

## RHINOLOGY

# Transnasal endoscopic treatment of cerebrospinal fluid leak: 17 years' experience

## *Il trattamento transnasale endoscopico di fistola liquorale: 17 anni di esperienza*

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## SUMMARY

Aim of this report is to describe the long-term results of endoscopic endonasal repair of cerebrospinal fluid leak using a septal mucoperichondrial graft. A case series of 52 patients operated for cerebrospinal fluid rhinorrhea between 1990 and 2006 is presented. All patients underwent surgical treatment for endoscopic endonasal closure of a cerebrospinal fluid leak using a septal mucoperichondrial graft. No lumbar drain and fluorescein tests were used. The intra-operative localization of the fistula was aided by Valsalva's manoeuvre by the anaesthetist. The success rate, after the first attempt, was 88.5% (46/52 patients); for the remaining 11.5% (6/52 patients), a second attempt was necessary which proved successful in 5 cases, raising the overall success rate to 98.1% (51/52 patients). Relapse occurred in only one case (1.9%), after the second attempt. In conclusion, a free mucoperichondrial graft offered good results for cerebrospinal fluid leak repair. In the Authors' experience, a high success rate can be achieved without the use of intrathecal fluorescein and lumbar drain.

KEY WORDS: Cerebrospinal fluid leak • Endoscopic treatment • Septal mucoperichondrial graft • Intrathecal fluorescein • Lumbar drain

## RIASSUNTO

*Lo scopo del nostro lavoro è quello di descrivere i risultati a lungo termine di riparazione endoscopica di fistole rinoliquorali mediante l'utilizzo di lembo mucopericondrale di setto nasale. Una casistica di 52 pazienti operati di fistola rinoliquorale tra il 1990 e il 2006 è presentata. Tutti i pazienti sono stati sottoposti a plastica di fistola rinoliquorale con tecnica endoscopica mediante l'utilizzo di lembo mucopericondrale prelevato dal setto nasale. Il drenaggio lombare e il test alla fluoresceina non sono stati mai utilizzati. L'identificazione intraoperatoria della sede della fistola è stata agevolata grazie alla manovra anestesiológica di Valsalva. Il successo operatorio è stato dell'88,5% (46/52 pazienti) dopo il primo intervento; per il restante 11,5% (6/52) si è reso necessario un secondo tempo chirurgico che è risultato risolutore in 5 casi, determinando un successo chirurgico del 98,1% (51/52 pazienti). In un solo caso (1,9%) si è rilevata la persistenza di fistola anche dopo il secondo tempo. In conclusione il lembo libero mucopericondrale di setto offre ottimi risultati per la riparazione della fistola rinoliquorale. Nella nostra esperienza, un'elevata percentuale di successo può essere ottenuta anche senza l'utilizzo del test alla fluoresceina e del drenaggio lombare.*

PAROLE CHIAVE: *Fistola rinoliquorale • Trattamento endoscopico • Lembo mucopericondrale • Test della fluoresceina • Drenaggio lombare*

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## Introduction

Cerebrospinal fluid (CSF) rhinorrhoea occurs from the breakdown of the barriers separating the nasal cavities from the subarachnoid spaces: skull base, *dura mater* and arachnoid membrane. Aetiologically, the causes of CSF rhinorrhoea can be classified as: traumatic, iatrogenic, congenital, neoplastic and idiopathic. The main symptom is the constant and uncontrollable unilateral watery rhinorrhoea. Surgical treatment is advised since this condition significantly increases the risk of meningitis and encephalitis<sup>1</sup>.

Since 1981, when Wigand<sup>2</sup> employed a transnasal endoscopic approach for the first time to repair anterior cranial base CSF rhinorrhoea, a growing number of Authors have performed the technique reporting a satisfactory success

rate<sup>3</sup>. A key point in this kind of surgery is the correct identification of the site of the CSF leak, and the intra-operative use of intrathecal fluorescein is often used for this.

In the literature, a variety of materials have been used for endoscopic endonasal repair: septal mucoperiosteal or mucoperichondrial grafts, free<sup>4</sup> or pedunculated<sup>5</sup>, middle turbinate<sup>6</sup>, *temporalis fascia*<sup>7,8</sup>, *fascia lata*<sup>9</sup>, or septal cartilage grafts<sup>10</sup>.

A retrospective report on surgical activity, covering the last 17 years, is presented, comprising 52 patients who underwent endoscopic endonasal repair of CSF leak performed using a mucoperichondrial graft from the septum, and without the use of intrathecal fluorescein and lumbar drain.

## Material and Methods

From January 1990 to December 2006, 52 patients underwent plastic surgery for a CSF by the same surgeon (L.P.). The aetiology of CSF leak was traumatic (car accident, blows and horse accident) in 16/52 (30.8%), iatrogenic (polypectomy, functional endoscopic sinus surgery and removal of hypophysary adenoma, fronto-basal meningioma and ethmoido-sphenoidal osteoma using a craniotomy approach) in 23/52 (44.2%) and spontaneous in 13/52 (25%).

Of these patients, 32 were male, 20 were female, median age was  $46.5 \pm 16.1$  years (age range 10-67 years for males and 15-64 for females).

The most common location of the defect, in this cohort, was the anterior ethmoid in 26/52 (50%) (12 lateral lamella, 10 cribriform plate and 4 ethmoid roof), followed by sphenoid sinus in 12/52 (23.1%) (5 lateral table, 5 posterior table, 2 sphenoid roof), posterior ethmoid in 9/52 (13.3%) and multiple in 5/52 (9.6%) (4 sphenoidal, 1 involving the ethmoid and orbital roof) (Table I).

The most frequent onset symptom was unilateral watery rhinorrhoea in 51/52 (98%) associated with pneumocephalus in 3/52 (5.8%), meningocele in 8/52 (15.4%) and meningoencephalocele in 11/52 (21.1%).

Overall, 17 patients (17/52: 32.7%) reported one or more meningitis episodes. In any patient of our case series an elevated intracranial pressure was relieved. The diagnostic algorithm for all patients was pre-operative nasal endoscopy,  $\beta$ -trace protein test (followed by a  $\beta$ -2-transferrin test in cases in which a doubt remained concerning interpretation), and 1 mm Computed Tomography (CT) scan slices of paranasal sinus and anterior cranial base in the axial and coronal plane. Magnetic Resonance (MR) was performed only in the case of meningocele and meningoencephalocele, identified by endoscopic exam or suspected on high-resolution Computed Tomography (HRCT).

All patients underwent cranial base plastic surgery through an endoscopic endonasal approach.

The surgical intervention was carried out under general anaesthesia; a preliminary local anaesthesia was performed by contact with a mixture of local anaesthetic and vasoconstrictor (Xylocain® 5% with naphazoline). 0° and 30° optics were used. With this technique anterior and posterior ethmoidectomy are performed with sacri-

fice of the middle turbinate. An intra-operative increase in intra-cranial pressure, as a result of a Valsalva's manoeuvre performed by the anaesthetist, helped the surgeon in the intra-operative identification of the site of the leak.

As a result, the intra-operative intra-thecal fluorescein test was not performed. Once dehiscence was located, the surrounding area was demucosized. A septal mucoperichondrial graft, of suitable dimensions, from the contra-lateral nasal fossa, was positioned with the overlay technique to cover the bony dehiscence region and later reinforced with gelatin sponge (Spongostan®), fibrin glue (Tissucol®), or oxidized regenerated cellulose (Tabotamp®).

In 3 cases, bone reinforcement from the middle turbinate of the vomer or perpendicular ethmoidal lamina was necessary, placed with the underlay technique, due to large defects (> 3 cm) associated with the presence of meningo-encephalocele. Nasal packing (Lyfoam® strips) was carried out, in all patients, and removed on the third post-operative day.

Post-operative management was based on diuretics (Acetazolamide 250 mg/day) and antibiotics, both for 5 days. Bed rest, in the supine position, with reverse-Trendelenburg (20-25°) was required for 72 h.

All patients were discharged after 72-96 h. Follow-up of asymptomatic patients consisted of evaluations once a month for the first 3 months, then twice yearly for the first year, and once yearly for the following 2 years. The mean follow-up was  $47 \pm 12.6$  months.

An Institutional Review Board approval was not requested as use of an endoscopic technique with mucoperichondrial graft has already been reported in the international literature. Moreover, although the use of fluorescein is a codified procedure in the international literature, its intrathecal use has not yet been approved by the Italian Ministry of Health.

## Results

Definitive closure of the CSF was achieved in 46 patients (46/52: 88.5%) after the first attempt. Of these, 22/46 (47.8%) had an anterior ethmoidal fistula, 7/46 (15.2%) a posterior ethmoidal fistula, 12/46 (26.1%) a sphenoidal fistula and 5/46 (10.9%) a multiple fistula. Relapse occurred in 6 patients (6/52: 11.5%) (Table II).

**Table I.** Site and aetiology of leak.

Site of leak	Traumatic	Iatrogenic	Spontaneous	No. patients
Anterior ethmoid	6	12	8	26
Posterior ethmoid	2	4	3	9
Sphenoid	5	5	2	12
Multiple	3	2	0	5
Total	16	23	13	52

**Table II.** Cause of failure.

Patient	Site of leak	Aetiology	Time of relapse (days)	Alleged cause of relapse
A	Cribriform plate with meningoencephalocele	Traumatic	11	Too small graft
B	Lateral lamella	Iatrogenic	7	Poor compliance; complete separation
C	Ethmoid roof	Iatrogenic	25	Partial separation
D	Posterior ethmoid	Traumatic	32	Partial separation
E	Lateral lamella	Spontaneous	58	Partial separation
F	Posterior ethmoid	Spontaneous	47	Partial separation

All 6 cases underwent a second surgical approach to reinforce the graft with the same type of material with a successful result in 5. Therefore, to the present day, 51/52 (98.1%) showed no further disturbances while in one patient (patient B) (1.9%), rhinorrhoea was still present 2 months after the second surgical procedure: this patient showed a poor compliance, and did not respect the post-operative advice of bed rest and avoiding blowing his nose and relapsed again after the second surgical attempt. He did not return for follow-up 2 months after the second surgical attempt.

In none of the treated patients were any intra-operative or post-operative complications observed, either after the first attempt, or after revision.

## Discussion

The first surgical intervention for repair of cerebrospinal fluid leak was carried out by Dandy, in 1926, using an intracranial approach through a bifrontal craniotomy. Although this technique allowed direct access to the fistula and visualization of the dural lesion, morbidity and complication risks were high and the success rate was as low as 60%<sup>10</sup>.

Some 20 years later, in 1948, Dohlman<sup>11</sup> was the first to use the extracranial approach, through naso-frontal incision, which reduced the risk of complications and offered a success rate between 60% and 80%.

It was not until 1981, that Wigand<sup>2</sup> successfully performed CSF leak closure for the first time using endonasal endoscopy. Low morbidity and high success rates (90% after the first attempt and 95-98% after the second attempt) have currently made endonasal endoscopy the preferred surgical technique for anterior cranial base CSF leak treatment<sup>2</sup>.

With respect to conventional intracranial or extracranial methods, endonasal endoscopy has some advantages such as an excellent field of vision, allowing exact localization of the leak, a better evaluation and quantification of bony dehiscence size, an increased chance for the operator to remove mucosa from the bony dehiscence, an increased chance for the operator to place the most suitable graft for the kind of lesion, reduced invasiveness of the surgical procedure and consequently a reduction in patient hospitalization time.

Nevertheless, co-existence of intracranial surgical haematomas, comminuted or depressed fractures of the ethmoid and fractures extending to the orbital roof or in the posterior wall of the frontal sinus<sup>12</sup> represent limitations for the endoscopic approach, and indicate an intracranial approach.

There is complete agreement, in the literature, regarding surgical treatment of fistulas with persistent leaks. If indications exist, the operation must be performed as soon as the general clinical conditions allow it and after having performed all due diagnostic assessments, in order to demonstrate the presence of CSF rhinorrhoea and to identify with accuracy the exact site of the leak. Therefore, in the case of suspected CSF leaks, clinical presentation and office-based endoscopic nasal exam are of primary importance to demonstrate its presence.

Also of great diagnostic advantage are laboratory tests of nasal secretions with special regard to  $\beta$ -trace protein testing<sup>13,14</sup>, especially since a new immunologic test has been introduced allowing the identification of much smaller concentrations of this protein (representing the second most profuse protein found in CSF after albumin). The  $\beta$ -trace protein test is highly sensitive and offers advantages with respect to  $\beta$ -2 transferrin testing: it is faster (only 20 min vs. 120 min necessary for the  $\beta$ -2 transferrin electrophoretic test), has a higher specificity (98-100%) and is much less expensive<sup>14</sup>.

In the present case series, the  $\beta$ -trace protein test was performed in all patients and, in cases where there was a doubt about interpretation, the result was confirmed with the  $\beta$ -2 transferrin test.

An important part of the diagnostic process is also the definition of the exact location of the leak.

Concerning this aspect, imaging, particularly HRCT, plays an essential role. In fact, HRCT is able to identify even the smallest bone defect along the skull base with high sensibility and is indispensable in providing the surgeon with important information regarding anatomical bone variations and landmarks for correct planning of the surgical intervention.

All 52 patients, in this case series, underwent 1 mm CT scan slices of the paranasal sinuses and anterior skull base, performed in the coronal plane and then reconstructed in the axial and sagittal plane.

In addition, MR (with T2-weight sequences) can repre-

sent a useful neuroradiological investigation, providing evidence of the presence of meningeal and/or encephalic herniation. Moreover, thanks to the elevated intrinsic contrast between CSF and the surrounding tissue, revealing the limits of the CSF space correlated with the cerebral parenchyma can help in the identification and location of the CSF leak<sup>15</sup> (particularly with MR-cisternography<sup>16,17</sup>, that emphasizes and enhances the CSF signal with suppression and subtraction of the adjacent background tissue signal). In this study, MR has been performed only in those cases in which parenchymal or meningeal herniation was suspected following endoscopic examination or HRCT.

Thanks to accurate endoscopic office-based examinations and CT scan and, when requested, MR the site of the leak, identified in the pre-operative period, was confirmed intra-operatively in 47/52 (90.4%) patients (89% of cases). Regarding the intrathecal use of fluorescein, although its efficacy for identification of CSF leaks has been established in the literature<sup>4,16,18</sup>, its use still remains controversial for many reasons. This technique involves injection of sodium fluorescein solution, at a concentration of 0.5% to 5% (2.5-50 mg) into the subarachnoid space through a lumbar puncture. Approximately 30 minutes should be allowed for diffusion of the fluorescein throughout the CSF. The investigator then uses either a blue light or standard operative lighting to detect fluorescence in the surgical field.

The finding of a green-yellow fluid reveals the site of a CSF leak<sup>18</sup>. First of all, multiple complications have been reported by some Authors<sup>19-21</sup> after intrathecal fluorescein administration, including headache, nausea and vomiting, dizziness, nuchal pain, lower limb weakness, numbness, generalized seizure activity, opisthotonus and cranial nerve deficit; the Authors also reported that these complications appear to be dose-dependent and transient at a concentration of 5% or preferably lower; about this, the fluorescein used for intrathecal use must not be only sterilized but filtered to exclude any particulate matter present in the ophthalmic preparation. Moreover, with intrathecal injection of fluorescein, the surgical procedure takes longer not only due to the time taken to perform the lumbar puncture, but also the time required to allow diffusion of the fluorescein in the CSF.

Furthermore, the intrathecal injection of fluorescein needs an efficient anaesthesiologist who is familiar with the lumbar puncture as well as the potential complications of its use. To avoid the complications and the technical problems of intrathecal use, Jones et al.<sup>22</sup> mentioned the possibility of using topical intranasal fluorescein to intra-operatively locate the site of CSF leak. A few years later, Saafan et al.<sup>23</sup> focused on the development and validation of the use of topical fluorescein in the intra-operative localization of CSF fistula, and to screen its use in pre-operative diagnosis of CSF rhinorrhoea as well as post-op-

erative detection of recurrence. As already mentioned, in our case series, the pre-operative use of topical intranasal fluorescein has been replaced with HRCT and laboratory tests.

Also regarding the intra-operative localization of the CSF leak, although intrathecal fluorescein is now the most commonly used method<sup>4,16,18</sup> based on the previous considerations and supported by the fact that its intrathecal use has still not been approved by the Italian Ministry of Health, it was not employed at the beginning of our surgical activity.

In this regard, the intra-operative increase in intracranial pressure has greatly benefited the surgeon in the identification of the site of the leak, without important complications. This was achieved in all our patients, by an easy and safe Valsalva's manoeuvre performed by the anaesthetist, using a manual increments of intra-thorax pressure which determines congestion and stasis of the internal jugular veins and a consequent increase in intracranial pressure, and an increased outflow of CSF from the leak, which thus becomes more identifiable. This manoeuvre has also been useful to confirm intra-operatively the validity of adequate CSF closure.

As far as concerns the graft, results from an analysis of the literature show how the experiences of several Authors differ with respect to the use of different kinds of graft in CSF leak repair: mucoperiosteal free flaps from the middle turbinate<sup>24</sup>, pedunculated mucoperiosteal flaps<sup>5</sup>, temporalis fascia<sup>7,8</sup>, fascia lata<sup>9</sup> and septal mucoperichondrial free flaps<sup>4</sup> have been employed. The majority of the Authors agree with the use of composite osteomucosal or chondromucosal grafts for repair of defects > 3-4 cm<sup>3,10</sup>. In the present case series, 49 patients were treated using only a septal mucoperichondrial graft, with an overlay technique for repair: the addition of a bone graft, positioned with an underlay technique was used only in 3 cases, where the skull defect measured > 3 cm with an associated meningoencephalocele. The success rate, at the first attempt, was 43/49 (87.8%) with septal mucoperichondrial graft and 3/3 (100%) with composite osteomucosal graft. Such grafts have offered good results regardless of leak site and bone defect size. The essential condition to allow optimal take of the flap is the scrupulous demucosization of the CSF leak site in order to enable contact of the perichondrium of the flap with the cranial base bone. In 5/6 patients that needed a second surgical approach, the cause of relapse was attributed to local failure of the flap (complete or partial separation of the graft, or too small dimensions of the graft) (Table II), rather than a mistake in defect localization: this was confirmed at the second operation, where the site of the leak was, in all cases, confirmed. Five of these relapses were successfully treated with a second surgical approach, raising the overall success rate to 98.1% (51/52).

The only failure after the second attempt (Patient B) was

attributed to insufficient cooperation of the patient after the operation as well as to failure of the graft.

In none of the patients, in our case series, was a lumbar drain used. Lumbar drain is advocated by many Authors to reduce CSF pressure and the flow of leakage in the case of large fistulae, but the indications for a post-operative lumbar drain are not clearly defined in the literature. A lumbar drain is often used depending on the surgeon's preference and/or tradition<sup>5</sup>. For some Authors, the use of a lumbar drain could be useful in patients with a spontaneous CSF leak in which an elevated intracranial pressure is relieved<sup>25</sup>, but in none of our patients has an elevated intracranial pressure been detected.

Moreover, although it cannot be excluded, in the present series, that a transitory elevation of intracranial pressure could have been co-responsible for some relapses (mainly in spontaneous fistulae), the success rate after the second attempt seems to confirm that the cause of relapses could have been more likely attributed to a local failure of flaps. The overall success rates, after the first and second attempts, in our case series, are comparable or better than

those of the most recent series reported in the international literature.

## Conclusions

In the last few years, endoscopic endonasal treatment has become the surgical approach of choice for anterior cranial base CSF leak treatment with a high success rate and low invasiveness.

The aim of this report on our experience is to underline how a free mucoperichondrial graft from the nasal septum, placed using an overlay technique, can be a useful technique for CSF leak repair regardless of site and bony defect size.

It should be emphasized that good results (comparable with those of the international literature), can be obtained without the use of intrathecal fluorescein and lumbar drain, but the current study, despite the large case series obtained, does not offer sufficient methodological power to draw definitive conclusions. Only further studies, possibly with a control group, will be able to clarify this controversial issue.

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