ORIGINAL ARTICLE

Management of Cerebrospinal Fluid Leaks According to Size. Our Experience

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Skull base;
Paranasal sinuses;
Endoscopic sinus surgery;
Meningitis

Abstract
Objective: We present our experience in the reconstruction of cerebrospinal fluid (CSF) leaks according to their size and location.

Materials and methods: Fifty-four patients who underwent advanced skull base surgery (large defects) and 62 patients with CSF leaks of different origin (small and medium-sized defects) were included. Large defects were reconstructed with a nasoseptal pedicled flap positioned on fat and fascia lata and lumbar drainage was used. In small and medium-sized leaks of other origin, intrathecal fluorescein 5% was applied previously to identify the defect. Fascia lata in an underlay position was used for reconstruction, which was then covered with mucoperiosteum from the turbinate. Perioperative antibiotics were administered for 5–7 days. Nasal packing was removed after 24–48 h.

Results: The most frequent aetiology for small and medium-sized defects was spontaneous (48.4%), followed by trauma (24.2%), iatrogenic (5%) and then others. The success rate was of 91% after the first surgery and 98% in large skull base defects and small/medium-sized respectively. After rescue surgery, the rate of closure achieved was 100%. The follow-up was 15.6 ± 12.4 months for large defects and 75.3 ± 51.3 months for small/medium-sized defects without recurrence.

Conclusions: Endoscopic surgery for closure of any type of skull base defect is the gold standard approach. Defect size does not play a significant role in the success rate. Fascia lata and mucoperiosteum allow a reconstruction of small/medium-sized defects. For larger skull base defects, a combination of fat, fascia lata and nasoseptal pedicled flaps provides a successful reconstruction.

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Introduction

Cerebrospinal fluid (CSF) fistulas (or leaks) into the nostrils consist of a continuous or intermittent leak of CSF into the fossae or nasopharynx caused by a disruption of the arachnoid and the dura mater, usually associated to a bone defect. Connections between the dura mater and the upper airway entail a risk of ascending bacterial meningitis which is calculated to exceed 10% annually. The most common symptoms are rhinoliquorrhea (mostly unilateral) and headache, especially if the fistula is associated to a meningocele or ascending meningitis. The most common location is at the level of the cribriform plate, followed by the roof of the ethmoid, sphenoid, frontal sinus, sella turcica and clivus.

Endoscopic sinonasal surgery is considered as the standard technique in the surgical closure of these fistulas as it decreases the morbidity associated to external approaches. However, the percentage of postoperative fistulas has increased due to the large endoscopic resections of tumours located throughout the skull base. The challenge in reconstructing these major defects is that they are often connected with the ventricular system (third ventricle), causing CSF fistulas with high flows and pressures. Initially, this caused a rate of CSF fistulas over 30%, leading this surgical approach to be questioned. However, recent innovations, particularly the introduction of vascularised flaps which allow large defects to be adequately sealed, have reduced this rate from 33% to 5.4%.

The objective of this study is to present our experience in the closure of CSF fistulas according to their size and location and, additionally, to create an algorithm for the diagnosis and management of CSF fistulas.

Materials and Methods

The study included patients undergoing endoscopic closure of CSF leaks (n=116) between 1997 and 2013. We conducted a review of medical records, causes, locations, methods of presentation, preoperative studies, surgical techniques, intraoperative findings, postoperative management, complications and closure success. The diagnostic and management protocol for CSF leaks presented in our algorithm (Fig. 1) was followed in all cases.

Patients were divided into two groups:

1. Extended skull base surgery group, including patients undergoing surgery for intracranial pathologies who required extensive endoscopic approaches between 2007 and 2013 (large defects).
2. Non-extended surgery group, including patients suffering rhinoliquorrhea for other causes between 1998 and 2013 (small to medium defects).

In both groups we used intravenous ceftriaxone for 5–7 days as prophylactic antibiotic therapy due to its penetration into the central nervous system (CNS). Levofloxacin and trimethoprim/sulfamethoxazole are other suitable prophylaxis alternatives for patients who are allergic to cephalosporins.

Group of Extended Skull Base Surgery

We studied 54 patients (66% females; mean age 47.7 ± 15.5 years; range: 22–82 years) with various skull base
pathologies who underwent resection through extended endoscopic surgery.

Reconstruction Technique
Before starting the operation we proceeded to place a lumbar drain and obtain suprapubic fat, especially in those cases where a high output fistula was expected. We prepared the nasoseptal flap (Hadad flap) at the start of surgery and prior to resecting the tumour, in order to avoid damaging the septal mucosa and the nasoseptal artery. We placed pledgets soaked in vasoconstrictor and subsequently injected lidocaine and epinephrine into the nasal septum using a number 22 lumbar puncture needle. The side and the size of the flap depended on the expected size of the defect and the location of the tumour. The flap was moved towards the nasopharynx and protected with a pledget while the tumour resection was carried out. In clival and nasopharyngeal tumours, the nasoseptal flap interfered with the surgical site so we carried out an extensive antrostomy of the maxillary sinus, where it was placed temporarily.

Following a standard protocol, once the tumour excision and thorough review of hemostasis were completed, suprapubic fat was placed in an intracranial position to fill the dead space between the dura mater and the underlying tissue. The fat was coated with lyophilised fascia lata (TSF, Barcelona) in an underlay position, that is, between the fat and above the dura mater (epidural). Next, the flap was replaced over the fascia lata and directly over the edges of the bone defect. It is important to avoid leaving foreign bodies (splinters, for example) between the defect and dura mater, as this may prevent closure. The use of fibrin glue may help the closure, but it is not required. The reconstruction was surrounded by fragments of Surgicel© or a similar agent, especially at the edges of the flap in contact with the bone defect in order to promote the growth of granulation tissue. Nasal packing was covered with the finger of a glove impregnated in antibiotic ointment so as to prevent the formation of adhesions (Fig. 2).

Group of Non-Extended Skull Base Surgery
The group included 62 patients (52% females; mean age: 48.8±14.1 years; range: 20–80 years) suffering from CSF fistula. A detailed medical history and a thorough nasal endoscopic examination were important for the diagnosis. Repeated otomicroscopic exploration associated with the Valsalva manoeuvre was essential to avoid confusion with fistulas of the middle ear with an outpour of CSF through the Eustachian tube. The most common symptom was unilateral rhinoliquorrhea. However, this finding was bilateral.

Figure 1 Algorithm for the diagnosis and management of cerebrospinal fluid fistulas.

![Figure 2](Image 350x98 to 519x268) Skull base reconstruction through pedicled nasoseptal flap.
in five patients due to a location of the fistula in the sphenoid sinus (n=4) or to a history of septal perforation (n=1). A total of 20 cases (32%) reported a history of bacterial meningitis and two patients reported recurrent meningitis. All patients with suspected spontaneous fistula were referred to the ophthalmologist of our centre in order to rule out intracranial hypertension.

Reconstruction Technique
We injected 1ml of 5% sodium fluorescein intrathecally 1h before surgery. Fluorescein helps to identify the bony defects of the skull base associated with CSF fistulas. Once the fistula was located, the surrounding mucosa was removed and the bone edges of the defect were identified. Some millimetric fistulas required the defect to be slightly extended in order to perform the reconstruction. In cases of meningocele or meningoencephalocele we removed the tissue by means of bipolar cautery until we reached the level of the skull base. The fascia lata (TSF, Barcelona) was placed in an underlay position and covered by a mucoperiosteal graft of the middle turbinate (in cases where it was resected to locate the fistula) or the inferior turbinate (Fig. 3). In some cases, it was difficult to place the fascia lata in an underlay position, especially in the cribriform plate and facing the crista galli, so we secured at least the lateral edges to attach the fascia, either in an inlay or overlay position (Figs. 4 and 5). The mucoperiosteal graft was supported at the defect site by oxidised cellulose sheets, followed by anterior packing covered with a glove finger soaked in antibiotic ointment as a fixing method. We did not use any fibrin glue or Foley probe and did not indicate lumbar drainage in any case of CSF fistula within this group.

Results

Group of Extended Skull Base Surgery (n=54)
All patients with skull base pathologies underwent complete radiographic studies with computed tomography (CT) and magnetic resonance imaging (MRI). The surgical approaches were selected according to the location of each tumour, with the most frequent being transcribiform, transubcicular/transplanar, transclival and ethmoid-pterygo-sphenoidal (Table 1). The nasoseptal flap was prepared on the left side in 42 cases (78%), depending on the condition of the nasal septum or the location of the tumour. No case of pituitary adenoma required a nasoseptal flap, so no adenoma patients were included in this study. Patients remained in total bed rest for 72 h with antibiotic and antithrombotic prophylaxis. They were advised to sneeze with an open mouth and avoid blowing their noses, and the use of laxatives was recommended in some cases to avoid an increase in abdominal pressure. The plugging was removed after 24–48 h and the lumbar drain after 72–96 h as long as there were no signs of an active fistula. CT and MRI scans were obtained at 24 h to rule out pneumocephalus and intracranial bleeding. In cases with suspected rhinoliquorrhea after removing the nasal packing we performed intrathecal injection of fluorescein through the lumbar drain.

![Figure 3](image1.png)  
**Figure 3** Skull base reconstruction through underlay *fascia lata* covered by a free graft of middle or inferior turbinate mucoperiosteum.

![Figure 4](image2.png)  
**Figure 4** Skull base reconstruction through inlay *fascia lata* covered by a free graft of middle or inferior turbinate mucoperiosteum.

![Figure 5](image3.png)  
**Figure 5** Skull base reconstruction through overlay *fascia lata* covered by a free graft of middle or inferior turbinate mucoperiosteum.
Table 1  Type of Lesion and Approach Carried Out by Endoscopic, Skull Base Surgery.

<table>
<thead>
<tr>
<th>Extended transnasal approach</th>
<th>Diagnosis</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcribiform</td>
<td>Olfactory sulcus meningioma</td>
<td>2</td>
</tr>
<tr>
<td>Transcribiform</td>
<td>Esthesioneuroblastoma</td>
<td>2</td>
</tr>
<tr>
<td>Transcribiform</td>
<td>Sinonasal carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Transtubercular/transplanar</td>
<td>Meningioma of the planum sphenoidale</td>
<td>5</td>
</tr>
<tr>
<td>Transtubercular/transplanar</td>
<td>Craniofaryngioma</td>
<td>6</td>
</tr>
<tr>
<td>Transtubercular/transplanar</td>
<td>Skull base sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Transtubercular</td>
<td>Tubercular meningioma</td>
<td>4</td>
</tr>
<tr>
<td>Transtubercular</td>
<td>Rathke cyst</td>
<td>2</td>
</tr>
<tr>
<td>Transtubercular</td>
<td>Suprasellar adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Transtubercular</td>
<td>Polycystic astrocytoma</td>
<td>1</td>
</tr>
<tr>
<td>Transclival</td>
<td>Chordoma</td>
<td>7</td>
</tr>
<tr>
<td>Transclival</td>
<td>Chondrosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Transclival</td>
<td>Myxofibrosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Transclival</td>
<td>Fibrous dysplasia</td>
<td>1</td>
</tr>
<tr>
<td>Transclival</td>
<td>Inflammatory pseudotumour</td>
<td>1</td>
</tr>
<tr>
<td>Transclival</td>
<td>Petroclival meningioma</td>
<td>3</td>
</tr>
<tr>
<td>Transclival</td>
<td>Cavity tumour with extension to the clivus</td>
<td>2</td>
</tr>
<tr>
<td>Transclival</td>
<td>Squamous carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Ethmoid-pterigo-sphenoidal</td>
<td>Adenoma with extension to cavernous sinus</td>
<td>3</td>
</tr>
<tr>
<td>Ethmoid-pterigo-sphenoidal</td>
<td>Neurofibroma</td>
<td>1</td>
</tr>
<tr>
<td>Transorbital</td>
<td>Neurofibroma</td>
<td>1</td>
</tr>
<tr>
<td>Transpalatal</td>
<td>Skull base teratoma</td>
<td>1</td>
</tr>
</tbody>
</table>

In total, five patients (9%) presented clear or incipient symptoms of meningitis. CSF leak was confirmed in all cases and resolved surgically through the use of flaps (3 patients with inferior turbinate pedicled flaps and two patients with nasal fossa floor rescue flaps). No recurrences of CSF fistulas were observed during the long-term follow-up (mean: 15.6±12.4 months; range 6–62 months).

Group of Non-Extended Skull Base Surgery (n=62)

All patients underwent a CT scan of the paranasal sinuses and skull base. In cases of suspected meningocoele or meningoencephalocele we also requested a cranial MRI. Until 2005, CSF fistulas were confirmed by the presence of beta-2 transferrin. After this date, we used a beta-trace kit to confirm fistulas, as the concentration of these proteins presents high sensitivity and specificity.

The most common cause of CSF fistulas was spontaneous, in almost half the cases, followed by traumatic andiatrogenic (Table 2) causes. Regarding location, half the cases were located in the cribiform plate, followed by the ethmoid, sphenoid and frontal sinuses (Table 3). The size of the defects ranged between 2 and 20 mm. We used 5% intrathecal fluorescein (very slow administration) in all cases (in the non-extended surgery group); only two patients presented transient severe headaches and one patient suffered mild weakness and paresthesias of the lower limbs in the immediate postoperative period which were resolved spontaneously without sequelae. The onlay technique (placement of reconstruction material between the dura mater and the bone of the skull base) was the most commonly used technique (59 patients; 95%), whilst the inlay and/or overlay (placement of the reconstruction material on the dura mater) was used in the remaining cases. We consider that both the fascia lata and the mucoperiosteal grafts should exceed the edges of the bone defect by about 2–5 mm in order to promote healing and prevent recurrence of the fistula. Hosemann et al. recommended mucoperiosteal grafts to be made at least 20% larger than the defect, as the healing process entails some shrinking.

Table 2  Most Frequent Aetiologies of Cerebrospinal Fluid Fistulas.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>30 (48.4)</td>
</tr>
<tr>
<td>Trauma</td>
<td>15 (24.2)</td>
</tr>
<tr>
<td>Iatrogenic/postoperative (ESNS)</td>
<td>5 (8.1)</td>
</tr>
<tr>
<td>Benign tumour (osteoma, mucocele, inverted papilloma)</td>
<td>5 (8.1)</td>
</tr>
<tr>
<td>Meningocele</td>
<td>3 (4.8)</td>
</tr>
<tr>
<td>Iatrogenic/postoperative (septorhinoplasty)</td>
<td>2 (3.2)</td>
</tr>
<tr>
<td>Congenital (meningoencephalocele of the Sternberg canal)</td>
<td>2 (3.2)</td>
</tr>
<tr>
<td>ESNS: endoscopic sinonasal surgery</td>
<td></td>
</tr>
</tbody>
</table>

Table 3  Locations of Cerebrospinal Fluid Fistulas.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cribriform plate</td>
<td>31 (50)</td>
</tr>
<tr>
<td>Anterior ethmoid sinus</td>
<td>13 (21)</td>
</tr>
<tr>
<td>Posterior ethmoid sinus</td>
<td>7 (11.3)</td>
</tr>
<tr>
<td>Sphenoid sinus</td>
<td>8 (12.9)</td>
</tr>
<tr>
<td>Frontal sinus</td>
<td>3 (4.8)</td>
</tr>
</tbody>
</table>
Complete closure of the fistula was achieved in 61 patients (98.4%). One patient presented signs of meningitis 2 weeks after surgery. Persistence of the CSF leak was confirmed, so the patient was reoperated for closure with no complications. Long-term follow-up lasted for 75.3±51.3 months (range: 6–177 months), with no evidence of recurrence of the CSF fistula.

Discussion

Our series had a 91% success rate in the first surgeries of large defects and 98% in small and medium defects, along with 100% for second interventions (or rescue surgery). Skull base defects secondary to extended endoscopic surgery were evident intraoperatively and did not require further diagnostic tests. Faced with a suspected CSF fistula with a different cause, we performed a thorough medical history including history of trauma, prior surgery and meningitis. Endoscopy may occasionally identify pulsating light reflex in the area of the fistula or a mass occupying the nostril with the suspected meningocele or meningoencephalocele. In cases of low pressure and intermittent fistulas, the examination may be completely normal. The biochemical study of nasal secretions enables a differential diagnosis, mainly with rhinorrhea secondary to chronic rhinitis which can cause similar symptoms to those described. In a review of 39 works published in the literature on the usefulness of certain tests, such as beta-trace protein and beta-2 transferrin, Bachmann-Herlisdorf proved them to be useful for diagnosing the presence of CSF. The beta-trace test has high specificity and sensitivity and is faster (20 versus 120 min) and less expensive.

We obtained high resolution CT scans of the paranasal sinuses of all patients (1 mm axial sections, with coronal and sagittal reconstructions). We believe that this radiographic examination is essential for diagnosis and to plan the surgical approach, as it offers details about bone structure. Furthermore, it sometimes allows the defect to be identified, associated or not to occupation of the affected sinus by soft part density. MRI scans are reserved for cases where the CT indicates extensive occupation by soft tissues, as in the case of meningocele and encephalocele, and when an expansive lesion is suspected.

The use of intrathecal 5% fluorescein as a diagnostic method and its intraoperative use to locate the defect and verify the closure of the fistula during surgery has been very helpful since its introduction by Kirchner in 1961. Intrathecal fluorescein was used as a diagnostic test in two cases of suspected fistula in which scarce or no CSF leakage made the biochemical study of the liquid impossible. Both cases presented an absence of fluorescein in the nasal cavity and skull base, so both were discarded from this study. In our series there were no serious complications following intrathecal administration of fluorescein, except for two cases reporting headaches and weakness of the lower limbs, respectively, which were resolved spontaneously without sequelae. A survey conducted among rhinologists revealed that the usual dose of fluorescein employed ranged between 0.5 and 1.0 ml, with a concentration of 10%, whilst another study demonstrated good efficacy with doses as low as 0.1 ml at 10%. Fluorescein injections do not normally cause any complications. When they do, they are related to high concentrations or administrations at a greater speed than recommended. Severe complications (epileptic crises, opisthotonos, peripheral paralysis) are always related to the direct chemical irritant action of fluorescein due to an overdose, as Symes et al. pointed out in an experimental study conducted with dogs.

It is worth highlighting that intrathecal application of 5% fluorescein is not contemplated in its prospectus. It is therefore important to obtain informed consent in writing from patients.

The most common aetiology of CSF fistulas in our series was spontaneous (48.4%), followed by trauma (24.2%), whilst the most common location was the cribiform plate (50%), followed by the anterior and posterior ethmoid (32.3%). In a literature review of 55 works which included 1778 fistulas repaired endoscopically, we found that the fistulas were generally distributed equally among traumatic (50.2%) and non-traumatic (49.8%) causes. In addition, we observed that spontaneous fistulas were the most common type, accounting for 41.1%, followed by postoperative (30.1%), trauma (23.2%), those related to tumours (5%) and those with congenital causes (3%).

Regarding our surgical repair technique, we highlight the use of the underlay technique in 95% of the cases and the inlay and/or overlay in the remaining cases. In the underlay technique, the dura mater was separated from the edge of the bone defect in the skull base to serve as a support framework to stabilise the graft. Mucosa from the middle or inferior turbinate as a free graft was used in all cases of small and medium bone defects. These grafts are simple to obtain and generate scarce morbidity at the donor site. In their metaanalysis of a total of 289 CSF fistulas, Hegazy et al. showed that both techniques had similar results and that mucosal grafts were used in 50% of the repairs, whereas fat was only used in 19%. The overlay technique is recommended for cases where there is a risk of nervous or vascular injury when dissecting the dura mater. In such cases, the graft is placed over the exposed bone margins of the mucosa.

In cases of extended surgery, the nasoseptal flap was conducted by the same otolaryngologist on the left side of the nasal septum in 78% of the patients. The following factors were considered when assessing the side from which to take the flap: preference of the surgeon, amplitude of the nostrils, possible anatomical abnormalities (septal deviation or spur), and the side with a greater possibility of vascular involvement of the flap by lateral extension of the surgical field. Recent studies have demonstrated the negative impact of these flaps on sinonasal symptoms, especially smell, mucociliary transport and quality of life. At present, we pay greater attention to these factors and modify the superior section of the nasoseptal flap in order to avoid damaging the olfactory mucosa. Furthermore, we also perform reverse flaps with contralateral mucoperichondrium to cover the bared cartilage.

The use of lumbar drainage remains controversial. In our series we only employed lumbar drains in patients with large defects following skull base surgery, and only as a measure to decrease the CSF pressure, which seemed to favour graft fixation.

On the other hand, the surgical procedure of lumbar drain placement has already been conducted if
intrathecal fluorescein has been injected, although its use is not without risks, such as headache, nausea, meningitis or pneumocephalus. 

55 Up to 67% of otolaryngologists surveyed used lumbar drainage routinely in the management of CSF fistulas. 

In a metaanalysis of 1568 CSF fistulas with a total of 761 lumbar drains, drainage duration varied from 1 to 10 days, although most studies used it between 2 and 5 days, as in our series. Unfortunately, the benefit of lumbar drainage cannot be calculated using the limited data provided by the studies reviewed. 

In our series we used ceftriaxone for 5–7 days in both groups due to its high penetration into the CNS. The effectiveness of prophylactic antibiotic therapy has not been proven by randomised studies, although it could be a reasonable attitude given the possible transmission of bacteria from the nasal cavity. In a review of 24 studies, 23 reported administering antibiotics routinely, four only perioperatively, whereas in 19 cases antibiotics were used between 2 and 14 days, especially in cases with lumbar drainage and nasal block. 

Wigand and Hosemann were the first to describe the complete closure of CSF fistulas. 

Subsequently, Hegazy et al. analysed 14 studies published between 1990 and 1999. Primary success rates for these studies ranged between 60% and 100%, with a mean value of 90%. In a recent review of 55 published studies on the closure of CSF fistulas, Psaltis et al. found a high rate of overall success of repair (90% for primary and 97% for secondary repairs), along with a low complication rate, less than 0.03%. In a recent meta-analysis, Harvey et al. concluded that current scientific studies suggested that the reconstruction of the skull base with vascularised tissue was associated with a lower rate of CSF leaks (6.7%) compared with free tissue grafts (15.6%) and reported similar closure rates to those obtained with open surgery. At present, several studies have concluded that endoscopic closure of CSF fistulas is safe and effective and should be considered the standard treatment for most cases.

Conclusion

Our study confirms that endoscopic sinus surgery is safe and very effective for the closure of CSF fistulas of any defect. Underlay fascia lata grafts and middle or inferior turbinate mucoperiosteum grafts placed on the fascia are able to repair fistulas and small and medium skull base defects. Vascularised nasoseptal flaps are the most adequate for reconstruction of large defects following advanced skull base surgery. Antibiotic therapy was used in all patients, whilst lumbar drainage was only employed for large defects.

Conflict of Interests

The authors have no conflict of interests to declare.

References


Management of Cerebrospinal Fluid Leaks

