordoma pathology** ($HR\ 9.48, p=0.045$)
 - Increased number of ETS sessions** ($HR\ 1.93, p=0.001$)
 - Increased number of RT sessions** ($HR\ 1.55, p=0.009$)
- Repair for delayed CSF leaks
One CSF leak recurrence: 26 months after non-vascularized multilayered closure
No CSF leak recurrence: Using mucosal flap-based multilayered closure

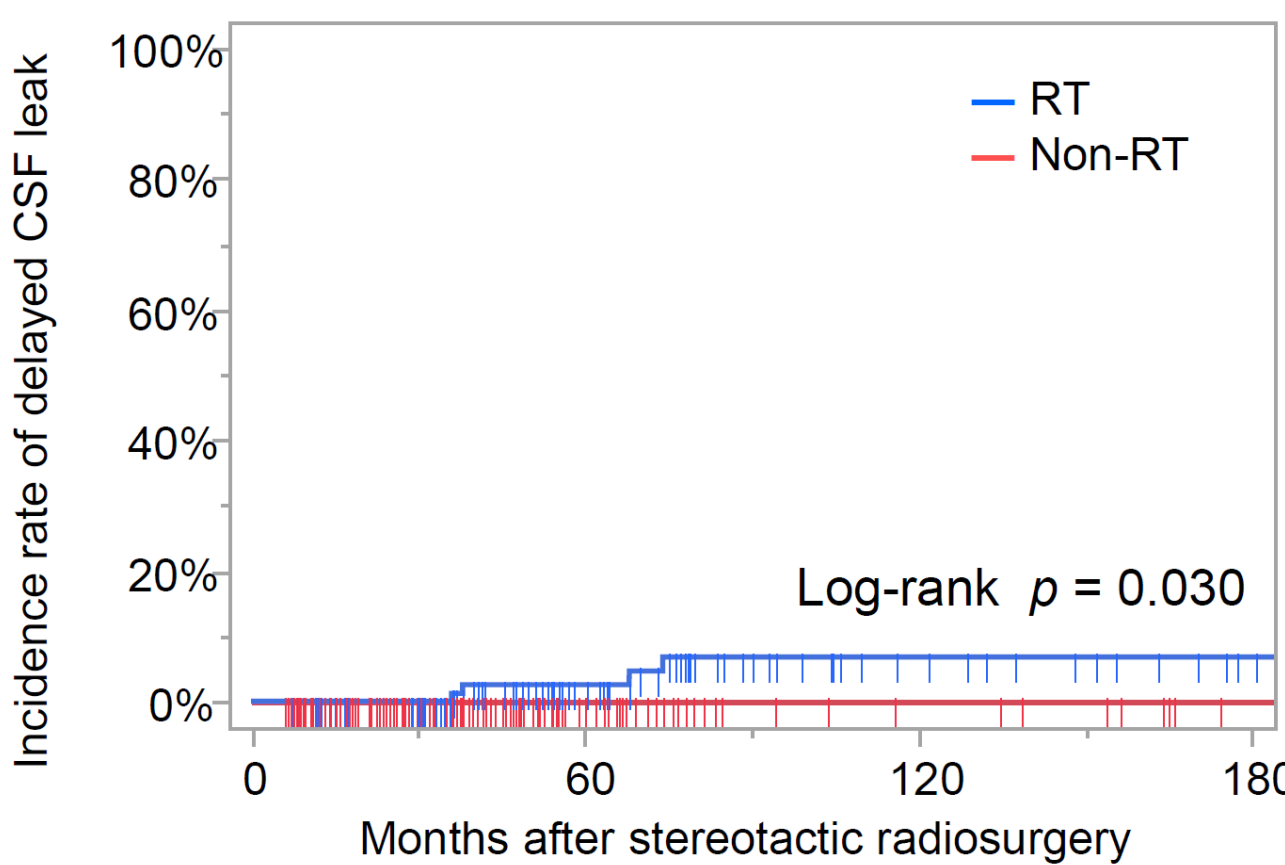


Figure 2. Cumulative incidence rate of delayed CSF leak

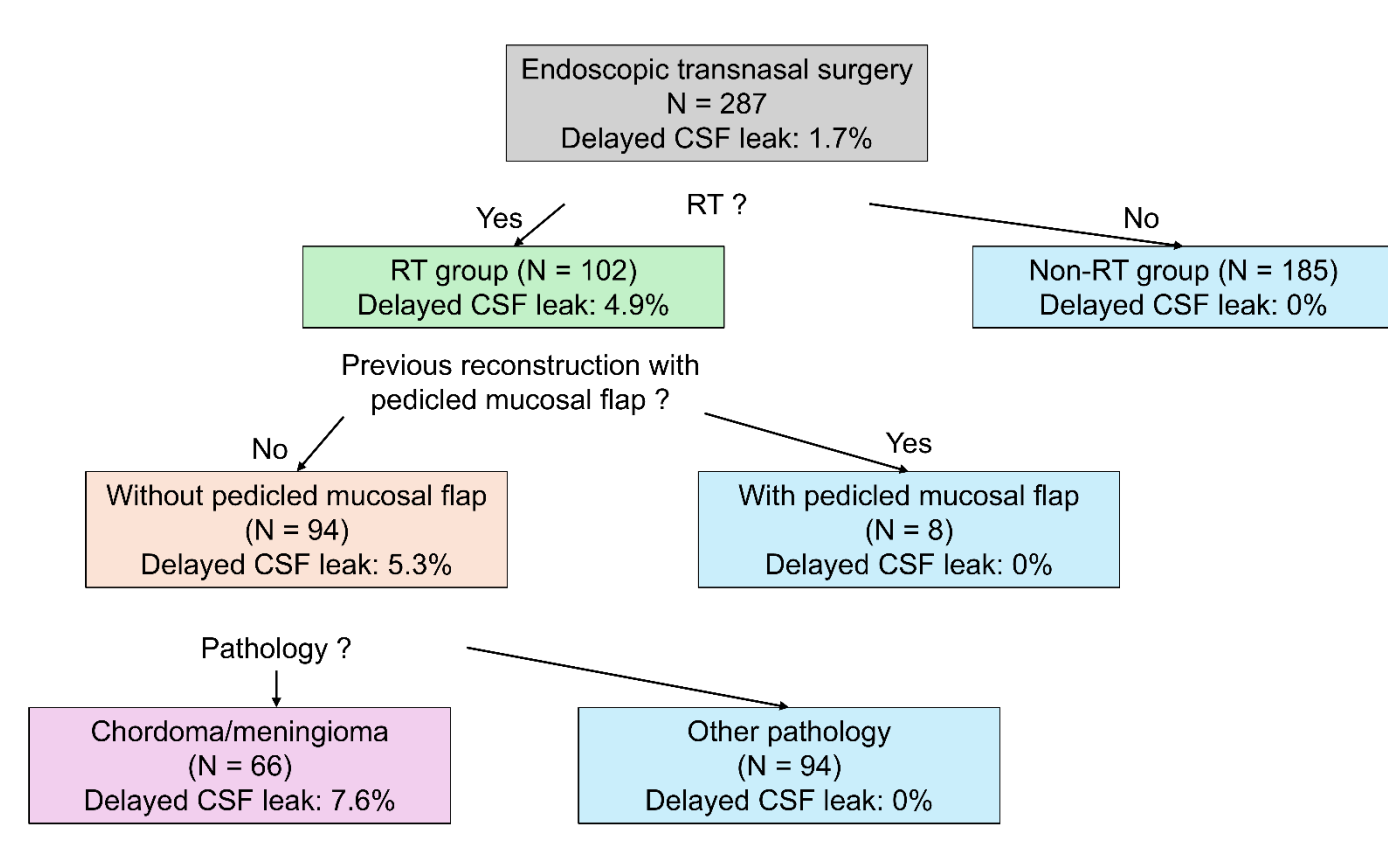
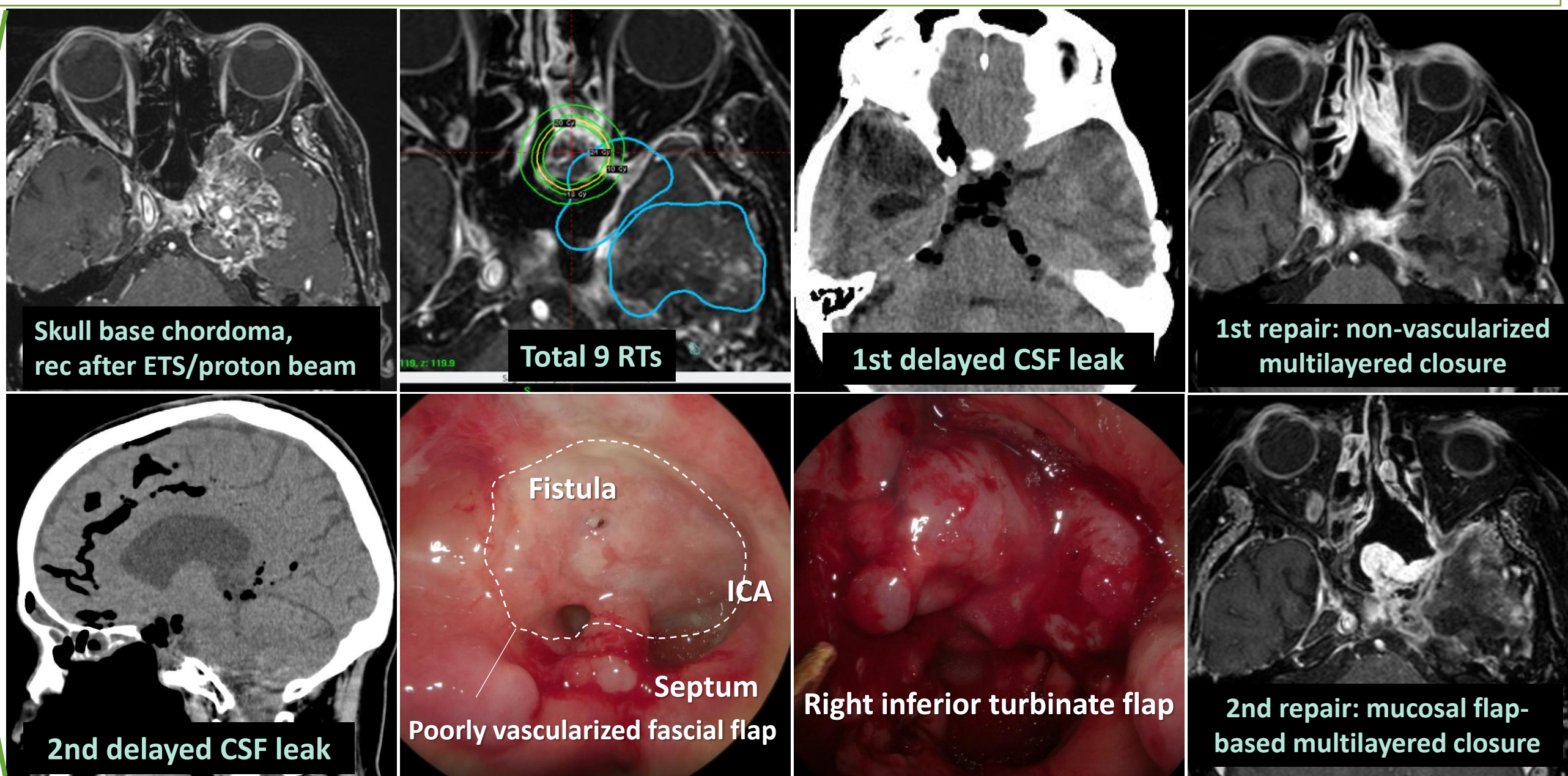


Figure 3. Recursive partitioning analysis for delayed CSF leak

Discussion

- Incidence of Delayed CSF Leak**
 - The **overall incidence was 1.7%**, which demonstrated robustness of non-vascularized multilayered closure.
 - Only observed in patients with a **history of RT**.
 - Patients requiring **multiple ETS and RT sessions** were at the highest risk.
 - These findings highlight the importance of long-term surveillance.
- The Role of Radiation Therapy in Skull Base Dehiscence**
 - High-dose RT (SRS, proton beam therapy)** increases the risk of skull base dehiscence.^{5,6}
 - Mechanisms of RT-induced damage^{7,8}:
 - Vascular endothelial injury → **reduced blood supply**
 - Fibrosis progression → **tissue breakdown**
 - Osteonecrosis → **delayed CSF leak**
 - RT should be planned to **minimize normal tissue damage** while maintaining tumor control.
- Mucosal Flap-Based Closure for Delayed CSF Leaks**
 - Pedicled mucosal flaps (e.g., **nasoseptal, inferior turbinate flaps**) improve **vascularization and tissue durability**.⁹
 - All patients who underwent mucosal flap-based repair had no recurrence** of delayed CSF leak.
 - Consideration for **early use of mucosal flaps** in high-risk patients may be beneficial, but **optimal mucosal flap use is needing further investigation**.



Conclusions

- Delayed CSF leaks** are rare but can occur in patients undergoing RT after ETS.
- Mucosal flap-based closure** may be an effective strategy for both prevention and repair of delayed CSF leaks.
- Careful **patient selection and reconstruction planning** are essential in cases requiring **multiple surgeries and RTs**.

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