Endoscopic repair of cerebrospinal fluid leaks

Mohammed Ben Husien

MHMBEN002

THE UNIVERSITY OF CAPE TOWN in the fulfillments of the requirements for the degree

MSc in Neuroscience

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Supervisors:

Professor Patrick Semple (Department of Neurosurgery)

Professor Darlene Lubbe (Department of ENT)

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

I cannot express enough thanks to my supervisors Professor Patrick Semple and Professor Darlene Lubbe for their continued support and encouragement. I Would also like to offer my sincere appreciation to them for the learning opportunities that they provided me over the period of my training in neurosurgery.

Thanks to my father Ibrahim and my mother Julie, for always being so proud of me

Finally, to my caring, loving and supportive wife, Haifa: my deepest gratitude. Your encouragement when the times got rough are much appreciated and duly noted. It was a great comfort and relief to know that you were willing to provide management of our three children and household activities while I completed my work. My heartfelt thanks.

MOHAMMED BEN HUSIEN

DECLARATION

I, MOHAMMED BEN HUSIEN hereby declare that the work on which this dissertation/thesis is based on my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for research either the whole or any portion of the contents in any manner whatsoever.

Signed by candidate

Signature Signature Removed

Date 03/07/2017

1. PART A: STUDY PROTOCOL

1.1. INRODUCTION:

Cerebrospinal fluid (CSF) leaks can be classified according to etiology into traumatic (accidental and iatrogenic trauma) and spontaneous (idiopathic) leaks. (1). Patients presenting with a CSF leak will have a spectrum of symptoms from clear nasal discharge and headaches to mental status changes, meningitis, or brain abscesses or it may be asymptomatic (1). The diagnosis of CSF leak can be assessed clinically by asking the patient to lean forward (reservoir test) to assess for watery rhinorrhea from the nose. A fluid sample can be sent for laboratory testing for Beta-2 transferrin or Beta-2 trace protein (2). The CSF can enter the nose through defects in the anterior cranial fossa such as the cribriform plate, frontal sinus, ethmoid sinus and sphenoid sinus; or through a defect in the middle cranial fossa via the sphenoid sinus. CSF can drain from the middle ear through the Eustachian tube into the nose in the event of a temporal bone fracture. Traumatic CSF leaks are usually initially managed conservatively, with strict bed rest. The majority will stop spontaneously within 2-3 weeks (2). Spontaneous CSF leaks, on the other hand, will always need surgical intervention (2). The evolution of CSF fistula repair has changed dramatically in the last 30 years, from craniotomy, that had a higher rate of failure and significant morbidity, to endoscopic repair (1) (2). Wigand reported the first successful endoscopic CSF leak repair in 1981 (5). The endoscopic approach has largely replaced open methods of repair as it is less invasive with a higher primary success rate (average of 90%) (1).

Endoscopic endonasal approaches allow for good exposure of the roof of the nasal cavity (fovea ethmoidalis) and improves access to certain areas of the skull base. Endoscopic surgery has numerous advantages over the standard craniotomy approach: (3) (4)

1. It is a minimally invasive surgical technique compared to a transcranial repair.
2. The endoscopic endonasal approach provides an excellent view of the surgical field.
3. Endoscopic repair requires standard endoscopic sinus surgery instrumentation and endoscopes.
4. Surgery time is often shorter compared to transcranial surgery.

5. There is no minimum age limit for children to undergo endoscopic endonasal repair.
6. Shorter hospital stay

Material used for Endoscopic endonasal repair of CSF leaks:

Various materials are used for CSF leak repair. The purpose of surgery is to seal the CSF fistula, thereby stopping the flow of CSF into the nasal cavity. Graft material can be classified into Autologous, Homologous, and Allograft materials

1. Autologous material includes septal mucosa, abdominal fat, fascia lata, or temporalis fascia (4).
2. Homologous material includes fascia lata or cadaveric pericardium (4).
3. Allograft material includes hydroxyapatite cement (4) and synthetic substrates.

The majority of surgeons recommend using autologous material, specifically from the nasal septum, turbinates, temporalis fascia or fascial lata for the first layer repair (underlay graft). The second layer usually consists of a local pedicle flap or second layer of fascia lata (as an overlay graft). Collagen glue is then used to keep the reconstruction in place (3) (4).

The surgical team will usually consist of a neurosurgeon and otolaryngologist.

1.2. Rational for the Study:

Numerous differences exist between traumatic and spontaneous CSF leaks, including presentation, etiology and recurrence after treatment. The endoscopic endonasal approach to repair traumatic and spontaneous CSF leaks is essentially the same and the technique has several advantages over an open craniotomy.

This study seeks to compare our results of endoscopic repair of CSF leaks in both groups to the published literature. We also describe our endoscopic technique and show that it is an effective treatment strategy that lowers recurrence rates.

1.3. STUDY AIM:

The aim of this study is to evaluate the results of our endoscopic repair of traumatic and spontaneous CSF leaks in patients who presented to Groote Schuur Hospital, UCT private Hospital, Panorama Hospital and Cape Town Mediclinic from February 2005 to August 2015 and to describe our developed endoscopic technique. This is a 10-year clinical audit retrospective analysis study. The patients will be collected from the neurosurgery and otolaryngology data bases with the same surgical team, comprising an otolaryngologist and neurosurgeon, having performed all the procedures.

1.4. Hypothesis:

Endoscopic repair of traumatic and spontaneous CSF leaks provides an excellent treatment modality when compared to the traditional open surgery methods. Our results are compared to those series with the international published literature. Our success rate in the traumatic group was above 90%, and in the spontaneous group was higher than 70% (The success rate being defined as the recurrence of a CSF leak within 12 months of the surgery).

We describe our new technique that resulted in an improved success rate in the spontaneous (100%) and traumatic (95%) groups of patients.

1.5. STUDY METHOD:

1.5.1 Study design:

A retrospective study of patients from Groote Schuur Hospital, UCT Private Academic Hospital, Panorama Mediclinic and Cape Town Mediclinic from January 2005 to December 2015. All the procedures were performed by the same surgeons (otolaryngologist and neurosurgeon).

1.5.2 Patient selection:

Patients were selected from theatre books, and included all patients who had endoscopic repair of CSF leaks. This included all patients presenting with spontaneous and traumatic leaks, confirmed with Beta-2-Transferrin, and a Computerized Tomography (CT) scan showing the bony defect.

1.5.3 Exclusion criteria.

Patients were excluded from the study if they did not have Beta-2-Transferrin confirmation or CT scan done, and if they were lost to follow-up with in 12 months period.

1.5.4 Data collection:

Data collection was being done on an electronic database with variables of

I. Age
II. Sex
III. Sinus involvement (Frontal, Sphenoid, Ethmoid)
IV. Symptoms of presentation (Headaches, Meningitis, Vomiting, watery discharge from the nose)
V. Modality of investigation.
   1. Beta-2 transferrin. Positive or Negative
   2. CT scan finding. Bony dehiscence. Present or Not

      Encephalocoele. Present or Absent

VI. Mechanism of injury in the trauma group (Penetrating, Blunt, Motor Vehicle Accident)
VII. Clinical outcome was evaluated using the recurrence of the leak within 12 months.

1.5.5 Intervention:

This was an observational study, and no intervention was planned.

1.6. Ethics:

The study protocol was presented to the Surgical Departmental Research Committee (DRC) for a MSc in Neuroscience, following which it was be presented to the Faculty Ethics Committee for approval, which was subsequently obtained.

The data collection was commenced as soon the protocol had been approved. The folders of patients with CSF leak (Traumatic and Spontaneous) as per the database where be requested for analysis. The folders were reviewed in the records department for safety and to maintain privacy.

Patient privacy and confidentiality was respected. As patient names are not required, the information will remain confidential and anonymous. Care was taken not to link any personal or identifiable characteristics of the subjects to the data collected or published.

The results of the study will be submitted to a peer review journal for publication and will be the basis of MSc Neuroscience dissertation.

1.7. References:

1. Anstead AS, Liu J. Cerebral spinal fluid leak repair. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2014 Jun;25(2):187–93.

2. Martín-Martín C, Martínez-Capoccioni G, Serramito-García R, Espinosa-Restrepo F. Surgical challenge: endoscopic repair of cerebrospinal fluid leak. BMC Research Notes. Springer Science + Business Media; 2012;5(1):459.

3. Cukurova İ, Cetinkaya EA, Aslan İB, Ozkul D. Endonasal endoscopic repair of ethmoid roof cerebrospinal fluid fistula by suturing the dura. Acta Neurochir (Wien). Springer Science + Business Media; 2008 Aug 23;150(9):897–900.

4. Paul P, Upadhyay K. Endoscopic endonasal repair of traumatic CSF rhinorrhoea. The Indian Journal of Neurotrauma. Elsevier BV; 2010 Jun;7(1):67–9.

5. Wigand ME, Haid T, Berg M. The enlarged middle cranial fossa approach for surgery of the temporal bone and of the cerebellopontine angle. Archives of Oto-Rhino-Laryngology. Springer Science + Business Media; 1989 Oct;246(5):299–302.

2. PART B: LITERATURE REVIEW

2.1. Introduction

Cerebrospinal fluid leaks (CSF) are caused by an abnormal communication between the extracranial space and the subarachnoid space (46). Leakage of spinal fluid into either the ear or nose is termed CSF otorrhea or rhinorrhea, respectively (25). CSF leaks were first characterised as a pathologic entity in 1899 by St Clair Thompson (1,25). Rhinorrhea, or the seeping of fluid through the nose, manifests in roughly 90% of CSF leaks that occur at the anterior skull base, and can become a life-threatening condition (46). When conservative treatment fails, surgical intervention is advised (19).

This review presents a comparison between traumatic and spontaneous CSF leak and the advantage that endoscopic repair has over open craniotomy surgery. It also presents the difference between the spontaneous and traumatic forms of CSF leaks, from presentation, to etiology, modes of treatment, and recurrence after treatment.

Overview of CSF leaks

2.1.1 Causes of CSF leaks

CSF leaks are classified into two etiologies: traumatic or non-traumatic (2,46). The system of classification, as developed by Ommaya in 1960, is the most widely accepted classification system today (25,53). Ommanya's etiological classification divides CSF rhinorrhea into two categories: traumatic and non-traumatic; with non-traumatic being further subdivided into non-traumatic with CSF hypertension and non-traumatic with normal pressure (53). A third category — spontaneous leaks, or primary CSF rhinorrhea — has been recently defined, which describes leaks in patients with no prior history of trauma, or with no other predisposition to CSF leaks (25). Spontaneous, or primary CSF rhinorrhea, is thus classified as a non-traumatic form of CSF leak (39). Bedrosian et al.(3), make the classification distinction that CSF-leaks are either iatrogenic or non-iatrogenic. Non-iatrogenic CSF leaks (or those not caused by surgical trauma) can be largely classified into three groups or categories: traumatic, tumour-related, and spontaneous.

CSF flow is higher in the non-traumatic aetiologies. Anosmia is more common in traumatic cases (53) and is rare among the non-traumatic forms. Headaches *are* common in the non-traumatic form.

2.1.2 Traumatic causes of CSF leaks

Traumatic CSF leaks are more common and can be divided into iatrogenic, and noniatrogenic leaks (3). Between 81% and 90% of CSF leaks are caused by trauma (7), with accidental trauma being the main cause of noniatrogenic traumatic CSF leaks in 70% to 80% of cases (3). The most common types of trauma observed in CSF leak cases are blunt trauma, such as industrial or motor vehicle accidents; penetrating injuries from stab or gunshot wounds; or from intracranial or extracranial surgical trauma (iatrogenic reasons) (7,39). CSF leaks occurs in approximately 2% of all cranial injuries (7). Traumatic CSF leaks show little relationship to gender, unlike the non-traumatic etiology, which predominantly effects adults over 30 years of age, and effects women twice as often as men (53). Posttraumatic CSF leaks are, however, less common in children than in adults, occurring in between 0.2% and 0.3% of cases childhood head trauma. Ibrahim et al. (18) attribute this to the greater flexibility of children's skull bones,. Anosmia is observed in 78% of traumatic cases, although CSF flow is typically higher in the non-traumatic etiologies (53). In more than 50% of traumatic cases, rhinorrhea stops within one week; and the remainder of leaks heal within six months (53).

The most common cause of iatrogenic CSF leaks is the transsphenoidal resection of pituitary tumours, with an incidence of between 0.5% and 15% (3); while acoustic neuroma surgery and functional endoscopic sinus surgeries account for between 7%-11%, and between 0.5%-3% of cases respectively (21). Iatrogenic injury most frequently occurs from an inadvertent violation of the cribriform plate or the roof of the posterior ethmoid sinus during endoscopic sinus surgery (ESS). Half of iatrogenic leaks present intraoperatively, or immediately following surgery, while the remaining 50% only present between one week and one month postoperatively. Theories for the delay in presentation are postoperative increase in intracranial pressure (ICP), resolving cerebral edema, wound contraction, or flap devascularisation (21).

2.1.3 Non-traumatic causes of CSF leaks

The less common, non-traumatic etiologies of CSF leak are typically a result of erosion of the skull base and raised intracranial pressure. These leaks can arise due to infections such as osteomyelitis of the skull and tuberculosis, congenital defects, meningoceles, encephaloceles, intracranial tumours such as osteomas and angiofibromas that destroy the bones of the skull base (26), intracranial pressure (ICP), or hydrocephalus (2,7,37,39,48). Meningoencephaloceles or meningoceles may, however, occur in both non-traumatic and traumatic cases (39).

Intracranial tumors can cause CSF leaks by obstructing CSF reabsorption, which results in increased ICP leading to high pressure leaks (3). Extracranial or intracranial tumour growth can cause an indirect erosion of the skull base (3).

Another more common cause of non-traumatic CSF leaks is congenital encephaloceles, which occurs in cases of open neural tube defects whereby herniations of the meninges and brain matter protrude through structural defects in the cranium (27). The incidence of congenital CSF leak with encephalocele has been reported in approximately one in every 4000-5000 live births (18,55) - often existing at birth in affected individuals. It is, however, typically only diagnosed once the patient presents symptoms of meningitis, an active CSF leak, nasal obstruction, or facial deformity (55).

2.1.4 Spontaneous CSF leaks

Spontaneous, or primary CSF fistulas, are classified as a separate etiological entity, since it describes patients that have “no other discernible etiology for their CSF leak” (25,). - such as a tumour or congenital abnormality, or any history of trauma. They are therefore classified as having originated from other idiopathic aetiologies (25,28).

According to current understanding, spontaneous or primary CSF leaks are typically associated with increased ICP, which is likely caused by Benign Intracranial Hypertension (BIH) (3). This is due to the finding that 70% of spontaneous CSF leak patients are diagnosed with BIH (51). Lopatin et al. (26) have also listed obesity, an overpneumatised sphenoid, and empty sella syndrome as etiological factors in the spontaneous generation of CSF fistulas. Spontaneous leaks are usually associated with the formation of encephaloceles. Bedrosian et al. (3) suggest that increased ICP may result in the formation of quite large encephaloceles that herniate through pre-existing skull base defects, pushing the brain contents through these small skull-base defects.

Spontaneous CSF leaks are most commonly observed in obese middle-aged women (3,25). Although spontaneous leaks are reported rarely, it is believed that that they may be more common than previously thought (25).

2.2. Anatomy and CSF leaks

In the cases of CSF rhinorrhea,the Leaks into the nasal cavity can occur directly from the anterior cranial fossa, namely the frontal sinus or the cribriform plate, or as a result of defects in the cranial fossa, namely the sphenoid sinus (22). Ultimately, defects leading to CSF rhinorrhea can occur at any point along the ventral skull base, including the cribriform plate, fovea ethmoidalis, sphenoid bone, temporal bone, or the posterior table of the frontal sinus (32,39), as shown in Figure 1(3). Although uncommon, CSF that enters into the nose indirectly through the eustachian tube via the mastoid air cell system in the middle or posterior fossa, is specifically referred to as CSF otorhinorrhea (22,34).

During spinal surgery, CSF fistulas may also occur which are attributed to inadvertent dural tears (DTs), or deliberate dural opening such as for marsupialisation of cysts, performing shunts or resecting intradural tumours or lesions (Epstein, 2013). DTs can arise inadvertently during primary spinal surgery, but are observed more often during revision spinal surgery as a result of epidural scarring. CSF fistulas or DTs may also be caused by resection of ossification of the posterior longitudinal ligament (OPLL), ossification of the yellow ligament (OYL), or epidural steroid injections (Epstein, 2013). Due to the extracranial localisation of most CSF fistulas and dural tears occurring during spinal surgery, they will not be considered in more detail for this review.

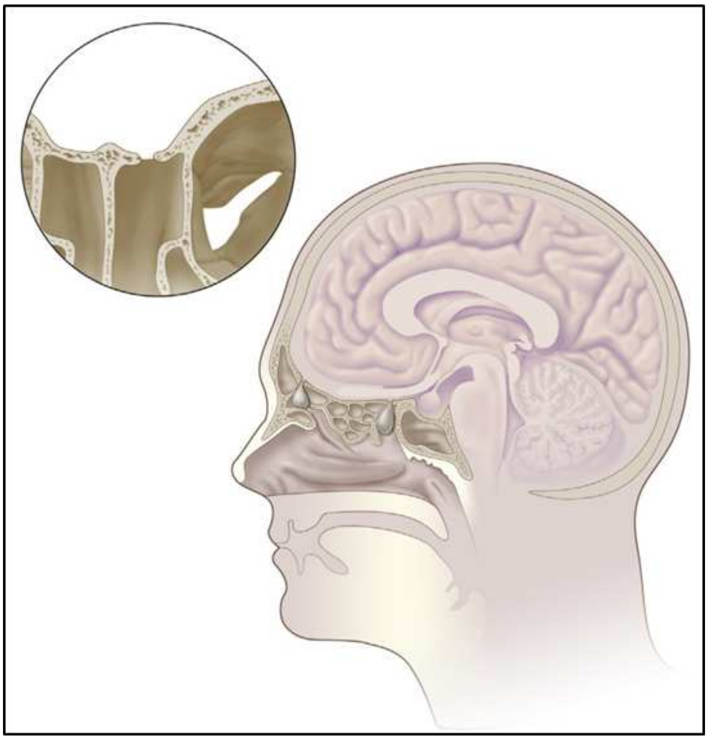

Figure 2.1: Illustration of the sagittal view of the skull base, depicting the locations of possible skull base defects, with defects shown at the cribriform region (posterior), and the foramen cecum (anterior). The inset also depicts the fovea ethmoidalis, a frequent site for iatrogenic skull-base violation. Source: Bedrosian et al. (3)

2.3. Dangers of CSF leaks

Defects that remain untreated expose patients to the risk of pneumocephalus, intracranial abscess, and meningitis (2,46). Meningitis, which is a primary hazard in the traumatic form, is far more common than in the non-traumatic varieties (53).

Surgical repair of skull base defects are also performed to prevent nasal obstruction, feeding difficulties, and problems with oral breathing that may be caused by the growth of defects in children (55).

2.4. Historical overview of CSF leak repair

When conservative treatment is not successful, surgical intervention is advised (19). Early attempts at repairing CSF leaks were performed by Grant (15) and Dandy (8) in 1923 and 1926 respectively, the latter having closed cranionasal fistulas through a frontal craniotomy (7,19,39).

Fascia lata was first used to repair CSF fistula through a transcranial extradural repair in 1937 by Cairns (5); however, the transnasal approach was limited to cauterisation until 1948, when the transnasal-transethmoid approach was described (11) by sealing off the cribriform plate leak with a septal and middle turbinate (MT) flap (53). The first reported extracranial repair of a CSF rhinorrhea was also performed by Dohlman in 1948 (11), using a naso-orbital incision (22,52). Subsequently, various endonasal approaches were developed using turbinate or septal flaps to repair the fistula site. In 1981, Wigand performed the first successful endoscopic endonasal repair of a CSF fistula, using a rod lens rigid endoscope (49).

Current advancements in surgical techniques and medical instrumentation have made endoscopic repair of anterior skull base CSF leaks a standard in otolaryngological care, and endoscopic sinus surgery (ESS) has become a common procedure in the field of otolaryngology (46). More than 90% of cases are treated successfully using this technique (2).

2.5. Detection of CSF leaks

Clinical confirmation of CSF rhinorrhea involves nasal inspection and laboratory testing for CSF markers (7,46). During nasal inspection, the common presenting symptom observed in patients with CSF rhinorrhea is the seeping of a clear fluid from one nostril (7).

The CSF has a low specific gravity, high sugar (higher than 30mg/dL, or 1.7 mmol/L), and low protein content (26,53). Measurement of the sugar content is performed on the nasal fluid using glucose oxidase test papers to provide preliminary confirmation of the presence of CSF (7). Drops of CSF from a traumatic leak, which are placed on absorbent filter paper, also typically form a “double-ring” pattern, due to a central ring of blood, and a perimeter ring of CSF (53, p.157).These are not reliable ways to confirm or refute the presence of CSF.

CSF markers that are used to confirm CSF rhinorrhea include β2-transferrin and β-trace protein. β2-transferrin is a protein that is only found in CSF, aqueous humour, perilymph and other pathilogies e.g tumours; thus, testing the nasal secretions for the presence of β2-transferrin represents a far more specific test than the glucose oxidase test (7). β-trace protein markers are economical and have a high specificity and sensitivity, while β2-transferrin markers have a high specificity and sensitivity; but are less economical than β-trace protein markers (45,46).

It should be noted that while the β2-transferrin assay is usually more specific for CSF than other methods, in the case of associated orbital injuries it can be unreliable since β2-transferrin also exists in the vitreous humour (46).

Confirmation of CSF leaks is accurate in more than 90% of cases (2); however, in some cases, the accurate localisation is difficult to determine (28). While the afore-mentioned tests are non-invasive and accurately diagnose the leakage of CSF, they offer little information on the actual location of the leak (7). Accurately identifying the location of a CSF fistula is important for planning the surgical approach (28). The identification of the site, size and etiology of CSF leaks have been described as the most important factors in determining the success of any reparative surgery (46).

Detection of the leak site is usually performed either through magnetic resonance imaging (MRI), or computed tomography (CT) scan. Radiolabeled cisternogram, CT/MRI cisternograms or nasoendoscopy with intrathecal fluorescein,are performed less frequently intraoperatively (2).

2.5.1 Intrathecal fluorescein

If the location of the defect is unknown, or less apparent following an MRI or CT (or in the case of spontaneous or multiple defects), a lumbar puncture is performed, and one hour before surgery, the doses fall in the range of 0.1 to 0.5ml of 5% to 10% Fluorescein in 10ml CSF mixture is slowly injected over more than one minute (53). The patient is then laid in a Trendelenburg position to aid the Fluorescein in reaching the intracranial compartment. Intrathecal Fluorescein is, however, not always used, as in the case of iatrogenic injury, where the defect is clearly visible on MRI or CT, and the location is known. Its use is also much debated in the literature (19,46,53). In the case of concurrent leaks, or multiple defect sites, many researchers argue that it is especially important that intrathecal Fluorescein is used (2). CSF is observed, and thus the location of a leak may be visualised, when Fluorescein-stained CSF is seen seeping as a bright yellow-green fluid that emanates from the defect site (39,53).

Martin-Martin et al. (46) argue that intrathecal Fluorescein should not be used during surgery, due to its possible complications. Instead, they recommend observing the leak during surgery by a valsalva manoeuvre, thereby increasing intracranial pressure by pressing on the abdomen, and locating the leak as a stream of transparent fluid. Sharma et al. (53) also suggest that there are risks of allergic reactions and transverse myelitis with Fluorescein. Fluorescein is neurotoxic in commercial doses, however, Javadi et al. (19) maintain that, based on the results of their study, diluted Fluorescein is safe in the low doses administered during endoscopic repair of CSF rhinorrhea. Authors of series have also suggested that identification of the fistula is one of the most difficult challenges in CSF leak repair, and successful identification is central to the success of any operation (3,25). The risks are therefore often weighed against the advantages of using intrathecal fluorescein.

Other methods of CSF observation have also been employed in the past, including dyes such as phenolsulfonphthalein, indigo carmine and methylene blue, which were introduced intranasally or into the subarachnoid spaces prior to surgery. However, these dyes are no longer in use as they can cause chemical meningitis, and carry a significant risk of morbidity (53).

2.5.2 MRI and CT Cisternography

For over a decade, the gold standard for CSF leak location detection has been CT cisternography with an accuracy of 92% in active leaks, and 40% in inactive leaks (28,44). A shortfall of CT cisternography, however, is that it is time-consuming, invasive, uncomfortable for the patient, and can carry the risk of headaches and infections (28). It is also contraindicated in patients with elevated ICP, or meningitis (28).

Unlike CSF site leak detection following trauma, CTscan is usually less sufficient in spontaneous CSF rhinorrhea, since patients with spontaneous CSF rhinorrhea naturally lack skull fracture sites that can be detected by high resolution CTscan in traumatic patients (28). CTscan only provides indirect evidence for CSF leaks, through abnormalities such as bone defects, or a fluid in the paranasal sinus, or pneumocephalus. Spontaneous leaks are also often associated with encephalocele formation (between 50 and 100%), and large meningoencephaloceles may herniate through relatively small bony defects, which may be mistaken on CTscan to be small bony defects or secretions of the paranasal sinus (28,41).

False positives have also been observed in CT scans during spontaneous CSF leaks, whereby dehiscence or thinning of the skull base, which would be observed under high-resolution CTscan, can be mistaken for small bone defects (4).

In some cases, MRI has advantages over CTscan in CSF leak detection (28). Firstly, MRI complements high-resolution CTscan, with an accuracy of 89%, sensitivity of 87% and specificity of 100%, in demonstrating the extracranial extension of the CSF column (41). MRI is also more effective in evaluating the leak point when the accurate evaluation of the CSF leak site(s) may be precluded by fibrous tissue or hematoma in the paranasal sinuses; or when there are multiple fractures of the skull base (28).

2.5.3 Pre-operative assessment

Patients are typically referred for neurosurgical evaluation prior to undergoing operative repair, which is ultimately determined by the location and size of the area for repair. The surgical approach will depend where the defect is located, though most often it is located in the cribriform region or ethmoid roof, as well as in the sphenoid sinus (37). In the case of iatrogenic injury, the most common location of CSF leak is at the ethmoid roof and the lateral lamella, as shown in Figure 2.

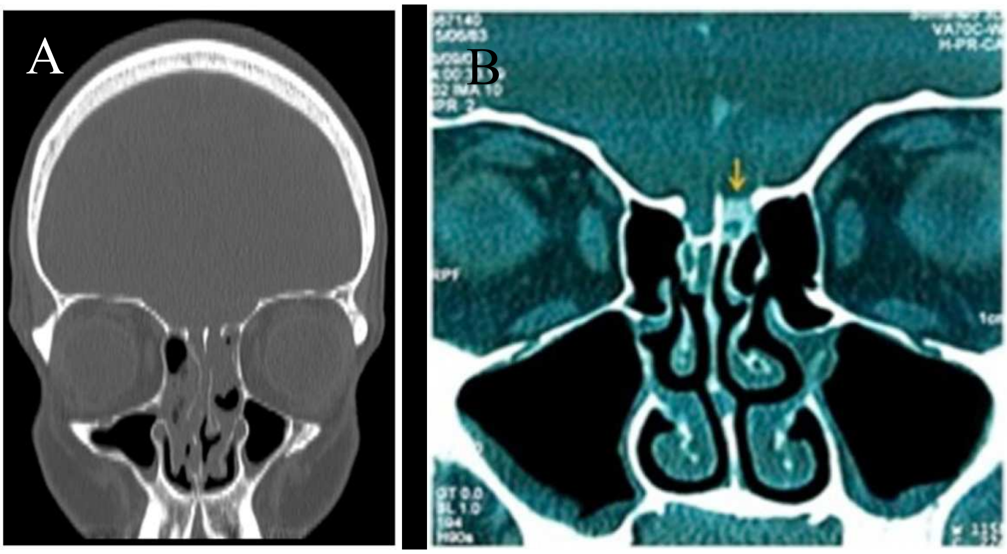

Figure 2.2: CT scan of an iatrogenic leak in the lateral lamella (left), and coronal CT of a spontaneous leak in the ethmoid roof (right) Sources: Anstead and Liu (2) (A); Martin-Martin et al. (46) (B)

2.6. Treatment of CSF leak

Most CSF leaks that result from iatrogenic or accidental causes, heal over the course of seven to ten days, following the implementation of conservative measures (39). Leaks that are less likely to spontaneously heal are those in which CSF rhinorrhea develops a few days or weeks after a trauma, leaks that are caused by gunshot wounds and large leaks that occur immediately after surgery (39).

The preliminary treatment includes bed rest with elevation of the head, avoiding straining activities such as coughing, sneezing nose blowing, and the use of stool softeners. Surgery is indicated if no resolution is detected within one-to-two weeks (39). The etiology of the leak also affects the risk of recurrence of CSF leaks, and therefore the method of repair of the defect, since the etiology would typically have a bearing on the location, size, degree of dural involvement, the probability of raised ICP, and the likelihood of meningoencephalocele protrusion (46).

2.7. Types of approaches to the skull base

Multiple approaches have been described for reaching defects at the base of the skull, including transsphenoidal, transethmoidal, transpterygoid, transcribiform, transplanum, and transclival; each depending on the site of injury (14,35,42). Three core approaches exist, however, for reaching CSF fistulas: Intracranial, extracranial, and endoscopic (53). Surgical repair of CSF leak defects may be achieved extracranially through a frontal sinusotomy or external ethmoidectomy, transcranially through a bifrontal craniotomy, or transnasally through visualisation with endoscopic or microscopic instruments (52). Conventionally, fistulas that persist, or those that do not respond to conservative treatment have been managed by a frontal craniotomy (52).

In the case of defects of the ethmoid roof or cribriform, a direct paraseptal approach may be recommended (34). To create adequate exposure, a complete ethmoidectomy and maxillary sinusotomy are often required, while frontal sinusotomies, middle-superior turbinectomies, and sphenoidotomies may also be required to provide added exposure.

In a study by Kirtane et al. (22, p.208) on 267 CSF leak repairs, the authors suggested that in the event of defects in the medial lamella of the cribriform plate, the preferred approach to the defect was between the septum and the middle turbinate, thereby allowing the defect to be localised and sealed, without “sacrificing the turbinate.”

2.7.1 Intracranial procedures

Originally described by Grant (15) and Dandy (8), intracranial procedures are still prescribed for most traumatic and non-traumatic cerebral fistulas. The critical element for surgical treatment is for the meningeal defect to be adequately closed (53), with careful patching of the fistula site typically accomplished using a fat graft — with or without fascia lata as a free graft, and often using the patient's own fat.

Although highly invasive, there are advantages of the transcranial approach (52). These include the ability to directly visualise the dural tear, the ability to treat any adjacent brain injuries that may exist, or the treatment of intracranial bleeding, especially in the case of trauma-related CSF leaks. Another advantage is the opportunity to use a pericranial vascularised flap to cover the anterior skull base, which is not possible during endonasal endoscopic approaches (EEA) (52).

The primary disadvantages of intracranial approaches are edema that is related to brain retraction, anosmia, and intracranial haemorrhaging (43). The success rate for transcranial repairs is only generally considered to be between 60% and 80% (23,24,52) with Sharma et al. (53) suggesting that success rate from the first attempt is only around 60%. Invasive techniques such as open transcranial repair, which traverse neurovascular structures, account for a substantial morbidity, and renders this type of repair a high-risk surgery (17). Reasons for the morbidity associated with the transcranial approaches for repair of CSF rhinorrhea include intracranial haemorrhage, venous infarction, cerebral contusion, bifrontal retraction injury, cerebral edema from frontal lobe retraction, pneumocephalus, anosmia from trauma to the cribriform plate and the olfactory bulb area, and bone flap infection (13,39,52).

Aside from increased risks of morbidity, other complications associated with the open transcranial approach are loss of smell and memory deficits (1,55). In transcranial approaches to the skull base, extensive bone drilling, nerve manipulation and brain retraction is required to expose the underlying pathology in the skull base (38). Transcranial surgery is a difficult operation that typically causes damage to the olfactory nerve fibres traversing the cribriform plate (28), since it requires mobilisation of one or both of the frontal lobes (18). It also carries the need for a large external incision, resulting in a large surgical wound (23,52). Various transcranial procedures have also been suggested for repairing anterior skull base defects in children; however, Ibrahim et al. (18) suggest that these approaches can potentially upset the growth centres in the craniofacial skeleton, causing facial asymmetry.

In many circumstances, however, intracranial approaches are the only possible option, such as in many of the traumatic etiologies, and often in the case of tumours (38). In spite of recent progress in microsurgical techniques, the location of lesions, and their contiguity to vital neurovascular structures can at times make surgical resection difficult. In the case of ventral midline tumours, transcranial approaches that use microscopic equipment need large bone openings to be made, that facilitate the passage of adequate light to the lateral extents of the lesion sites (38). This may require a range of open-skull base techniques to allow the surgeon to pass either sub-frontally or laterally, thereby providing a convoluted pathway to the lesion site. As alluded to previously, these techniques typically require large areas of bone to be removed, retraction of the brain to some degree, and manipulation of the cranial nerves across the operative trajectory between the surgeon and the lesion (38).

2.7.2 Extracranial procedures

Recommended by Aboulker et al. in 1966 (53), the extracranial approach to CSF leaks involves access to the defect through the frontal and ethmoidal sinus. Sharma et al. (53, p.159) assert that leaks occurring through the sphenoid sinus and sella turcica are best approached via the "microneurosurgical trans-sphenoid" route.

The primary advantages of the extracranial approach are higher rates of success than the intracranial approaches, lower rates of morbidity, and far less risk of anosmia (6,10,29,33). These approaches also offer the best exposure of the parasellar, sphenoid, and posterior ethmoid regions, and allow superior visualisation of fistulas in the cribriform plate, fovea ethamoidalis, and the posterior wall of the frontal sinus.However, not all parts of the cranial base can be accessed using these techniques (30,53).

2.7.3 Endoscopic approaches

The endoscopic approach to CSF fistulas is a "subset" of the extradural, extracranial, approaches to CSF leaks (53, p.159). As noted previously, since the first performance of an endoscopic treatment of CSF rhinorrhea by Wigand (49), the technique has become popular, globally, due to its benefits, including shortened operation time, good visualisation, and precise graft placement (47).

The endoscope-assisted ventral endonasal approaches utilise less-invasive means, since they take advantage of natural anatomic corridors that exist, in order to reach the defects of the midline skull base, while providing maximal preservation of the anatomic structures. Other prime advantages of the transnasal, or endoscopic endonasal approach (EEA) are that it minimises the intranasal trauma to the patient while preserving the bony framework that supports the frontal recess and other critical regions of the face (53,54). EEAs also offer higher efficacy of repair, and lower incidences of complications relative to the traditional cranial base techniques (38).

Since they provide an accessible trajectory to reaching the anterior skull base through the ethmoid and sphenoid sinuses, EEA can be used either as an adjunct to the microscope for reaching more lateral components of the target, or the sole means of illumination in accessing the ventral and midline regions (38).

Since the first successful repair of a CSF leak performed by Wigand in 1981 (49), minimally invasive endoscopic endonasal surgery (EES) for repair of CSF rhinorrhea has largely replaced the more invasive open transcranial approaches to the skull base (7,39).

2.7.4 Open transcranial versus endoscopic endonasal approaches

Endoscopic endonasal approaches allow excellent exposure of the nasal cavity roof, and improved access, which in turn offer the opportunity to reach and treat defects efficiently (31,46). Numerous other advantages of EEA exist over open transcranial and extracranial interventions (46). These are summarised as follows:

- EES is a less invasive surgical technique, as compared to open transcranial repair, as it provides a “direct short-cut access” to the anterior and middle skull base, without the need for traversing any important neurovascular structures;
- EES provides an excellent, panoramic view of the surgical field (53);
- EES does not require specific material or instruments for performing the procedure, aside from a rod lens rigid endoscope and FESS instruments;
- Nasal endoscopes are available with different angled lenses, which can clearly expose the roof of the sinonasal tract, and facilitate the precise localisation of CSF fistulas (52);
- There is no minimum age limit for children or infants to undergo EES; and
- EES may be performed in a shorter surgery time than transcranial procedures (53).

Defects that are smaller than 1.5 cm in size, and located within the cribriform, sphenoid, ethmoid, and frontal sinuses, which are most easily accessed transnasally, are best repaired by EES (34). Increased success rates for the EES types of treatment have also been cited, whereby the success rate for leak closure of endoscopic CSF leak repairs was observed in a systematic review (28) to be 90.6% after the first attempt, and as high as 96.6% following a second attempt; with very little chance of complications (0.03%). Additionally, in a study by Martin-Martin et al. (46), the success rate of 30 patients who underwent CSF leak repair surgery by EES was even higher, at 93.4%, and none of the patients that required a second procedure required a craniotomy for closure.Looking at the success rates between endoscopic and open approaches generally compares two different types of patients.Literature on endoscopic cases reflects a small skull base defect.Open approch series tend to come from a time when imaging was far less complex and also includes patoients with larger defects.

As described above, there appears to be no minimum age limit for EES (55), and in a study by Di Rocco et al. (9), the youngest reported CSF leak repair patient was 1.5 months old. Similarly, in a study by Ma et al. (55), the youngest patient was 3 months old, while a large number of the study's patients were younger than 1 year of age.

It should be noted that EES is not an option in all cases, and as described previously, in the event that fistulas occur in the posterior wall of the frontal sinus, open transcranial techniques are still the only option (46). Situations where a craniotomy are still required include oncologic procedures, as described previously,multiple and extensive fractures of skull base, frontal sinus defects with lateral extensions; defects that are greater than 1.5cm in size, or defects of the posterior wall of the frontal sinus where an open technique best addresses the primary lesion site (32,34).

Furthermore, Cukurova et al. (7) assert that while a leak in the ethmoid roof or cribriform plate can be treated with standard EES, a full endoscopic ethmoidectomy is often required to provide suitable exposure of a skull-base defect and leak; and at times, a frontal sinusotomy, sphenoidotomy, and middlesuperior turbinectomy may be needed if additional exposure is required.

2.8. Material used for CSF leak repair

Various materials are used for CSF leak repair (52). The ultimate purpose of surgical intervention is to insert a seal or blockage to the CSF fistula, thereby stemming the flow of CSF. For this purpose, numerous grafting materials, and intraoperative instruments have been prescribed (12,56).

2.8.1 Grafting materials

Grafting materials used for CSF repair are most often cartilage, fascia, fat, local pedicle tissue, cadaveric fascia or dermis, mucoperichondrium, turbinate, septal mucosa, free mucosal grafts, or composite grafts (34). In high-flow or large skull base defects, pedicle nasoseptal flaps (PNSFs) have been widely used since their inception in 2006 (12,16,20). Zweig et al. (52) categorise the materials used for grafting as either autologous, homologous, or allografts:

- Autologous materials include septal mucosa, abdominal fat, turbinate bone, or temporalis fascia;
- Homologous materials include fascia lata, or cadaveric pericardium; and
- Allografts include materials such as hydroxyapatite cement or other artificially produced medical devices.

Often, surgeons recommend obtaining grafts of the nasal passages, and specifically from the nasal septum, turbinates or the nose floor. The temporalis fascia is also considered appropriate (40). Each Fistula should be treated uniquely, though, and Martin-Martin et al. (46, p.4) recommend that a surgeon should "know the different options" available, in order to "solve the problem".

Saafan et al. (39)In his own experience he suggests that in the event that the patient has increased CSF pressures, a rigid underlay graft should be used, such as bone. Conversely, in the event of leaks that have normal intracranial pressures, soft tissue grafts are often suitable, and rigid grafts are typically not necessary (39).

Material that can be used for rigid grafts includes bone grafts from the mastoid, turbinates or septum; while soft tissue materials for overlay or underlay grafts can include fascia lata, temporalis fascia, free mucosal or mucoperichondrial grafts, or cadaveric dermis or fascia (39,50). These may be to used overlay, such as over the nasal side of the defect, or underlay — between the skull base bone and dura — to seal the affected region (39).

Zweig et al. (52, p.139) argue that, regardless of the choice of material and the specific technique performed in the repair, "if the surgical technique is sound", the endoscopic repair of CSF leaks should still be "highly successful".

2.9. Intraoperative instruments

Instruments used in the endonasal endoscopic surgical (EES) repair of CSF rhinorrhea include various endoscopic nasal instruments, such as 0-, 30-, and 45-degree rigid nasal endoscopes. In the event that fluorescein is to be used for the purposes of the CSF leak, a yellow light filter is applied to the endoscope, and a blue light filter is used for identifying the leak site,this is not usually necessary as the defect is often obvious to the naked eye (34).

Although its use is disputed (56), a perioperative lumbar drain may be used to regulate ICP, administer intrathecal fluorescein, and aid in reducing encephaloceles (34). The drain typically remains in situ, postoperatively, for between 24 and 72 hours (34). A low rate (5 mL/h) lumbar drain for a short duration postoperatively also assists in avoiding pooling at the defect reconstruction site following placement of the graft, thereby allowing any sealant to fully harden with a watertight seal(32) .There is currently a controversy around the use of lumbar drain in the repair of CSF leaks and no evidance to show that they are of any benefit,complication rate with LD are not insignificant,they include headache, cellulitis at the punture site, meningitis, pneumocephalus and in rare instances, uncal herniation.

2.9.1 Repair of CSF leaks by Endoscopic Endonasal Surgery

The team involved in an EES repair of a CSF rhinorrhea typically involves an otolaryngologist and neurosurgeon. General anaesthesia is almost always induced (19,23), and a topical decongestion of the nose is achieved using cottonoids soaked in phenylephrine, oxymetazoline, or 4% cocaine (32). The nasal mucosa is typically treated with epinephrine to achieve a complete contraction of the blood vessels, and the nasal cavity is also disinfected with iodoform (23). The patient is then usually placed in a supine position with their head elevated by 15° (19,23).

A lumbar drain may be placed; and prior to the injection of fluorescein, the patient should receive a dose of diphenhydramine and dexamethasone (32). Standard procedure then dictates the slow injection of 0.2 ml of 10% fluorescein, intrathecally, diluted in 10 mL CSF, up to one hour before surgery (2). A blue light filter positioned on the endoscopic light source enhances the fluorescein dye, and helps to locate the CSF leak (32,34). In the event that the defect location is known, such as in the case of iatrogenic or traumatic injuries, or if the defect is clearly visible on MRI or CT, intrathecal fluorescein is not necessarily used (2).

In the first phase of the surgical procedure, adequate exposure of the entire bony defect must be obtained, which may necessitate an extended approach to allow visualisation of the skull base defect (32). In the case of lateral sphenoid defects, a transmaxillary, transpterygoidal approach may be required as an adjunct to the standard transsphenoidal, transethmoidal approach. Furthermore, in the case of cribriform plate defects, a partial or total resection of the middle turbinate (MT) may be required in order to access the defect (32). Thus, while one school of thought is that the middle turbinate should be excised, another belief is that the operation should simply lateralise the middle turbinate (53).

Surgery can be performed with or without the use of a nasal speculum; however, a nasal speculum can obviate the need for a middle turbinectomy, thereby widening the nasal passage to facilitate the placement of the telescope and other instruments (53). A middle turbinectomy also prevents accidental knocking of the telescope against the turbinate (53).

Once the defect has been located, the mucosa must be entirely stripped away from the defect site, and a bed fashioned in preparation for a graft (34). Curettes or a diamond burr are often used for this purpose (18). A wide exposure of the defect site may assist graft placement and improve the rate of success of closure (32).

In preparation of the site, any encephaloceles or dural protrusions must be resected or reduced into the intracranial cavity — for example, by bipolar elecrocautery at the stalk — to prevent them from retracting into, and haemorrhaging within the skull (32,18). Careful use of a microdebrider, or otherwise thru-cut forceps can be used to reduce or resect the herniated dura (32). In the case of any encephaloceles, herniated brain tissue within the nasal cavity is seldom functional, and is deemed a source of intracranial infection if not resected (57). It is also important to ensure that any contact between the prolapsed brain and the bony defect is severed (32).

A graft is then placed over the site to cover the defect (34). Closure of the grafted repair site is performed using either an overlay, underlay, combined, or obliteration technique, depending on the nature and size of the defect (34).

2.9.2 Onlay or overlay technique

The onlay or overlay technique is generally recommended in small leaks less than 10 mm, or in cases where the underlay technique is not possible (32,46). In the overlay technique, the graft is placed extrinsically, or on the nasal side of the defect, as shown in Figure 3.

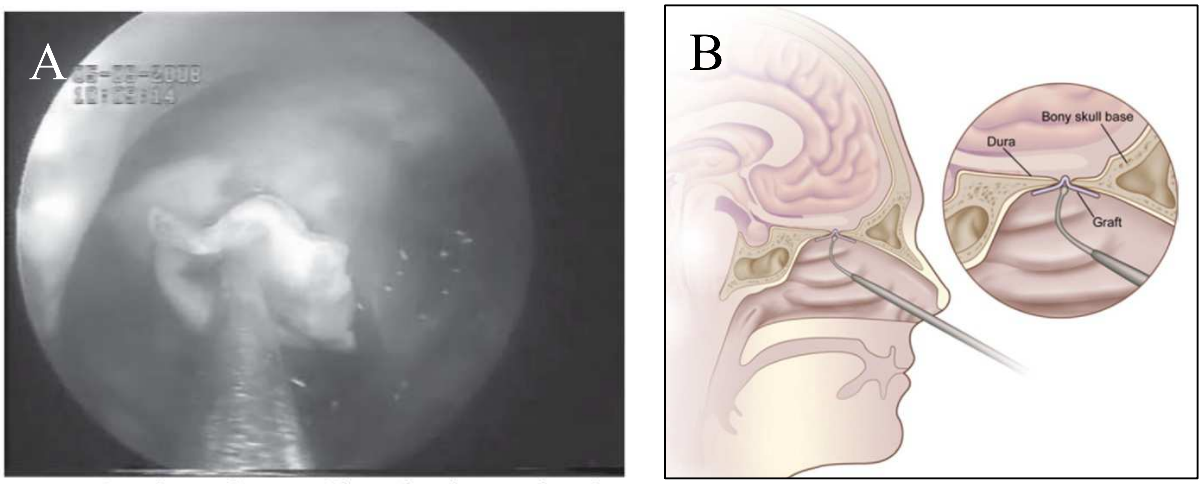

Figure 2.3: Photograph of the overlay technique, with fascia being grafted into a defect of the sphenoid roof (A), and a schematic sagittal diagram of a defect being plugged by soft tissue using a seeker probe (B). Source: Paul and Upadhyay (34) (A); Nyquist et al. (32) (B)

Small defects are usually sealed by placing an inlay of graft material, or simply by "plugging" tissue into the defect using a seeker probe, as shown in Figure 3 . The bony defect is transcended by the graft with both a sinonasal and an intracranial component, which circles the defect with a surrounding, watertight seal (32). Materials that are commonly used for the onlay graft include fascia lata, fat, and medical device products such as Alloderm by LifeCell Corporation in Branchburg, New Jersey, or DuraGuard by Biovascular Corporation in Minneapolis (32). Often, a tissue sealant such as Duraseal by Covidien in Mansfield, Massachusetts, can be used to secure the graft in place (32).

2.9.3 Underlay technique

In the underlay technique, the graft material is placed between the dura and the bone of the skull base, as shown in Figure 4. Various CSF leakage repair strategies have been described that use an underlay technique, and it is widely accepted that the preferred method of treatment for large defects is through the underlay technique (46). In this method, fistulas are closed by placing mucoperichondrium, which is combined with a grafting of cartilage, and sealed with fibrin glue into the fistula site (34).

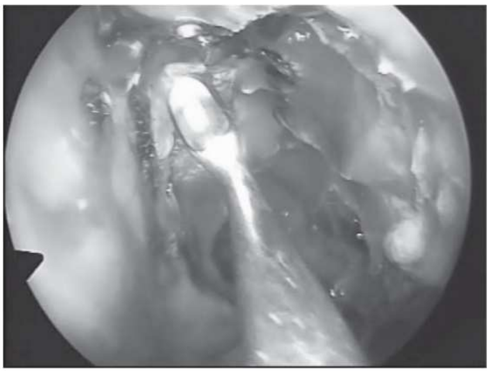

Figure 2.4: Photograph of the underlay technique, with conchal cartilage being grafted into a defect of the medial lamella. Source: Paul and Upadhyay (34)

2.9.4 Combined technique

In combined techniques of CSF leak repair, the graft is placed below the dura, between dura and bone, while an extracranial overlay is also used (34). Otherwise described as the ‘sandwich-grafting technique’, this technique often incorporates two layers of facia lata (underlay and overlay), interposed with a layer of conchal bone or septal cartilage in-between (39). Saafan et al. (39) argue that using a three-layered sandwich-grafting technique of facia lata provides added security to the sealing of CSF leaks, and enhances the chances of success of the surgery.

Various other authors also describe multilayer techniques (18,32). The method used by Ibrahim et al. (18), for example, consists of the following five layers:

1. Layer one is an intracranial intradural underlay fat graft harvested from the anterior aspect of the thigh;
2. Layer two is an intracranial extradural layer of fascia lata slipped underneath the bony edge of the defect;
3. Layer three is an intracranial extradural layer of bone to close the bone defect, harvested from the bony septum or MT;
4. Layer four is an extracranial overlay graft of fascia lata over the defect; and
5. Layer five is a free mucoperiosteal graft from the MT in the event a middle turbinectomy has been performed, or otherwise an extracranial vascularised nasoseptal rotational flap.

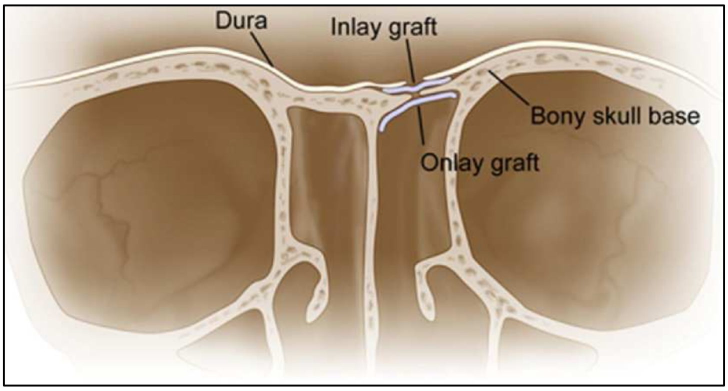

Figure 2.5: Schematic diagram of the coronal view of a defect being plugged by both an onlay, and an underlay graft. Source: Nyquist et al. (32)

In many larger defects, and for those along the ventral skull base, a multi-layered gasket seal is often favoured, which consists of a soft tissue graft of fascia lata centred over the defect, and with the surrounding edges of the graft circumferentially surpassing the bony defect (32). A rigid graft is often shaped to roughly the size of the bony defect, and surgeons such as Nyquist et al. (32) recommend vomer bone, or medical devices such as Medpor by Porex Surgical in Newnan for this purpose. Approximately 5 mm of excess soft tissue is left around the rigid graft, which is gently countersunk into the bony defect to form a watertight seal, or gasket seal. The gasket seal is then covered by a vascularised flap, which is adhered to the surrounding bony skull base around the gasket seal with a tissue sealant, as shown in Figure 5

In some clinical situations, such as after the removal of large intracranial tumours, dead space should first be eliminated with a filling of fat before placement of the gasket seal; unless communication exists between the defect and the third ventricle, whereby fat may migrate and cause an obstructive hydrocephalus (32).

2.9.5 Obliteration technique

When repairing a CSF leak with obliteration, firstly the mucosa is completely stripped, before a graft of abdominal fat is inserted into the defect graft bed. Fibrin glue is then often used to assist in wound healing by facilitating the contact of the graft to the recipient site (34).

2.10. Challenges to CSF leak repair

In many cases, CSF leaks are completely repaired through a minimally invasive endoscopic endonasal surgery, though this requires a complete and accurate preoperative determination of the leak site to be performed (28). Javadi et al. (19) assert that identifying and locating the dural defects and CSF leaks are a significant challenge, since CSF is translucent, and the operative field is typically obscured with mucosal secretions or blood.

As noted previously, various studies have listed the identification of the site, size and etiology of CSF leaks as being the most important factor in determining the success of any surgery (46). However, CSF leaks that occur in the anterior skull base form one of the more difficult of the endonasal endoscopic surgeries, due to the location, which is technically demanding to access, and anatomically complicated (46).

Another significant challenge exists when recreating the barrier between the nasal cavity and the cranial vault to eliminate the CSF leak, and in turn, protect the brain from exposure to infection (46).

Ma et al. (55) assert that in the case of paediatric CSF leak repair, such as in infants and small children, diagnosis and surgical intervention is challenging. Furthermore, according to Ma et al. (55, p.2), “the general principles and results of endoscopic transnasal surgery in adults cannot be directly extrapolated to infants and children.” Endoscopic procedures are known to be more challenging in children because of their narrow nasal fossae, which require a higher surgical experience to navigate successfully (18).

Bedrosian et al. (3, p.87) argue that “in many ways, spontaneous CSF leaks are the most difficult to treat”. They assert that this is because the small, slow leaks that are typical of spontaneous CSF leaks can often be difficult to locate, while the broad attenuation of the skull-base bones makes the complete watertight sealing of leaks difficult. Furthermore, associated meningoencephaloceles or encephaloceles are observed in between 50% and 100% of patients, with rates of postoperative recurrence being generally higher than any of the other causes (between 25% and 87% in many cases). While repair techniques are similar to the other etiologies, postoperative management of spontaneous leak patients is “critical” (3, p.87).

A debate exists over the use of fixators for CSF leak repair. These include compounds such as fibrin glue and/or packing, as well as postoperative adjunctive management, such as the use of perioperative antibiotics and lumbar drains (39). Upon placement of the graft, a sealant such as fibrin glue can be applied to secure the graft in place. Absorbable nasal packing, or gel-foam, is also usually applied for between five and seven days postoperatively, directly on the mucosal edge of the graft to improve support. This is followed by a non-absorbable packing that provides additional support and hemostasis, and these packs are typically removed after between five and seven days (36).

A controversy also exists in which technique of graft placement to use. Depending on the size of the leak, either the onlay technique or the underlay technique is used. Authors such as Martin-Martin et al. (46) use curettes of different sizes to determine the size of the fistula. Sizes of defects vary greatly, and a study by Ma et al. (55) observed defect sizes with expanses of between 4 and 150mm^2 in size.

Bacterial meningitis may also be caused following surgery when a repair has not healed sufficiently, or when a lumbar drain still remains after the procedure, or if prophylactic antibiotics have been administered that promote the growth of bacterial resistance and infection (46).

2.11. Recurrence of CSF leak

Traditionally, defects that have been managed via lateral rhinotomy or craniotomy have been associated with considerable recurrence rates, with studies reporting up to 40% recurrence rates following these techniques (1,55).

Endoscopic endonasal repair of CSF leak has been shown to be effective, and minimises morbidity. However, general principles of adequate bridgement of the surrounding mucosa should be ensured, and suitable postoperative care should also be followed (2). Recurrence of CSF leak has been seen, though it is typically associated with benign intracranial hypertension, and high-flow CSF leaks. In such patients, postoperative acetazolamide, ventriculoperitoneal shunts, or lumbar drains may be indicated (2).

Persistent leaks that require a second operation occur in between five and ten percent of endoscopic repairs. A second EES increases the rate of success to 97%. Rates of persistent leaks that do not respond even after a second EES include the following (34):

- Frontal lobe abscess (0.9%);
- Anosmia (0.6%);

- Pneumocephalus (0.6);
- Meningitis (0.3%);
- Intracranial haemorrhage or hematoma (0.3%); and
- Chronic headache (0.3%).

2.12. Conclusion

Numerous differences exist between traumatic and spontaneous CSF leak from presentation, etiology, modes of treatment, and recurrence after treatment. Endoscopic endonasal approaches to repair have several advantages over open craniotomy surgery; however, it is not always possible to perform EES. Therefore, each of the primary forms of surgery are still prevalent, and research is needed to continue to improve them.

2.13. References

1. Aarabi B, Leibrock LG. Neurosurgical approaches to cerebrospinal fluid rhinorrhea. Ear Nose Throat J. 1992;71:300–5.
2. Anstead AS, Liu J. Cerebral spinal fluid leak repair. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2014 Jun;25(2):187–93.
3. 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 Neurosurgery. Elsevier BV; 2014 Dec;82(6):S86–94.
4. Bleier BS. Comprehensive techniques in CSF leak repair and skull base reconstruction. Adv Otorhinolaryngol. Vol. 74. Basel: Karger; 2013. p. 92–103.
5. Cairns H. Injuries of the Frontal and Ethmoidal Sinuses with Special Reference to Cerebrospinal Rhinorrhœa and Aeroceles. The Journal of Laryngology & Otology. Cambridge University Press (CUP); 1937 Sep;52(09):589–623.

6. Calcaterra TC. Extracranial Surgical Repair of Cerebrospinal Rhinorrhea. Annals of Otology, Rhinology & Laryngology. SAGE Publications; 1980 Mar 1;89(2):108–16.

7. Cukurova İ, Cetinkaya EA, Aslan İB, Ozkul D. Endonasal endoscopic repair of ethmoid roof cerebrospinal fluid fistula by suturing the dura. Acta Neurochir (Wien). Springer Science + Business Media; 2008 Aug 23;150(9):897–900.

8. Dandy WE. Pneumocephalus (Intracranial Pneumatocele or Aerocele). Archives of Surgery. American Medical Association (AMA); 1926 May 1;12(5):949–82.

9. 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. Journal of Neurosurgery: Pediatrics. Journal of Neurosurgery Publishing Group (JNSPG); 2010 Nov;6(5):459–63.

10. Dodson E, Gross C, Swerdloff J, Gustafson L. Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea and skull base defects: A review of twenty-nine cases. Otolaryngology - Head and Neck Surgery. Elsevier BV; 1994 Nov;111(5):600–5.

11. Dohlman G. Spontaneous cerebrospinal rhinorrhoea: Case operated by rhinologic methods. Acta Oto-laryngologica. Informa UK; 1948 Jan;36(s67):20–3.

12. Eloy JA, Kalyoussef E, Choudhry OJ, Baredes S, Gandhi CD, Govindaraj S, et al. Salvage endoscopic nasoseptal flap repair of persistent cerebrospinal fluid leak after open skull base surgery. American Journal of Otolaryngology. Elsevier BV; 2012 Nov;33(6):735–40.

13. Eloy JA, Kuperan AB, Choudhry OJ, Harirchian S, Liu JK. Efficacy of the pedicled nasoseptal flap without cerebrospinal fluid (CSF) diversion for repair of skull base defects: incidence of postoperative CSF leaks. International Forum of Allergy & Rhinology. Wiley-Blackwell; 2012 Apr 23;2(5):397–401.

14. Eloy JA, Shukla PA, Choudhry OJ, Singh R, Liu JK. Challenges and surgical nuances in reconstruction of large planum sphenoidale tuberculum sellae defects after endoscopic endonasal resection of parasellar skull base tumors. The Laryngoscope. Wiley-Blackwell; 2013 Mar 11;123(6):1353–60.

15. Grant FC. Intracranial aerocele following fracture of the skull: report of a case with review of the literature. Surg Gynecol Obstet. 1923;36:251–5.

16. 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. The Laryngoscope. Wiley-Blackwell; 2006;116(10):1882–6.

17. Hegazy HM, Carrau RL, Snyderman CH, Kassam A, Zweig J. Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea: A meta-analysis. The Laryngoscope. Wiley-Blackwell; 2000;110(7):1166–72.

18. Ibrahim AA, Magdy EA, Eid M. Endoscopic endonasal multilayer repair of traumatic ethmoidal roof cerebrospinal fluid rhinorrhea in children. International Journal of Pediatric Otorhinolaryngology. Elsevier BV; 2012 Apr;76(4):523–9.

19. Javadi SA, Samimi H, Naderi F, Shirani M. The use of low-dose intrathecal fluorescein in endoscopic repair of cerebrospinal fluid rhinorrhea. Arch Iran Med. 2013;16(5):264–6.

20. Kassam AB, Prevedello DM, Carrau RL, Snyderman CH, Thomas A, Gardner P, et al. Endoscopic endonasal skull base surgery: analysis of complications in the authors' initial 800 patients. Journal of Neurosurgery. Journal of Neurosurgery Publishing Group (JNSPG); 2011 Jun;114(6):1544–68.

21. Kerr JT, Chu FWK, Bayles SW. Cerebrospinal Fluid Rhinorrhea: Diagnosis and Management. Otolaryngologic Clinics of North America. Elsevier BV; 2005 Aug;38(4):597–611.

22. Kirtane M, Gautham K, Upadhyay S. Endoscopic CSF rhinorrhea closure: Our experience in 267 cases. Otolaryngology - Head and Neck Surgery. Elsevier BV; 2005 Feb;132(2):208–12.

23. Kong Y-G, Deng Y-Q, Wang Y. Transnasal Endoscopic Repair of Cerebrospinal Fluid Rhinorrhea: An Analysis of 22 Cases. Indian Journal of Otolaryngology and Head & Neck Surgery. Springer Science + Business Media; 2013 Feb 15;65(S2):409–14.

24. Lindstrom DR, Toohill RJ, Loehrl TA, Smith TL. Management of Cerebrospinal Fluid Rhinorrhea: The Medical College of Wisconsin Experience. The Laryngoscope. Wiley-Blackwell; 2004;114(6):969–74.

25. Lloyd KM, DelGaudio JM, Hudgins PA. Imaging of Skull Base Cerebrospinal Fluid Leaks in Adults 1. Radiology. Radiological Society of North America (RSNA); 2008 Sep;248(3):725–36.

26. Lopatin AS, Kapitanov DN, Potapov AA. Endonasal Endoscopic Repair of Spontaneous Cerebrospinal Fluid Leaks. Archives of Otolaryngology–Head & Neck Surgery. American Medical Association (AMA); 2003 Aug 1;129(8):859–63.

27. Mahajan C, Rath GP, Dash HH, Bithal PK. Perioperative Management of Children With Encephalocele. Journal of Neurosurgical Anesthesiology. Ovid Technologies (Wolters Kluwer Health); 2011;23(4):352–6.

28. Matsubara T, Akutsu H, Tanaka S, Yamamoto T, Ishikawa E, Matsumura A. A case of spontaneous cerebrospinal fluid rhinorrhea: Accurate detection of the leak point by magnetic resonance cisternography. Surgical Neurology International. Medknow; 2014;5(1):54.

29. Mattox DE, Kennedy DW. Endoscopic Management of Cerebrospinal Fluid Leaks and Cephaloceles. The Laryngoscope. Wiley-Blackwell; 1990;100(8):857???862.

30. McCormack B, Cooper PR, Persky M, Rothstein S. Extracranial repair of cerebrospinal fluid fistulas. Neurosurgery. Ovid Technologies (Wolters Kluwer Health); 1990 Sep;412.

31. Mirza S, Thaper A, McClelland L, Jones NS. Sinonasal Cerebrospinal Fluid Leaks: Management of 97 Patients Over 10 Years. The Laryngoscope. Wiley-Blackwell; 2005;115(10):1774–7.

32. Nyquist GG, Anand VK, Schwartz TH. Endoscopic management of cerebrospinal fluid rhinorrhea. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2011 Sep;22(3):229–31.

33. Park JL, Strelzow VV, Friedman WH. Current management of cerebrospinal fluid rhinorrhea. Laryngoscope. 1983;93:1294–300.

34. Paul P, Upadhyay K. Endoscopic endonasal repair of traumatic CSF rhinorrhoea. The Indian Journal of Neurotrauma. Elsevier BV; 2010 Jun;7(1):67–9.

35. Prosser J, Vender J, Alleyne C, Solares C. Expanded Endoscopic Endonasal Approaches to Skull Base Meningiomas. Journal of Neurological Surgery Part B: Skull Base. Thieme Publishing Group; 2012 Feb 22;73(3):147–56.

36. Prosser JD, Vender JR, Solares CA. Traumatic Cerebrospinal Fluid Leaks. Otolaryngologic Clinics of North America. Elsevier BV; 2011 Aug;44(4):857–73.

37. Psaltis AJ, Schlosser RJ, Banks CA, Yawn J, Soler ZM. A Systematic Review of the Endoscopic Repair of Cerebrospinal Fluid Leaks. Otolaryngology -- Head and Neck Surgery. SAGE Publications; 2012 Jun 15;147(2):196–203.

38. Raper DMS, Komotar RJ, Starke RM, Anand VK, Schwartz TH. Endoscopic versus open approaches to the skull base: A comprehensive literature review. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2011 Dec;22(4):302–7.

39. Saafan ME, Albirmawy OA, Tomoum MO. Sandwich grafting technique for endoscopic endonasal repair of cerebrospinal fluid rhinorrhoea. European Archives of Oto-Rhino-Laryngology. Springer Science + Business Media; 2013 Aug 28;271(5):1073–9.

40. Schaberg MR, Anand VK, Schwartz TH. 10 Pearls for Safe Endoscopic Skull Base Surgery. Otolaryngologic Clinics of North America. Elsevier BV; 2010 Aug;43(4):945–54.

41. Schlosser RJ, Bolger WE. Nasal Cerebrospinal Fluid Leaks: Critical Review and Surgical Considerations. The Laryngoscope. Wiley-Blackwell; 2004 Feb;114(2):255–65.

42. Schmidt RF, Choudhry OJ, Raviv J, Baredes S, Casiano RR, Eloy JA, et al. Surgical nuances for the endoscopic endonasal transpterygoid approach to lateral sphenoid sinus encephaloceles. Neurosurgical Focus. Journal of Neurosurgery Publishing Group (JNSPG); 2012 Jun;32(6):E5.

43. Sethi DS, Pillay PK. Endoscopic management of lesions of the sella turcica. The Journal of Laryngology & Otology. Cambridge University Press (CUP); 1995 Oct;109(10).

44. Shetty PG, Shroff MM, Sahani D, Kirtane M. Evaluation of high‑resolution CT and MR cisternography in the diagnosis of cerebrospinal fluid fistula. AJNR Am J Neuroradiol. 1998;19:633–9.

45. Skedros DG, Cass SP, Hirsch BE, Kelly RH. Sources of error in use of beta-2 transferrin analysis for diagnosing perilymphatic and cerebral spinal fluid leaks. Otolaryngology - Head and Neck Surgery. 1993;109(5):861–4.

46. Martín-Martín C, Martínez-Capoccioni G, Serramito-García R, Espinosa-Restrepo F. Surgical challenge: endoscopic repair of cerebrospinal fluid leak. BMC Research Notes. Springer Science + Business Media; 2012;5(1):459.

47. Stankiewicz JA. Cerebrospinal Fluid Fistula and Endoscopic Sinus Surgery. The Laryngoscope. Wiley-Blackwell; 1991;101(3):250-256.

48. Wang EW, Vandergrift WA, Schlosser RJ. Spontaneous CSF Leaks. Otolaryngologic Clinics of North America. Elsevier BV; 2011 Aug;44(4):845–56.

49. Wigand ME, Haid T, Berg M. The enlarged middle cranial fossa approach for surgery of the temporal bone and of the cerebellopontine angle. Archives of Oto-Rhino-Laryngology. Springer Science + Business Media; 1989 Oct;246(5):299–302.

50. Woodworth BA, Bolger WE, Schlosser RJ. Nasal cerebrospinal fluid leaks and encephaloceles. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2006 Jun;17(2):111–6.

51. 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. Otolaryngology - Head and Neck Surgery. SAGE Publications; 2008 Jun;138(6):715–20.

52. Zweig JL, Carrau RL, Celin SE, Snyderman CH, Kassam A, Hegazy H. Endoscopic Repair of Acquired Encephaloceles, Meningoceles, and Meningo-Encephaloceles: Predictors of Success. Skull Base. Thieme Publishing Group; 2002;12(3):133–40.

53. Sharma D, Singh D, Sinha S, Srivastva A, Singh H, Jagetia A, et al. CSF rhinorrhea: An overview of endoscopic repair. The Indian Journal of Neurotrauma. Elsevier BV; 2010 Dec;7(2):157–62.

54. Schaefer SD, Manning S, Close LG. Endoscopic Paranasal Sinus Surgery. The Laryngoscope. Wiley-Blackwell; 1989 Jan;99(1):1-5.

55. Ma J, Huang Q, Li X, Huang D, Xian J, Cui S, et al. Endoscopic transnasal repair of cerebrospinal fluid leaks with and without an encephalocele in pediatric patients: from infants to children. Child's Nervous System. Springer Science + Business Media; 2015 May 15;

56. Casiano R. Endoscopic cerebrospinal fluid rhinorrhea repair: Is a lumbar drain necessary? Otolaryngology - Head and Neck Surgery. SAGE Publications; 1999 Dec;121(6):745–50.

57. Buchman CA, Civantos FJ, Casiano RR. Skull base cerebrospinal fluid leaks and encephaloceles. Advances in Otolaryngology - Head and Neck Surgery. SAGE Publications; 1999;13

3. PART C: MANUSCRIPT

3.1. ABSTRACT

3.1.1 BACKGROUND

Cerebrospinal fluid leaks (CSFL) can be classified into traumatic and spontaneous (1,6). The CSFL may arise from defects in the cribriform plate, frontal sinus, sphenoid sinus or in the middle cranial fossa (22,32). Traumatic CSFL are usually managed conservatively, but repair may be indicated in persistent leaks, recurrent leaks or if the patient develops meningitis. The management of spontaneous leaks is always surgical repair. Prior to endoscopic surgery, CSF leaks were repaired through a craniotomy (10).

3.1.2 Study Aim

The aim of this study is to evaluate endoscopic repair of patients with traumatic and spontaneous CSF leaks that presented to Groote Schuur Hospital, Red Cross Hospital and Cape Town Medi-clinic from 2005 to 2015. This is retrospective study and the Neurosurgery and ENT databases was used to select patients.

3.1.3 Results

A total of 48 patients had an endoscopic repair of a CSF leak in the study period; 30 traumatic and 18 spontaneous. In the group of patients with a traumatic CSF fistula, 20 presented with an intermittent CSF leak, 2 had a continuous CSF leak and 8 presented with meningitis. In the group of patients who presented with a spontaneous CSF leak 17 had an intermittent leak and one presented with meningitis.

The method of repair consisted of utilizing fat (or other material) to plug the defect; followed by a multi-layer closure - usually incorporating a mucosal flap, then tissue collagen glue to hold the construct in place. Utilizing this method of repair our success rate in the traumatic group of patients was above 93%, and in the spontaneous group was higher than 77%(the success rate was defined as no recurrence of a CSF leak within 12 months' period in both

groups). Changing our technique and using a vascularized mucosal flap pedicled on the posterior septal artery has led to 100% success rate in the spontaneous group.

3.1.4 Conclusion

Endoscopic repair is a safe and effective method of treatment of spontaneous and traumatic CSF fistulas.

3.2. INRODUCTION

Cerebrospinal fluid leaks (CSFL) can be classified, based on the etiology, into traumatic (accidental and iatrogenic trauma) and spontaneous (idiopathic) leaks. (1). Patients presenting with a CSF leak can have a spectrum of symptoms from clear nasal discharge and headaches to mental status changes, meningitis, or even a brain abscess (1). The diagnosis of CSF leak can be assessed clinically by asking the patient to lean forward (reservoir test) to assess for watery rhinorrhea from the nose (4). A fluid sample can be sent for Beta-2 transferrin or Beta-2 trace protein (2). The CSF can enter the nose through defects in the anterior cranial fossa such as the cribriform plate, frontal sinus, ethmoid sinus and sphenoid sinus or through a defect in the middle cranial fossa (via the sphenoid sinus) (8). CSF can drain from the middle ear through the eustachian tube into the nose in the event of a temporal bone fracture (8,11). Traumatic CSF leaks are usually initially managed conservatively with strict bed rest. Most will stop spontaneously within 2-3 weeks (2). The spontaneous CSF leak, on the other hand, will always need surgical intervention (2).

The evolution of CSF fistula repair has changed dramatically in the last 30 years, from previous craniotomy to endoscopic repair (1) (2). Wigand did the first successful endoscopic CSF leak repair in 1981 (5). The endoscopic approach has largely replaced open methods of repair since it is less invasive with a higher primary success rate (average of 90%) (1). The team involved in the endoscopic repair of CSF leaks are typically an otolaryngologist and neurosurgeon (12,13). The patient is anaesthetised in a supine position and the head slightly elevated (12,13), the nasal mucosa is injected with epinephrine to achieve vasoconstriction of the blood vessels (8). The first step is to identify the boney defect, this is followed by stripping of the entire mucosa from and around the defect (8), a graft is used to plug the defect -usually using fat or fascia lata as graft -then this is followed with an overlay technique (11). The other method used is an underlay technique (2), usually when the defect is large

(8). This is done by placing the material between the dura and the bone of the skull base. The third method is using the combined technique, where the graft is placed below the dura and between the dura and the skull base - what is commonly known as the sandwich-graft technique (9).

The leaks managed with a craniotomy have been associated with high rate of recurrence, that has been reported to reach 40% (14,15). Endoscopic repair has shown to be more effective with less morbidity Recurrence of leaks appears to be more common in the spontaneous CSF leak group, mainly in patients with intracranial hypertension and the high flow CSF leaks (1). A second endoscopic repair increases the success rate to 97% (11)

3.3. Methods

This is a 10-year clinical audit retrospective analysis study and the patients were collected from the neurosurgery and otolaryngology databases. The aim was to look at our endoscopic repair results of patients with traumatic and spontaneous CSF leaks that presented to Groote Schuur Hospital, UCT private Hospital and Cape Town Medi-clinic from February 2005 to August 2015 and to describe our modified endoscopic technique of repair.

3.4. Results

A total number of 48 cases had endoscopic repair over a period of 10 years: There were thirty traumatic cases; 19 males (63.4%) and 11 females (36.6 %). The mechanism of injury was as follows: 8 blunt, 4 penetrating, 10 motor vehicle accidents and 8 cases were iatrogenic post-surgery.

There were 18 spontaneous CSF leaks :4 males (22.3%) and 14 females (77.7%).

The trauma group presented as follows:

- 20 cases presented with an intermittent leak,
- 2 cases presented with a continuous leak
- 8 presented with meningitis having had 3 or more episodes.

In the group of patients with a spontaneous CSF leak,17 presented with an intermittent leak and only 1 presented with meningitis.

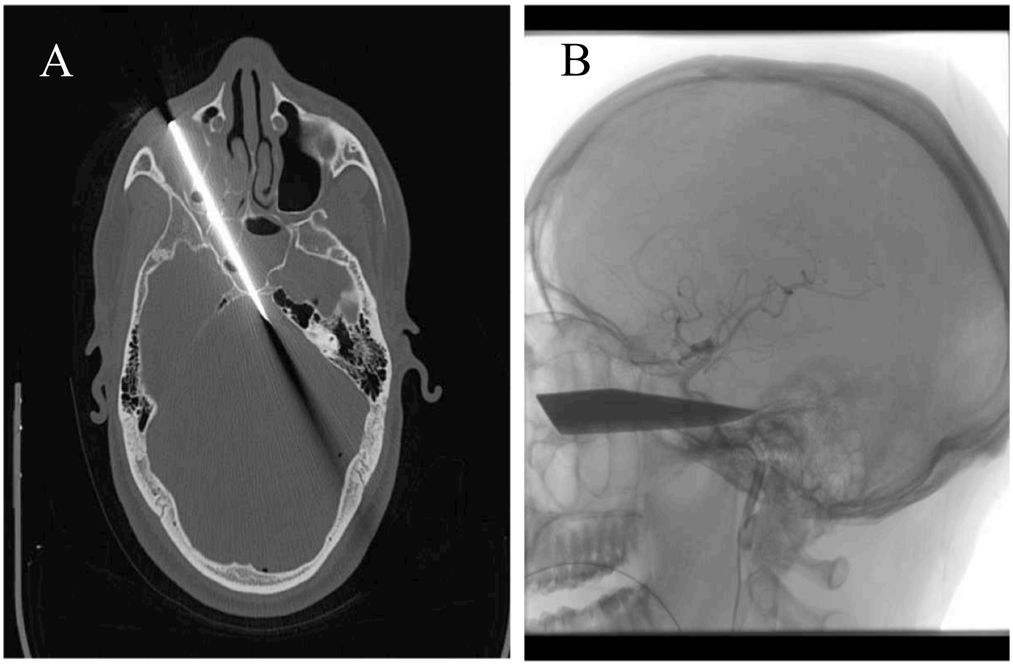

Figure 3.1: Penetrating injury through the right orbit with blade extending through ethmoid and sphenoid sinus (A). Digital subtraction angiography(DSA) to exclude vascular injury (B). Source: Groote Schuur Hospital.

The most common sinus involved in the traumatic and spontaneous leak groups was the sphenoid sinus, followed by the ethmoid sinus. Seventeen traumatic cases involved the sphenoid sinus, 7 the ethmoid sinuses and the 6 the frontal sinus. In the spontaneous group of patients with CSF leaks, 12 involved the sphenoid sinus, 5 the ethmoid sinus and in 1 patient the frontal sinus. An encephalocele was found in 4 cases (13.3%) in the traumatic group of patients, while the spontaneous group had 8 (44.4%).

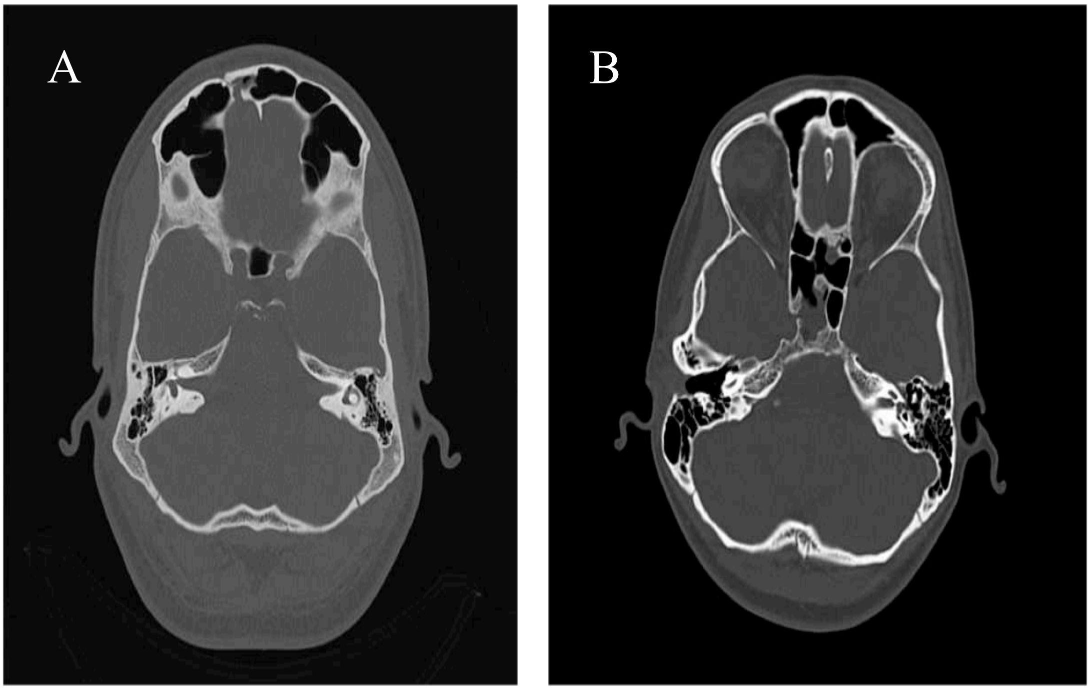

Figure 3.2: Defect of the Frontal sinus(A) Defect of the Sphenoid and Ethmoid sinus(B). Source: Groote Schuur Hospital.

There were 2 cases of recurrence of a CSF leak after endoscopic repair, representing a failure of 6.6%. On the other hand, in the spontaneous group, we had 4 cases of recurrence after endoscopic repair, a failure rate of 22.2%; Two patients had to be repaired twice and one needed to be repaired 3 times.

The repair was carried out by a combined otolaryngology and neurosurgery team. The first step was to identify the defect and visualize the edges of the bony defect., Fat or other material such as fascia lata or a muscle graft was then used to plug the defect. The third step was using a multiple layer technique usually incorporating a mucosal flap. Finally collagen glue was used to keep the reconstruction in place.

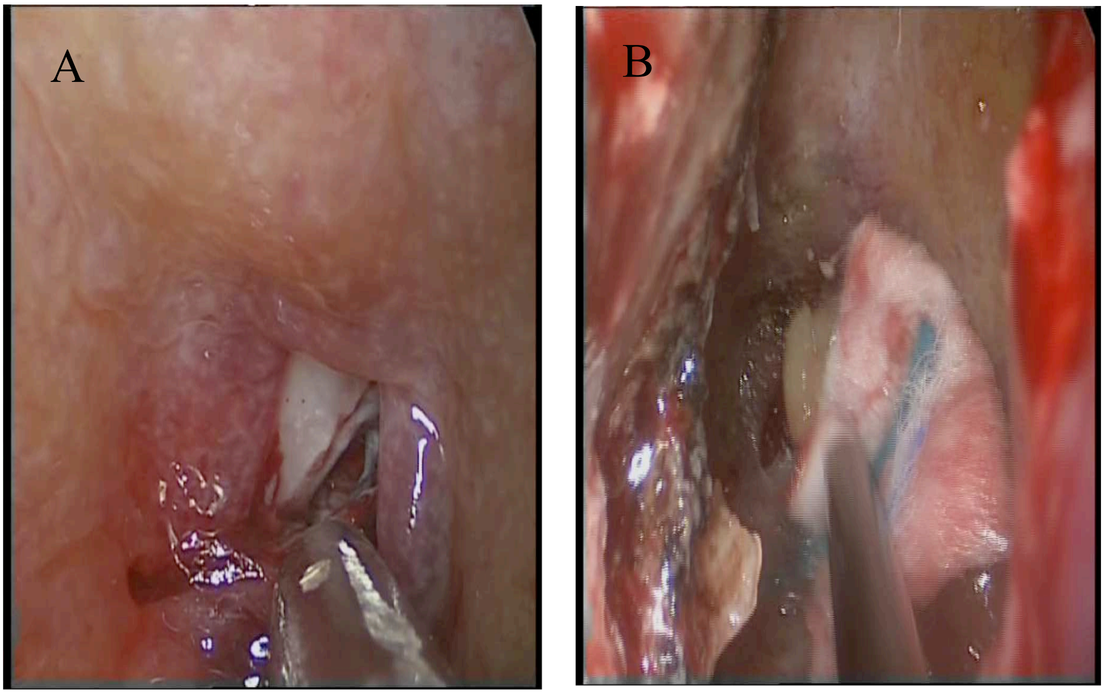

Figure 3.3: (A) Identification of the defect. (B) Plugging the defect using utilized fat. Source: Groote Schuur Hospital.

Utilizing this method of repair, we had a success rate of 93.3%. In the spontaneous group we had 77.7% success rate, in which 4 cases had to be taken back for repair. There were no complications in this series of patients and no lumbar drains were used in any of the 48 cases. The average hospital stay was between 2 and 4 days.

The duration of symptoms in the traumatic group of patients with CSF leaks was between 1 to 3 years before presenting to the hospital. In the iatrogenic group the CSF leaks were diagnosed during their hospital stay. In the spontaneous group the duration of symptoms were between 3 months to 2 years.

We modified our endoscopic repair technique for both groups - but more specifically initially for the spontaneous group - as this group had a higher rate of recurrence. The modification involved identification of the defect, plugging the defect using harvested fat or other material, and most importantly using a vascualarised mucosal flap. This improved technique resulted in a 100% success rate in the spontaneous group (introduced in the last 6 patients who presented with spontaneous leaks). We believe the use of a vascularised mucosal flap is the reason for the improved success rate. The defects were all small less than a one centimetre and all were easibly accessible.

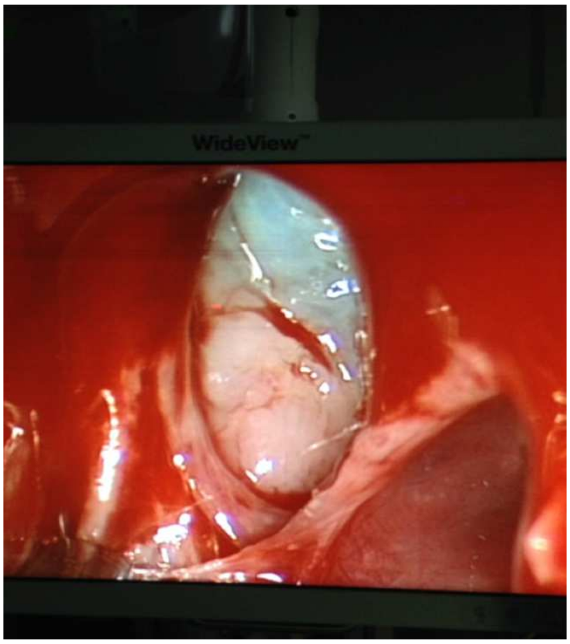

Figure 3.4: A defect in a spontenous leak,Showing a Encephalocoele.

3.5. Discussion

The introduction of endoscopic repair of CSF leaks by Wigand in 1981(3), has improved the outcome of patients with CSF leaks. Less complications, shorter recovery time and hospital stay, and most importantly, the high success rate with an average of 90% success (1), makes endoscopic repair the favoured approach.,

The first step is to confirm the leak. A CSF leak is confirmed on history and clinical examination using the reservoir test. The next step is to send a sample of the fluid to check biochemically for Beta-2-ransferrin (4) and finally radiology is performed. , A Computerized tomography (CT) scan is done to demonstrate a bony defect in either the ethmoid (cribriform plate), frontal sinus or sphenoid sinus (5).

The traumatic group of patients with CSF leaks were managed conservatively initially with bed rest. A pneumoococcal vaccine was given to all base of skull fractures with an CSF leaks. Antibiotics were not administered unless there was evidence of meningitis. Most leaks stopped spontaneously, within 2 to 3 weeks, and a repair was only indicated with persistent leaks or meningitis. The spontaneous group were all offered surgery on presentation.

Two thirds (66.6%) of patients in the traumatic group presented with intermittent leaks. In the spontaneous group, intermittent leaks were found in 94.4%. The second most common presentation in the traumatic group was meningitis (26.6%)., In the spontaneous group only 5.5% presented with meningitis.. In both groups the most frequent involved sinus was the sphenoid sinus. In the traumatic group it represented 56.66% (17 cases) of the sinuses involved. In the spontaneous group it was slightly higher at 66.6% (12 cases) An encephalocoele was found in 4 cases (13.3%) in the traumatic group, while in the spontaneous group it was higher (8 cases (44.4%). Sixty three percent of traumatic group of patients were male but in the spontaneous group 77.7% of the cases were female. The hospital stay on average was 2 to 4 days.

We have changed and modified our endoscopic repair technique for both groups, but more specifically to the spontaneous group - This has led to improved success rate. The changes were specifically, identification of the defect, plugging the defect, and most importantly using a mucosal flap. This has resulted in 100% success in the spontaneous group of patients since it has been introduced (in the last 6 patients). Using a mucosal flap is thought to have been vital in improving the repair success rate.

3.6. Conclusion

Numerous differences exist between the traumatic and spontaneous CSF leaks - from presentation, to their aetiology, modes of treatment and their recurrence. Endoscopic repair is an effective and safe method of repair with a high success rate. The most important key points during the repair of a defect is to plug the defect, using endogenous material and using a vascualarized mucosal flap in a multiple layer technique.

3.7. References:

1. Anstead AS, Liu J. Cerebral spinal fluid leak repair. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2014 Jun;25(2):187–93.
2. Martín-Martín C, Martínez-Capoccioni G, Serramito-García R, Espinosa-Restrepo F. Surgical challenge: endoscopic repair of cerebrospinal fluid leak. BMC Research Notes. Springer Science + Business Media; 2012;5(1):459.
3. Wigand ME, Haid T, Berg M. The enlarged middle cranial fossa approach for surgery of the temporal bone and of the cerebellopontine angle. Archives of Oto-Rhino-Laryngology. Springer Science + Business Media; 1989 Oct;246(5):299–302.
4. Cukurova İ, Cetinkaya EA, Aslan İB, Ozkul D. Endonasal endoscopic repair of ethmoid roof cerebrospinal fluid fistula by suturing the dura. Acta Neurochir (Wien). Springer Science + Business Media; 2008 Aug 23;150(9):897–900.
5. Shetty PG, Shroff MM, Sahani D, Kirtane M. Evaluation of high‐resolution CT and MR cisternography in the diagnosis of cerebrospinal fluid fistula. AJNR Am J Neuroradiol. 1998;19:633–9.
6. Martín-Martín C, Martínez-Capoccioni G, Serramito-García R, Espinosa-Restrepo F. Surgical challenge: endoscopic repair of cerebrospinal fluid leak. BMC Research Notes. Springer Science + Business Media; 2012;5(1):459.
7. Kirtane M, Gautham K, Upadhyay S. Endoscopic CSF rhinorrhea closure: Our experience in 267 cases. Otolaryngology - Head and Neck Surgery. Elsevier BV; 2005 Feb;132(2):208–12.
8. Nyquist GG, Anand VK, Schwartz TH. Endoscopic management of cerebrospinal fluid rhinorrhea. Operative Techniques in Otolaryngology-Head and Neck Surgery. Elsevier BV; 2011 Sep;22(3):229–31.
9. Saafan ME, Albirmawy OA, Tomoum MO. Sandwich grafting technique for endoscopic endonasal repair of cerebrospinal fluid rhinorrhoea. European Archives of Oto-Rhino-Laryngology. Springer Science + Business Media; 2013 Aug 28;271(5):1073–9.
10. Sharma D, Singh D, Sinha S, Srivastva A, Singh H, Jagetia A, et al. CSF rhinorrhea: An overview of endoscopic repair. The Indian Journal of Neurotrauma. Elsevier BV; 2010 Dec;7(2):157–62.
11. Paul P, Upadhyay K. Endoscopic endonasal repair of traumatic CSF rhinorrhoea. The Indian Journal of Neurotrauma. Elsevier BV; 2010 Jun;7(1):67–9.
12. Javadi SA, Samimi H, Naderi F, Shirani M. The use of low-dose intrathecal fluorescein in endoscopic repair of cerebrospinal fluid rhinorrhea. Arch Iran Med. 2013;16(5):264–6.

13. Kong Y-G, Deng Y-Q, Wang Y. Transnasal Endoscopic Repair of Cerebrospinal Fluid Rhinorrhea: An Analysis of 22 Cases. Indian Journal of Otolaryngology and Head & Neck Surgery. Springer Science + Business Media; 2013 Feb 15;65(S2):409–14.
14. Ma J, Huang Q, Li X, Huang D, Xian J, Cui S, et al. Endoscopic transnasal repair of cerebrospinal fluid leaks with and without an encephalocele in pediatric patients: from infants to children. Child's Nervous System. Springer Science + Business Media; 2015 May 15;
15. Aarabi B, Leibrock LG. Neurosurgical approaches to cerebrospinal fluid rhinorrhea. Ear Nose Throat J. 1992;71:300–5.