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Case report

3D Slicer reconstruction combined with neuroendoscopic keyhole approach for the treatment of cerebrospinal fluid rhinorrhea : 2 cases report and literature review

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A R T I C L E I N F O

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A B S T R A C T

Background and importance: Explore the techniques, advantages and disadvantages of 3D Slicer reconstruction combined with transcranial neuroendoscopy in cerebrospinal fluid rhinorrhea surgery.
Clinical presentation: We collected complete clinical data of two patients with cerebrospinal fluid rhinorrhea who underwent minimally invasive surgery using 3D Slicer reconstruction combined with transcranial neuroendoscopy through the supraorbital eyebrow arch keyhole approach in our hospital from June 2022 to May 2023. The patients were one male and one female, aged 50 and 63 years old. At the same time, a retrospective summary of relevant literature at home and abroad in recent years was conducted. 1 case had spontaneous cerebrospinal fluid rhinorrhea with secondary cribriform plate lesion, and the other 1 case had traumatic cerebrospinal fluid rhinorrhea. Both 2 patients were ineffective after long-term conservative treatment, and ultimately recovered after detailed preoperative evaluation and preparation and surgical treatment.
Conclusion: Cerebrospinal fluid rhinorrhea is a challenging disease in neurosurgery, and improper management can lead to serious complications such as meningitis. Our team used 3D Slicer reconstruction combined with transcranial endoscopic minimally invasive keyhole surgery to treat cerebrospinal fluid rhinorrhea, achieving good results, proving that this combined technology has certain advantages and is a new surgical technique worth promoting. However, the widespread application and promotion of this technology in anterior skull base surgery still require comprehensive and reliable prospective clinical studies to test.

1. Introduction

In the past 30 years, the surgical methods for cerebrospinal fluid rhinorrhea have rapidly developed, and before the emergence of

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neuroendoscopy, the success rate and complication rate of craniotomy surgery varied. Retrospective studies [1] have shown that traumatic cerebrospinal fluid rhinorrhea accounts for about 44 %, spontaneous cerebrospinal fluid rhinorrhea accounts for about 28 %, and iatrogenic cerebrospinal fluid rhinorrhea accounts for about 12 %. Traumatic cerebrospinal fluid leakage is a common complication of traumatic brain injury (TBI), accounting for about 1 %–3% of all brain injuries and 10 %–30 % of anterior basilar fracture. More than 50 % cerebrospinal fluid leakage occurs immediately or within 48 hours of injury. About 2/3 of them can naturally heal after active conservative treatment such as raising the head of the bed, dehydration to reduce intracranial pressure, anti-infection, and lumbar cistern drainage. If they do not heal after long-term observation or still have cerebrospinal fluid leakage, complications such as secondary meningitis may lead to serious consequences and often require surgical treatment [2]. Due to β-2 transferrin has specificity in cerebrospinal fluid and is a highly sensitive biological marker for diagnosing cerebrospinal fluid leakage. However, most medical institutions do not have this testing program, and radiological examinations are still needed in clinical practice to supplement diagnosis [3]. The commonly used radiological examinations currently include high-resolution thin-layer CT scans and three-dimensional reconstruction, CT cisternography, and intrathecal or cerebrospinal fluid cine MRI (CSF Cine MRI) . 3D Slicer is a free open-source software application for medical image processing, similar to a radiology workstation [4]. It is easy to operate and supports various semi-automatic and visual reconstructions, allowing neurosurgeons to process thin layer raw data of patients' brain CT or MRI like radiologists [5–7], and combine clinical examinations to purposefully search for and discover fistulas, guiding surgical design and preoperative planning. In the past two to three decades, with the development of endoscopy and the maturity of surgical techniques, the repair of cerebrospinal fluid leaks has undergone a smooth transition from craniotomy intracranial repair to endoscopic extracranial repair. However, a large number of literature reports have reported endoscopic surgery through nasal or orbital approaches for treatment [2,8–10]. Our team recently completed two surgeries using 3D Slicer reconstruction combined with neuroendoscopic supraorbital keyhole approach to repair traumatic cerebrospinal fluid rhinorrhea. There was no recurrence of cerebrospinal fluid rhinorrhea during postoperative follow-up, and the treatment effect was good.

2. Materials and methods

2.1. General data

We collected complete clinical data of two patients with cerebrospinal fluid rhinorrhea who underwent minimally invasive surgery using 3D Slicer reconstruction combined with transcranial neuroendoscopy through the supraorbital eyebrow arch keyhole approach in our hospital from June 2022 to May 2023. The patients were one male and one female, aged 50 and 63 years old. 1 case had spontaneous cerebrospinal fluid rhinorrhea with secondary cribriform plate lesion, and the other one had traumatic cerebrospinal fluid rhinorrhea. Both 2 patients were ineffective after long-term conservative treatment, and ultimately recovered after detailed preoperative evaluation and preparation and surgical treatment. The size of the skull opening is approximately 2.5cm*4.0cm. Routine use of antibiotics and mannitol dehydration treatment after surgery. Within 3 months of discharge, both patients did not experience any discomfort during outpatient follow-up or telephone follow-up.

2.2. 3D slicer reconstruction of anterior skull base virtual reality model for preoperative planning

Before surgery, raw data of thin layer CT of the patient's skull was collected in DICOM format. The above data of the patient was imported into the 3D-Slicer (https://www.slicer.org) system, and the bony structure of the anterior skull base was reconstructed to create a 3D virtual reality model and a 3D printed model. The 3D virtual reality model helps us understand the location of the fistula, while also evaluating the feasibility of surgical approaches and simulating surgical operations in advance. Both 2 patients underwent 3D Slicer reconstruction before surgery to fully simulate and evaluate the feasibility, and an eyebrow keyhole approach combined with neuroendoscopic technology was designed for repair surgery.

2.3. Cases presentation

Case 1. .

A 50 years old male patient, admitted to the department for more than 2 months due to unexplained nasal discharge. Upon admission, the brain CT revealed high-density shadows in the right ethmoid sinus and bilateral lateral ventricular pneumatosis. The CSF Cine MRI showed anterior skull base cerebrospinal fluid rhinorrhea, meningocele, right frontal floor air accumulation, and bilateral lateral ventricles anterior horn air accumulation. After conducting sufficient preoperative evaluation and simulating surgery using a 3D Slicer reconstruction model, the surgical approach was chosen as the eyebrow arch keyhole approach, and repair surgery was performed under neuroendoscopy. During the surgery, abnormal proliferation of the ethmoid sinus bone plate was clearly visible under the neuroendoscope, with bone spurs eroding and penetrating the dura mater. Bubbles could be seen at the fistula opening, and the hyperplastic bone plate was ground flat. Bone wax was used to seal the ethmoid sinus, but the dura mater suturing was difficult. Artificial meninges and multiple layers of biological glue were used to seal and repair the fistula opening. Within 3 months of discharge, the patient did not experience any discomfort during telephone follow-up. We affirm that the patient has provided written informed consent. (Fig. 1A–P)

Case 2. .

A 63 years old female patient, admitted to the department for more than 16 years due to cerebrospinal leakage post-TBI. Initially, there was a slight intermittent leakage from the right nasal cavity without surgical intervention. Three years ago, due to the worsening of the leakage, the patient sought treatment at another hospital for transnasal cerebrospinal fluid rhinorrhea repair and improved. Half a year ago, the patient experienced a recurrence of left nasal leakage. Three months ago, the patient underwent another transnasal cerebrospinal fluid rhinorrhea repair surgery, but there was no significant improvement after surgery. They immediately sought medical attention from our department. The patient was obese, had a history of hypertension and diabetes in the past, and had good oral drug control. After admission, the nasal sinus CT showed thickening of the mucosa in the left maxillary sinus, ethmoid sinus, and left frontal sinus, with patchy slightly low-density shadows visible. There was a localized bone defect in the posterior wall of the left frontal sinus. Brain MRI and cerebrospinal fluid film show soft tissue shadows in the left frontal sinus, with meningocele visible. The patient underwent bilateral nasal cavity surgery before this surgery, which resulted in poor results in blocking the outlet of cerebrospinal fluid rhinorrhea. Analysis of the causes may be related to the patient's obesity, intracranial hypertension, and diabetes history [10,11]. Drawing lessons from the failure of the previous two external hospital surgeries, we have chosen the intracranial repair method this time. We used a 3D Slicer to reconstruct a 3D virtual reality image of the fistula opening and evaluated the feasibility of

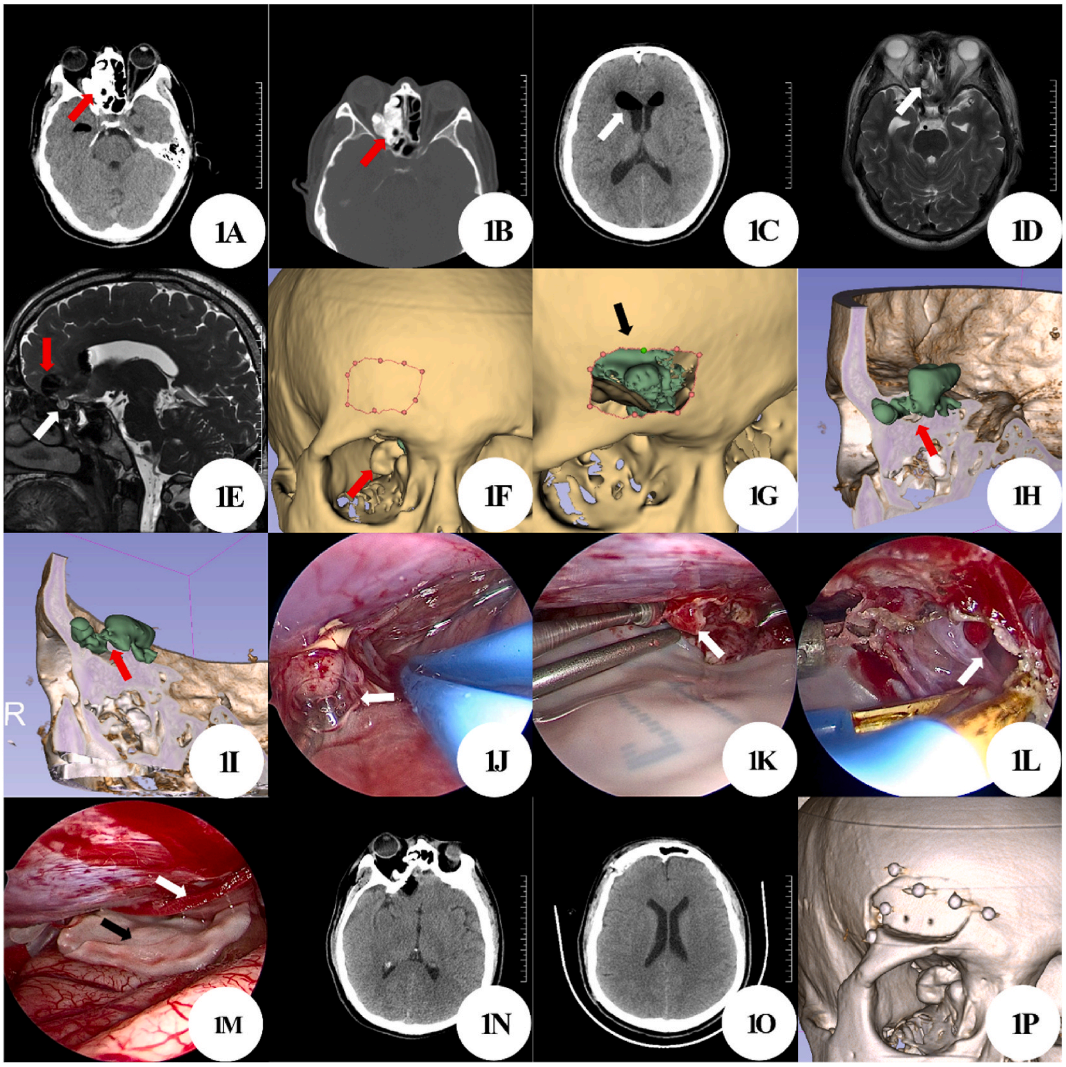

Fig. 1. A–B: Preoperative brain CT revealed abnormal bone hyperplasia in the right ethmoid sinus (red arrow). C: Preoperative brain CT indicates intraventricular gas accumulation (white arrow). D–E: Preoperative brain MRI indicates brain tissue swelling (white arrow) and intracranial gas accumulation (red arrow). F–G: Preoperative planning, 3D Slicer reconstruction of virtual reality images to simulate minimally invasive surgery of orbital eyebrow arch keyhole. H–I: Virtual reality image of 3D Slicer reconstruction of fistula opening (red arrow). J: Gas overflow visible under neuroendoscopy (white arrow). K：Endoscopic examination reveals bone erosion and proliferation towards the intracranial area (white arrow). L: Dural fistula seen under neuroendoscopy (white arrow). M: Multi-layer artificial meningeal repair (white and black arrows). N–O: Brain CT re-examination after operation. P: Eyebrow arch lock hole bone window size. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

this approach through virtual endoscopic surgery. During the surgery, fragments of a fracture at the base of the frontal sinus were punctured through the dura mater under neuroendoscopy, and brain tissue herniated from the incision into the frontal sinus with inflammatory granulation tissue proliferation. At the same time, cerebrospinal fluid overflow was observed. After thoroughly cleaning the fragmented bone fragments and frontal sinus, suturing the dura mater of the fistula opening and using artificial meninges and biological glue for repair. Within 3 months of discharge, the patient did not experience any discomfort during outpatient follow-up. We affirm that the patient has provided written informed consent. (Fig. 2A–O)

3. Discuss

Cerebrospinal fluid leakage is caused by tearing of the arachnoid membrane and dura mater at the base of the skull, resulting in cerebrospinal fluid overflowing from the subarachnoid space through natural cavities such as sinuses and the nasal cavity. It can be divided into non traumatic and traumatic cerebrospinal fluid leakage. The former is mostly caused by skull base tumors, skull lesions, or elevated intracranial pressure combined with skull base defects, while the latter can be divided into traumatic and iatrogenic. Risk factors for spontaneous cerebrospinal fluid rhinorrhea include obesity and obstructive sleep apnea [12]. Traumatic cerebrospinal fluid leakage is caused by traumatic skull base fractures that puncture or tear the dura mater and arachnoid membranes. The degree of skull base fracture, the size of dura mater rupture, the degree of arachnoid membrane tear, and the level of intracranial pressure after trauma all affect the occurrence of cerebrospinal fluid leakage. The common clinical manifestation is clear water like fluid flowing through the nasal or external ear canal, sometimes accompanied by blood, and some patients may complain of a salty taste in the throat. Therefore, early conservative treatment is advocated for traumatic cerebrospinal fluid leakage [13]. Conservative treatment measures include strict bed rest, head height of about 30°, no blowing of nose, coughing or holding breath, dehydration to reduce intracranial pressure, preventive use of antibiotics, etc. If necessary, continuous lumbar puncture or lumbar cistern drainage can increase the success rate of conservative treatment to 70%–90 %, and can improve the success rate of various surgical repairs [3,12]. Most traumatic cerebrospinal fluid rhinorrhea self closes within one week, but strict attention needs to be paid during the observation process. Excessive loss of cerebrospinal fluid can lead to pneumocephalosis, brain tissue displacement, cerebral hernia, etc. Prolonged cerebrospinal fluid leakage may also worsen the condition and even endanger life. According to literature reports [12,14], the incidence of meningitis in patients with persistent cerebrospinal fluid leakage is 6%–58 %, with an average of about 20 % and a mortality rate of about 10 %. The incidence of meningitis is 2.5 % for prophylactic use and 10 % for non-antibiotic use, respectively.

The traditional surgical method is craniotomy to repair the fistula, which has many complications such as compression of brain tissue, loss of smell, delayed intracranial hemorrhage, edema of brain tissue, epilepsy, and memory impairment [9,13]. With the development of endoscopy and technological advancements, transnasal endoscopic surgery is gradually replacing craniotomy as the preferred method for repairing cerebrospinal fluid leaks [3]. Compared with craniotomy, endoscopic surgery has the advantages of good visualization and close observation, with a higher overall success rate and a lower incidence of complications [13,15]. The other literature reports on the treatment of cerebrospinal fluid leakage through endoscopic transorbital or combined orbital and nasal approaches [2,9]. However, regardless of the surgical approach, it is crucial to fully understand the location of the fistula. The use of high-resolution thin slice CT raw data to reconstruct the three-dimensional structure of the anterior skull base can clearly display the bony structure of the skull base. However, due to artifacts, there is a certain false positive rate, with a sensitivity of about 89 % [14], which is considered a good diagnostic method. CT cisternography requires lumbar puncture injection of contrast agent, which is an invasive examination with low sensitivity and increases the risk of complications such as infection and epilepsy, and is gradually being abandoned [14]. The CSF Cine MRI for active cerebrospinal fluid rhinorrhea is approximately 90 % [14]. Our team reconstructed three-dimensional virtual reality images of the anterior skull base and sinuses by using 3D Slicer, in order to understand the specific location of the fistula and its three-dimensional relationship with surrounding structures. Our team used virtual reality images to simulate minimally invasive surgery through the combination of virtual endoscopy and eyebrow arch keyhole approach before the surgery, and evaluated the feasibility of the above plan. During the actual surgical process, the frontal lobe brain tissue naturally collapses backwards, exposing sufficient subdural space for better surgical operation. At the same time, the skin and bone window trauma are smaller and more minimally invasive, and it also takes into account aesthetics. Transnasal and intraorbital surgeries are limited by the narrow surgical channels of the nasal cavity or eye socket, making it impossible to use multiple surgical instruments simultaneously, and are also powerless to suture fistulas. Therefore, there are certain limitations. Transnasal and intraorbital surgeries are limited by the narrow surgical channels of the nasal cavity or eye socket, making it impossible to use multiple surgical instruments simultaneously, and are also powerless to suture fistulas. Therefore, there are certain limitations. The supraorbital eyebrow arch keyhole approach is a variable conical channel, and the closer it is to the target range, the larger the operating space, and even instruments can be used for fistula closure surgery (Fig. 2L) , which can make repair surgery more reliable. Meanwhile, theoretically speaking, internal repair methods are significantly superior to external repair methods. In our surgical practice, we can have enough space to suture the damaged dura mater, restore the damaged and twisted fracture fragments, and theoretically greatly improve the success rate of repair. For delayed cerebrospinal fluid leakage or recurrence, possible reasons may be due to wound contraction, displacement of fracture fragments, soft tissue necrosis, retraction of repair materials, or incomplete repair of all fistula openings. Literature has reported that obesity, women, and sleep apnea are also risk factors for cerebrospinal fluid leakage [10]. The possible reason is that obesity leads to increased abdominal pressure and further increases intracranial pressure, while abnormal levels of coagulation factors and lipoprotein in obese patients may lead to occult thrombosis of venous sinuses and also increase intracranial pressure [11]. In our case, there is a female obese patient who has experienced repeated cerebrospinal fluid leaks and multiple repair surgeries for nearly 16 years, and ultimately recovered through our surgical treatment.

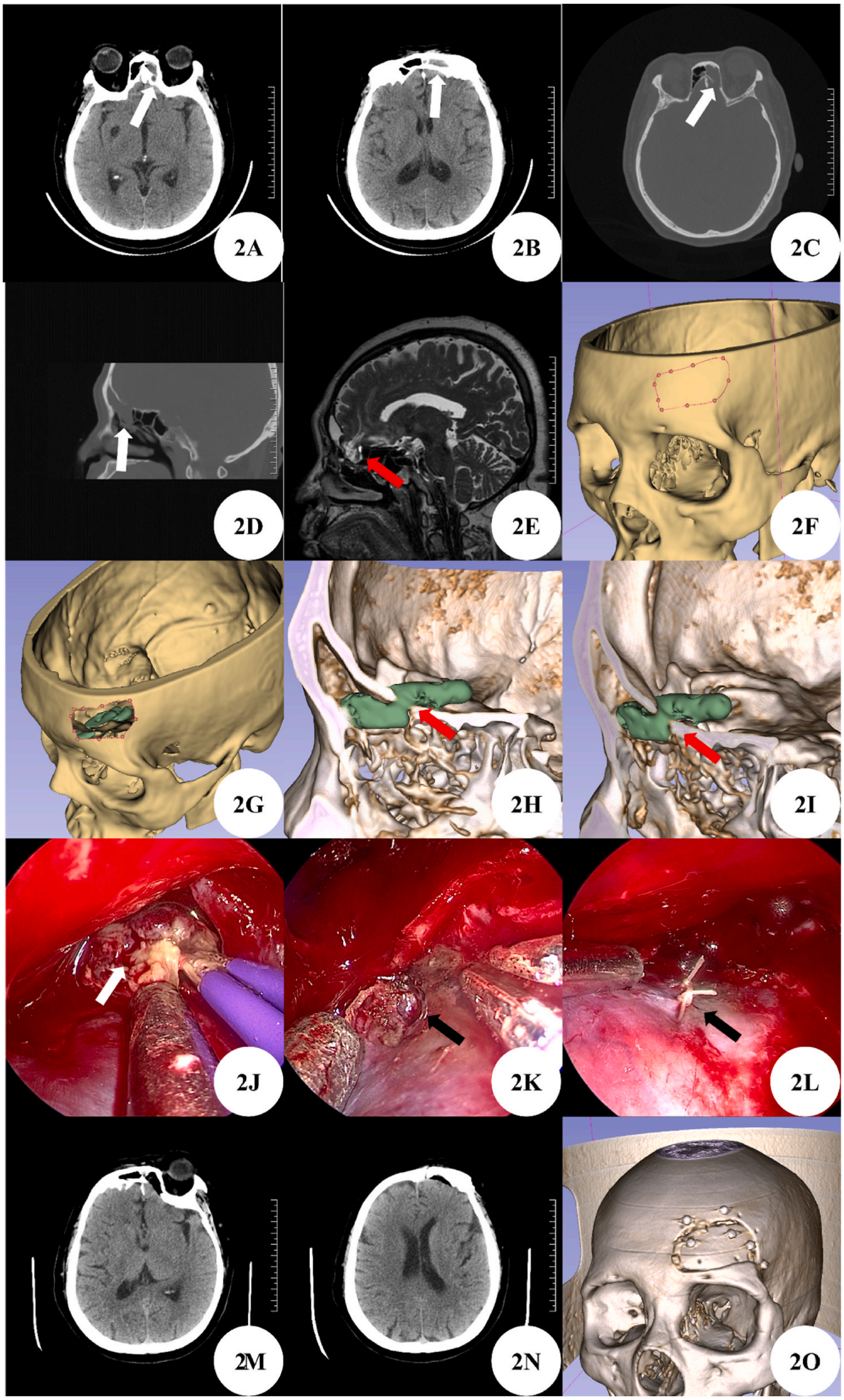

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Fig. 2. A–D: Preoperative CT scan revealed soft tissue manifestations in the left frontal and ethmoid sinuses. E: Preoperative brain MRI suggests anterior skull base brain tissue swelling. F–G: Preoperative planning, 3D Slicer reconstruction of virtual reality images to simulate minimally invasive surgery of orbital eyebrow arch keyhole. H–I: Virtual reality image of 3D Slicer reconstruction of fistula opening (red arrow). J: Hernia tissue visible under intraoperative neuroendoscopy (white arrow). K: Obvious fistula visible under intraoperative neuroendoscopy (black arrow). L: Suture the fistula with silk thread, and then repair it with biological glue and artificial meninges (black arrow). M–N: Brain CT re-examination after operation. O: Eyebrow arch lock hole bone window size. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

4. Summarize

Cerebrospinal fluid rhinorrhea is a challenging disease in neurosurgery, and improper management can lead to serious complications such as meningitis. Our team used 3D Slicer reconstruction combined with transcranial endoscopic minimally invasive keyhole surgery to treat cerebrospinal fluid rhinorrhea, achieving good results, proving that this combined technology has certain advantages and is a new surgical technique worth promoting. However, the widespread application and promotion of this technology in anterior skull base surgery still require comprehensive and reliable prospective clinical studies to test.

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Ethical approval

The families of two patients have signed and agreed to the surgery. This retrospective clinical study was approved by the ethics committee of Clinical Research, Renmin Hospital of Wuhan University (WDRY2023-K139).

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

CRediT authorship contribution statement

Long Zhou: Writing – original draft, Software, Methodology, Data curation, Conceptualization. **Yuan Lv:** Writing – original draft, Software, Methodology, Data curation, Conceptualization. **Zhiyang Li:** Writing – original draft, Software, Methodology, Data curation, Conceptualization. **Huikai Zhang:** Data curation. **Pan Lei:** Data curation. **Ping Song:** Data curation. **Lun Gao:** Data curation. **Qianxue Chen:** Data curation. **Hui Ye:** Data curation. **Qiang Cai:** Writing – review & editing, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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