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Endoscopic skull base reconstruction with the nasoseptal flap: complications and risk factors

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Abstract

Purpose The endoscopic endonasal approach is increasingly being used for resection and reconstruction of anterior skull base lesions. The vascularized nasoseptal flap (NSF) has become the workhorse for reconstruction of anterior skull base defects, resulting in a significant decrease in the incidence of cerebrospinal fluid (CSF) leak. This study presents a single center's experience with NSFs and reports associated complications.

Methods Patients who underwent endoscopic skull base defect repair with a NSF between 2008 and 2014 were retrospectively evaluated. Complications reviewed were divided into major and minor. Major complications included new-onset and continuing CSF leak and meningitis. Minor complications included long-standing crust formation, synechia, epistaxis, septal perforation, sinusitis and anosmia.

Results Of the 77 patients included in the study, 47 (61%) underwent trans-sphenoidal surgery for pituitary lesions during which CSF leak was observed. The other 30 patients underwent reconstructive surgeries for post-traumatic CSF leaks or extirpation of lesions involving the anterior skull base. A high-flow intra-operative CSF leak was observed in 25 patients (25/77, 32%). The median follow-up was 16 months (range 3–81 months). 9 patients had major complications and 27 patients had minor complications. Only high-flow intra-operative CSF leak correlated with major complications ($p = 0.012$).

Conclusion NSF is an extremely effective tool for skull base reconstruction. While it is associated with a low rate of major complications, minor complications are frequent and require local treatment, although they tend to resolve in the late post-operative period.

Keywords Endoscopy · Paranasal sinuses · Nasoseptal flap · Reconstruction · Skull base

Introduction

The endoscopic endonasal approach (EEA) has become increasingly popular for the treatment of skull base and sellar lesions and for the reconstruction of ventral skull base defects [1–3]. As with the open surgical approach, persistent communication between the cranial cavity and the sinonasal tract makes reconstruction one of the most challenging surgical procedures. A cerebrospinal fluid (CSF) leak is the primary postoperative complication. Numerous reconstructive techniques have been described based upon different types of grafting materials, including avascular grafts, intranasal vascular flaps and regional flaps [4–7]. Since its introduction in 2006, the use of a vascularized pedicled nasoseptal flap in a multilayered reconstruction technique has resulted in a significant decrease in the rates of CSF leak which have dropped from 16 to 5% [3, 4]. Although it has become the workhorse for anterior skull base reconstruction and has been used in a variety of procedures, complications related to nasoseptal flaps (NSF) are rarely discussed [8, 9].

The purpose of this article is to present one center's 6-year experience of skull base endoscopic reconstruction with NSF and to analyze associated complications and risk factors.

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Materials and methods

Study design

After obtaining institutional review board approval, a retrospective review was conducted of medical records of all patients who underwent endoscopic skull base surgery and defect repair by means of a NSF between January 2008 and August 2014. Patients who had less than 3 months follow-up were excluded from the study. The extracted data included selected demographics, preoperative clinical and radiological findings, intra-operative details and postoperative complications. Complications reviewed were divided into major and minor. Major complications were limited to those that occurred within 3 months post-surgery and they included both new-onset and continuing CSF leak and meningitis. Minor complications were defined as being local and lasting up to 1 year post-surgery, and they included long-standing crust formation, synechia, epistaxis, septal perforation, sinusitis and anosmia.

Surgical technique of NSF reconstruction

The NSF is typically raised at the beginning of surgery when a high-flow CSF leak is expected, e.g., large lesions or significant supra-sellar component. The nasal cavity is decongested with 1% lidocaine and adrenalin (10:1), and infiltrated with lidocaine HCl 2% and epinephrine 1:100,000. The septal mucosa is incised with a #10 blade and a monopolar electrocautery needle beginning at the level of the sphenoid osteum along the septum, curving down at level of the anterior edge of the inferior turbinate to partly include the nasal floor. If the defect is anterior and the flap required needs a better arc of rotation, mucosa can be harvested anteriorly up to the nasal spine. If the defect size is large, the flap can be extended to include the inferior meatus mucosa. After incisions have been performed, the flap is raised antero-posteriorly by a Freer elevator after which it is tucked in the nasopharynx or maxillary sinus for the duration of surgery. A posterior septectomy is performed to reduce exposed bone tissue once surgery is completed. If bone or cartilage remains exposed, it is either covered by a reverse flap or left for secondary healing. The region of the skull base defect is prepared to receive the flap by drilling any existing bony septations in the vicinity of the defect and removing the mucosa circumferentially. Reconstruction of skull base defects typically involves the use of a multilayer closure with abdominal fat, thrombin glue or fascia lata. The NSF is layered as an overlay flap to cover the defect, taking care to avoid torsion of the pedicle and to orient the mucosal surface of the flap towards the nasal cavity.

Perioperative treatment protocol

Prior to the beginning of the surgery, patients are treated with metronidazole and cefuroxime. Postoperative antibiotic treatment is continued with amoxicillin and clavulanic acid, and is ceased after 4 days. Postoperative protocol includes bed rest with head elevation of 30°, limited mobility and stool softeners. Continuous drainage is inserted if required.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics version 24.0. Univariate analysis was performed using the Cox proportional-hazards regression (HR), with significance set at a p level of < 0.05. All potential preoperative and intra-operative predictor variables were tested for an association with postoperative complications as the primary outcome measure. Kaplan–Meier survival plots were used to describe the occurrence of complications over time.

Results

A total of 77 patients (40 males and 37 females) who underwent endoscopic skull base surgery and defect repair by means of a NSF were identified. The patient characteristics are summarized in Table 1. The cohort's mean age was 48 years (range 2–83 years). Forty-seven patients (61%) underwent trans-sphenoidal surgery for pituitary lesions during which CSF leaks were observed. The remaining patients underwent reconstructive surgeries for post-traumatic,

Table 1 Patient characteristics

Age (y), mean (range)	48 (range 2–83)
Female, *n* (%)	37 (48%)
Male, *n* (%)	40 (52%)
Comorbidities, *n* (%)	
Cardiovascular	36 (46%)
Respiratory	8 (10%)
Endocrine	15 (19%)
Obesity	5 (6%)
Previous surgery, *n* (%)	
Yes	38 (49%)
No	39 (50.6%)
Malignant lesion, *n* (%)	
Yes	13 (17%)
No	64 (83%)
Adjuvant radiotherapy, *n* (%)	
Yes	64 (83%)
No	13 (17%)

postoperative or spontaneous CSF leaks or extirpation of lesions involving the anterior skull base. Four patients had post-traumatic CSF leak which was induced by head trauma, while indication for surgical repair was either previous conservative management failure or documented meningitis.

NSF alone was used for reconstruction in 27 (38.9%) patients, while abdominal fat or fascia lata grafts were used in conjunction with NSF in the remaining 50 patients. Location of the defect and the surgical approach, i.e., transsphenoidal, trans-cribriform or trans-clival, influenced the selection of the reconstruction technique. Reconstruction with the NSF alone was used in 26 (53%) cases in the transsphenoidal approach, whereas there was a clear shift towards reconstruction in a multilayer fashion with abdominal fat and fascia lata for skull base surgeries in the trans-clival or trans-cribriform approach.

Notably, 25 patients (32%) had a high-flow intra-operative CSF leak and 46 patients (62%) had continuous drainage during the postoperative period. The median follow-up was 16 months (range 3–81 months).

During the first 3 months following the operation, nine patients had a major complication: five patients had a postoperative CSF leak, three patients had meningitis and one patient had both (Table 2). Most of the major complications occurred during the first 30 postoperative days (Fig. 1). All patients who had a postoperative CSF leak were first treated conservatively as detailed in the perioperative treatment protocol, but all had eventually undergone reoperation. During reoperation, two cases of flap necrosis were identified, one of which was partial; in both cases debridement of the necrotic flap and redo multilayer reconstruction was undertaken. Patients who had postoperative meningitis were given a 10–14 days course of vancomycin and meropenem.

A univariate analysis of variables (Table 3) revealed that only a high-flow intra-operative CSF leak correlated with major complications [HR 7.531 (1.564–36.236), $p=0.012$]. A survival analysis comparing major complications over time by the presence or absence of intra-operative high-flow CSF leak is shown in Fig. 2. Evidently, a high-flow CSF leak shows a correlation with the occurrence of major complications following surgery.

Twenty-seven patients (35%) had minor complications, including primarily prolonged crust formation, synechia and anosmia. Patients who had anterior cribriform lesions and had documented anosmia prior to surgery were not regarded as having a postoperative minor complication; patients who had anterior cribriform lesions and had undergone transcribriform approach to the skull base had expected postoperative anosmia which did not resolve in most cases. Most minor complications occurred during the first 4 months following surgery (Fig. 3) and majority of them resolved during follow-up with large volume nasal saline irrigation and in-office cleansing. In a univariate analysis, no single factor was found significant for the occurrence of minor complications (Table 4).

Discussion

The endoscopic management of skull base defects and postoperative CSF leaks remains a challenge for skull base surgeons. The goal of reconstruction after an EEA is similar to that after conventional external approaches to the skull base, which is essentially to separate the cranial cavity from the sinonasal tract and avoid complications, mainly postoperative CSF leak. The occurrence of a postoperative CSF leak could be expected in cases of an intra-operative high-flow CSF leak with a widely opened third ventricle [10]. While different reconstruction techniques have been described in the literature since the 1950s, among them the septal flap and its modifications or the middle turbinate flap, the vascularized pedicled nasoseptal flap was shown to be superior in its versatility, area of coverage and arc of rotation [4].

Although the NSF is reportedly superior to the other flaps [4, 5], the use of a NSF is also associated with a variety of complications which have been infrequently reported in the literature. Most studies focus on CSF leak as the major complication, whereas other complications, such as meningitis or local complications, are hardly mentioned. A recently published systematic review of complications and morbidities related to the NSF by Lavigne et al. [8] reports local complications or quality of life in 27 studies. These include NSF necrosis, mucocele formation, septal perforation, nasal dorsum collapse, reduced quality of life and olfactory loss. Most studies reported on anosmia and prolonged crusting, but only few studies reported on flap necrosis, septal perforation, epistaxis or synechia. The review concludes that some NSF complications are underreported and that high-quality evidence is missing. One of the studies reviewed, by Soudri et al. [9], focused on complication rates and their analyses. They reported an overall complication rate of 30% in association with the NSF procedure, of which 60% were donor site complications, such as prolonged crusting and septal perforation (the most common complication in their series). Early CSF leak was reported in 7% of the cohort in that study.

Another relevant study by Jalessi et al. [11] evaluated the impact of NSF elevation on sinonasal quality of life (QOL) in patients with pituitary adenomas using the Sinonasal Outcome Test (SNOT-22) questionnaire. While this study did not report on local complications rate, it did interestingly show that although nasal symptoms deteriorated in the 1st postoperative month (compared to preoperative data) in the NSF group of patients, no negative impact on the sinonasal QOL was shown compared to the control group.

Table 2 Characteristics of patients with major complications ($n=9$)

#	Complication	Pathology	Reconstruction type	Intra-operative high-flow CSF leak	Previous surgery	Flap failure	CD postop	Other intra-operative complications	Revision surgery
1	CSF leak	Huge anterior skull base fibrous dysplasia	NSF + fascia lata	+	−	Necrosis	+	ICA rupture + Stenting	Debridement and closure with bilateral inferior turbinate flap and fascia lata
2	Meningitis	CSF leak post-TSS for pituitary adenoma	NSF	–	TSS	–	+	–	–
3	CSF leak	Craniopharyngioma	NSF + abdominal fat	+	–	Failed positioning	+	–	Repositioning
4	CSF leak	CSF leak post-FESS	NSF	–	FESS	Flap not covering additional site of CSF leak in lateral sphenoid wall	–	–	Pterygoid meningocele debridement and sphenoid obliteration with abdominal fat, repositioned NSF
5	CSF leak	Craniopharyngioma	NSF + abdominal fat	+	–	Failed positioning	+	–	Repositioning
6	Meningitis	Craniopharyngioma	NSF + abdominal fat	+	TSS and insertion of Ommaya catheter	–	+	–	–
7	CSF leak	Temporal encephalocele with CSF leak	NSF + fascia lata	+	TSS	Flap not covering additional site of CSF leak in cribriform plate	+	–	Reconstruction with fascia lata and nasal mucosa flap
8	CSF leak + Meningitis	CSF leak post-TSS for pituitary adenoma with ICA rupture and stenting	NSF + fascia lata	+	TSS	Failed positioning and partial necrosis	+	–	Reconstruction with abdominal fat plug, fascia lata and bilateral inferior turbinate flap
9	Meningitis	CSF leak post-encephalocele resection	NSF + fascia lata	+	TSS	–	+	–	–

CSF cerebrospinal fluid, *CD* continuous drainage, *TSS* trans-sphenoidal surgery, *ICA* internal carotid artery

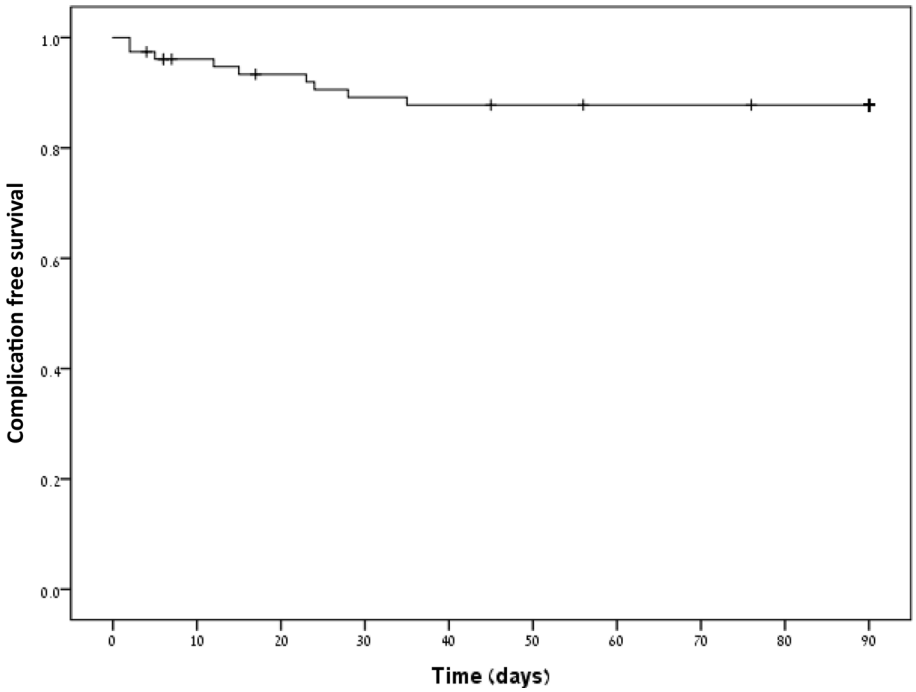

Fig. 1 Time to major complications

Table 3 Results of the univariate analysis of variables associated with major postoperative complications

	No major complication ($n=68$)	Major complication ($n=9$)	HR (95% CI)	p
Age *(y)*, mean	48.1	48	0.998 (0.96–1.03)	0.924
Male	33 (48.5%)	7 (77.8%)	3.61 (0.75–17.4)	0.11
Diabetes mellitus	12 (17.6%)	3 (33.3%)	2.057 (0.514–8.225)	0.308
Cardiovascular disease	31 (45.6%)	4 (44.4%)	0.874 (0.235–3.256)	0.841
Malignancy	13 (19.1%)	0 (0%)	0.036 (0.0–49.815)	0.368
Preoperative radiotherapy	1 (1.5%)	0 (0%)	0.049 (0.000–2193596373)	0.809
Previous surgery	33 (48.5%)	5 (55.6%)	1.395 (0.374–5.199)	0.62
Approach, *n* (%)				
Trans-sphenoidal	39 (57.4)	8 (88.9%)	5.635 (0.704–45.075)	0.103
Trans-clival	9 (13.2%)	0 (0%)	0.4 (0–197.4)	0.459
Trans-cribriform	20 (29.4%)	1 (11.1%)	0.316 (0.039–2.525)	0.277
Reconstruction type	25 (35%)	2 (22%)	0.588 (0.122–2.829)	0.507
Intra-operative HF CSF leak	18 (26.5%)	7 (77.8%)	7.531 (1.564–36.236)	**0.012**
Postoperative CD	40 (58.8%)	8 (88.9%)	4.94 (0.618–39.502)	0.132

Statistically significant p-value is in bold

HF high flow, *CSF* cerebrospinal fluid, *CD* continuous drainage

CSF leak in the early postoperative period in our cohort was observed in six patients (7.7%), which is comparable with the published literature. It was associated only when there had been a high-flow CSF leak intra-operatively. Importantly, all of those six patients had significant comorbidities or had undergone previous surgery (either transsphenoidal surgery, endoscopic sinus surgery or craniotomy), but neither variable reached a level of significance in the univariate analysis.

Local complications were observed in 27 patients (35%), and they consisted mainly of crust formation ($n=14$, 52%), synechia ($n=7$, 25%) and anosmia ($n=7$, 25%). Fewer patients had sinusitis, two had epistaxis and anterior septal perforation was not observed.

As we gained experience over the years, we found there are few surgical principles and postoperative measures that reduce occurrence of local complications ; to reduce crusting, we suggest harvesting a flap designed for defect

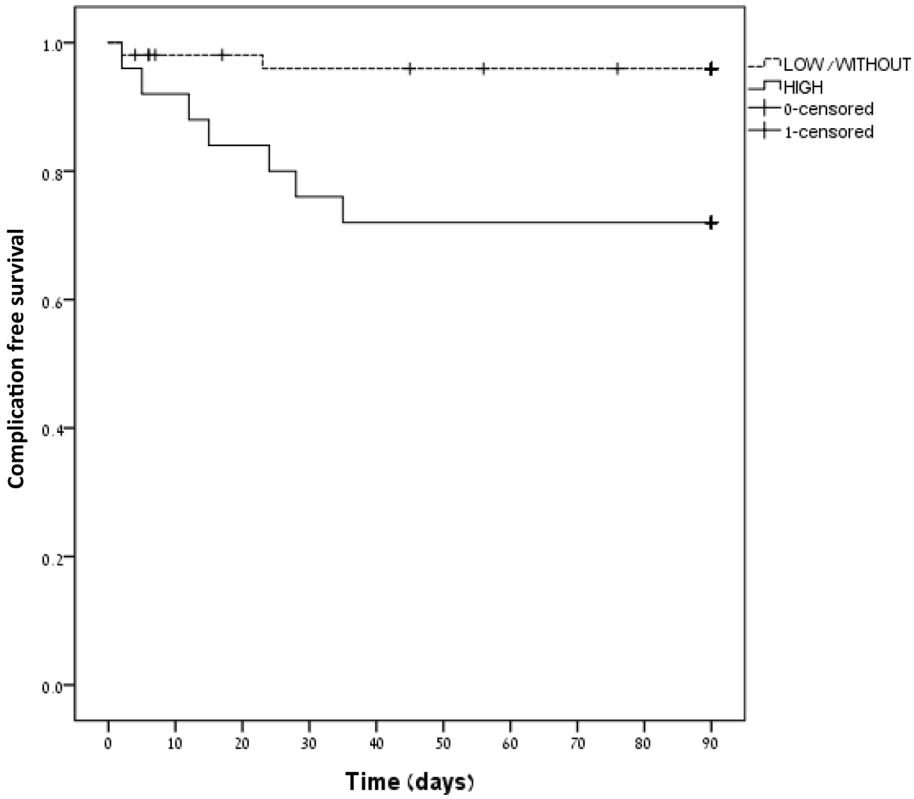

Fig. 2 Kaplan–Meier plot comparing the occurrence of major complications in the presence or absence of intra-operative high-flow cerebrospinal fluid leak

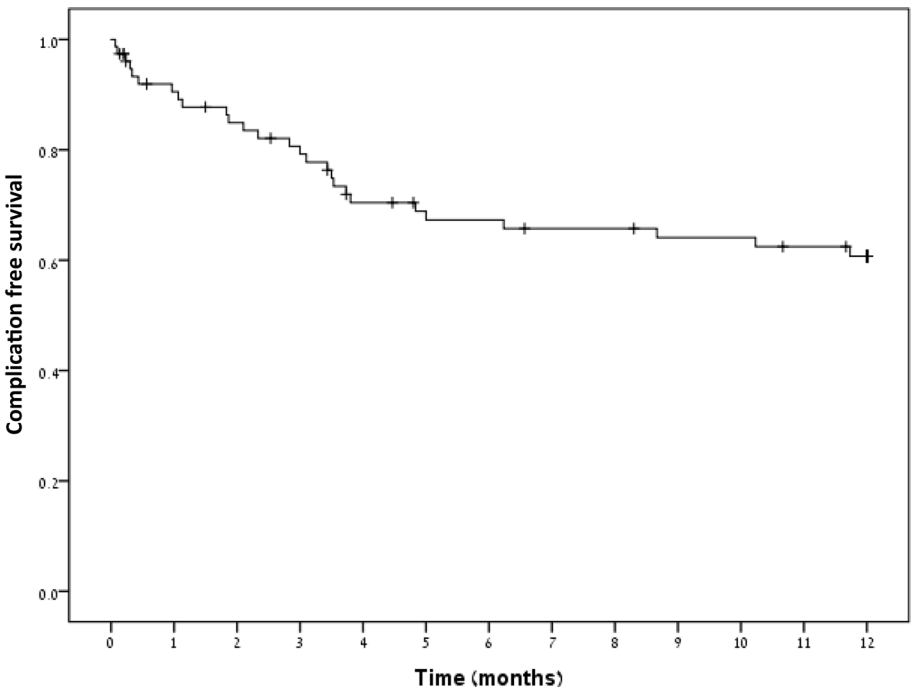

Fig. 3 Time to minor complications

size and location while trying to elevate as little mucosa as possible from the cartilaginous septum, taking care to cover all exposed cartilage at the end of the procedure. A reverse flap could be used for coverage. Suturing silicone strips along the nasal septum and removing them at postoperative day 14 reduces synechia formation and allows for a better mucosal coverage in the early postoperative period. We also noticed that harvesting the flap no higher than the lower border of the middle turbinate or the sphenoid sinus ostium contributed to a better sense of

Table 4 Results of the univariate analysis of variables associated with postoperative minor complications

	No minor complication ($n=50$)	Minor complication ($n=27$)	HR (95% CI)	p
Age (y), mean	47.7	48.9	0.997 (0.977–1.017)	0.773
Male	26 (52%)	14 (51.9%)	1.153 (0.541–2.456)	0.712
Diabetes mellitus	8 (16%)	7 (26%)	1.564 (0.661–3.704)	0.309
Cardiovascular disease	21 (42%)	14 (52%)	1.146 (0.539–2.438)	0.724
Malignancy	6 (12%)	7 (25.9%)	1.934 (0.818–4.577)	0.133
Preoperative XRT	0 (0%)	1 (3.7%)	2.62 (0.353–19.456)	0.347
Previous surgery	26 (52%)	12 (44.4%)	0.901 (0.421–1.928)	0.788
Approach, n (%)				
Trans-sphenoidal	32 (64%)	15 (55.6%)	0.836 (0.391–1.787)	0.644
Trans-clival	4 (8%)	5 (18.5%)	2.215 (0.837–5.858)	0.109
Trans-cribriform	14 (28%)	7 (26%)	0.788 (0.333–1.864)	0.587
Reconstruction type	16 (30%)	11 (40.7%)	1.713 (0.793–3.698)	0.170
Intra-operative HF CSF leak	15 (30%)	10 (37%)	1.069 (0.489–2.335)	0.868
CD postop	30 (60%)	18 (66.7%)	1.114 (0.50–2.481)	0.791

HF high flow, *CSF* cerebrospinal fluid, *CD* continuous drainage

smell at the postoperative period, this is especially important in the older population.

The important effect of local complications on quality of life was not addressed in the current study, yet most complications resolved following frequent cleansing and local treatments (large volume nasal saline irrigation) during the follow-up period.

Meningitis is another significant complication that is rarely reported in association with the extended endoscopic approach. Moreover, when it is mentioned, it is not specifically associated with a reconstruction technique. One meta-analysis published in 2013 reported an overall ~ 1.9% rate of meningitis after an EEA [12]. The 5% rate of meningitis in the early postoperative period in the current study was higher than the rates cited in earlier publications. This could be partly due to the use of continuous lumbar drainage in the majority of the patients (62%) who underwent EEA during the study period.

The statistical analysis suggested a non-significant increased HR for patients with continuous drainage to develop a major complication ($p=0.132$). The issue of bacterial meningitis secondary to the use of lumbar catheters has yet to be studied in depth. The reported catheter-related meningitis rates are between 3 and 10% [13, 14]. The use of continuous lumbar drainage in EEA is controversial, with some reports showing benefit with regard to postoperative CSF leak and meningitis rates [13] while others showing the opposite [15–18]. The small sample size and the low rate of major complications may have precluded the ability for demonstrating any association between continuous lumbar drainage and major complications to reach a level of significance. Based on the possibility that preventive insertion of continuous drainage during extended endoscopic approach with the nasoseptal flap reconstruction being unnecessary and harmful, it is no longer a routine procedure in the study institution.

Study limitations

The main limiting factor of this study is the retrospective data analysis. Another issue is that the patient population included in the study ranges from the earliest period of endoscopic skull base reconstruction in our institution and so data presented here are likely not reflective of recent surgical results as over the years and along the learning curve, surgical skills were gained and improved.

Conclusion

The NSF is a highly effective means of skull base reconstruction. It has dramatically decreased the postoperative risk of CSF leak following endoscopic procedures. CSF leak in the current series was associated solely with intra-operative high-flow CSF leak and not with reconstruction type or surgical approach, nor with flap necrosis. NSF is associated with minor complications which are rarely discussed in the literature; most of them require no more than frequent cleansing and local treatment, and tend to resolve during the late postoperative period. Additional quality of life studies are warranted to evaluate the advantages and disadvantages of NSF for patients undergoing skull base operations.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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