

ARTICLE ONLINE FIRST

This provisional PDF corresponds to the article as it appeared upon acceptance.

A copyedited and fully formatted version will be made available soon.

The final version may contain major or minor changes.

## Management of anterior fossa cephaloceles: an overview

Vittorio RAMPINELLI, Davide MATTAVELLI, Marco FERRARI, Alberto SCHREIBER,  
Marco RAVANELLI, Davide FARINA, Alberto DEGANELLO, Marco FONTANELLA,  
Francesco DOGLIETTO, Piero NICOLA

*Journal of Neurosurgical Sciences* 2020 Dec 15

DOI: 10.23736/S0390-5616.20.05099-7

Article type: Original Article

© 2020 EDIZIONI MINERVA MEDICA

Article first published online: December 15, 2020

Manuscript accepted: December 1, 2020

Manuscript revised: November 6, 2020

Manuscript received: July 13, 2020

**Subscription:** Information about subscribing to Minerva Medica journals is online at:

<http://www.minervamedica.it/en/how-to-order-journals.php>

**Reprints and permissions:** For information about reprints and permissions send an email to:

[journals.dept@minervamedica.it](mailto:journals.dept@minervamedica.it) - [journals2.dept@minervamedica.it](mailto:journals2.dept@minervamedica.it) - [journals6.dept@minervamedica.it](mailto:journals6.dept@minervamedica.it)

## **Management of anterior fossa cephaloceles: an overview**

### **Running title**

Anterior skull base cephaloceles

### **Authors**

Vittorio Rampinelli<sup>1</sup>, Davide Mattavelli<sup>1</sup>, Marco Ferrari<sup>1,2</sup>, Alberto Schreiber<sup>1</sup>, Marco Ravanelli<sup>3</sup>, Davide Farina<sup>3</sup>, Alberto Deganello<sup>1</sup>, Marco Maria Fontanella<sup>4</sup>, Francesco Doglietto<sup>4\*</sup>, Piero Nicolai<sup>2</sup>.

### **Affiliations**

1 Unit of Otorhinolaryngology - Head and Neck Surgery, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

2 Section of Otorhinolaryngology – Head and Neck Surgery, Department of Neurosciences, University of Padua, Padua, Italy

3 Unit of Radiology, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

4 Unit of Neurosurgery, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

### **\* Corresponding author**

Francesco Doglietto, MD, PhD

Associate Professor

Unit of Neurosurgery, Department of Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia

Piazzale Spedali Civili 1, 25123 Brescia, Italy

Telephone number: +39 0303995587

Fax number: +39 0303995008

E-mail address: francesco.doglietto@unibs.it

## ABSTRACT

Skull base cephaloceles (SBCs) are defined as herniation of intracranial content through the skull base and are classified based on composition, etiology, and topographic location. Anterior SBCs frequently protrude in the sinonasal cavity, and consequently are at potential risk of infection. Therefore, the current recommendation is to treat SBCs with the primary intent of preventing meningitis, and surgery represents the mainstay of treatment. Anterior SBCs may display a wide spectrum of severity and complexity, and in each case the risks and benefits of surgical approaches are to be carefully weighted based on thorough assessment of symptoms, age, general conditions, location and size of the lesion, as well as expertise of the surgeon. In the last 30 years, the evolution and diffusion of transnasal endoscopic surgery have substantially changed the surgical management of the majority of SBC. In the past, they were treated exclusively with open transcranial approaches that may be burdened by relevant morbidity and risk for severe complications. The transnasal endoscopic corridor now provides easy access to the lesion and different reconstructive strategies using endonasal pedicled flaps, without any external incision, cranioplasty or brain manipulation. However, there are still scenarios in which an exclusive transnasal endoscopic route is contraindicated. The aim of the present review is to provide an overview on the comprehensive management of anterior SBC, with a particular focus on lesions suitable for endoscopic surgery. Furthermore, special aspects of SBC management in children and adults will be highlighted.

## KEY WORDS

**Skull base, cephalocele, CSF leak.**

## INTRODUCTION

The prevalence of intracranial content herniation through the skull is estimated to range between 1:10,000 and 1:2500,<sup>1</sup> with an unexplained higher rate in Southeast Asia compared to other geographical areas.<sup>2</sup> Herniations are classified according to topographic location, histological composition in terms of brain and meningeal tissue, and congenital *versus* acquired onset, but univocal consensus is lacking. In the present review, any herniation of the intracranial content through the skull will be defined as “cephalocele” (“cephalo-” referring to the skull and “-cele” to herniation). Although from a theoretical standpoint cephaloceles could be further classified in either encephaloces, meningoceles, or meningoencephaloces if, respectively, made up by only brain, only meninges, or both neural and meningeal tissues, this distinction would be irrelevant in terms of practical implications in most cases, since the treatment of the vast majority of skull base cephaloces (SBC) is independent of its content.

Cephaloces developing through certain areas of the skull base have the chance to reach a mucosa-lined air cavity early, which can be either the sinonasal tract, nasopharynx, or middle ear. This anatomical relationship can lead cephaloces to manifest through nasal and/or ear cerebrospinal fluid (CSF) leak, provided that the mucoperiosteal layer and meningeal sac spontaneously dehiscence at some point. Otherwise, the herniated tissue can become clinically appreciable through a mass effect or because of transmission of brain pulsation towards a non-air-containing area such as the orbit. The main concern when a cephalocele is diagnosed nearby a mucosal area is the risk for infectious meningitis, which can occur through ascending infection of the intracranial cavity by microbes in a mucosal cavity. In a series cumulatively analyzing 111 CSF leaks with different causes, the incidence of meningitis was 0.3 episodes/year, with most occurring within 1 year from leak onset.<sup>3</sup> Specifically focusing on CSF-leaking ethmoidal meningoencephaloces, Ziade *et al.* found that 30% of patients present with infectious meningitis.<sup>4</sup> The risk of meningitis in patients bearing nonleaking, incidentally found cephaloces is unknown. However, episodes of meningitis in patients with a nonleaking cephalocele lined by intact mucosa have been reported.<sup>5</sup>

Based on the aforesaid evidence, the current recommendation is to manage SBCs with the primary intent of preventing ascending meningitis, with surgery representing the mainstay of treatment.

Traditionally, SBC were treated with open transcranial approaches,<sup>6-8</sup> which are burdened by relevant morbidity and/or complications, such as significant blood loss, injury to the olfactory apparatus and supraorbital/supratrochlear nerves, brain manipulation, aesthetic impairment, and, with special reference to children, damage of bone growth centers.<sup>7</sup>

In the last 30 years, the evolution and popularization of transnasal endoscopic surgery (TES) have dramatically changed the surgical management of anterior and middle SBC, taking advantage from the enhanced collaboration between neurosurgeons and otolaryngologists.

The aim of the present paper is to provide an overview on the comprehensive management of anterior SBC, with a particular focus on those suitable for TES. Furthermore, even if formally belonging to middle skull base, SBCs herniating through the lateral wall of the sphenoid sinus will also be discussed. Aspects of SBC management in children and adults will be highlighted.

## CLASSIFICATION AND ETIOLOGY

SBC can be classified based on timing of development as congenital or acquired. Congenital cephaloceles result from incomplete closure of the neural tube during gestation and occur in approximately 1:3000-5000 live births.<sup>9</sup> Those encroaching on the sinonasal tract are especially sincipital (further divided in nasofrontal, nasoethmoidal, and naso-orbital) and basal (further divided in transethmoidal, sphenothmoidal, trans-sphenoidal, and frontosphenoidal) cephaloceles.<sup>10</sup>

Congenital cephaloceles can be found either alone or in the context of malformation syndromes,<sup>11</sup> whose discussion is beyond the aim of the present review. The causes of congenital cephaloceles are unknown. Familiar and geographical clustering would suggest a genetic predisposition, whereas association with low socioeconomic status, advanced maternal age, and long interpregnancy period hint unfavorable intrauterine environment as a potential cause.<sup>2,11</sup>

Acquired cephaloceles can occur through two main mechanisms (or via their combination): 1) increased intracranial pressure, and 2) newly-onset defect (or weakening) of the skull base. Idiopathic intracranial hypertension (IIH) perfectly fits this pathogenetic model, as it embraces both mechanisms by increasing CSF pressure while relentlessly enfeebling the weakest areas of the skull base through chronic pathological CSF pulsation. Acquired cephaloceles might represent a late manifestation of IIH causing an initially nonleaking herniation, as witnessed by the significant association between IIH and meningoceles.<sup>12</sup> On the other hand, patients with CSF early leaking through the skull base due to intracranial hypertension might represent an earlier manifestation of IIH with no frank herniation of intracranial tissues. An intermediate scenario is the “excavating meningoencephalocele”, a recently described entity consisting of a tunnel-like meningeal protrusion through the skull base, which possibly represent an early-leaking meningeal herniation.<sup>13</sup> Association between IIH and cephaloceles is also corroborated by the overlap in terms of risk factors, high body mass index (BMI), and female gender being the most relevant.<sup>4,14,15</sup> The prevalence of cephalocele in IIH patients treated for spontaneous CSF leak ranges from 69% to 97%.<sup>16,17</sup>

Less frequently, increased intracranial pressure or weakening of the skull base might result from other causes such as an intracranial mass,<sup>18,19</sup> previous surgery, and trauma,<sup>20-22</sup> respectively. Finally, some cephaloceles diagnosed in adult patients might also represent congenital herniation that remain unnoticed until adulthood. In fact, series on patients treated for a congenital cephalocele include subjects aged 18 or older.<sup>5-7</sup>

Classification of SBC according to subsite of herniation includes the cribriform plate, ethmoidal roof, posterior frontal plate, and sphenoidal walls. Distribution throughout these subsites is as follows: 40-100%, 6-40%, 9-71%, and 16-38%, respectively (**Figure 1**).<sup>4,6,7,23,24</sup> A remarkable difference in topographical distribution can be observed when comparing pediatric and adult series,

with the former being more frequently associated with frontal cephaloceles. Sphenoidal cephaloceles most frequently develop through the lateral wall, whereas other sphenoidal subsites (e.g. planum sphenoidale, tuberculum sellae, clivus) are involved with exceeding rarity.<sup>25-27</sup>

## CLINICAL PRESENTATION

SBCs manifest across a diverse clinical spectrum, which can vary from episodic rhinorrhea to large sinonasal or nasopharyngeal masses that can cause obstruction or craniofacial deformities. Etiology, size and site of the cephalocele, along with the age of the patient, largely dictate the clinical picture.

Overall, nasal obstruction, CSF rhinorrhea, and headache are the leading symptoms. In general, SBC manifest as pulsating, cystic masses protruding in the face (covered by skin), in sinonasal cavities and nasopharynx (covered by mucosa), or in the orbit. Furstenberg sign (i.e. increased swelling and pulsatility in association with Valsalva maneuver or jugular vein compression) is a simple but effective clinical finding to guide differential diagnosis.<sup>28</sup>

Congenital cephaloceles are usually large and can display a relevant mass effect leading to deformities of the nasal bones, maxillofacial skeleton and sinonasal structures (severe septal deviation and turbinates dislodgement). Sincipital cephaloceles are often more obvious, since they can be associated with external, visible pulsating masses and other craniofacial deformities, such as telecanthus.<sup>7</sup> Conversely, basal cephaloceles may be more insidious, and diagnosed at a later age. They usually present with nasal obstruction, but can be also associated with other conditions, including hypertelorism, facial clefts, and Morning Glory Syndrome (congenital optic disc dysplasia).<sup>29,30</sup>

In a recent study analyzing 15 congenital cephaloceles, the average age at diagnosis was six years, ranging from 2 months to 22 years, and the most frequent symptom was nasal obstruction. Associated anomalies were found in almost half of cases, with craniofacial deformities being the most frequent (30%). The majority of cephaloceles occurred at the foramen cecum and presented relevant dimension in view of the limited size of the craniofacial skeleton (mean diameter, 2.44 cm).<sup>7</sup> Fronto-orbital cephaloceles are almost exclusively congenital, and can cause proptosis, orbital displacement, pain, and interfere with eye-ball mobility (diplopia) and venous drainage (chemosis).<sup>7</sup>

Acquired cephaloceles more frequently occur in adults. In general, nasal obstruction has a marginal relevance, since cephaloceles tend to be smaller and do not impact nasal flow. The most important symptom is CSF rhinorrhea, followed by previous (or present) episodes of meningitis and persistent headache.<sup>14</sup>

Traumatic and iatrogenic cephaloceles can be easily ruled out with careful anamnesis. Spontaneous or idiopathic CSF leaks are almost invariably associated with increased intracranial pressure. IIH typically occurs in overweight women in their 5<sup>th</sup>-6<sup>th</sup> decade of life.<sup>31</sup> This epidemiological trait, together with a clinical history consistent for CSF leak, is highly suggestive for cephaloceles and warrants further clinical and radiological examinations. The diagnosis of IIH is



defined by the modified Dandy criteria (**Table 1**);<sup>32-34</sup> in particular, indirect radiological signs of intracranial hypertension (i.e. empty sella, enlargement of the space between the optic nerve and optic sheath) can strongly support the diagnosis before other invasive procedures are carried out (i.e., CSF opening pressure at lumbar puncture).

Noteworthy, IIH-induced CSF-leaks may show a valve mechanism, which translates into an intermittent leak that can delay correct diagnosis.

Meningitis may complicate the clinical condition in a non-negligible group of patients. Focusing on CSF-leaking ethmoidal meningoencephaloceles, Ziade *et al.* reported that 30% of patients present with infectious meningitis.<sup>4</sup> Furthermore, episodes of meningitis in patients with a nonleaking cephalocele lined by intact mucosa have been reported.<sup>5</sup>

## DIAGNOSTIC WORK-UP

The diagnostic work-up is aimed at: a) confirming the diagnosis of cephalocele; b) defining its size and site; c) establishing the etiology.

### Clinical examination

Careful inspection of the face and palpation are adequate to evaluate external cephaloceles and possible abnormalities of the maxillofacial skeleton.

In case of fronto-ethmoidal and basal cephaloceles, endoscopic endonasal evaluation has a pivotal role in confirming diagnosis and localizing the cephalocele. Congenital cephalocele are often more obvious and their location is easier to define. Conversely, acquired cephaloceles can be more subtle, and they can be so small that they can be hidden beneath the mucosa and be impossible to visualize.

The presence of CSF leak is a helpful hint to confirm diagnosis. From a clinical perspective, CSF is indistinguishable from serous nasal secretion unless an evident and high-flow leak is clearly detectable. Therefore, laboratory tests on fluid collection (i.e. identification of beta-2-transferrin or beta-trace protein) are invaluable tools to confirm CSF-leak.

Identification of the site of the meningoencephalocele can be challenging in case of very small defects.

In IIH induced cephaloceles, an important clue is provided by a non-random distribution of these defects in the ASB. In fact, they mostly occur at the level of the posterior portion of the cribriform plate, probably because the presence of olfactory foramina combined with the larger width of the olfactory cleft makes the bony skull base more susceptible to dehiscence.<sup>35</sup>

An interesting method to increase the efficacy of nasal endoscopy is intradural injection of fluorescein. In a retrospective series on 103 CSF-leak repairs, fluorescein was used in 47 patients, and showed 73.8% sensitivity and 100% specificity for detection of the leak site.<sup>36</sup> Sensitivity can be even higher with the use of a blue light filter, which allows for visual detection of fluorescein at 1 part in 10 million.<sup>37</sup> Being an off-label indication, proper patient consent is needed. Safety of lumbar fluorescein injection has been debated in the literature; however, authors' personal experience and other published evidence suggest that the specific risks related to fluorescein injection are minimal.<sup>33</sup>

Overall, clinical and endoscopic evaluations are useful to address diagnostic suspicion, but are rarely conclusive. It is of utmost importance to avoid any interventional procedure such as biopsy before a complete radiological workup has been concluded.

### Radiological diagnosis

Radiological examinations are imperative to confirm diagnosis and define the content of the cephalocele, detect its location, and suggest a possible etiology. Furthermore, a combination of different radiological techniques is usually required.

High-resolution computed tomography (HRCT) and magnetic resonance (MR) with or without contrast medium are the mainstay in the diagnostic workup.

HRCT is highly effective in the study of the bony skull base, and can detect even millimetric bony defects. In a retrospective study on 42 CSF leaks, the site of the skull base defect was identified preoperatively by HRCT in all cases, with successful intraoperative detection via intraoperative image guidance.<sup>38</sup> Conversely, the drawbacks are exposure to ionizing radiation, and the impossibility to distinguish between skull base dehiscence and skull base defect with cephaloceles, as a consequence of its low capability of soft tissue discrimination (risk of false positive). The latter issue is brilliantly resolved by combining HRCT with MR.

The great advantage of MR is the power to discriminate between brain tissue, CSF, and nasal secretion by combining T2-weighted, three-dimensional (3D) constructive interference in steady state (CISS) and fluid attenuated inversion recovery (FLAIR) sequences. In particular, image contrast in 3D-CISS is characterized by a high T2-T1 ratio, i.e. tissues (like fat and water) with both long T2 and short T1 relaxation times have increased signal intensity. This allows for an excellent contrast between CSF (hyperintense) and other structures; other relevant advantages of this sequence are high signal-to-noise ratio, high contrast-to-noise ratio, and intrinsic insensitivity to motion.<sup>39,40</sup> In FLAIR, the signal of CSF is suppressed and will appear completely black, while the brain is predominantly gray and the mucosa hyperintense. Therefore, the combination of 3D-CISS and FLAIR is extremely useful to detect the site of the cephalocele and to define its content.

Other relevant advantages of MR are the absence of radiation (important in young patients or in case of repeated examinations) and the ability to rule out possible causes of cephalocele (brain tumors, IIH, thrombosis of the dural sinuses, etc.). Overall, the combination of HRCT and MR can resolve the vast majority of suspected cephaloceles.

Accordingly, CT and MR cisternography should be considered as second-line examinations for very selected cases, in view of the need for an intrathecal injection of contrast medium via a lumbar puncture. CT cisternography is 85% sensitive for active leaks, but this can decrease to 48% in case of intermittent leakage.<sup>33</sup> Performance of MR cisternography are better, with 100% detection rate for continuous leaks, and 70% for intermittent ones.<sup>40,41</sup> A common drawback of these two tests is the dependence on contrast medium diffusion in CSF, with a risk of false negativity in case of poor distribution.

As previously stated, the most critical scenario in terms of diagnosis is intermittent CSF leak. To increase diagnostic accuracy, radionuclide cisternography has been proposed and investigated. This examination is based on the intrathecal injection of technetium-99; the detection of a possible leak may last several days, and theoretically this should allow capturing even intermittent or low volume leakage. However, preliminary results are discouraging. First, spatial resolution is very poor, which limits an effective localization of the defect. In addition, sensitivity is quite low, ranging between 62% and 76%, while the false positive rate is not negligible (33%).<sup>33</sup>

## SURGICAL TREATMENT

Surgery is the mainstay of treatment of SBC. To date, TES is the preferred surgical strategy to address basal and sincipital cephaloceles that are not associated with craniofacial deformity and do not show far lateral extension.<sup>42</sup> In a systematic review of 1178 patients from 71 studies, Komotar *et al.* reported no significant difference in the rate of successful repair of skull base defects when comparing open and endoscopic cohorts.<sup>43</sup> Complications and mortality were significantly lower in the endoscopic group, most probably because brain retraction is avoided and neurovascular manipulation minimized.<sup>43</sup> Moreover, skin incision and large craniotomies are avoided, resulting in negligible cosmetic alterations.<sup>33,43</sup> TES has also been associated with lower costs compared to open surgery.<sup>44</sup>

Despite these indisputable advantages, some perils of TES have to be highlighted, with special reference to pediatric patients. In contrast to adults, pediatric sinonasal anatomy can substantially restrict the working space for surgical instrumentation. Children may also lack key anatomical landmarks as a consequence of early-stage pneumatization of craniofacial bones, and performing surgery requires a thorough understanding of age-dependent structural patterns.<sup>6,45</sup> For instance, sphenoid sinus pneumatization usually occurs 7 years after birth, thus invariably presenting a non-pneumatized sphenoid body if surgery is performed earlier.<sup>45,46</sup> Furthermore, surgeons must be mindful of potential damage to facial and skull growth centers, and in particular the sphenodorsal zone, which extends from the sphenoid septum to the nasal dorsum, being consequently at risk of impairment during TES.<sup>6,47,48</sup> Finally, endonasal pedicled flaps are smaller and possibly inadequate to reconstruct large, congenital defects. Despite these concerns, a number of studies have validated the feasibility of TES in children, showing satisfactory outcomes with low complication rates.<sup>6,7,45,47,48</sup>

While the paradigm continues to shift towards endoscopic approaches, there are still situations which contraindicate an exclusive TES. Sincipital congenital cephaloceles with external mass involving facial and nasal bones and traumatic encephaloceles accompanied with skull base multifracture and orbital/intracerebral complications require external approaches, yet frequently in combination with TES.<sup>42,49</sup> Furthermore, selected defects of the posterior frontal plate located nearby frontal recess can be addressed through TES, but an osteoplastic flap approach is needed for laterally and/or cranially located defects (**Figure 2**).<sup>42</sup>

The optimal surgical strategy has to be chosen based on extension, size, location of the lesion, and expertise of the surgical team (**Table 2**). The possibility to rely on different surgical approaches is pivotal, as well as being flexible and prepared to switch or add another approach when forced by

unexpected intraoperative findings. In this view, adequate preoperative counseling is of paramount importance.

## **Surgical timing**

Because of the rarity of SBCs and consequent paucity of sound data, the optimal timing for surgical intervention still needs to be fully defined.<sup>7</sup>

In children, presence of airway obstruction, CSF leak, meningitis, and pronounced facial deformities require prompt intervention.<sup>6,7</sup> On the other hand, in the absence of these risk factors, and in particular in case of newborns with limited blood reservoir, surgery can be delayed and the patient carefully followed.

In adults, active CSF leak and/or history of meningitis suggest the need for intervention, even if in the setting of nonurgent care.

Patients with small and asymptomatic SBCs, in the absence of any major contraindication to the surgical procedure, should undergo elective surgery, as the risk of developing infectious meningitis cannot be excluded.<sup>5</sup>

## **Endoscopic surgical technique**

### *Resection phase*

TES takes advantage of the corridor offered by the nasal cavities and paranasal sinuses to reach the skull base.<sup>50</sup> Cephaloceles can present in several areas of the skull base and the endoscopic corridor to expose the area of interest accordingly varies from case to case (**Table 2**). However, there are some surgical principles that are essential regardless of the endoscopic corridor employed.

The first phase of any procedure consists of a careful exploration of olfactory fissures, nasal meati, and nasopharynx, taking advantage of intrathecal fluorescein use in non-obvious cases, since multiple or hidden sources of CSF leak can be present simultaneously.<sup>33</sup>

A wide exposure of the area of the defect is pivotal. The base of the cephalocele (*i.e.* the area where the herniated tissue crosses the skull base) needs to be adequately exposed, which is achieved by removing the surrounding structures. The lesion should then be reduced or cauterized flush with the skull base, as herniated brain tissue is typically nonfunctional.<sup>33</sup>

Cephaloceles originating from the caudal aspect of the posterior frontal plate or through a patent and widened foramen cecum can be addressed endoscopically via a transfrontal approach,<sup>51,52</sup>

provided that lateral extension over the orbital cavity is limited (**Figure 3**). However, the surgeon needs to be prepared to switch to an open approach in far anteriorly located cephaloceles, with the frontal osteoplastic flap approach best addressing this anatomical area.

As illustrated above, the cribriform plate is the typical localization of SBCs in adults, most frequently in the posterior third, likely because of the lack of significantly thick bone buttress.<sup>35</sup> Herniations in the olfactory cleft can be addressed by sparing the ethmoidal complex. Wide SBCs of this area may force the need to perform a partial septectomy by removing the perpendicular plate of the ethmoid bone to expose the entire circumference of their base.<sup>33</sup> When the skull base defect includes the vertical portion of the cribriform plate and/or the ethmoidal roof, a more lateral access through the ethmoidal complex is required. For defects of the cribriform plate and ethmoidal roof, the middle and superior turbinate can be spared (and possibly used as source of vascularized flap)<sup>53-56</sup> if their insertion on the skull base is sufficiently far from the bone defect. Otherwise, middle and superior turbinectomy is necessary to adequately expose the skull base defect.

SBCs of the sphenoid sinus are managed through transsphenoidal approaches. The removal of the rostrum allows to gain exposure and working volume, both for lesions of the planum sphenoidalis (**Figure 4**), cranially, and the clivus, caudally,<sup>52,57,58</sup> while simple parasagittal sphenoidotomy usually does not provide proper cranial-caudal exposure. However, it is worth remembering that most sphenoidal SBCs herniate through the lateral wall, whose exposure is achieved by drilling the pterygoid root through a transethmoidal, transpterygoid approach.<sup>33,52,57,59-61</sup>

For uncommon cases of SBC involving the pterygopalatine or infratemporal fossa, the necessary wider exposure can be reached through a combined transsphenoidal-transmaxillary approach.<sup>59</sup>

Preservation of vascular pedicles is always highly recommended during the resection phase even though their use is not in the surgical plan, since they can be helpful to provide a back-up reconstruction in a possible revision setting. In particular, the septal branch of the sphenopalatine artery needs to be spared, possibly through a rescue flap.<sup>62</sup>

### *Reconstructive phase*

Reconstruction usually represents the most critical phase of the entire surgical procedure, as its failure would imply a postoperative CSF leak.

In every case, when preparing the reconstruction bed, the mucosa around the bone defect needs to be removed. In fact, there should be no overlap between the in-situ skull-base mucosa and the graft applied, which could result in suboptimal adhesion between reconstructive layers and

subsequent development of a mucocele.<sup>33</sup> The surrounding bone surface is to be flattened in order to improve adhesion of overlay covering materials.

The bone defect is usually widened beyond the limits of the dural opening to allow proper positioning of grafts for reconstruction. Grafting may be performed with underlay or overlay techniques, or through a combination of both.<sup>33</sup> Placement of an underlay graft for defects smaller than 4 mm may be difficult,<sup>33</sup> but for larger defects multi layer reconstruction is recommended in most circumstances to optimize the chances of success.<sup>63</sup>

Options for graft materials are numerous. Iliotibial tract, fascia lata, temporalis fascia, collagen matrix, cadaveric fascia, dermis, and pericardium are valuable materials as intradural and epidural layers. Fat can be used as transcranial plug in case of small defects,<sup>64</sup> as well as a filler for bone depression to flatten the surface where the extracranial layer is positioned (typically for SBC of the lateral wall of the sphenoid, with highly pneumatized lateral recess). A rigid graft may be indicated in a gasket-seal closure for large, high-flow, high-pressure defects.

Small SBCs no longer leaking after cauterization can be covered by a single overlay graft of fascia or mucoperiosteum. Bedrosian *et al.* proposed the interposition of a fat graft between these small defects and mucosal graft.<sup>33</sup>

There are many pedicled options for extracranial coverage. Nasoseptal flap (NSF) is the most frequently used, based on easy harvesting, reliability, and vast surface cover provided. It allows proper reconstruction of cribriform plate, fovea ethmoidalis, and sphenoidal walls. However, it is poorly adequate to cover defects of the posterior frontal plate. In the pediatric population, the application of NSF may be technically difficult due to the narrow nasal corridor. As such, it may be best reserved for older children, large defects, significant intraoperative CSF leak, or other high-risk situations.<sup>6</sup>

In addition to NSF, other nasal mucoperiosteal flaps pedicled on the maxillary or ethmoidal artery systems can be taken into consideration. These are primarily represented by the ethmoidal arteries pedicled septal flap (*i.e.* septal flip-flap),<sup>65</sup> and middle turbinate (MTF), inferior turbinate (ITF), turbinal, and lateral nasal wall flaps.<sup>53-56,66</sup> Given their anteriorly located pivot, septal flip-flap and turbinal flaps perfectly suit defects of the cribriform plate and fovea ethmoidalis.<sup>54,65</sup> Sphenoidal wall defects are best covered with posteriorly pedicled flaps, such as NSF, MTF, ITF, and lateral nasal wall flap.<sup>53</sup> Of note, flaps based on branches of the sphenopalatine artery might be technically difficult to harvest, but represent a valuable option when NSF is unavailable, as is frequently the case in revision surgery.

### *Post-operative management*



Careful post-operative management is imperative for a successful post-operative course. Outpatient repeated meticulous debridement of nasal crusting and fibrin, as well as check of the status of the skull base reconstruction should be performed until complete healing. Non-collaborative pediatric patients can be scheduled for endoscopic second look with sedation at 15-20 days after surgery.

Maneuvers increasing intracranial pressure, such as lifting anything heavy, blowing the nose, air travel, and doing physical and sexual activity, should be discouraged.<sup>46</sup> Obese patients should be sent for nutritional counseling and weight loss should be accordingly planned.

In the literature on adult patients, the indications for a lumbar drain (LD) lacks univocal consensus and, with special reference to anterior skull base defects, is usually deemed unnecessary given the unfavorable risk-benefit ratio. In fact, complications of LD may be more frequent than postoperative CSF leak in these circumstances.<sup>46,67</sup> In our opinion, LD should be positioned in case of large high-flow dural defects, especially in the presence of significant risk factors for postoperative CSF leak such as intracranial hypertension and/or relapsing leak. Furthermore, in patients with significant IIH, reduction of intracranial pressure can be obtained with oral acetazolamide administration,<sup>16,68</sup> remarkably increasing the success rate of reconstruction as highlighted in the systematic review by Teachey *et al.*<sup>69</sup>

### **Surgical outcomes and complications**

Several studies clearly showed that the transnasal endoscopic route is efficient and safe to approach SBCs, irrespective of the patient's age.<sup>6,7,46,70</sup>

A recent systematic review by Lee *et al.* on 110 pediatric patients treated endoscopically for cephaloceles found that the recurrence rate was 5.2% after an average follow up of 25.3 months.<sup>6</sup> In the same paper, failure of reconstruction with post-operative CSF leak occurred in 6.0% of cases across all studies analyzed.<sup>6</sup> These results are in line with what observed in the literature after the introduction of endonasal vascularized pedicled flaps, which have dramatically decreased the incidence of post-operative CSF leak from 15% to about 5% to 6%.<sup>71,72</sup> The post-operative CSF leak rate reported by Nation *et al.* on a cohort of 39 pediatric patients was 0% using a reconstruction strategy including an underlay-overlay allograft alone for low-flow or nonleaking defects, with NSF being indicated to line the reconstruction only in case of high-flow intraoperative leaks.<sup>46</sup> Of note, NSF has been demonstrated to also be effective in children, while not leading to craniofacial growth abnormalities.<sup>73</sup> In patients with no NSF available, other vascularized flaps are likely to provide comparable results in terms of postoperative CSF leak rate.<sup>74</sup> However, a single-institution study on

pediatric patients did not show a significant difference in terms of postoperative CSF leak rate when comparing vascularized flap-including reconstruction to purely graft-based ones.<sup>75</sup>

Meningitis occurred in 3.7% of cases analyzed in the review by Lee *et al.*,<sup>6</sup> being associated with post-operative CSF leak, especially when persisting for more than 7 days after surgery.<sup>46,76</sup> Other complications include alar collapse, nasal stenosis, transient diabetes insipidus, pneumonia, and neurologic injury, cumulatively occurred in 7.0% of cases.<sup>6</sup> Mucocele formation was observed in 14% of cases treated by Di Rocco *et al.*, highlighting the risk of skull base reconstruction to obstruct the mucous drainage pathways, especially when the defect is located anteriorly, near the frontal sinus drainage pathway.<sup>70</sup>

Death is exceedingly rare in studies on pediatric SBC treated with TES. The systematic review by Lee *et al.* revealed a single case of death occurred post-operatively following a convulsive episode and attributed to compression of the respiratory center near the site of repair.<sup>6</sup> This low rate of fatal complications is consistent with findings in the adult endoscopic literature.<sup>6</sup> In fact, in the systematic review by Komotar *et al.* on endoscopic skull base surgery in adults, meningitis and perioperative mortality occurred in 0–1% of cases.<sup>43</sup>

## CONCLUSIONS

The comprehensive management of SBC requires a multidisciplinary approach, with assessment of the general conditions of the patient and specific characteristics of the lesion to select the best treatment strategy.

Two distinct pathological scenarios are usually encountered when dealing with SBC: on one hand malformative pathology in the child, on the other acquired pathology due to traumas or IIH in adults.

The current recommendation is to manage SBC with the primary intent of preventing ascending meningitis, with surgery representing the mainstay of treatment. The choice of the surgical approach (endoscopic, open or combined) is usually dictated by size and location of the lesion. When feasible, endoscopic surgery represents the first choice in virtue of its efficacy and more favorable complication profile compared to open techniques.

Reconstruction usually represents the most critical phase of the entire surgical procedure, with the choice of the reconstruction technique relying on the size, site and pressure/flow of the leak, and always favoring use of autologous material.

## REFERENCES

1. Kiyamaz N, Yilmaz N, Demir I, Keskin S. Prognostic factors in patients with occipital encephalocele. *Pediatr Neurosurg*. 2010;46(1):6–11.
2. Suphapeetiporn K, Mahatumarat C, Rojvachiranonda N, Taecholam C, Siriwan P, Srivuthana S, et al. Risk factors associated with the occurrence of frontoethmoidal encephalomeningocele. *Eur J Paediatr Neurol*. 2008 Mar;12(2):102–7.
3. Daudia A, Biswas D, Jones NS. Risk of meningitis with cerebrospinal fluid rhinorrhea. *Ann Otol Rhinol Laryngol*. 2007 Dec;116(12):902–5.
4. Ziade G, Hamdan AL, Homsy MT, Kazan I, Hadi U. Spontaneous Transethmoidal Meningoceles in Adults: Case Series with Emphasis on Surgical Management. *ScientificWorldJournal*. 2016;2016:3238297.
5. Woodworth BA, Schlosser RJ, Faust RA, Bolger WE. Evolutions in the management of congenital intranasal skull base defects. *Arch Otolaryngol Head Neck Surg*. 2004 Nov;130(11):1283–8.
6. Lee JA, Byun YJ, Nguyen SA, Schlosser RJ, Gudis DA. Endonasal endoscopic surgery for pediatric anterior cranial fossa encephaloceles: A systematic review. *Int J Pediatr Otorhinolaryngol*. 2020 Feb 1;132:109919.
7. Thompson HM, Schlosser RJ, McCarty Walsh E, Cho D-Y, Grayson JW, Kamezis TT, et al. Current management of congenital anterior cranial base encephaloceles. *Int J Pediatr Otorhinolaryngol*. 2020 Apr;131:109868.
8. Rahbar R, Resto VA, Robson CD, Perez-Atayde AR, Goumnerova LC, McGill TJ, et al. Nasal glioma and encephalocele: diagnosis and management. *Laryngoscope*. 2003 Dec;113(12):2069–77.
9. Kennedy EM, Gruber DP, Billmire DA, Crone KR. Transpalatal approach for the extracranial surgical repair of transsphenoidal cephaloceles in children. *J Neurosurg*. 1997 Nov;87(5):677–81.
10. Suwanwela C, Suwanwela N. A morphological classification of sincipital encephalomeningoceles. *J Neurosurg*. 1972 Feb;36(2):201–11.
11. Som P., Curtin H. *Head and Neck Imaging: Expert Consult*. 5th ed. Vol. 1st. Elsevier; 2011.
12. Bialer OY, Rueda MP, Bruce BB, Newman NJ, Biousse V, Saindane AM. Meningoceles in idiopathic intracranial hypertension. *AJR Am J Roentgenol*. 2014 Mar;202(3):608–13.
13. Loftus PA, Wise SK, Daraei P, Baugnon K, DeGaudio JM. Excavating meningoencephaloceles: A newly recognized entity. *Am J Rhinol Allergy*. 2017 Mar 1;31(2):127–34.

14. Nyquist GG, Anand VK, Mehra S, Kacker A, Schwartz TH. Endoscopic endonasal repair of anterior skull base non-traumatic cerebrospinal fluid leaks, meningoceles, and encephaloceles. *J Neurosurg*. 2010 Nov;113(5):961–6.
15. Kreatsoulas DC, Shah VS, Otto BA, Carrau RL, Prevedello DM, Hardesty DA. Surgical outcomes of the endonasal endoscopic approach within a standardized management protocol for repair of spontaneous cerebrospinal fluid rhinorrhea. *J Neurosurg*. 2020 Feb 28;1–7.
16. Martínez-Capoccioni G, Serramito-García R, Martín-Bailón M, García-Allut A, Martín-Martín C. Spontaneous cerebrospinal fluid leaks in the anterior skull base secondary to idiopathic intracranial hypertension. *Eur Arch Otorhinolaryngol*. 2017 May;274(5):2175–81.
17. Campbell RG, Farquhar D, Zhao N, Chiu AG, Adappa ND, Palmer JN. Cerebrospinal fluid rhinorrhea secondary to idiopathic intracranial hypertension: Long-term outcomes of endoscopic repairs. *Am J Rhinol Allergy*. 2016 Jul;30(4):294–300.
18. Radovnický T, Bartoš R, Vachata P, Sameš M. Cerebrospinal Fluid Rhinorrhea due to Transethmoidal Encephalocele Following Occipital Meningioma Resection in an Adult: A Case Report. *J Neurol Surg A Cent Eur Neurosurg*. 2019 Mar;80(2):138–40.
19. Akhaddar A. Brain Herniation into Nasal Cavity Secondary to Large Convexity Meningioma. *World Neurosurg*. 2019;125:398–9.
20. Battaglia P, Turri-Zanoni M, Castelnovo P, Prevedello DM, Carrau RL. Brain Herniation After Endoscopic Transnasal Resection of Anterior Skull Base Malignancies. *Neurosurgery*. 2015 Sep;11 Suppl 3:457–62; discussion 462.
21. Koutourousiou M, Filho FVG, Costacou T, Fernandez-Miranda JC, Wang EW, Snyderman CH, et al. Pontine encephalocele and abnormalities of the posterior fossa following transclival endoscopic endonasal surgery. *J Neurosurg*. 2014 Aug;121(2):359–66.
22. Renaud M, Fath L, Cheptou M, Dillenseger L, Riehm S, Venkatasamy A, et al. Iatrogenic meningoencephalocele after traumatic perforation of the cribriform plate during nasal intubation of a preterm infant. *Int J Pediatr Otorhinolaryngol*. 2019 Mar;118:120–3.
23. Stavrakas M, Karkos PD, Triaridis S, Constantinidis J. Endoscopic management of paediatric meningoencephaloceles: a case series. *Eur Arch Otorhinolaryngol*. 2018 Nov;275(11):2727–31.
24. Rawal RB, Sreenath SB, Ebert CS, Huang BY, Dugar DR, Ewend MG, et al. Endoscopic sinonasal meningoencephalocele repair: a 13-year experience with stratification by defect and reconstruction type. *Otolaryngol Head Neck Surg*. 2015 Feb;152(2):361–8.
25. Govindaraju R, Tang IP, Prepageran N. Management of sphenoid lateral recess encephaloceles. *Curr Opin Otolaryngol Head Neck Surg*. 2019 Feb;27(1):37–46.

26. Hanz SZ, Arko L, Schmidt F, Kacker A, Tsiouris AJ, Anand VK, et al. Low incidence of true Sternberg's canal defects among lateral sphenoid sinus encephaloceles. *Acta Neurochir (Wien)*. 2020 May 6;
27. Rajasekar G, Nair P, Abraham M, Jaiswal P, Deepti A N null. Endoscopic Endonasal Repair of a Persistent Craniopharyngeal Canal and Sphenoid Meningoencephalocele: Case Report and Review of Literature. *World Neurosurg*. 2019 Feb;122:196–202.
28. Albright AL, Pollack IF, Adelson PD. *Principles and Practice of Pediatric Neurosurgery*. 2<sup>nd</sup> ed. USA. Thieme; 2008.
29. Chen CS, David D, Hanieh A. Morning glory syndrome and basal encephalocele. *Childs Nerv Syst*. 2004 Feb;20(2):87–90.
30. Tirumandas M, Sharma A, Gbenimacho I, Shoja MM, Tubbs RS, Oakes WJ, et al. Nasal encephaloceles: a review of etiology, pathophysiology, clinical presentations, diagnosis, treatment, and complications. *Childs Nerv Syst*. 2013 May;29(5):739–44.
31. Woodworth BA, Prince A, Chiu AG, Cohen NA, Schlosser RJ, Bolger WE, et al. Spontaneous CSF leaks: a paradigm for definitive repair and management of intracranial hypertension. *Otolaryngol Head Neck Surg*. 2008 Jun;138(6):715–20.
32. Dandy We. Intracranial pressure without brain tumor: diagnosis and treatment. *Ann Surg*. 1937 Oct;106(4):492–513.
33. Bedrosian JC, Anand VK, Schwartz TH. The endoscopic endonasal approach to repair of iatrogenic and noniatrogenic cerebrospinal fluid leaks and encephaloceles of the anterior cranial fossa. *World Neurosurg*. 2014 Dec;82(6 Suppl):S86-94.
34. Hesham Atef Elshitany, Ehab Abd ELHaleem Ali. Management of idiopathic intracranial hypertension with repeated lumboperitoneal shunt malfunction. *Egyptian Journal of Neurosurgery*. 2019;34:1.
35. Murray RD, Friedlander R, Hanz S, Singh H, Anand VK, Schwartz TH. Nonrandom spatial clustering of spontaneous anterior fossa cerebrospinal fluid fistulas and predilection for the posterior cribriform plate. *J Neurosurg*. 2017 May;126(5):1720–4.
36. Seth R, Rajasekaran K, Benninger MS, Batra PS. The utility of intrathecal fluorescein in cerebrospinal fluid leak repair. *Otolaryngol Head Neck Surg*. 2010 Nov;143(5):626–32.
37. Kerr JT, Chu FWK, Bayles SW. Cerebrospinal fluid rhinorrhea: diagnosis and management. *Otolaryngol Clin North Am*. 2005 Aug;38(4):597–611.
38. Zuckerman JD, DelGaudio JM. Utility of preoperative high-resolution CT and intraoperative image guidance in identification of cerebrospinal fluid leaks for endoscopic repair. *Am J Rhinol*. 2008 Apr;22(2):151–4.

39. Hingwala D, Chatterjee S, Kesavadas C, Thomas B, Kapilamoorthy TR. Applications of 3D CISS sequence for problem solving in neuroimaging. *Indian J Radiol Imaging*. 2011 Apr;21(2):90–7.
40. Algin O, Hakyemez B, Gokalp G, Ozcan T, Korfali E, Parlak M. The contribution of 3D-CISS and contrast-enhanced MR cisternography in detecting cerebrospinal fluid leak in patients with rhinorrhoea. *Br J Radiol*. 2010 Mar;83(987):225–32.
41. Selcuk H, Albayram S, Ozer H, Ulus S, Sanus GZ, Kaynar MY, et al. Intrathecal gadolinium-enhanced MR cisternography in the evaluation of CSF leakage. *AJNR Am J Neuroradiol*. 2010 Jan;31(1):71–5.
42. Gun R, Tosun F, Durmaz A, Yorgancilar E, Bakir S, Kamasak K, et al. Predictors of surgical approaches for the repair of anterior cranial base encephaloceles. *Eur Arch Otorhinolaryngol*. 2013 Mar;270(4):1299–305.
43. Komotar RJ, Starke RM, Raper DMS, Anand VK, Schwartz TH. Endoscopic endonasal versus open repair of anterior skull base CSF leak, meningocele, and encephalocele: a systematic review of outcomes. *J Neurol Surg A Cent Eur Neurosurg*. 2013 Jul;74(4):239–50.
44. Jeswani S, Nuño M, Wu A, Bonert V, Camichael JD, Black KL, et al. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study. *J Neurosurg*. 2016 Mar;124(3):627–38.
45. Tatreau JR, Patel MR, Shah RN, McKinney KA, Wheless SA, Senior BA, et al. Anatomical considerations for endoscopic endonasal skull base surgery in pediatric patients. *Laryngoscope*. 2010 Sep;120(9):1730–7.
46. Nation J, Schupper AJ, Deconde A, Levy M. CSF leak after endoscopic skull base surgery in children: A single institution experience. *Int J Pediatr Otorhinolaryngol*. 2019 Apr;119:22–6.
47. Chen W, Gardner PA, Branstetter BF, Liu S-D, Chang YF, Snyderman CH, et al. Long-term impact of pediatric endoscopic endonasal skull base surgery on midface growth. *J Neurosurg Pediatr*. 2019 11;23(4):523–30.
48. Parasher AK, Lerner DK, Glicksman JT, Storm PB, Lee JYK, Vossough A, et al. The impact of expanded endonasal skull base surgery on midfacial growth in pediatric patients. *Laryngoscope*. 2020 Feb;130(2):338–42.
49. Tosun F, Gonul E, Yetiser S, Gerek M. Analysis of different surgical approaches for the treatment of cerebrospinal fluid rhinorrhea. *Minim Invasive Neurosurg*. 2005 Dec;48(6):355–60.

50. Schwartz TH, Fraser JF, Brown S, Tabaei A, Kacker A, Anand VK. Endoscopic cranial base surgery: classification of operative approaches. *Neurosurgery*. 2008 May;62(5):991–1002; discussion 1002-1005.
51. Woodworth B, Schlosser RJ. Endoscopic repair of a congenital intranasal encephalocele in a 23 months old infant. *Int J Pediatr Otorhinolaryngol*. 2005 Jul;69(7):1007–9.
52. Nicolai P, Ferrari M, Maroldi R, Hirtler L, Tschabitscher M, Rodella LF. Endoscopic Transnasal Anatomy of the Skull Base and Adjacent Areas: A Lab Dissection and Radiological Atlas. 1<sup>st</sup> ed. Italy. Thieme; 2019.
53. Prevedello DM, Barges-Coll J, Fernandez-Miranda JC, Morera V, Jacobson D, Madhok R, et al. Middle turbinate flap for skull base reconstruction: cadaveric feasibility study. *Laryngoscope*. 2009 Nov;119(11):2094–8.
54. Schreiber A, Mattavelli D, Ferrari M, Rampinelli V, Lancini D, Belotti F, et al. The turbinal flap: an additional option for anterior skull base reconstruction. Cadaveric feasibility study and case report. *Int Forum Allergy Rhinol*. 2017;7(2):199–204.
55. Tamura R, Toda M, Kohno M, Watanabe Y, Ozawa H, Tomita T, et al. Vascularized middle turbinate flap for the endoscopic endonasal reconstruction of the anterior olfactory groove. *Neurosurg Rev*. 2016 Apr;39(2):297–302; discussion 302.
56. Wang X, Zhang X, Hu F, Yu Y, Gu Y, Xie T, et al. Middle Turbinate Mucosal Flap in Endoscopic Skull Base Reconstruction. *Turk Neurosurg*. 2016;26(2):200–4.
57. Belotti F, Doglietto F, Schreiber A, Ravanelli M, Ferrari M, Lancini D, et al. Modular Classification of Endoscopic Endonasal Transsphenoidal Approaches to Sellar Region: Anatomic Quantitative Study. *World Neurosurg*. 2018 Jan;109:e281–91.
58. Doglietto F, Ferrari M, Mattavelli D, Belotti F, Rampinelli V, Kheshaifati H, et al. Transnasal Endoscopic and Lateral Approaches to the Clivus: A Quantitative Anatomic Study. *World Neurosurg*. 2018 May;113:e659–71.
59. Zoli M, Farneti P, Ghirelli M, Giulioni M, Frank G, Mazzatenta D, et al. Meningocele and Meningoencephalocele of the Lateral Wall of Sphenoidal Sinus: The Role of the Endoscopic Endonasal Surgery. *World Neurosurg*. 2016 Mar;87:91–7.
60. Castelnuovo P, Dallan I, Pistochini A, Battaglia P, Locatelli D, Bignami M. Endonasal endoscopic repair of Sternberg's canal cerebrospinal fluid leaks. *Laryngoscope*. 2007 Feb;117(2):345-9.
61. Tabaei A, Anand VK, Cappabianca P, Stamm A, Esposito F, Schwartz TH. Endoscopic management of spontaneous meningoencephalocele of the lateral sphenoid sinus. *J Neurosurg*. 2010 May;112(5):1070-7.



62. Rivera-Serrano CM, Snyderman CH, Gardner P, Prevedello D, Wheless S, Kassam AB, et al. Nasoseptal “rescue” flap: a novel modification of the nasoseptal flap technique for pituitary surgery. *Laryngoscope*. 2011 May;121(5):990–3.
63. Simal-Julián JA, Miranda-Lloret P, Pérez de San Román Mena L, Sanromán-Álvarez P, García-Piñero A, Sanchis-Martín R, et al. Impact of Multilayer Vascularized Reconstruction after Skull Base Endoscopic Endonasal Approaches. *J Neurol Surg B Skull Base*. 2020 Apr;81(2):128–35.
64. Lam K, Luong AU, Yao WC, Citardi MJ. Use of Autologous Fat Grafts for the Endoscopic Reconstruction of Skull Base Defects: Indications, Outcomes, and Complications. *Am J Rhinol Allergy*. 2018 Jul;32(4):310–7.
65. Battaglia P, Turri-Zanoni M, De Bernardi F, Dehgani Mobaraki P, Karligkiotis A, Leone F, et al. Septal flip flap for anterior skull base reconstruction after endoscopic resection of sinonasal cancers: preliminary outcomes. *Acta Otorhinolaryngol Ital*. 2016 Jun;36(3):194–8.
66. Choby GW, Pinheiro-Neto CD, de Almeida JR, Ruiz-Valdepeñas EC, Wang EW, Fernandez-Miranda JC, et al. Extended inferior turbinate flap for endoscopic reconstruction of skull base defects. *J Neurol Surg B Skull Base*. 2014 Aug;75(4):225–30.
67. Soudry E, Turner JH, Nayak JV, Hwang PH. Endoscopic reconstruction of surgically created skull base defects: a systematic review. *Otolaryngol Head Neck Surg*. 2014 May;150(5):730–8.
68. Chaaban MR, Illing E, Riley KO, Woodworth BA. Spontaneous cerebrospinal fluid leak repair: a five-year prospective evaluation. *Laryngoscope*. 2014 Jan;124(1):70–5.
69. Teachey W, Grayson J, Cho D-Y, Riley KO, Woodworth BA. Intervention for elevated intracranial pressure improves success rate after repair of spontaneous cerebrospinal fluid leaks. *Laryngoscope*. 2017;127(9):2011–6.
70. Di Rocco F, Couloigner V, Dastoli P, Sainte-Rose C, Zerah M, Roger G. Treatment of anterior skull base defects by a transnasal endoscopic approach in children. *J Neurosurg Pediatr*. 2010 Nov;6(5):459–63.
71. Harvey RJ, Parmar P, Sacks R, Zanation AM. Endoscopic skull base reconstruction of large dural defects: a systematic review of published evidence. *Laryngoscope*. 2012 Feb;122(2):452–9.
72. Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. *Laryngoscope*. 2006 Oct;116(10):1882–6.
73. Ghosh A, Hatten K, Learned KO, Rizzi MD, Lee JY, Storm PB, et al. Pediatric nasoseptal flap reconstruction for suprasellar approaches. *Laryngoscope*. 2015 Nov;125(11):2451–6.

74. Patel MR, Taylor RJ, Hackman TG, Germanwala AV, Sasaki-Adams D, Ewend MG, et al. Beyond the nasoseptal flap: outcomes and pearls with secondary flaps in endoscopic endonasal skull base reconstruction. *Laryngoscope*. 2014 Apr;124(4):846–52.
75. Stapleton AL, Tyler-Kabara EC, Gardner PA, Snyderman CH, Wang EW. Risk factors for cerebrospinal fluid leak in pediatric patients undergoing endoscopic endonasal skull base surgery. *Int J Pediatr Otorhinolaryngol*. 2017 Feb;93:163–6.
76. Abuabara A. Cerebrospinal fluid rhinorrhoea: diagnosis and management. *Med Oral Patol Oral Cir Bucal*. 2007 Sep 1;12(5):E397-400.

## NOTES

### **Conflicts of interest:**

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

### **Funding:**

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

### **Authors' Contribution:**

Dr Vittorio Rampinelli, Dr Davide Mattavelli, Dr Marco Ferrari, Dr Alberto Schreiber, and Dr Marco Ravanelli designed the paper, drafted the initial manuscript and reviewed and revised the manuscript. Prof. Davide Farina, Prof. Alberto Deganello, Prof. Marco Maria Fontanella, Prof. Francesco Doglietto, and Prof. Piero Nicolai have contributed to design the paper and reviewed and revised the manuscript.

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

## TABLES

**Table 1.** Modified Dandy criteria.

1. Symptoms and signs of augmented intracranial pressure.
2. No localizing signs at the neurological examination (except abducens nerve palsy).
3. Normal imaging (except for empty sella).
4. Opening pressure of lumbar puncture greater than 250 mm of water, with normal CSF
5. Alert and awake patient
6. No other cause of augmented intracranial pressure

**Table 2.** Selection of the surgical approach based on location and specifics of anterior skull base cephalocele.

<b>Cephalocele location and specifics</b>	<b>Surgical approach</b>
Ethmoidal roof	Endoscopic transethmoidal
Cribriform plate	Endoscopic transnasal +/- transethmoidal
Planum sphenoidalis	Endoscopic transplanum
Lateral wall of the sphenoid sinus	Endoscopic transsphenoidal +/- transpterygoid
Caudal aspect of the posterior frontal plate and foramen cecum	Endoscopic transfrontal
Lateral and cranial aspects of the posterior frontal plate	External osteoplastic flap +/- combined endoscopic
External mass involving facial and nasal bones	External transfacial +/- combined endoscopic
Traumatic cephaloceles accompanied with skull base multifracture and orbital/intracerebral complications	External transfacial/transcranial +/- combined endoscopic

## FIGURES

**Figure 1.** Main sites of anterior SBCs distribution: Cribriform Plate (CrP) (40-100%), Ethmoidal Roof (ER) (6-40%), Posterior Frontal Plate (PFP) (9-71%), sphenoidal walls (16-38%).<sup>4,6,7,23,24</sup>

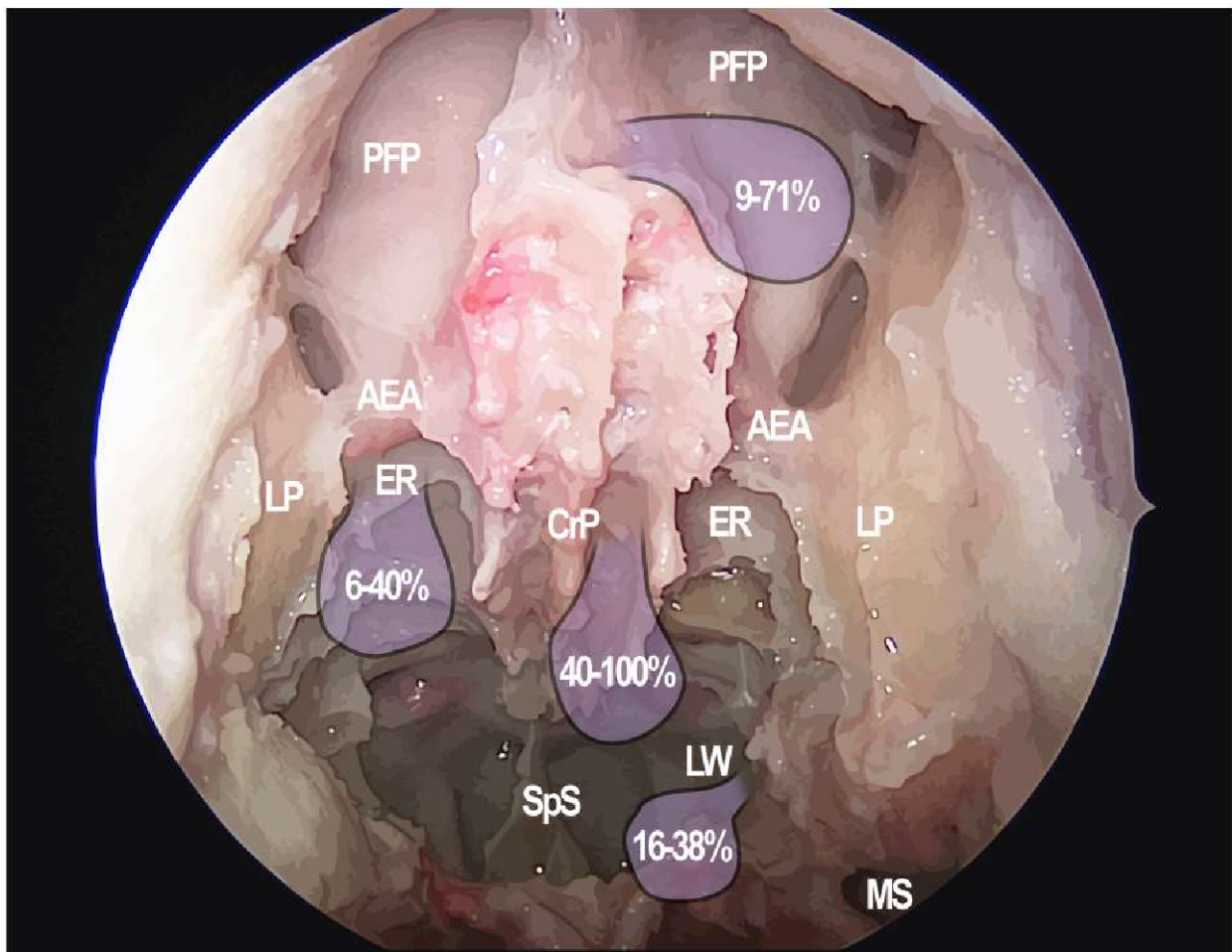
AEA - Anterior Ethmoidal Artery; LP – Lamina Papiracea; LW – Lateral Wall of the sphenoid sinus; MS – Maxillary sinus; SpS – Sphenoid Sinus.

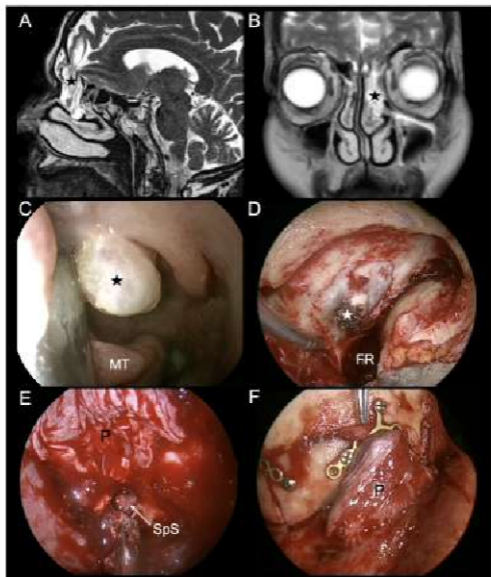
**Figure 2.** Case of a 36-year-old male complaining of chronic left frontal headache, with onset of intermittent left CSF leak. Imaging showed the presence of a meningoencephalocele of the cranial portion of the posterior frontal plate occupying the frontal recess and reaching the middle meatus (black asterisk in figure A and B, sagittal and coronal MRI T2 weighted sequences, respectively). The caudal aspect of the lesion (black asterisk in figure C) was visible at endoscopic examination by means of lateral displacement of the middle turbinate (MT). Surgical strategy consisted in endoscopic removal of the caudal portion, cleaning the frontal recess from below, combined with pericranium and external osteoplastic flap harvesting. The lesion was removed and its base isolated and coagulated (black asterisk in figure D). Pericranium flap (P in figure E and F) was distended along the left anterior skull base (figure E). Osteoplastic flap was then repositioned and fixed with plates (figure F). FR- Frontal Recess; SpS – Sphenoid Sinus.

**Figure 3.** Case of a 48-year-old female complaining about headache treated for years as it was atypical migraine, without CSF leak. Sagittal cone-beam CT showed an enlarged foramen cecum (black asterisk in figure A). MRI confirmed the suspect of meningoencephalocele: in sagittal T2 weighted sequences (figure B) an extension of tissue with mixed hyperintense (CSF) and intermediate (brain) signal protrudes on the midline below and anteriorly to the normal boundary of the anterior skull base; the FLAIR sagittal sequence (figure C) is characterized by the fall of signal in the fluid component between the cerebral parenchyma. The lesion was treated with endoscopic transfrontal approach. The meningoencephalocele (black asterisks in figure D) was isolated and resected after performing a Draf III procedure. Multilayer reconstruction consisted in positioning inlay epidural fat, inlay septal cartilage (C in figure E), fat fixed with fibrin glue, and lateral nasal wall pedicled mucosa (FI in figure F). NS – Nasal Septum.

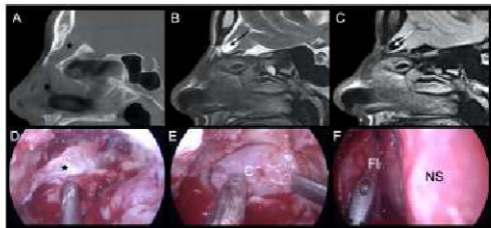
**Figure 4.** Case of a 28-year-old male with CSF leak consequent to facial trauma. Imaging showed the presence of a meningocele of the right planum sphenoidalis (asterisks in figure A and B, coronal CT scan and sagittal CISS weighted MRI, respectively). Arrows indicate the point of fracture of the skull base). Transsphenoidal approach allowed exposure of the meningocele (black asterisk in figure

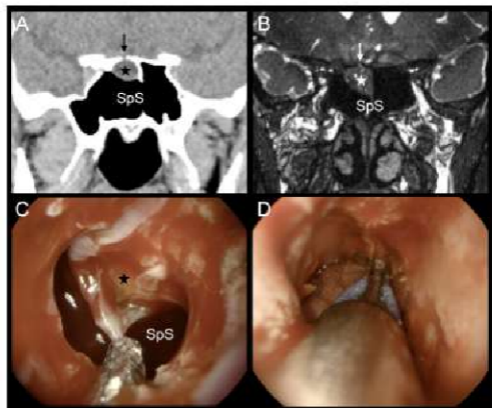
C), covered by mucosa. It was coagulated with bipolar forceps (Figure D) and, in view of CSF leak ceasing, covered with fat and mucosal graft. SpS – Sphenoid Sinus.











## **Management of anterior fossa cephaloceles: an overview**

### **Running title:**

Anterior skull base cephaloceles

### **Authors:**

Vittorio Rampinelli<sup>1</sup>, Davide Mattavelli<sup>1</sup>, Marco Ferrari<sup>1,2</sup>, Alberto Schreiber<sup>1</sup>, Marco Ravanelli<sup>3</sup>,  
Davide Farina<sup>3</sup>, Alberto Deganello<sup>1</sup>, Marco Maria Fontanella,<sup>4</sup> Francesco Doglietto<sup>4\*</sup>, Piero Nicolai<sup>2</sup>.

### **Affiliations**

1 Unit of Otorhinolaryngology - Head and Neck Surgery, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

2 Section of Otorhinolaryngology – Head and Neck Surgery, Department of Neurosciences, University of Padua, Padua, Italy

3 Unit of Radiology, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

4 Unit of Neurosurgery, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

### **\* Corresponding author**

Francesco Doglietto, MD, PhD

Associate Professor

Unit of Neurosurgery, Department of Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia

Piazzale Spedali Civili 1, 25123 Brescia, Italy

Telephone number: +39 0303995587

Fax number: +39 0303995008

E-mail address: francesco.doglietto@unibs.it

**ABSTRACT**

Skull base cephaloceles (SBCs) are defined as herniation of intracranial content through the skull base and are classified based on composition, etiology, and topographic location. Anterior SBCs frequently protrude in the sinonasal cavity, and consequently are at potential risk of infection. Therefore, the current recommendation is to treat SBCs with the primary intent of preventing meningitis, and surgery represents the mainstay of treatment. Anterior SBCs may display a wide spectrum of severity and complexity, and in each case the risks and benefits of surgical approaches are to be carefully weighted based on thorough assessment of symptoms, age, general conditions, location and size of the lesion, as well as expertise of the surgeon. In the last 30 years, the evolution and diffusion of transnasal endoscopic surgery have substantially changed the surgical management of the majority of SBC. In the past, they were treated exclusively with open transcranial approaches that may be burdened by relevant morbidity and risk for severe complications. The transnasal endoscopic corridor now provides easy access to the lesion and different reconstructive strategies using endonasal pedicled flaps, without any external incision, cranioplasty or brain manipulation. However, there are still scenarios in which an exclusive transnasal endoscopic route is contraindicated. The aim of the present review is to provide an overview on the comprehensive management of anterior SBC, with a particular focus on lesions suitable for endoscopic surgery. Furthermore, special aspects of SBC management in children and adults will be highlighted.

**KEY WORDS**

**Skull base, cephalocele, CSF leak.**

## INTRODUCTION

The prevalence of intracranial content herniation through the skull is estimated to range between 1:10,000 and 1:2500,<sup>1</sup> with an unexplained higher rate in Southeast Asia compared to other geographical areas.<sup>2</sup> Herniations are classified according to topographic location, histological composition in terms of brain and meningeal tissue, and congenital *versus* acquired onset, but univocal consensus is lacking. In the present review, any herniation of the intracranial content through the skull will be defined as “cephalocele” (“cephalo-” referring to the skull and “-cele” to herniation). Although from a theoretical standpoint cephaloceles could be further classified in either encephaloceles, meningoceles, or meningoencephaloceles if, respectively, made up by only brain, only meninges, or both neural and meningeal tissues, this distinction would be irrelevant in terms of practical implications in most cases, since the treatment of the vast majority of skull base cephaloceles (SBC) is independent of its content.

Cephaloceles developing through certain areas of the skull base have the chance to reach a mucosa-lined air cavity early, which can be either the sinonasal tract, nasopharynx, or middle ear. This anatomical relationship can lead cephaloceles to manifest through nasal and/or ear cerebrospinal fluid (CSF) leak, provided that the mucoperiosteal layer and meningeal sac spontaneously dehisce at some point. Otherwise, the herniated tissue can become clinically appreciable through a mass effect or because of transmission of brain pulsation towards a non-air-containing area such as the orbit. The main concern when a cephalocele is diagnosed nearby a mucosal area is the risk for infectious meningitis, which can occur through ascending infection of the intracranial cavity by microbes in a mucosal cavity. In a series cumulatively analyzing 111 CSF leaks with different causes, the incidence of meningitis was 0.3 episodes/year, with most occurring within 1 year from leak onset.<sup>3</sup> Specifically focusing on CSF-leaking ethmoidal meningoencephaloceles, Ziade *et al.* found that 30% of patients present with infectious meningitis.<sup>4</sup> The risk of meningitis in patients bearing nonleaking, incidentally found cephaloceles is unknown. However, episodes of meningitis in patients with a nonleaking cephalocele lined by intact mucosa have been reported.<sup>5</sup>

Based on the aforesaid evidence, the current recommendation is to manage SBCs with the primary intent of preventing ascending meningitis, with surgery representing the mainstay of treatment.

Traditionally, SBC were treated with open transcranial approaches,<sup>6-8</sup> which are burdened by relevant morbidity and/or complications, such as significant blood loss, injury to the olfactory apparatus and supraorbital/supratrochlear nerves, brain manipulation, aesthetic impairment, and, with special reference to children, damage of bone growth centers.<sup>7</sup>

In the last 30 years, the evolution and popularization of transnasal endoscopic surgery (TES) have dramatically changed the surgical management of anterior and middle SBC, taking advantage from the enhanced collaboration between neurosurgeons and otolaryngologists.

The aim of the present paper is to provide an overview on the comprehensive management of anterior SBC, with a particular focus on those suitable for TES. Furthermore, even if formally belonging to middle skull base, SBCs herniating through the lateral wall of the sphenoid sinus will also be discussed. Aspects of SBC management in children and adults will be highlighted.

## CLASSIFICATION AND ETIOLOGY

SBC can be classified based on timing of development as congenital or acquired. Congenital cephaloceles result from incomplete closure of the neural tube during gestation and occur in approximately 1:3000-5000 live births.<sup>9</sup> Those encroaching on the sinonasal tract are especially sincipital (further divided in nasofrontal, nasoethmoidal, and naso-orbital) and basal (further divided in transethmoidal, sphenothmoidal, trans-sphenoidal, and frontosphenoidal) cephaloceles.<sup>10</sup>

Congenital cephaloceles can be found either alone or in the context of malformation syndromes,<sup>11</sup> whose discussion is beyond the aim of the present review. The causes of congenital cephaloceles are unknown. Familiar and geographical clustering would suggest a genetic predisposition, whereas association with low socioeconomic status, advanced maternal age, and long interpregnancy period hint unfavorable intrauterine environment as a potential cause.<sup>2,11</sup>

Acquired cephaloceles can occur through two main mechanisms (or via their combination): 1) increased intracranial pressure, and 2) newly-onset defect (or weakening) of the skull base. Idiopathic intracranial hypertension (IIH) perfectly fits this pathogenetic model, as it embraces both mechanisms by increasing CSF pressure while relentlessly enfeebling the weakest areas of the skull base through chronic pathological CSF pulsation. Acquired cephaloceles might represent a late manifestation of IIH causing an initially nonleaking herniation, as witnessed by the significant association between IIH and meningoceles.<sup>12</sup> On the other hand, patients with CSF early leaking through the skull base due to intracranial hypertension might represent an earlier manifestation of IIH with no frank herniation of intracranial tissues. An intermediate scenario is the “excavating meningoencephalocele”, a recently described entity consisting of a tunnel-like meningeal protrusion through the skull base, which possibly represent an early-leaking meningeal herniation.<sup>13</sup> Association between IIH and cephaloceles is also corroborated by the overlap in terms of risk factors, high body mass index (BMI), and female gender being the most relevant.<sup>4,14,15</sup> The prevalence of cephalocele in IIH patients treated for spontaneous CSF leak ranges from 69% to 97%.<sup>16,17</sup>

Less frequently, increased intracranial pressure or weakening of the skull base might result from other causes such as an intracranial mass,<sup>18,19</sup> previous surgery, and trauma,<sup>20-22</sup> respectively. Finally, some cephaloceles diagnosed in adult patients might also represent congenital herniation that remain unnoticed until adulthood. In fact, series on patients treated for a congenital cephalocele include subjects aged 18 or older.<sup>5-7</sup>

Classification of SBC according to subsite of herniation includes the cribriform plate, ethmoidal roof, posterior frontal plate, and sphenoidal walls. Distribution throughout these subsites is as follows: 40-100%, 6-40%, 9-71%, and 16-38%, respectively, (Figure 1).<sup>4,6,7,23,24</sup> A remarkable difference in topographical distribution can be observed when comparing pediatric and adult series,

with the former being more frequently associated with frontal cephaloceles. Sphenoidal cephaloceles most frequently develop through the lateral wall, whereas other sphenoidal subsites (*e.g.* planum sphenoidale, tuberculum sellae, clivus) are involved with exceeding rarity.<sup>25-27</sup>



## CLINICAL PRESENTATION

SBCs manifest across a diverse clinical spectrum, which can vary from episodic rhinorrhea to large sinonasal or nasopharyngeal masses that can cause obstruction or craniofacial deformities. Etiology, size and site of the cephalocele, along with the age of the patient, largely dictate the clinical picture.

Overall, nasal obstruction, CSF rhinorrhea, and headache are the leading symptoms. In general, SBC manifest as pulsating, cystic masses protruding in the face (covered by skin), in sinonasal cavities and nasopharynx (covered by mucosa), or in the orbit. Furstenberg sign (i.e. increased swelling and pulsatility in association with Valsalva maneuver or jugular vein compression) is a simple but effective clinical finding to guide differential diagnosis.<sup>28</sup>

Congenital cephaloceles are usually large and can display a relevant mass effect leading to deformities of the nasal bones, maxillofacial skeleton and sinonasal structures (severe septal deviation and turbinates dislodgement). Sincipital cephaloceles are often more obvious, since they can be associated with external, visible pulsating masses and other craniofacial deformities, such as telecanthus.<sup>7</sup> Conversely, basal cephaloceles may be more insidious, and diagnosed at a later age. They usually present with nasal obstruction, but can be also associated with other conditions, including hypertelorism, facial clefts, and Morning Glory Syndrome (congenital optic disc dysplasia).<sup>29,30</sup>

In a recent study analyzing 15 congenital cephaloceles, the average age at diagnosis was six years, ranging from 2 months to 22 years, and the most frequent symptom was nasal obstruction. Associated anomalies were found in almost half of cases, with craniofacial deformities being the most frequent (30%). The majority of cephaloceles occurred at the foramen cecum and presented relevant dimension in view of the limited size of the craniofacial skeleton (mean diameter, 2.44 cm).<sup>7</sup> Fronto-orbital cephaloceles are almost exclusively congenital, and can cause proptosis, orbital displacement, pain, and interfere with eye-ball mobility (diplopia) and venous drainage (chemosis).<sup>7</sup>

Acquired cephaloceles more frequently occur in adults. In general, nasal obstruction has a marginal relevance, since cephaloceles tend to be smaller and do not impact nasal flow. The most important symptom is CSF rhinorrhea, followed by previous (or present) episodes of meningitis and persistent headache.<sup>14</sup>

Traumatic and iatrogenic cephaloceles can be easily ruled out with careful anamnesis. Spontaneous or idiopathic CSF leaks are almost invariably associated with increased intracranial pressure. IIH typically occurs in overweight women in their 5<sup>th</sup>-6<sup>th</sup> decade of life.<sup>31</sup> This epidemiological trait, together with a clinical history consistent for CSF leak, is highly suggestive for cephaloceles and warrants further clinical and radiological examinations. The diagnosis of IIH is

defined by the modified Dandy criteria (**Table 1**);<sup>32-34</sup> in particular, indirect radiological signs of intracranial hypertension (i.e. empty sella, enlargement of the space between the optic nerve and optic sheath) can strongly support the diagnosis before other invasive procedures are carried out (i.e., CSF opening pressure at lumbar puncture).

Noteworthy, IHH-induced CSF-leaks may show a valve mechanism, which translates into an intermittent leak that can delay correct diagnosis.

Meningitis may complicate the clinical condition in a non-negligible group of patients. Focusing on CSF-leaking ethmoidal meningoencephaloceles, Ziade *et al.* reported that 30% of patients present with infectious meningitis.<sup>4</sup> Furthermore, episodes of meningitis in patients with a nonleaking cephalocele lined by intact mucosa have been reported.<sup>5</sup>

## **DIAGNOSTIC WORK-UP**

The diagnostic work-up is aimed at: a) confirming the diagnosis of cephalocele; b) defining its size and site; c) establishing the etiology.

### **Clinical examination**

Careful inspection of the face and palpation are adequate to evaluate external cephaloceles and possible abnormalities of the maxillofacial skeleton.

In case of fronto-ethmoidal and basal cephaloceles, endoscopic endonasal evaluation has a pivotal role in confirming diagnosis and localizing the cephalocele. Congenital cephalocele are often more obvious and their location is easier to define. Conversely, acquired cephaloceles can be more subtle, and they can be so small that they can be hidden beneath the mucosa and be impossible to visualize.

The presence of CSF leak is a helpful hint to confirm diagnosis. From a clinical perspective, CSF is indistinguishable from serous nasal secretion unless an evident and high-flow leak is clearly detectable. Therefore, laboratory tests on fluid collection (i.e. identification of beta-2-transferrin or beta-trace protein) are invaluable tools to confirm CSF-leak.

Identification of the site of the meningoencephalocele can be challenging in case of very small defects.

In IIH induced cephaloceles, an important clue is provided by a non-random distribution of these defects in the ASB. In fact, they mostly occur at the level of the posterior portion of the cribriform plate, probably because the presence of olfactory foramina combined with the larger width of the olfactory cleft makes the bony skull base more susceptible to dehiscence.<sup>35</sup>

An interesting method to increase the efficacy of nasal endoscopy is intradural injection of fluorescein. In a retrospective series on 103 CSF-leak repairs, fluorescein was used in 47 patients, and showed 73.8% sensitivity and 100% specificity for detection of the leak site.<sup>36</sup> Sensitivity can be even higher with the use of a blue light filter, which allows for visual detection of fluorescein at 1 part in 10 million.<sup>37</sup> Being an off-label indication, proper patient consent is needed. Safety of lumbar fluorescein injection has been debated in the literature; however, authors' personal experience and other published evidence suggest that the specific risks related to fluorescein injection are minimal.<sup>33</sup>

Overall, clinical and endoscopic evaluations are useful to address diagnostic suspicion, but are rarely conclusive. It is of utmost importance to avoid any interventional procedure such as biopsy before a complete radiological workup has been concluded.

### **Radiological diagnosis**

Radiological examinations are imperative to confirm diagnosis and define the content of the cephalocele, detect its location, and suggest a possible etiology. Furthermore, a combination of different radiological techniques is usually required.

High-resolution computed tomography (HRCT) and magnetic resonance (MR) with or without contrast medium are the mainstay in the diagnostic workup.

HRCT is highly effective in the study of the bony skull base, and can detect even millimetric bony defects. In a retrospective study on 42 CSF leaks, the site of the skull base defect was identified preoperatively by HRCT in all cases, with successful intraoperative detection via intraoperative image guidance.<sup>38</sup> Conversely, the drawbacks are exposure to ionizing radiation, and the impossibility to distinguish between skull base dehiscence and skull base defect with cephaloceles, as a consequence of its low capability of soft tissue discrimination (risk of false positive). The latter issue is brilliantly resolved by combining HRCT with MR.

The great advantage of MR is the power to discriminate between brain tissue, CSF, and nasal secretion by combining T2-weighted, three-dimensional (3D) constructive interference in steady state (CISS) and fluid attenuated inversion recovery (FLAIR) sequences. In particular, image contrast in 3D-CISS is characterized by a high T2-T1 ratio, i.e. tissues (like fat and water) with both long T2 and short T1 relaxation times have increased signal intensity. This allows for an excellent contrast between CSF (hyperintense) and other structures; other relevant advantages of this sequence are high signal-to-noise ratio, high contrast-to-noise ratio, and intrinsic insensitivity to motion.<sup>39,40</sup> In FLAIR, the signal of CSF is suppressed and will appear completely black, while the brain is predominantly gray and the mucosa hyperintense. Therefore, the combination of 3D-CISS and FLAIR is extremely useful to detect the site of the cephalocele and to define its content.

Other relevant advantages of MR are the absence of radiation (important in young patients or in case of repeated examinations) and the ability to rule out possible causes of cephalocele (brain tumors, IIH, thrombosis of the dural sinuses, etc.). Overall, the combination of HRCT and MR can resolve the vast majority of suspected cephaloceles.

Accordingly, CT and MR cisternography should be considered as second-line examinations for very selected cases, in view of the need for an intrathecal injection of contrast medium via a lumbar puncture. CT cisternography is 85% sensitive for active leaks, but this can decrease to 48% in case of intermittent leakage.<sup>33</sup> Performance of MR cisternography are better, with 100% detection rate for continuous leaks, and 70% for intermittent ones.<sup>40,41</sup> A common drawback of these two tests is the dependence on contrast medium diffusion in CSF, with a risk of false negativity in case of poor distribution.

As previously stated, the most critical scenario in terms of diagnosis is intermittent CSF leak. To increase diagnostic accuracy, radionuclide cisternography has been proposed and investigated. This examination is based on the intrathecal injection of technetium-99; the detection of a possible leak may last several days, and theoretically this should allow capturing even intermittent or low volume leakage. However, preliminary results are discouraging. First, spatial resolution is very poor, which limits an effective localization of the defect. In addition, sensitivity is quite low, ranging between 62% and 76%, while the false positive rate is not negligible (33%).<sup>33</sup>

## SURGICAL TREATMENT

Surgery is the mainstay of treatment of SBC. To date, TES is the preferred surgical strategy to address basal and sincipital cephaloceles that are not associated with craniofacial deformity and do not show far lateral extension.<sup>42</sup> In a systematic review of 1178 patients from 71 studies, Komotar *et al.* reported no significant difference in the rate of successful repair of skull base defects when comparing open and endoscopic cohorts.<sup>43</sup> Complications and mortality were significantly lower in the endoscopic group, most probably because brain retraction is avoided and neurovascular manipulation minimized.<sup>43</sup> Moreover, skin incision and large craniotomies are avoided, resulting in negligible cosmetic alterations.<sup>33,43</sup> TES has also been associated with lower costs compared to open surgery.<sup>44</sup>

Despite these indisputable advantages, some perils of TES have to be highlighted, with special reference to pediatric patients. In contrast to adults, pediatric sinonasal anatomy can substantially restrict the working space for surgical instrumentation. Children may also lack key anatomical landmarks as a consequence of early-stage pneumatization of craniofacial bones, and performing surgery requires a thorough understanding of age-dependent structural patterns.<sup>6,45</sup> For instance, sphenoid sinus pneumatization usually occurs 7 years after birth, thus invariably presenting a non-pneumatized sphenoid body if surgery is performed earlier.<sup>45,46</sup> Furthermore, surgeons must be mindful of potential damage to facial and skull growth centers, and in particular the sphenodorsal zone, which extends from the sphenoid septum to the nasal dorsum, being consequently at risk of impairment during TES.<sup>6,47,48</sup> Finally, endonasal pedicled flaps are smaller and possibly inadequate to reconstruct large, congenital defects. Despite these concerns, a number of studies have validated the feasibility of TES in children, showing satisfactory outcomes with low complication rates.<sup>6,7,45,47,48</sup>

While the paradigm continues to shift towards endoscopic approaches, there are still situations which contraindicate an exclusive TES. Sincipital congenital cephaloceles with external mass involving facial and nasal bones and traumatic encephaloceles accompanied with skull base multifracture and orbital/intracerebral complications require external approaches, yet frequently in combination with TES.<sup>42,49</sup> Furthermore, selected defects of the posterior frontal plate located nearby frontal recess can be addressed through TES, but an osteoplastic flap approach is needed for laterally and/or cranially located defects (**Figure 42**).<sup>42</sup>

The optimal surgical strategy has to be chosen based on extension, size, location of the lesion, and expertise of the surgical team (**Table 2**). The possibility to rely on different surgical approaches is pivotal, as well as being flexible and prepared to switch or add another approach when forced by

unexpected intraoperative findings. In this view, adequate preoperative counseling is of paramount importance.

### **Surgical timing**

Because of the rarity of SBCs and consequent paucity of sound data, the optimal timing for surgical intervention still needs to be fully defined.<sup>7</sup>

In children, presence of airway obstruction, CSF leak, meningitis, and pronounced facial deformities require prompt intervention.<sup>6,7</sup> On the other hand, in the absence of these risk factors, and in particular in case of newborns with limited blood reservoir, surgery can be delayed and the patient carefully followed.

In adults, active CSF leak and/or history of meningitis suggest the need for intervention, even if in the setting of nonurgent care.

Patients with small and asymptomatic SBCs, in the absence of any major contraindication to the surgical procedure, should undergo elective surgery, as the risk of developing infectious meningitis cannot be excluded.<sup>5</sup>

### **Endoscopic surgical technique**

#### *Resection phase*

TES takes advantage of the corridor offered by the nasal cavities and paranasal sinuses to reach the skull base.<sup>50</sup> Cephaloceles can present in several areas of the skull base and the endoscopic corridor to expose the area of interest accordingly varies from case to case (**Table 2**). However, there are some surgical principles that are essential regardless of the endoscopic corridor employed.

The first phase of any procedure consists of a careful exploration of olfactory fissures, nasal meati, and nasopharynx, taking advantage of intrathecal fluorescein use in non-obvious cases, since multiple or hidden sources of CSF leak can be present simultaneously.<sup>33</sup>

A wide exposure of the area of the defect is pivotal. The base of the cephalocele (*i.e.* the area where the herniated tissue crosses the skull base) needs to be adequately exposed, which is achieved by removing the surrounding structures. The lesion should then be reduced or cauterized flush with the skull base, as herniated brain tissue is typically nonfunctional.<sup>33</sup>

Cephaloceles originating from the caudal aspect of the posterior frontal plate or through a patent and widened foramen cecum can be addressed endoscopically via a transfrontal approach,<sup>51,52</sup>

provided that lateral extension over the orbital cavity is limited (**Figure 23**). However, the surgeon needs to be prepared to switch to an open approach in far anteriorly located cephaloceles, with the frontal osteoplastic flap approach best addressing this anatomical area.

As illustrated above, the cribriform plate is the typical localization of SBCs in adults, most frequently in the posterior third, likely because of the lack of significantly thick bone buttress.<sup>35</sup> Herniations in the olfactory cleft can be addressed by sparing the ethmoidal complex. Wide SBCs of this area may force the need to perform a partial septectomy by removing the perpendicular plate of the ethmoid bone to expose the entire circumference of their base.<sup>33</sup> When the skull base defect includes the vertical portion of the cribriform plate and/or the ethmoidal roof, a more lateral access through the ethmoidal complex is required. For defects of the cribriform plate and ethmoidal roof, the middle and superior turbinate can be spared (and possibly used as source of vascularized flap)<sup>53-56</sup> if their insertion on the skull base is sufficiently far from the bone defect. Otherwise, middle and superior turbinectomy is necessary to adequately expose the skull base defect.

SBCs of the sphenoid sinus are managed through transsphenoidal approaches. The removal of the rostrum allows to gain exposure and working volume, both for lesions of the planum sphenoidalis (**Figure 34**), cranially, and the clivus, caudally,<sup>52,57,58</sup> while simple parasseptal sphenoidotomy usually does not provide proper cranial-caudal exposure. However, it is worth remembering that most sphenoidal SBCs herniate through the lateral wall, whose exposure is achieved by drilling the pterygoid root through a transethmoidal, transpterygoid approach.<sup>33,52,57,59,61</sup>

For uncommon cases of SBC involving the pterygopalatine or infratemporal fossa, the necessary wider exposure can be reached through a combined transsphenoidal-transmaxillary approach.<sup>59</sup>

Preservation of vascular pedicles is always highly recommended during the resection phase even though their use is not in the surgical plan, since they can be helpful to provide a back-up reconstruction in a possible revision setting. In particular, the septal branch of the sphenopalatine artery needs to be spared, possibly through a rescue flap.<sup>60,62</sup>

#### *Reconstructive phase*

Reconstruction usually represents the most critical phase of the entire surgical procedure, as its failure would imply a postoperative CSF leak.

In every case, when preparing the reconstruction bed, the mucosa around the bone defect needs to be removed. In fact, there should be no overlap between the in-situ skull-base mucosa and the graft applied, which could result in suboptimal adhesion between reconstructive layers and



subsequent development of a mucocele.<sup>33</sup> The surrounding bone surface is to be flattened in order to improve adhesion of overlay covering materials.

The bone defect is usually widened beyond the limits of the dural opening to allow proper positioning of grafts for reconstruction. Grafting may be performed with underlay or overlay techniques, or through a combination of both.<sup>33</sup> Placement of an underlay graft for defects smaller than 4 mm may be difficult,<sup>33</sup> but for larger defects multilayer reconstruction is recommended in most circumstances to optimize the chances of success.<sup>6463</sup>

Options for graft materials are numerous. Iliotibial tract, fascia lata, temporalis fascia, collagen matrix, cadaveric fascia, dermis, and pericardium are valuable materials as intradural and epidural layers. Fat can be used as transcranial plug in case of small defects,<sup>6464</sup> as well as a filler for bone depression to flatten the surface where the extracranial layer is positioned (typically for SBC of the lateral wall of the sphenoid, with highly pneumatized lateral recess). A rigid graft may be indicated in a gasket-seal closure for large, high-flow, high-pressure defects.

Small SBCs no longer leaking after cauterization can be covered by a single overlay graft of fascia or mucoperiosteum. Bedrosian *et al.* proposed the interposition of a fat graft between these small defects and mucosal graft.<sup>33</sup>

There are many pedicled options for extracranial coverage. Nasoseptal flap (NSF) is the most frequently used, based on easy harvesting, reliability, and vast surface cover provided. It allows proper reconstruction of cribriform plate, fovea ethmoidalis, and sphenoidal walls. However, it is poorly adequate to cover defects of the posterior frontal plate. In the pediatric population, the application of NSF may be technically difficult due to the narrow nasal corridor. As such, it may be best reserved for older children, large defects, significant intraoperative CSF leak, or other high-risk situations.<sup>6</sup>

In addition to NSF, other nasal mucoperiosteal flaps pedicled on the maxillary or ethmoidal artery systems can be taken into consideration. These are primarily represented by the ethmoidal arteries pedicled septal flap (*i.e.* septal flip-flap),<sup>6465</sup> and middle turbinate (MTF), inferior turbinate (ITF), turbinal, and lateral nasal wall flaps.<sup>53-56,6466</sup> Given their anteriorly located pivot, septal flip-flap and turbinal flaps perfectly suit defects of the cribriform plate and fovea ethmoidalis.<sup>54,6465</sup> Sphenoidal wall defects are best covered with posteriorly pedicled flaps, such as NSF, MTF, ITF, and lateral nasal wall flap.<sup>53</sup> Of note, flaps based on branches of the sphenopalatine artery might be technically difficult to harvest, but represent a valuable option when NSF is unavailable, as is frequently the case in revision surgery.

#### *Post-operative management*

Careful post-operative management is imperative for a successful post-operative course. Outpatient repeated meticulous debridement of nasal crusting and fibrin, as well as check of the status of the skull base reconstruction should be performed until complete healing. Non-collaborative pediatric patients can be scheduled for endoscopic second look with sedation at 15-20 days after surgery.

Maneuvers increasing intracranial pressure, such as lifting anything heavy, blowing the nose, air travel, and doing physical and sexual activity, should be discouraged.<sup>46</sup> Obese patients should be sent for nutritional counseling and weight loss should be accordingly planned.

In the literature on adult patients, the indications for a lumbar drain (LD) lacks univocal consensus and, with special reference to anterior skull base defects, is usually deemed unnecessary given the unfavorable risk-benefit ratio. In fact, complications of LD may be more frequent than postoperative CSF leak in these circumstances.<sup>46,66,67</sup> In our opinion, LD should be positioned in case of large high-flow dural defects, especially in the presence of significant risk factors for postoperative CSF leak such as intracranial hypertension and/or relapsing leak. Furthermore, in patients with significant IHH, reduction of intracranial pressure can be obtained with oral acetazolamide administration,<sup>16,66,68</sup> remarkably increasing the success rate of reconstruction as highlighted in the systematic review by Teachey *et al.*<sup>62,69</sup>

### **Surgical outcomes and complications**

Several studies clearly showed that the transnasal endoscopic route is efficient and safe to approach SBCs, irrespective of the patient's age.<sup>6,7,46,66,70</sup>

A recent systematic review by Lee *et al.* on 110 pediatric patients treated endoscopically for cephaloceles found that the recurrence rate was 5.2% after an average follow up of 25.3 months.<sup>6</sup> In the same paper, failure of reconstruction with post-operative CSF leak occurred in 6.0% of cases across all studies analyzed.<sup>6</sup> These results are in line with what observed in the literature after the introduction of endonasal vascularized pedicled flaps, which have dramatically decreased the incidence of post-operative CSF leak from 15% to about 5% to 6%.<sup>69,70,71,72</sup> The post-operative CSF leak rate reported by Nation *et al.* on a cohort of 39 pediatric patients was 0% using a reconstruction strategy including an underlay-overlay allograft alone for low-flow or nonleaking defects, with NSF being indicated to line the reconstruction only in case of high-flow intraoperative leaks.<sup>46</sup> Of note, NSF has been demonstrated to also be effective in children, while not leading to craniofacial growth abnormalities.<sup>74,75</sup> In patients with no NSF available, other vascularized flaps are likely to provide comparable results in terms of postoperative CSF leak rate.<sup>72,73</sup> However, a single-institution study

on pediatric patients did not show a significant difference in terms of postoperative CSF leak rate when comparing vascularized flap-including reconstruction to purely graft-based ones.<sup>33,75</sup>

Meningitis occurred in 3.7% of cases analyzed in the review by Lee *et al.*,<sup>6</sup> being associated with post-operative CSF leak, especially when persisting for more than 7 days after surgery.<sup>46,74,76</sup> Other complications include alar collapse, nasal stenosis, transient diabetes insipidus, pneumonia, and neurologic injury, cumulatively occurred in 7.0% of cases.<sup>6</sup> Mucocele formation was observed in 14% of cases treated by Di Rocco *et al.*, highlighting the risk of skull base reconstruction to obstruct the mucous drainage pathways, especially when the defect is located anteriorly, near the frontal sinus drainage pathway.<sup>68,70</sup>

Death is exceedingly rare in studies on pediatric SBC treated with TES. The systematic review by Lee *et al.* revealed a single case of death occurred post-operatively following a convulsive episode and attributed to compression of the respiratory center near the site of repair.<sup>6</sup> This low rate of fatal complications is consistent with findings in the adult endoscopic literature.<sup>6</sup> In fact, in the systematic review by Komotar *et al.* on endoscopic skull base surgery in adults, meningitis and perioperative mortality occurred in 0–1% of cases.<sup>43</sup>

## CONCLUSIONS

The comprehensive management of SBC requires a multidisciplinary approach, with assessment of the general conditions of the patient and specific characteristics of the lesion to select the best treatment strategy.

Two distinct pathological scenarios are usually encountered when dealing with SBC: on one hand malformative pathology in the child, on the other acquired pathology due to traumas or IHH in adults.

The current recommendation is to manage SBC with the primary intent of preventing ascending meningitis, with surgery representing the mainstay of treatment. The choice of the surgical approach (endoscopic, open or combined) is usually dictated by size and location of the lesion. When feasible, endoscopic surgery represents the first choice in virtue of its efficacy and more favorable complication profile compared to open techniques.

Reconstruction usually represents the most critical phase of the entire surgical procedure, with the choice of the reconstruction technique relying on the size, site and pressure/flow of the leak, and always favoring use of autologous material.

## REFERENCES

1. Kiyamaz N, Yilmaz N, Demir I, Keskin S. Prognostic factors in patients with occipital encephalocele. *Pediatr Neurosurg.* 2010;46(1):6–11.
2. Suphapeetiporn K, Mahatumarat C, Rojvachiranonda N, Taecholarn C, Siriwan P, Srivuthana S, et al. Risk factors associated with the occurrence of frontoethmoidal encephalomeningocele. *Eur J Paediatr Neurol.* 2008 Mar;12(2):102–7.
3. Daudia A, Biswas D, Jones NS. Risk of meningitis with cerebrospinal fluid rhinorrhea. *Ann Otol Rhinol Laryngol.* 2007 Dec;116(12):902–5.
4. Ziade G, Hamdan AL, Homsy MT, Kazan I, Hadi U. Spontaneous Transethmoidal Meningoceles in Adults: Case Series with Emphasis on Surgical Management. *ScientificWorldJournal.* 2016;2016:3238297.
5. Woodworth BA, Schlosser RJ, Faust RA, Bolger WE. Evolutions in the management of congenital intranasal skull base defects. *Arch Otolaryngol Head Neck Surg.* 2004 Nov;130(11):1283–8.
6. Lee JA, Byun YJ, Nguyen SA, Schlosser RJ, Gudis DA. Endonasal endoscopic surgery for pediatric anterior cranial fossa encephaloceles: A systematic review. *Int J Pediatr Otorhinolaryngol.* 2020 Feb 1;132:109919.
7. Thompson HM, Schlosser RJ, McCarty Walsh E, Cho D-Y, Grayson JW, Karnezis TT, et al. Current management of congenital anterior cranial base encephaloceles. *Int J Pediatr Otorhinolaryngol.* 2020 Apr;131:109868.
8. Rahbar R, Resto VA, Robson CD, Perez-Atayde AR, Goumnerova LC, McGill TJ, et al. Nasal glioma and encephalocele: diagnosis and management. *Laryngoscope.* 2003 Dec;113(12):2069–77.
9. Kennedy EM, Gruber DP, Billmire DA, Crone KR. Transpalatal approach for the extracranial surgical repair of transsphenoidal cephaloceles in children. *J Neurosurg.* 1997 Nov;87(5):677–81.
10. Suwanwela C, Suwanwela N. A morphological classification of sincipital encephalomeningoceles. *J Neurosurg.* 1972 Feb;36(2):201–11.
11. Som P., Curtin H. *Head and Neck Imaging: Expert Consult.* 5th ed. Vol. 1st. Elsevier; 2011.
12. Bialer OY, Rueda MP, Bruce BB, Newman NJ, Biousse V, Saindane AM. Meningoceles in idiopathic intracranial hypertension. *AJR Am J Roentgenol.* 2014 Mar;202(3):608–13.
13. Loftus PA, Wise SK, Daraei P, Baugnon K, DelGaudio JM. Excavating meningoencephaloceles: A newly recognized entity. *Am J Rhinol Allergy.* 2017 Mar 1;31(2):127–34.

14. Nyquist GG, Anand VK, Mehra S, Kacker A, Schwartz TH. Endoscopic endonasal repair of anterior skull base non-traumatic cerebrospinal fluid leaks, meningoceles, and encephaloceles. *J Neurosurg.* 2010 Nov;113(5):961–6.
15. Kreatsoulas DC, Shah VS, Otto BA, Carrau RL, Prevedello DM, Hardesty DA. Surgical outcomes of the endonasal endoscopic approach within a standardized management protocol for repair of spontaneous cerebrospinal fluid rhinorrhea. *J Neurosurg.* 2020 Feb 28;1–7.
16. Martínez-Capoccioni G, Serramito-García R, Martín-Bailón M, García-Allut A, Martín-Martín C. Spontaneous cerebrospinal fluid leaks in the anterior skull base secondary to idiopathic intracranial hypertension. *Eur Arch Otorhinolaryngol.* 2017 May;274(5):2175–81.
17. Campbell RG, Farquhar D, Zhao N, Chiu AG, Adappa ND, Palmer JN. Cerebrospinal fluid rhinorrhea secondary to idiopathic intracranial hypertension: Long-term outcomes of endoscopic repairs. *Am J Rhinol Allergy.* 2016 Jul;30(4):294–300.
18. Radovnický T, Bartoš R, Vachata P, Sameš M. Cerebrospinal Fluid Rhinorrhea due to Transethmoidal Encephalocele Following Occipital Meningioma Resection in an Adult: A Case Report. *J Neurol Surg A Cent Eur Neurosurg.* 2019 Mar;80(2):138–40.
19. Akhaddar A. Brain Herniation into Nasal Cavity Secondary to Large Convexity Meningioma. *World Neurosurg.* 2019;125:398–9.
20. Battaglia P, Turri-Zanoni M, Castelnuovo P, Prevedello DM, Carrau RL. Brain Herniation After Endoscopic Transnasal Resection of Anterior Skull Base Malignancies. *Neurosurgery.* 2015 Sep;11 Suppl 3:457–62; discussion 462.
21. Koutourousiou M, Filho FVG, Costacou T, Fernandez-Miranda JC, Wang EW, Snyderman CH, et al. Pontine encephalocele and abnormalities of the posterior fossa following transclival endoscopic endonasal surgery. *J Neurosurg.* 2014 Aug;121(2):359–66.
22. Renaud M, Fath L, Cheptou M, Dillenseger L, Riehm S, Venkatasamy A, et al. Iatrogenic meningoencephalocele after traumatic perforation of the cribriform plate during nasal intubation of a preterm infant. *Int J Pediatr Otorhinolaryngol.* 2019 Mar;118:120–3.
23. Stavrakas M, Karkos PD, Triaridis S, Constantinidis J. Endoscopic management of paediatric meningoencephaloceles: a case series. *Eur Arch Otorhinolaryngol.* 2018 Nov;275(11):2727–31.
24. Rawal RB, Sreenath SB, Ebert CS, Huang BY, Dugar DR, Ewend MG, et al. Endoscopic sinonasal meningoencephalocele repair: a 13-year experience with stratification by defect and reconstruction type. *Otolaryngol Head Neck Surg.* 2015 Feb;152(2):361–8.
25. Govindaraju R, Tang IP, Prepageran N. Management of sphenoid lateral recess encephaloceles. *Curr Opin Otolaryngol Head Neck Surg.* 2019 Feb;27(1):37–46.

26. Hanz SZ, Arko L, Schmidt F, Kacker A, Tsiouris AJ, Anand VK, et al. Low incidence of true Sternberg's canal defects among lateral sphenoid sinus encephaloceles. *Acta Neurochir (Wien)*. 2020 May 6;
27. Rajasekar G, Nair P, Abraham M, Jaiswal P, Deepti A N null. Endoscopic Endonasal Repair of a Persistent Craniopharyngeal Canal and Sphenoid Meningoencephalocele: Case Report and Review of Literature. *World Neurosurg*. 2019 Feb;122:196–202.
28. Albright AL, Pollack IF, Adelson PD. *Principles and Practice of Pediatric Neurosurgery*. 2<sup>nd</sup> ed. USA. Thieme; 2008.
29. Chen CS, David D, Hanieh A. Morning glory syndrome and basal encephalocele. *Childs Nerv Syst*. 2004 Feb;20(2):87–90.
30. Tirumandas M, Sharma A, Gbenimacho I, Shoja MM, Tubbs RS, Oakes WJ, et al. Nasal encephaloceles: a review of etiology, pathophysiology, clinical presentations, diagnosis, treatment, and complications. *Childs Nerv Syst*. 2013 May;29(5):739–44.
31. Woodworth BA, Prince A, Chiu AG, Cohen NA, Schlosser RJ, Bolger WE, et al. Spontaneous CSF leaks: a paradigm for definitive repair and management of intracranial hypertension. *Otolaryngol Head Neck Surg*. 2008 Jun;138(6):715–20.
32. Dandy We. Intracranial pressure without brain tumor: diagnosis and treatment. *Ann Surg*. 1937 Oct;106(4):492–513.
33. Bedrosian JC, Anand VK, Schwartz TH. The endoscopic endonasal approach to repair of iatrogenic and noniatrogenic cerebrospinal fluid leaks and encephaloceles of the anterior cranial fossa. *World Neurosurg*. 2014 Dec;82(6 Suppl):S86–94.
34. Hesham Atef Elshitany, Ehab Abd ELHaleem Ali. Management of idiopathic intracranial hypertension with repeated lumboperitoneal shunt malfunction. *Egyptian Journal of Neurosurgery*. 2019;34:1.
35. Murray RD, Friedlander R, Hanz S, Singh H, Anand VK, Schwartz TH. Nonrandom spatial clustering of spontaneous anterior fossa cerebrospinal fluid fistulas and predilection for the posterior cribriform plate. *J Neurosurg*. 2017 May;126(5):1720–4.
36. Seth R, Rajasekaran K, Benninger MS, Batra PS. The utility of intrathecal fluorescein in cerebrospinal fluid leak repair. *Otolaryngol Head Neck Surg*. 2010 Nov;143(5):626–32.
37. Kerr JT, Chu FWK, Bayles SW. Cerebrospinal fluid rhinorrhea: diagnosis and management. *Otolaryngol Clin North Am*. 2005 Aug;38(4):597–611.
38. Zuckerman JD, DeGaudio JM. Utility of preoperative high-resolution CT and intraoperative image guidance in identification of cerebrospinal fluid leaks for endoscopic repair. *Am J Rhinol*. 2008 Apr;22(2):151–4.

39. Hingwala D, Chatterjee S, Kesavadas C, Thomas B, Kapilamoorthy TR. Applications of 3D CISS sequence for problem solving in neuroimaging. *Indian J Radiol Imaging*. 2011 Apr;21(2):90–7.
40. Algin O, Hakyemez B, Gokalp G, Ozcan T, Korfali E, Parlak M. The contribution of 3D-CISS and contrast-enhanced MR cisternography in detecting cerebrospinal fluid leak in patients with rhinorrhoea. *Br J Radiol*. 2010 Mar;83(987):225–32.
41. Selcuk H, Albayram S, Ozer H, Ulus S, Sanus GZ, Kaynar MY, et al. Intrathecal gadolinium-enhanced MR cisternography in the evaluation of CSF leakage. *AJNR Am J Neuroradiol*. 2010 Jan;31(1):71–5.
42. Gun R, Tosun F, Durmaz A, Yorgancilar E, Bakir S, Kamasak K, et al. Predictors of surgical approaches for the repair of anterior cranial base encephaloceles. *Eur Arch Otorhinolaryngol*. 2013 Mar;270(4):1299–305.
43. Komotar RJ, Starke RM, Raper DMS, Anand VK, Schwartz TH. Endoscopic endonasal versus open repair of anterior skull base CSF leak, meningocele, and encephalocele: a systematic review of outcomes. *J Neurol Surg A Cent Eur Neurosurg*. 2013 Jul;74(4):239–50.
44. Jeswani S, Nuño M, Wu A, Bonert V, Carmichael JD, Black KL, et al. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study. *J Neurosurg*. 2016 Mar;124(3):627–38.
45. Tatreau JR, Patel MR, Shah RN, McKinney KA, Wheless SA, Senior BA, et al. Anatomical considerations for endoscopic endonasal skull base surgery in pediatric patients. *Laryngoscope*. 2010 Sep;120(9):1730–7.
46. Nation J, Schupper AJ, Deconde A, Levy M. CSF leak after endoscopic skull base surgery in children: A single institution experience. *Int J Pediatr Otorhinolaryngol*. 2019 Apr;119:22–6.
47. Chen W, Gardner PA, Branstetter BF, Liu S-D, Chang YF, Snyderman CH, et al. Long-term impact of pediatric endoscopic endonasal skull base surgery on midface growth. *J Neurosurg Pediatr*. 2019 11;23(4):523–30.
48. Parasher AK, Lerner DK, Glicksman JT, Storm PB, Lee JYK, Vossough A, et al. The impact of expanded endonasal skull base surgery on midfacial growth in pediatric patients. *Laryngoscope*. 2020 Feb;130(2):338–42.
49. Tosun F, Gonul E, Yetiser S, Gerek M. Analysis of different surgical approaches for the treatment of cerebrospinal fluid rhinorrhea. *Minim Invasive Neurosurg*. 2005 Dec;48(6):355–60.



50. Schwartz TH, Fraser JF, Brown S, Tabae A, Kacker A, Anand VK. Endoscopic cranial base surgery: classification of operative approaches. *Neurosurgery*. 2008 May;62(5):991–1002; discussion 1002–1005.
51. Woodworth B, Schlosser RJ. Endoscopic repair of a congenital intranasal encephalocele in a 23 months old infant. *Int J Pediatr Otorhinolaryngol*. 2005 Jul;69(7):1007–9.
52. Nicolai P, Ferrari M, Maroldi R, Hirtler L, Tschabitscher M, Rodella LF. *Endoscopic Transnasal Anatomy of the Skull Base and Adjacent Areas: A Lab Dissection and Radiological Atlas*. 1<sup>st</sup> ed. Italy. Thieme; 2019.
53. Prevedello DM, Barges-Coll J, Fernandez-Miranda JC, Morera V, Jacobson D, Madhok R, et al. Middle turbinate flap for skull base reconstruction: cadaveric feasibility study. *Laryngoscope*. 2009 Nov;119(11):2094–8.
54. Schreiber A, Mattavelli D, Ferrari M, Rampinelli V, Lancini D, Belotti F, et al. The turbinal flap: an additional option for anterior skull base reconstruction. Cadaveric feasibility study and case report. *Int Forum Allergy Rhinol*. 2017;7(2):199–204.
55. Tamura R, Toda M, Kohno M, Watanabe Y, Ozawa H, Tomita T, et al. Vascularized middle turbinate flap for the endoscopic endonasal reconstruction of the anterior olfactory groove. *Neurosurg Rev*. 2016 Apr;39(2):297–302; discussion 302.
56. Wang X, Zhang X, Hu F, Yu Y, Gu Y, Xie T, et al. Middle Turbinate Mucosal Flap in Endoscopic Skull Base Reconstruction. *Turk Neurosurg*. 2016;26(2):200–4.
57. Belotti F, Doglietto F, Schreiber A, Ravanelli M, Ferrari M, Lancini D, et al. Modular Classification of Endoscopic Endonasal Transsphenoidal Approaches to Sellar Region: Anatomic Quantitative Study. *World Neurosurg*. 2018 Jan;109:e281–91.
58. Doglietto F, Ferrari M, Mattavelli D, Belotti F, Rampinelli V, Khshaifati H, et al. Transnasal Endoscopic and Lateral Approaches to the Clivus: A Quantitative Anatomic Study. *World Neurosurg*. 2018 May;113:e659–71.
59. Zoli M, Farneti P, Ghirelli M, Giulioni M, Frank G, Mazzatenta D, et al. Meningocele and Meningoencephalocele of the Lateral Wall of Sphenoidal Sinus: The Role of the Endoscopic Endonasal Surgery. *World Neurosurg*. 2016 Mar;87:91–7.
- [6060. Castelnovo P, Dallan I, Pistochini A, Battaglia P, Locatelli D, Bignami M. Endonasal endoscopic repair of Sternberg's canal cerebrospinal fluid leaks. \*Laryngoscope\*. 2007 Feb;117\(2\):345-9.](#)
- [61. Tabae A, Anand VK, Cappabianca P, Stamm A, Esposito F, Schwartz TH. Endoscopic management of spontaneous meningoencephalocele of the lateral sphenoid sinus. \*J Neurosurg\*. 2010 May;112\(5\):1070-7.](#)

- [62](#). Rivera-Serrano CM, Snyderman CH, Gardner P, Prevedello D, Wheless S, Kassam AB, et al. Nasoseptal “rescue” flap: a novel modification of the nasoseptal flap technique for pituitary surgery. *Laryngoscope*. 2011 May;121(5):990–3.
- [6463](#). Simal-Julián JA, Miranda-Lloret P, Pérez de San Román Mena L, Sanromán-Álvarez P, García-Piñero A, Sanchis-Martín R, et al. Impact of Multilayer Vascularized Reconstruction after Skull Base Endoscopic Endonasal Approaches. *J Neurol Surg B Skull Base*. 2020 Apr;81(2):128–35.
- [6264](#). Lam K, Luong AU, Yao WC, Citardi MJ. Use of Autologous Fat Grafts for the Endoscopic Reconstruction of Skull Base Defects: Indications, Outcomes, and Complications. *Am J Rhinol Allergy*. 2018 Jul;32(4):310–7.
- [6365](#). Battaglia P, Turri-Zanoni M, De Bernardi F, Dehgani Mobaraki P, Karligkiotis A, Leone F, et al. Septal flip flap for anterior skull base reconstruction after endoscopic resection of sinonasal cancers: preliminary outcomes. *Acta Otorhinolaryngol Ital*. 2016 Jun;36(3):194–8.
- [6466](#). Choby GW, Pinheiro-Neto CD, de Almeida JR, Ruiz-Valdepeñas EC, Wang EW, Fernandez-Miranda JC, et al. Extended inferior turbinate flap for endoscopic reconstruction of skull base defects. *J Neurol Surg B Skull Base*. 2014 Aug;75(4):225–30.
- [6567](#). Soudry E, Turner JH, Nayak JV, Hwang PH. Endoscopic reconstruction of surgically created skull base defects: a systematic review. *Otolaryngol Head Neck Surg*. 2014 May;150(5):730–8.
- [6668](#). Chaaban MR, Illing E, Riley KO, Woodworth BA. Spontaneous cerebrospinal fluid leak repair: a five-year prospective evaluation. *Laryngoscope*. 2014 Jan;124(1):70–5.
- [6769](#). Teachey W, Grayson J, Cho D-Y, Riley KO, Woodworth BA. Intervention for elevated intracranial pressure improves success rate after repair of spontaneous cerebrospinal fluid leaks. *Laryngoscope*. 2017;127(9):2011–6.
- [6870](#). Di Rocco F, Couloigner V, Dastoli P, Sainte-Rose C, Zerah M, Roger G. Treatment of anterior skull base defects by a transnasal endoscopic approach in children. *J Neurosurg Pediatr*. 2010 Nov;6(5):459–63.
- [6971](#). Harvey RJ, Parmar P, Sacks R, Zanation AM. Endoscopic skull base reconstruction of large dural defects: a systematic review of published evidence. *Laryngoscope*. 2012 Feb;122(2):452–9.
- [7072](#). Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. *Laryngoscope*. 2006 Oct;116(10):1882–6.
- [7473](#). Ghosh A, Hatten K, Learned KO, Rizzi MD, Lee JY, Storm PB, et al. Pediatric nasoseptal flap reconstruction for suprasellar approaches. *Laryngoscope*. 2015 Nov;125(11):2451–6.

- [7274](#). Patel MR, Taylor RJ, Hackman TG, Germanwala AV, Sasaki-Adams D, Ewend MG, et al. Beyond the nasoseptal flap: outcomes and pearls with secondary flaps in endoscopic endonasal skull base reconstruction. *Laryngoscope*. 2014 Apr;124(4):846–52.
- [7375](#). Stapleton AL, Tyler-Kabara EC, Gardner PA, Snyderman CH, Wang EW. Risk factors for cerebrospinal fluid leak in pediatric patients undergoing endoscopic endonasal skull base surgery. *Int J Pediatr Otorhinolaryngol*. 2017 Feb;93:163–6.
- [7476](#). Abuabara A. Cerebrospinal fluid rhinorrhoea: diagnosis and management. *Med Oral Patol Oral Cir Bucal*. 2007 Sep 1;12(5):E397–400.

## NOTES

### **Conflicts of interest:**

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

### **Funding:**

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

### **Authors' Contribution:**

Dr Vittorio Rampinelli, Dr Davide Mattavelli, Dr Marco Ferrari, Dr Alberto Schreiber, and Dr Marco Ravanelli designed the paper, drafted the initial manuscript and reviewed and revised the manuscript. Prof. Davide Farina, Prof. Alberto Deganello, Prof. Marco Maria Fontanella, Prof. Francesco Doglietto, and Prof. Piero Nicolai have contributed to design the paper and reviewed and revised the manuscript.

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

## TABLES

**Table 1.** Modified Dandy criteria.

1. Symptoms and signs of augmented intracranial pressure.
2. No localizing signs at the neurological examination (except abducens nerve palsy).
3. Normal imaging (except for empty sella).
4. Opening pressure of lumbar puncture greater than 250 mm of water, with normal CSF
5. Alert and awake patient
6. No other cause of augmented intracranial pressure

**Table 2.** Selection of the surgical approach based on location and specifics of anterior skull base cephalocele.

Cephalocele location and specifics	Surgical approach
Ethmoidal roof	Endoscopic transethmoidal
Cribriform plate	Endoscopic transnasal +/- transethmoidal
Planum sphenoidalis	Endoscopic transplanum
Lateral wall of the sphenoid sinus	Endoscopic transsphenoidal +/- transpterygoid
Caudal aspect of the posterior frontal plate and foramen cecum	Endoscopic transfrontal
Lateral and cranial aspects of the posterior frontal plate	External osteoplastic flap +/- combined endoscopic
External mass involving facial and nasal bones	External transfacial +/- combined endoscopic
Traumatic cephaloceles accompanied with skull base multifracture and orbital/intracerebral complications	External transfacial/transcranial +/- combined endoscopic

## FIGURES

**Figure 1.** Main sites of anterior SBCs distribution: Cribriform Plate (CrP) (40-100%), Ethmoidal Roof (ER) (6-40%), Posterior Frontal Plate (PFP) (9-71%), sphenoidal walls (16-38%).<sup>4,6,7,23,24</sup> AEA - Anterior Ethmoidal Artery; LP - Lamina Papiracea; LW - Lateral Wall of the sphenoid sinus; MS - Maxillary sinus; SpS - Sphenoid Sinus.

**Figure 2.** Case of a 36-year-old male complaining of chronic left frontal headache, with onset of intermittent left CSF leak. Imaging showed the presence of a meningoencephalocele of the cranial portion of the posterior frontal plate occupying the frontal recess and reaching the middle meatus (black asterisk in figure A and B, sagittal and coronal MRI T2 weighted sequences, respectively). The caudal aspect of the lesion (black asterisk in figure C) was visible at endoscopic examination by means of lateral displacement of the middle turbinate (MT). Surgical strategy consisted in endoscopic removal of the caudal portion, cleaning the frontal recess from below, combined with pericranium and external osteoplastic flap harvesting. The lesion was removed and its base isolated and coagulated (black asterisk in figure D). Pericranium flap (P in figure E and F) was distended along the left anterior skull base (figure E). Osteoplastic flap was then repositioned and fixed with plates (figure F). FR- Frontal Recess; SpS - Sphenoid Sinus.

**Figure 33.** Case of a 48-year-old female complaining about headache treated for years as it was atypical migraine, without CSF leak. Sagittal cone-beam CT showed an enlarged foramen cecum (black asterisk in figure A). MRI confirmed the suspect of meningoencephalocele: in sagittal T2 weighted sequences (figure B) an extension of tissue with mixed hyperintense (CSF) and intermediate (brain) signal protrudes on the midline below and anteriorly to the normal boundary of the anterior skull base; the FLAIR sagittal sequence (figure C) is characterized by the fall of signal in the fluid component between the cerebral parenchyma. The lesion was treated with endoscopic transfrontal approach. The meningoencephalocele (black asterisks in figure D) was isolated and resected after performing a Draf III procedure. Multilayer reconstruction consisted in positioning inlay epidural fat, inlay septal cartilage (C in figure E), fat fixed with fibrin glue, and lateral nasal wall pedicled mucosa (Fl in figure F). NS - Nasal Septum.

**Figure 34.** Case of a 28-year-old male with CSF leak consequent to facial trauma. Imaging showed the presence of a meningocele of the right planum sphenoidalis (asterisks in figure A and B, coronal CT scan and sagittal CISS weighted MRI, respectively). Arrows indicate the point of fracture of the

skull base). Transsphenoidal approach allowed exposure of the meningocele (black asterisk in figure C), covered by mucosa. It was coagulated with bipolar forceps (Figure D) and, in view of CSF leak ceasing, covered with fat and mucosal graft. SpS – Sphenoid Sinus.