

# Graded Reconstruction Strategy Using a Multi-Layer Technique without Lumbar Drainage After Endoscopic Endonasal Surgery

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## Research Article

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# Abstract

## Introduction

Sellar reconstruction following endoscopic endonasal surgery (EES) requires modification based on the degree of cerebrospinal fluid (CSF) leak. For high-flow (grade II or III) intraoperative CSF leak, lumbar drainage (LD), in addition to the multi-layer closing technique, is generally recommended. However, LD has complications occasionally, including post-puncture headache, over-drainage symptoms, and increased length of stay (LOS). We retrospectively evaluated the outcome of our graded reconstruction strategy using a multi-layer technique with a novel material, without LD, after EES.

## Methods

Ninety-seven patients who underwent EES with grade II or III intraoperative CSF leak between June 2020 and March 2021 were retrospectively reviewed. For grade II CSF leak, fibrin sealant and a nasoseptal flap (NSF) were placed; for grade III CSF leak, a multi-layer technique was utilized in combination with collagen matrix, an acellular dermal graft, injectable hydroxyapatite (HXA), and an NSF. Postoperatively, routine LD was not performed.

## Results

This study included 48 (49.5%) grade II and 49 (50.5%) grade III CSF leaks. Upon follow-up period (mean, 8.7 months), no patient showed postoperative CSF leak in either group. The postoperative LOS was not significantly different between the grade II (6.68 [range, 3–14] days) and grade III CSF leak groups (7.38 [range, 4–15] days) ( $p>0.05$ ). No HXA-associated complications occurred.

## Conclusions

A graded surgical repair strategy after EES could avoid postoperative CSF leak. Combined use of injectable HXA and acellular dermal grafts for high-flow CSF leak can limit LD requirement, without significant risks.

## Introduction

Recent advances in endoscopic neurosurgical techniques have made the endoscopic endonasal surgery (EES) a primary surgical option for the treatment of skull base lesions [1–5]. Despite its widespread application in a variety of skull base lesions and several clinical advantages, complications related to EES should not be overlooked [6, 7]. Among them, postoperative cerebrospinal fluid (CSF) leak is the most common and fatal complication to occur after the introduction of endoscopic skull base surgery [8, 9].

Since Hadad et al. suggested a vascularized nasoseptal flap (NSF) for skull base reconstruction [10], many authors have reported that cases of postoperative CSF leak have decreased surprisingly [11–13]. Nonetheless, postoperative placement of lumbar drainage (LD) for CSF diversion is still required,

especially in cases with a high body mass index (BMI), opening of the third ventricle, previous history of surgery or radiation treatment, or involvement of the posterior cranial fossa [14–17]. However, LD is frequently associated with unlethal complications, such as post-puncture headache, radiculopathy, symptoms associated with over-drainage, and immobilization [18], all of which could increase the postoperative length of stay (LOS). Therefore, the development of safe and effective alternative reconstruction methods that do not require LD is necessary to reduce the incidence of LD-associated complications.

Injectable hydroxyapatite (HXA) was introduced in 1996 and is has been widely used in various fields, including orthopedic surgery, otorhinolaryngology, plastic surgery, and neurosurgery [19–21]. The HXA hardens within 5 min after injection under drying conditions; hence, it could be a suitable material to cover bony defects. In skull base surgery for sellar reconstruction, Chung et al. recommended injectable HXA as a substitute for NSF [7], and Kitano et al. proposed injectable HXA as a component of the multi-layer technique [22]. In this study, we retrospectively evaluated the outcome of our graded reconstruction strategy after EES with injectable HXA, but without LD.

## Materials And Methods

A total of 250 patients who underwent EES between June 2020 and March 2021 were retrospectively reviewed in this consecutive series. During this period, we performed EES for skull base tumors such as pituitary adenoma, craniopharyngioma, tuberculum sellae meningioma, and Rathke's cleft cyst. The degree of intraoperative CSF leak was assessed using the grading scale suggested by Esposito et al [17]. Ninety-seven patients showed an intraoperative grade II or III CSF leak and were included in the study. Patients without an intraoperative CSF leak, patients with a grade I CSF leak, and those with tumors involving the posterior fossa were excluded from this study. The study was approved by the institutional review board of our institution and was performed in compliance with relevant ethical guidelines.

Medical records of the included patients were reviewed to collect data, including demographic variables (sex, age, and BMI), diagnosis, intraoperative CSF leak grade, sellar reconstruction method used, and length of stay (LOS) in the hospital postoperatively. To investigate the integrity of NSF, postoperative MRI and rhinological status were also examined by a dedicated neuroradiologist and otorhinolaryngologist, respectively.

## Surgical technique

Details of the EES have been described previously [8, 23]. The entire surgery was performed by an endoscopic skull base surgery team comprising a neurosurgeon (D.S.K.) and an otorhinolaryngologist (S.D.H.) at a single institution. During the EES, rigid endoscopes (diameter, 4 mm; length, 18 cm; with 0°, 30°, or 45° angle of view lenses; KARL STORZ Endoscopy Korea Co., Ltd., Seoul, Korea) were used in combination with a robotic holding arm (POINT SETTER, Mitaka Kohki Co., Ltd., Tokyo, Japan). All

endoscopic procedures were recorded using a high-resolution camera and video recording system (KARL STORZ Endoscopy Korea Co., Ltd., Seoul, Korea).

For grade II CSF leak, we placed a fibrin sealant patch (TachoSil®, Takeda Pharmaceutical Co., Ltd., Osaka, Japan), followed by an NSF. In contrast, for cases involving grade III CSF leaks, the sellar reconstructive method included the following multi-layer technique. In this technique, (i) a collagen matrix (DuraGen®, Integra LifeSciences, New Jersey, USA) was first placed into the arachnoid defect. Thereafter, (ii) an acellular dermal graft (AlloDerm®, BioHorizons®, Alabama, USA or MegaDerm®, L&C BIO, Gyeonggi-do, Korea), tailored according to the size of the sellar bone defect, was overlaid as an on-layer dura graft. (iii) HXA (Hydroset®, Stryker Leibinger, Freiburg, Germany) was then injected for additional closure of the sellar defect; at this step, no intraoperative CSF leak was observed from the reconstructed graft site 5–10 min after HXA injection. Finally, (iv) the NSF, already harvested at the beginning of EES, was used to cover the layered materials; thus, HXA was not exposed to the nasal cavity. Compression was applied with (v) a 12-Fr balloon catheter or two pieces of Merocel® (Medtronic, Minneapolis, USA) to stabilize the graft. Postoperatively, LD was not routinely performed.

## Postoperative management

Three antibiotics (third-generation cephalosporin, quinolone, and metronidazole) were intravenously administered for 3–5 days. Intravenous or oral steroid (hydrocortisone) replacement was performed pre- and postoperatively. To identify the degree of tumor resection and the integrity of NSF, sellar MRI was performed one day after surgery, and otorhinolaryngological examination was performed on days 2 and 5 postoperatively. All patients were followed up at an otorhinolaryngology and endocrinology outpatient clinic at 1 week after discharge and at a neurosurgery outpatient clinic 3 weeks after discharge.

## Statistical analysis

Independent variables associated with CSF leaks were analyzed using univariate analysis. The postoperative LOS was compared between the CSF leak grade II and grade III groups using an independent sample t-test.  $P < 0.05$  was considered statistically significant. Statistical evaluations were accomplished by SPSS® Statistics 27 (IBM Co., New York, USA)

## Results

### Baseline characteristics

Among the 97 consecutive patients included in this study, 47 (48.5%) were men and 50 (51.5%) were women. The mean age at the time of surgery was 48.5 (range, 5–75) years, and the mean BMI was 25.7 (range, 13.9–37.1) kg/m<sup>2</sup>. Pituitary adenoma (n = 57) was the most common tumor (including four cases of Cushing's disease, three cases of acromegaly, and three cases of prolactinoma) followed by craniopharyngioma (n = 18), meningioma (n = 11), Rathke's cleft cyst (n = 4), germinoma (n = 4), chordoma (n = 1), cavernous malformation (n = 1), and pilocytic astrocytoma (n = 1) (Table 1).

Table 1  
Baseline patient characteristics

		Number of cases (%)
Total number		97 (100)
Sex	Male	47 (48.5)
	Female	50 (51.5)
Age (years)	<20	4 (4.1)
	20–59	70 (72.2)
	≥ 60	23 (23.7)
BMI <sup>a</sup> (kg/m <sup>2</sup> )	<18	5 (5.2)
	18–25	42 (43.3)
	≥ 25	50 (51.5)
Diagnosis	Pituitary adenoma	57 (58.8)
	Non-functional	47 (48.5)
	Cushing’s disease	4 (4.1)
	Acromegaly	3 (3.1)
	Prolactinoma	3 (3.1)
	Craniopharyngioma	18 (18.6)
	Meningioma	11 (11.3)
	Rathke’s cleft cyst	4 (4.1)
	Germinoma	4 (4.1)
	Chordoma	1 (1.0)
	Cavernous malformation	1 (1.0)
	Pilocytic astrocytoma	1 (1.0)
<sup>a</sup> BMI, body mass index		

## Clinical and reconstruction outcome

During the follow-up period (mean, 8.7 months), overall gross- and near-total resection was achieved in 50 (51.5%) and 39 patients (40.2%), respectively (Table 2). Among the 97 patients, grade II and grade III CSF leaks were noted in 48 (49.5%) and 49 (50.5%) patients, respectively (Table 3). We applied the modified reconstructive methods according to the CSF leak grade. We placed a fibrin sealant patch

(TachoSil®, Takeda Pharmaceutical Co., Ltd., Osaka, Japan), followed by an NSF in patients with grade II CSF leak; for patients with grade III CSF leak, we applied a multi-layer technique using a collagen matrix, an acellular dermal graft, HXA, and an NSF. During the follow-up period, no postoperative CSF leak was observed in any of the patients. On univariate analysis, we found that no significant variable affected the outcome of the reconstruction.

Table 2  
Extent of tumor removal and pathological diagnosis of patients

Diagnosis	Extent of removal <sup>a</sup>			Number of cases
	GTR	NTR	STR	
Pituitary adenoma	34	21	2	57
Non-functional	28	18	1	47
Cushing's disease	2	1	1	4
Acromegaly	2	1	0	3
Prolactinoma	2	1	0	3
Craniopharyngioma	8	9	1	18
Meningioma	6	3	2	11
Rathke's cleft cyst	1	3	0	4
Germinoma	0	1	3	4
Chordoma	1	0	0	1
Cavernous malformation	0	1	0	1
Pilocytic astrocytoma	0	1	0	1
Total	50	39	8	97

<sup>a</sup>GTR, gross total resection; NTR, near-total resection; STR, subtotal resection

Table 3  
CSF leak grade and pathological diagnosis of patients

Variable	Number of cases		p-value <sup>a</sup>
	Grade II	Grade III	
Female sex	27	23	0.419
Age < 50 years	20	25	0.418
BMI <sup>b</sup> ≥ 25 (kg/m <sup>2</sup> )	23	27	0.545
Pituitary adenoma	41	16	0.000*
Non-functional	33	14	0.000*
Cushing's disease	4	0	0.056
Acromegaly	2	1	0.617
Prolactinoma	2	1	0.617
Craniopharyngioma	0	18	0.000*
Meningioma	4	7	0.524
Rathke's cleft cyst	2	2	1.000
Germinoma	1	3	0.617
Chordoma	0	1	1.000
Cavernous malformation	0	1	1.000
Pilocytic astrocytoma	0	1	1.000
Total	48	49	
<sup>a</sup> Fisher's exact test, <sup>b</sup> BMI, body mass index, *p-value < 0.05, statistically significant			

We compared the postoperative LOS between the grade II and grade III CSF leak groups. The mean LOS was 6.68 (range, 3–14) days in the grade II CSF leak group and 7.38 (range, 4–15) days in the grade III CSF leak group. There was no significant difference in the LOS between the two groups ( $p = 0.212$ ) (Table 4).

Table 4  
Postoperative length of stay (LOS) and CSF leak grade

<sup>a</sup> CSF leak grade	LOS (days)	p-value <sup>b</sup>
Grade II	6.68*	0.212
Grade III	7.38**	
<sup>a</sup> CSF, cerebrospinal fluid		
<sup>b</sup> Independent sample t-test		
*One patient was excluded due to postoperative subarachnoid hemorrhage and required a longer admission period for consequent management.		
**One patient was excluded due to ongoing management of perioperative hydrocephalus.		

## Status of integrity of the NSF

To evaluate the integrity of the NSF, postoperative MRI was performed within a day after surgery. A C-shaped configuration of the flap adjacent to the skull base covering the sellar defect in both coronal and sagittal views was reviewed by an authoritative neuroradiologist (S.T.K.). Additionally, rhinological examination was performed by a dedicated otorhinolaryngologist. MRI results showed that NSF was not enhanced in 12 of the 97 patients examined (12.4%, 7 with grade II and 5 with grade III CSF leaks), which was confirmed by rhinological examination.

## Adverse effects associated with HXAgraft

During the overall follow-up period, we did not observe crust, seroma, or infection around the NSF or HXA in routine rhinological examinations. In addition, there was no allergic reaction or aseptic meningitis in the group that received the HXA graft.

## Discussion

Recently, EES for skull base tumors has become a major surgical technique in modern skull base surgery. Despite its surgical and technical limitations compared with the transcranial approach, it provides a favorable surgical outcome [24–26]. However, postoperative CSF leak, a recognized complication associated with EES [27, 28], remains a matter of concern, and reconstruction of the barriers between the arachnoid space and sinonasal tract continues to be a challenge [10]. For grade III CSF leaks, which is an inevitable result after the suprasellar or transclival approach, lumbar CSF diversion can contribute to improved reconstruction outcomes [17, 18]. However, LD often poses risks of associated complications such as post-puncture headache, radiculopathy, symptoms associated with over-drainage, and long-standing immobilization.

The recommended maintenance period of LD varies among studies [17, 18], with no consensus. In clinical practice, postoperative LD should be maintained for a minimum of 3–5 days, resulting in prolonged LOS in hospitals. Therefore, an alternative technique without LD is required to manage grade III CSF leaks. Herein, we analyzed the efficacy of HXA and its potential to replace LD in high-flow intraoperative CSF leaks by comparing the LOS between patients with grade II and grade III CSF leaks. We found no significant difference in the LOS between the two groups, and no serious complications associated with injectable HXA were identified.

In contrast to a previous study on the complications of HXA [29], our study showed acceptable clinical results with HXA. For successful grafting of HXA, optimal condition of the perigraft environment is crucial because HXA weakens in humid environments and can fracture easily. Some materials, such as HXA, reabsorb too slowly, which can cause inflammation. Therefore, it is critical to maintain minimal or zero infection rate after HXA grafting. We suggest that the acellular dermis for dural grafting might function as a barrier between the arachnoid space and the injected HXA, and it may prevent stray HXA particles from entering the intradural space. In addition, in the study, placement of a vascularized NSF completely covered the grafted HXA and prevented it from exposure to the outer side of the sinonasal tract. Thus, the combination of acellular dermal graft with HXA could have contributed to our favorable results; no patient showed HXA-related complications, such as aseptic meningitis or foreign body reaction.

Our study had several limitations. Since this study was designed as a retrospective consecutive series, we did not compare the LOS between patients treated with injectable HXA and those who required LD. Furthermore, data were collected from a single institution by a single surgery team, and thus, might not represent the patient-group in general. Although the size of the tumor and the extent of the sellar defect varied among individual patients, these were not considered in our study.

## Conclusions

The graded surgical repair strategy using injectable HXA in combination with acellular dermal grafts provided effectiveness and safety in sellar reconstruction after EES without postoperative CSF leak. Combined use of injectable HXA and acellular dermal grafts for high-flow CSF leak can limit LD requirement, without significant risks. By decreasing the need for LD, HXA may allow early ambulation and shorten the LOS after surgery.

## Abbreviations

BMI, body mass index; CSF, cerebrospinal fluid; CT, computed tomography; EES, endoscopic endonasal surgery; GTR, gross total resection; HXA, hydroxyapatite; LD, lumbar drainage; LOS, length of stay; MRI, magnetic resonance imaging; NSF, nasoseptal flap; NTR, near-total resection; STR, subtotal resection

## Declarations

**Funding:** This research received no external funding.

**Conflicts of interest/Competing interests:** The authors declare no conflict of interest.

**Ethics approval:** This retrospective study was reviewed and approved by the Institutional Review Board of Samsung Medical Center in Seoul, Korea. The study was performed in accordance with the World Medical Association Declaration of Helsinki.

**Availability of data and material:** The data are available upon reasonable request to the corresponding author.

**Code availability:** Not applicable

**Consent to participate:** Patient consent was waived due to the retrospective study design.

**Consent for publication:** Patient consent was waived due to the retrospective study design

**Contributions:** Conceptualization: Chang-Min Ha, Doo-Sik Kong; Methodology: Chang-Min Ha, Doo-Sik Kong; Data curation: Sang Duk Hong, Doo-Sik Kong; Resources: Chang-Min Ha, Sang Duk Hong, Doo-Sik Kong; Validation: Chang-Min Ha, Sang Duk Kong, Doo-Sik Kong; Formal Analysis: Chang-Min Ha; Investigation: Doo-Sik Kong; Project administration: Doo-Sik Kong; Supervision: Jung Won Choi, Ho Jun Seol, Do-Hyun Nam, Jung-Il Lee; Visualization: Chang-Min Ha, Doo-Sik Kong; Writing – original draft: Chang-Min Ha; Writing – review & editing: Doo-Sik Kong

All authors have read and agreed to the published version of the manuscript.

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