

Advances in Skull Base Reconstruction during Neuroendoscopic Transsphenoidal Pituitary Adenectomy

Guangyu Zhang, Ninghui Zhao*

The Neurosurgery Department of the Second Affiliated Hospital, Kunming Medical University, Kunming, Yunnan, China.

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***Corresponding author:** Ninghui Zhao, The Neurosurgery Department of the Second Affiliated Hospital, Kunming Medical University, Kunming, Yunnan, China.

Abstract

With the development of endoscopic equipment and technology in recent years, endoscopic transnasal skull base surgery has been more widely used in clinical practice. Endoscopic transsphenoidal approach is currently the mainstream surgical approach for the surgical treatment of pituitary adenomas, but a series of complications such as postoperative cerebrospinal fluid leakage and consequent intracranial infections still pose a serious challenge to surgeons. Complete and reliable skull base reconstruction is an important method to improve patient prognosis, reduce postoperative cerebrospinal fluid and improve the effect of endoscopic transnasal skull base surgery, which can reconstruct the dural barrier of the skull base and restore the original anatomy of the skull base. With the development of endoscopic skull base surgery and innovations in skull base repair materials, skull base reconstruction techniques have made substantial progress, with a significant increase in repair success rates and a decreased risk of postoperative cerebrospinal fluid leak. This article reviews the materials, technical methods, and related advances in skull base reconstruction.

Keywords

Nasocranial base surgery, neuroendoscopy, pituitary adenoma, cerebrospinal fluid leak, skull base reconstruction

The endoscopic endonasal transsphenoidal approach (EETSA) is widely used in endoscopic anterior skull base surgery (EASB) because of its low tissue trauma, short operative time, wide operator field of view, and rapid postoperative recovery. However, postoperative cerebrospinal fluid leakage and consequent intracranial infection are common complications that hinder the further development of endoscopic skull base surgery [1]. Severe postoperative cerebrospinal fluid leak will cause a series of complications, including intracranial infection, intracranial pneumonia, secondary surgery, and lumbar pool drainage, which will affect the patient's postoperative recovery, increase the financial burden, and prolong the length of hospital stay. Complete and effective skull base reconstruction has been reported to be a core factor in improving patient prognosis and preventing postoperative cerebrospinal fluid leakage [2, 3]. The purpose of skull base reconstruction is to reconstruct the hydrophobic tissue barrier between the sterile intracranial environment and the contaminated nasopharyngeal space, to tightly close the operative area, to eliminate dead space, to block intracranial communication with the outside world, to restore the original anatomical structure, and to enable adequate support and protection of intracranial tissues [4]. With the improvement of endoscopic techniques and the development and utilization of skull base repair materials, skull base reconstruction techniques have made substantial progress, the success rate of skull base repair has increased significantly,

the risk of postoperative cerebrospinal fluid leakage has decreased, and skull base surgery has developed in compliance. The current strategies, materials, and technical developments of skull base reconstruction are reviewed as follows.

1. Grading strategy for skull base reconstruction

Among the factors that reduce the risk of postoperative cerebrospinal fluid leak, Conger pointed out that the most important factor in reducing the risk of postoperative cerebrospinal fluid leak is the selection of the appropriate skull base reconstruction according to the different intraoperative cerebrospinal fluid leak flows [5]. The classification of cerebrospinal fluid leak is controversial, but is usually based on the size of the skull base defect and the degree of cerebrospinal fluid leak. Harvey summarized the size of the skull base defect and defined an area of <1 cm as a small defect and >3 cm as a large defect [6], and selected different recommended grades of repair strategies according to the area of the saddle base defect. According to the dural defect diameter and cerebrospinal fluid flow, the skull base defect was divided into 3 grades [7]. Grade I, the dural defect is only fissure-like or small hole-like, with a small amount of cerebrospinal fluid leakage; Grade II, the dural defect diameter ≤ 5 mm, with obvious cerebrospinal fluid leakage; Grade III, the dural defect diameter > 5mm, with a large amount of cerebrospinal fluid leakage, and according to the different grades of intraoperative cerebrospinal fluid leakage, different skull base reconstruction strategies were finally developed. The grading of cerebrospinal fluid leakage based on the flow of cerebrospinal fluid leakage and saddle-diaphragm defect in endoscopic transsphenoidal saddle area tumor resection (Kelly grading) proposed by Kelly of the Department of Neurosurgery at the University of California Hospital has been widely used in clinical saddle-base repair [8].

2. Skull base reconstruction materials

Richard showed from a review of the literature that in small skull base defects, more satisfactory repair results can be achieved regardless of the repair material used [6]. Mihir showed that in complex skull base reconstruction, the selection of repair materials and reconstruction techniques should not only consider the extent and size of the skull base defect itself, but also the nature, location, and invasiveness of the responsible lesion, etc. Mihir pointed out that in endoscopic transsphenoidal skull base reconstruction, the selection of repair materials and tissues is an important factor for successful reconstruction [9]. The selection of repair materials should refer to their functions in the repair: (i) filling the empty tumor cavity to achieve space-filling effect; (ii) reconstructing the hydrophobic threshold of the skull base; (iii) mechanical support to strengthen the rigid strength of the skull base; (iv) enhancing the stability of the surgical opening in the operative area; (v) strengthening the anti-infective power of the repair materials. Therefore, different from the traditional saddle base repair, the modern skull base reconstruction strategy emphasizes more on multi-level and multi-functional reconstruction [10]. With the rapid development of 3D printing technology, 3D printed materials are expected to replace some traditional materials and show a wider range of applications in the provision of materials for endoscopic skull base surgery with the advantages of high plasticity, high biocompatibility and no artifacts [11]. Therefore, in the face of a wide variety of skull base reconstruction materials, clinicians need to adopt corresponding repair strategies and select appropriate repair materials according to intraoperative conditions regarding cerebrospinal fluid leakage flow and skull base defect grading to avoid the occurrence of postoperative cerebrospinal fluid leakage to the greatest extent.

2.1 Free grafts

Skull base reconstruction materials can be broadly divided into two types: free materials and tipped tissue flaps, and free materials include cellular free grafts and non-cellular free grafts [12]. Free materials include both cellular and non-cellular free grafts. Non-cellular free grafts include common artificial materials such as gelatin sponges, absorbable hemostatic gauze, artificial duramater, bioclays, tumescentsponges, iodoformgauze, etc. All of which can be selected flexibly according to the intraoperative repair needs. Among them, artificial meninges/biomembranes are often used as the main material for low-flow cerebrospinal fluid leak saddle base repair. The artificial meninges can be placed on the inner or outer layer of the dura mater to enhance the adhesion and tightness of the saddle base repair material by covering the dura mater [13]. The gelatin sponge provides a degree of protection. Gelatin sponge provides a degree of space occupancy and mechanical support and can be used as a filler for the empty tumor cavity after tumor resection. Various non-cellular free materials provide easy and versatile repair options to ensure the feasibility and success of skull base reconstruction in the face of different complex

defects and dysplastic skull base conditions during surgery.

2.1.1 Autologous free material

Although there are a wide variety of material options for skull base reconstruction with different characteristics, autologous materials are widely preferred by skull base surgeons because of their wide source of extraction, high tissue compatibility, and generally no rejection reactions. Among them, fat, muscle, and fascia lata are the most applicable in the choice of skull base repair materials because of their wide sources, easy access, and affordability. Because of its hydrophobic nature, adipose tissue can provide support for arachnoid leaks, isolate cerebrospinal fluid outflow, and serve as a hydrophobic layer for skull base reconstruction, and because of its large size and irregular edges, it can provide tighter filling and sealing of arachnoid leaks. Mehendale concluded that the "fat plugs" formed by adipose tissue could not only achieve good closure of the skull base leaks, but also promote the fusion of the fat and dural interstitial defects, which is beneficial for the long-term reconstruction [14]. The muscle tissue is strong because of its tissue. The muscle tissue, because of its toughness and plasticity, can evenly distribute the pressure on the skull base and make the repair material fit better, the fascia lata, because of its flexibility and resistance to infection, can provide good support and closure of the saddle base after repair.

2.1.2 Free mucosal flap

Free mucosal flaps are cellular free grafts along with the common autologous free materials. Compared to other autologous materials, free mucosal flaps are often used for epidural placement in saddle base repair because of their good coverage, good fit, and strong seal. A meta-analysis by Cai showed that both free and tipped mucosal flaps were superior repair materials for intraoperative high-flow cerebrospinal fluid leaks, significantly reducing the incidence of postoperative cerebrospinal fluid leaks [15]. A prospective study in Fishpool, which included 32 patients with pituitary adenomas, showed no postoperative cerebrospinal fluid leaks in patients who had intraoperative saddle septal repair with a free mucosal flap [16]. Li used free turbinate mucosa to perform skull base repair in 24 patients with saddle septal defects < 1.5 cm in size, and all had satisfactory repair results were satisfactory [17].

2.2 Tissue flap with tip

As early as the 1950s, Oscar first proposed the use of a nasal septal mucosal flap for saddle-base repair to prevent cerebrospinal fluid leakage [18]. At the beginning of this century, Haded improved the nasal septal mucosal flap by preserving the posterior nasal septal artery as a vascular tip, which strengthened the mucosal flap's resistance to infection, improved tissue viability, and effectively increased the success rate of saddle base repair, establishing the importance of the tipped nasal septal mucosal flap in skull base reconstruction^[19]. The importance of the septal mucosal flap in skull base reconstruction was established. Ross reported that the use of tipped nasal septal mucosal flap in saddle base reconstruction on the basis of traditional autologous repair materials could effectively improve the success rate of skull base repair and reduce the incidence of postoperative cerebrospinal fluid to less than 5% [20]. Eloy retrospectively analyzed 74 patients who underwent skull base reconstruction with a tipped nasal septal mucosal flap after neuroendoscopic transsphenoidal approach to remove anterior skull base tumors [21]. Charles reported an improvement in quality of life in most patients after resection of anterior skull base tumors with a tipped nasal septal mucosal flap and skull base repair by long-term follow-up (67.4±14.2 months) [22]. However, the use of a tipped nasal septal mucosal flap is limited in that it cannot be prepared when the vessels or mucosa in the nasal cavity are invaded by a tumor or when the defect is located in a partially inaccessible location. Some scholars also pointed out that the preparation of mucosal flap disturbs and damages the normal mucosa of the nasal cavity and disrupts the physiological structure of the nasal cavity, which affects the quality of life of patients to different degrees after surgery, such as the development of olfactory impairment [23].

In addition to the tipped nasal septal mucosal flap with the posterior nasal septal artery as the vascular tip, various tipped tissue flaps are widely used in different skull base defect repairs because of their different coverage locations. The temporal muscle flap and temporo-occipital fascial flap with the superficial temporal artery as the tip can cover the lateral skull base, pterygoid saddle, saddle node, and pterygoid plateau; The mucosal flap of the middle turbinate and lateral wall of the nasal cavity with the middle turbinate artery as the tip and the mucosal flap of the inferior turbinate with the inferior turbinate artery as the vascular tip can respectively cover the pterygoid saddle, saddle node and slope, respectively. The frontal osteochondral flap with the supraorbital and superior talocrural arteries as the tips can cover the pterygoid plateau and sieve plate. Gaye noted that the tipped mucosal flap is a common choice for revascularization because it is easy to obtain, has a high survival rate and wide coverage, which can be clipped as needed or rotated to cover saddle, supra-saddle, slope, and anterior skull base defects [24]. The

operator needs to select the tipped mucosal flap reasonably according to the actual situation such as the location of the intraoperative defect and the condition of the mucosa in the patient's nasal cavity.

3. Skull base reconstruction techniques

With the update of saddle base repair materials, the skull base reconstruction technique has also been innovated and developed by scholars' practical exploration. Many neurosurgeons have improved the traditional repair techniques, used new repair materials, introduced multidisciplinary treatment models, and integrated different surgical operations in their clinical practice to make more innovations and reforms in skull base reconstruction techniques.

3.1 Gasket-Seal Technology

The Gasket-Seal technique, often referred to as the gasket technique or the closed gasket technique, is a technique that allows for the complementary biological properties of multiple layers of material by taking advantage of the tissue properties of each repair material [25]. The Gasket-Seal technique first used autologous fat to fill the arachnoid leak to eliminate the dead space inside the defect and achieve the closure of the first irregular hydrophobic layer; after that, a piece of fascia lata larger than the area of the defect (at least 1 cm radius than the leak) was cut to wrap the fat and applied outside the fat layer to achieve the middle layer of the closure gasket; then a rigid structure such as titanium plate and bone flap was selected to The mechanical strength of the closure gasket is strengthened and the structure is embedded in the material of the previous layer to achieve watertight closure; finally, bioglue is dripped on the edge of the closure gasket to strengthen the closure of the surrounding subtle parts and achieve the integrity of the whole gasket. The active role of Gasket-Seal technology in achieving skull base reconstruction, repairing skull base defects and treating cerebrospinal fluid leaks has now been recognized by many neurosurgeons [4].

3.2 Dural suture technique

With the development of endoscopic technology, more scholars began to pursue more solid and reliable skull base reconstruction techniques, among which the application of dural suture technology can effectively prevent postoperative cerebrospinal fluid leakage, especially intraoperative high-flow cerebrospinal fluid leakage, by mechanically reinforcing the saddle base, cushioning cerebrospinal fluid pulsation, dispersing intracranial pressure, and accelerating blood supply reconstruction [26][27]. However, due to the deep location of the skull base, the narrow operating space and the limitation of endoscopic two-dimensional imaging, the difficulty of suturing and knotting the saddle base is significantly increased, and there are still many problems to be solved in the application of dural sutures in skull base reconstruction [28]. Ahn used a newly designed instrument consisting of a suture forceps, needle holder and grasping forceps for skull base reconstruction [29]. Heng introduced the idea of laparoscopic instrumentation with the innovative use of two needle holders with rotatable tips and a 30° upward tilt angle for saddle base suture tying [30]. Sakamoto reported a sliding knotting technique to optimize the endoscopic knotting method and improve the dural suture rate [31]. These improvements and advances in endoscopic dural suturing techniques have enhanced the operability of the technique, reduced the prolonged operative time due to suturing, and increased the success rate of suturing.

3.3 In situ bone flap technique

Yang proposed the "in situ bone flap" technique by endoscopically cutting a 1×1.5 cm rectangular bone window in the skull base with a high-speed grinding drill, preserving the bone flap of the open saddle base and returning it in situ after surgery, thus promoting bony healing, strengthening bony support, and promoting a more durable and stable reconstruction of the skull base, which significantly reduces the incidence of postoperative cerebrospinal fluid leakage. The incidence of postoperative cerebrospinal fluid leakage is significantly reduced, especially in patients with hydrocephalus [32]. Oostra showed that the bony reconstruction of the skull base facilitated the mechanical support of the skull base and strengthened the intertissue confinement [33]. A study by Xia also pointed out that in situ bone flaps, because they are derived from autologous bone tissue, are more biocompatible with surrounding tissues and facilitate the early healing of bony structures, plus the postoperative bony reconstruction of the block patients, strengthen the rigid support of the skull base, and provide good bony conditions during periods of high risk of cerebrospinal fluid leakage [34].

3.4 Other repair techniques

The "bathtub plug" technique was first applied by Wormald and reported satisfactory skull base reconstruction results [35]. This technique makes full use of the hydrophobic and irregular characteristics of adipose tissue by implanting large fat blocks and free grafts such as gelatin sponges and free mucosal flaps under the dura, and then fixing these composite materials like "bathtub plugs" to the upper lateral cartilage of the nasal cavity with sutures that pass through the fat plugs to give a tighter filling and sealing of the leak. In the experience of Zhang, this technique has been widely used in their center for intraoperative skull base reconstruction of small cerebrospinal fluid leaks or epidural lesions (e.g. pituitary adenoma), with good closure results [36].

The "double button" technique is achieved by overlapping two pieces of fascia lata of different sizes, with the larger part of the fascia lata being at least 25% larger than the area of the dura mater to ensure complete coverage of the duramater, and the larger part of the overlapping pieces being embedded below the dura mater and the smaller part being fixed outside the duramater, forming a firm structure similar to a bearing, or two layers of buttons that are nested together. Adam, the author of this technique, recommends this repair technique for skull base repair in patients with high cerebrospinal fluid flow or large dural defects and has successfully reduced the incidence of postoperative cerebrospinal fluid leakage from 45% to 10% at his center [37].

The "sandwich" repair technique involves the use of a composite, multilayered free autologous tissue for joint sealing between the different layers of the saddle base repair, allowing each layer to give full play to its own biological properties and achieving complementary properties of the multilayered materials to improve the success rate of the repair. Saafan, the designer of this technique, reported that the first layer uses a piece of fascia lata, which is slightly larger than the saddle base defect, to cover the skull base; the second layer uses nasal septum cartilage to seal the bone defect and strengthen the bone support; and the third layer covers a piece of fascia lata larger than the first layer, which has achieved a 95% repair success rate in his center [38]. Li replaced the middle repair layer of the "sandwich" technique with mashed muscle instead of septal cartilage, and also achieved satisfactory repair results [17]. Based on the experience of many operators, the "sandwich" repair technique is more suitable for low-flow cerebrospinal fluid leaks or small leaks in the saddle base with small areas.

Cavallo used the 3F (Fat, Flap, and Flash) technique to participate in skull base reconstruction by combining intraoperative fat block and tipped nasal septal mucosal flap, and then asked the patients to get out of bed early after the operation to enhance their activities, and achieved good results in the skull base reconstruction of 25 patients undergoing neuroendoscopic extended transsphenoidal approach [39].

In conclusion, a solid and reliable skull base reconstruction is an important factor in reducing postoperative cerebrospinal fluid leakage and other complications after neuroendoscopic transsphenoidal surgery. The development of biotechnology and material technology has greatly promoted the great progress of skull base surgery, urging more scholars to improve skull base reconstruction strategies and innovate skull base reconstruction techniques, which have greatly improved the success rate of repair and made the risk of postoperative cerebrospinal fluid leakage in patients significantly reduced.

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