# Transnasal endoscopic repair of adult spontaneous cerebrospinal fluid rhinorrhea with assistance of computer-assisted navigation system: an analysis of 21 cases

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## Abstract

**Objective** The purpose of this study was to investigate and summarize the characteristics of spontaneous cerebrospinal fluid rhinorrhea cases and the efficacy of transnasal endoscopic repair of spontaneous cerebrospinal fluid rhinorrhea with the assistance of computer-assisted navigation system.

**Methods** This is a retrospective study including 21 adult patients with spontaneous cerebrospinal fluid rhinorrhea who underwent transnasal endoscopic repair with the assistance of computer-assisted navigation system between January 2007 and December 2017. Data collected included patient demographics, body mass index, patient symptoms, biochemical findings, radiographic findings, location of defect, type and size of defect, type of repair, follow-up time, reoccurrence, and complications.

**Results** Spontaneous cerebrospinal fluid rhinorrhea was more commonly seen in females who were middle-aged and overweight in our series. The effluent was determined as cerebrospinal fluid by testing of glucose concentration and $\beta_2$-transferrin. The location of the lesion was determined by rigid nasal endoscopy combined with radiologic study. Intraoperatively, the skull base defects were found most frequently on the ethmoid roof in 12 cases (57.1%), followed by the cribriform plate in seven cases (33.3%), and sphenoid sinus in two cases (9.5%). The size of the skull base defect was < 5 mm in 13 cases, 5 mm ~ 10 mm in six cases and two cases involved defects of ≥ 10 mm. The graft materials were chosen based on the size of the defect. In small leaks, the thigh muscle was dumbbell-shaped herniated into the bony defect, reinforced by fascia lata. Larger defects were packed with the anterior part of middle turbinate with an overlay of fascia lata. All 21 patients had no recurrence of cerebrospinal fluid rhinorrhea during the follow-up period, which ranged from 11 to 24 months.

**Conclusion** The transnasal endoscopic approach with assistance of computer-assisted navigation system is a safe and effective procedure for the repair of spontaneous cerebrospinal fluid rhinorrhea.

**Keywords** Spontaneous cerebral fluid rhinorrhea · Cerebral fluid rhinorrhea · Repair · Endoscopy · Computer-assisted navigation system

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## Introduction

Cerebrospinal fluid (CSF) rhinorrhea occurs due to a breakdown of the layers of the arachnoid membrane, dura matter, the bony skull base and periosteum, and the nasal mucosa [1]. CSF rhinorrhea origin can be traumatic, iatrogenic, tumor induced and spontaneous. Spontaneous CSF rhinorrhea (SCSFR) forms in the absence of trauma, surgery, or another inciting event, thus it's easily to be misdiagnosed when the clinical symptoms are not typical. Spontaneous leaks can be congenital, idiopathic, or related to a meningoencephalocele [2]. Initial reports suggested that spontaneous leaks accounts for only 4% of CSF leaks. However,

current data showed a significant increase in SCSFR ranging from 20 to 40%, necessitating an increased emphasis on awareness and the need for early and accurate detection [3, 4]. SCSFR do not typically self-resolve and require surgical repair. Timely and effective closure of defects is critical to avoid potentially serious consequences including brain abscess and meningitis due to the spread of infection from the sinonasal cavity. Transnasal endoscopic surgery for CSF leaks is currently the standard approach for management due to the higher successful rate and lower morbidity compared to the transcranial or open approaches [5, 6].

Since the advent of image-guided sinus surgery in Germany in the 1920s, this technique has gained widespread popularity throughout the world. Recently, the increased efficacy and safety of computer-assisted navigation system (CANS) used in endoscopic sinus surgery for rhinosinusitis have been described [7, 8]. CANS allows for easy maneuverability, fast registration and calibration, and accurate localization [9, 10]. Reports of the use of CANS for endoscopic sinus closure of spontaneous CSF leaks, however, remain limited. In our study, CANS was routinely used in the procedure of transnasal endoscopic repair of SCSFR. CANS allowed accurate intraoperative identification of skull base defects, especially when the defects was ≤ 3 mm [11].

In this report, we described our experience with 21 patients who presented to our department with SCSFR and underwent transnasal endoscopic surgery with assistance of CANS between January 2007 and December 2017.

## Materials and methods

### Patients

We retrospectively reviewed all cases of CSF rhinorrhea submitted for surgical treatment between January 2007 and December 2017. During this period, 92 cases of CSF rhinorrhea were treated in our department, among which 29 cases were traumatic, 20 cases were iatrogenic, 22 cases were congenital, and 21 cases were spontaneous. Thus, 21 adult patients treated for SCSFR were enrolled in our study. Data collected included patient demographics, body mass index (BMI), patient symptoms, biochemical findings, radiographic findings, location of defect, type and size of defect, type of repair, follow-up time, reoccurrence, and complications. Descriptive statistics of the study population were performed with mean and standard deviation calculated for continuous variables and frequencies for category variables.

### Diagnostic techniques

Patients with clinical symptoms manifested as persistent or intermittent unilateral clear nasal drainage, exacerbated

by bending over or performing a Valsalva maneuver were highly suspected of SCSFR. Then possible nasal fluid was collected and evaluated for glucose concentration and $\beta_2$-transferrin. The effluent was determined as CSF if the glucose concentration in the fluid was over 1.7 mmol/L and the test for $\beta_2$-transferrin was positive. $\beta_2$-transferrin is a protein only found in CSF, aqueous humor, and perilymph that should be absent from other nasal and body secretions. Testing for $\beta_2$-transferrin is a reliable non-invasive test to confirm CSF rhinorrhea [8].

For localization of the defect there are several modalities that offer identification of the site of leak. Rigid nasal endoscopy was performed on both sides of the nasal cavity with a 2.7-mm Storze 0° endoscope in patients' awake state to identify the possible leak site. Every patient in this study underwent a preoperative high-resolution computed tomography (HRCT) scan of paranasal sinuses with submillimeter cuts and triplanar reconstructions were obtained to evaluate the site of the defect. In cases with glucose content and β2-transferrin confirmed leaks where there is no obvious skull base defect on HRCT, magnetic resonance image (MRI) would be benefit to identify the possible location of the CSF leak by showing high signal intensity of the CSF using T2-weighted sequences.

## CANS

The DigiPointeur® Surgical Navigation System (Collin, French) has been used in all surgical repair of SCSFR cases. We have used the same CANS system during the research period. 1 or 2 days prior to the operation, axial spiral CT was used to scan the nasal sinuses. The CT imaging follows a set of protocol that allows the acquired data to be transferred to a computer workstation. Following anesthesia, patients were placed in the supine position, and were fitted with a headset with electromagnetic reference. The position of the probe was adjusted and then registered in the navigator. The screen was divided into four parts for the view of axial, coronal and sagittal CT scan views plus the intraoperative endoscopic view. During surgery, the navigation system deduced the position of the operator's instrument by extrapolating the calibration points (the tip of the aspirator). Since the point was stereoscopically displayed, the surgeon could clearly distinguish the adjacent anatomical structure and resection range of the lesion (Fig. 1).

### Surgical techniques

Transnasal endoscopic approach under general anesthesia was used in all patients to repair the CSF leak. Functional endoscopic sinus surgery was performed to expose the skull base and isolate the leak site. The ethmoid sinus was exposed from anterior to posterior if the CSF rhinorrhea was
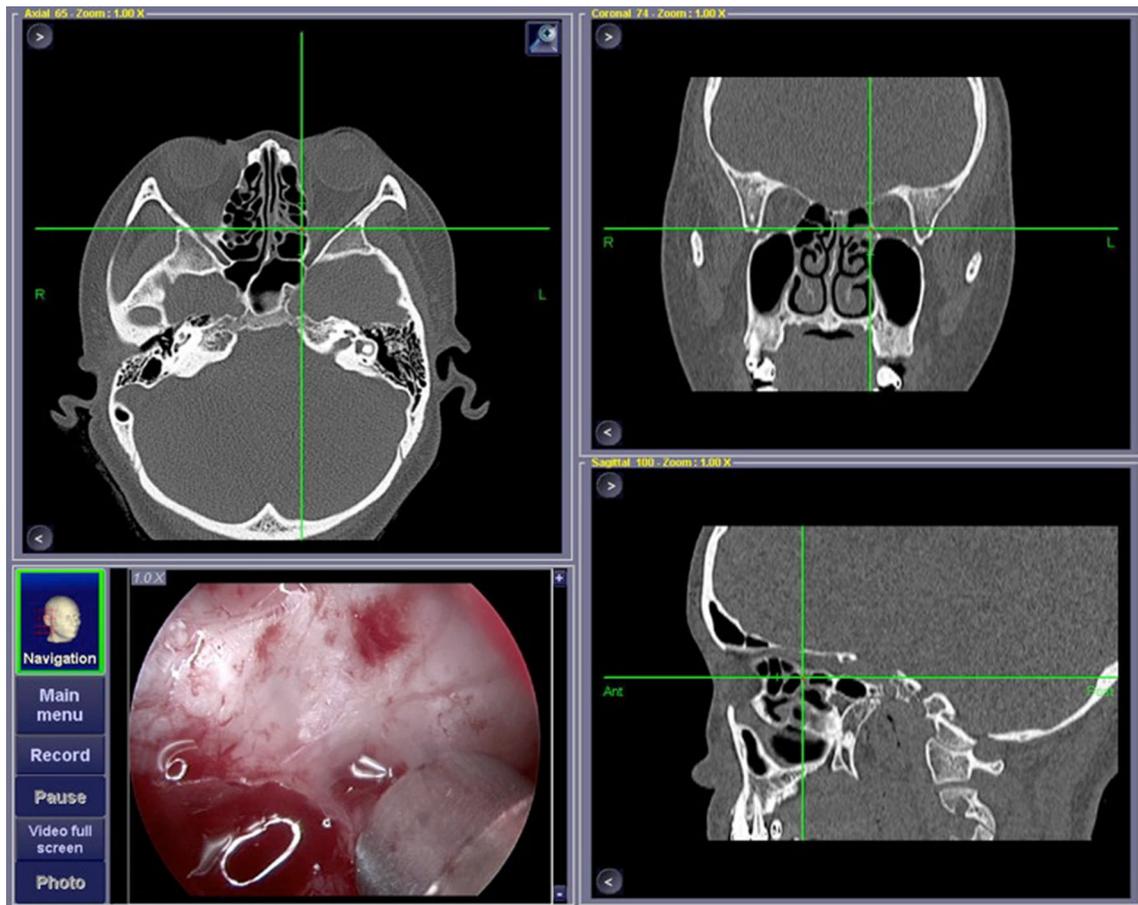
**Fig.1** The DigiPointeur® Surgical Navigation System was able to display the position of the tip of the surgical instrument (aspirator) relative to the position of the site of skull base defect with multi-plane (axial, coronal and sagittal)

located on the top of the ethmoid sinus; the sphenoid sinus was exposed through the nature ostium if the CSF leak was in the sphenoid sinus. If the leak site could not be clearly identified before the surgery, the ethmoid sinus and sphenoid sinus were routinely exposed. If the leak flow was slow and not obvious, the internal jugular vein was compressed to force CSF out of the lesion and can assist in intraoperative leak identification. Mucosa surrounding the defect was then removed and an area of bone 2 mm in diameter around the lesion was exposed. Graft materials for repair included thigh muscle, thigh muscle fascia, turbinate graft and abdominal fat tissue. The repair graft material was chosen based on the defect size and different surgeons' preference. Generally, small leaks (< 10 mm) were repaired by thigh muscle, which was dumbbell-shaped herniated into the small bony defect, and an overlay of fascia lata. In cases of larger leaks (≥ 10 mm), multilayer repair was performed with an underlay of the anterior part of middle turbinate (both bone and mucosa) and an overlay of fascia lata. Fibrin glue was injected to the defect area to reinforce the graft materials. A gelatin sponge impregnated with antibiotics (such

as neomycinsulphate, aureomycin, and polymyxin) was attached to the graft surface, and intranasal gauze packing containing iodoform was placed afterward.

## Adjuvant treatment

Postoperatively, patients were advised to adhere to strict bed rest and avoid vigorous coughing and nose blowing. A low salt diet and higher energy intake were recommended. 20% mannitol was used routinely after surgery to control intracranial pressure. Meanwhile prophylactic antibiotics were administered to prevent intracranial infection. Intranasal iodoform gauze was removed on the 14th post-operative day. An endoscopic inspection of the operative site with removal of crusts was performed on the 14th day, leaving the operative site untouched. Monthly nasal endoscopic follow-up examinations were recommended for 3 month, and once 6 month thereafter. After discharge, patients must be discouraged from engaging in any activity that places stress on the graft or increases intracranial pressure, including heaving lifting, intense exercise, and other strenuous activities. We

recommended avoiding strenuous activities for 3 months in patients with small leaks (< 5 mm) and 6 months in patients with large defects (≥ 5 mm).

## Results

Between January 2007 and December 2017, 21 patients met the criteria of present study. They consisted of 18 (85.7%) female and 3(14.3%) male patients, ranging in age from 29 to 68 years (mean $51.0 \pm 9.8$ years). The mean BMI was $27.2 \pm 1.6$ kg/m$^2$, while 18 out of 21 (85.7%) patients were overweight (BMI > 25) at diagnosis. Patients' clinical symptoms were all manifested as persistent or intermittent unilateral clear nasal drainage, exacerbated by bending over. One female patient's symptoms appeared after severe coughing while diving, and there were no obvious inducements in other cases. The mean duration of CSF rhinorrhea was $9.8 \pm 5.9$ weeks (range: 2–22 weeks). Twelve of the 21 patients had a left-sided leak, nine had a right-sided leak. Among them, four cases were complicated with type 2 diabetes along with hypertension, seven cases with hypertension and one case with type 2 diabetes (Table 1).

All patients' nasal fluid was collected and evaluated for glucose concentration and $\beta_2$-transferrin, all of which met the diagnostic standard of CSF. Visualization of clear fluid discharge can be found through nature ostium of sphenoid sinus in one case and through olfactory sulcus in three cases by preoperative rigid nasal endoscopic examination. All patients received a CT scan for perioperative planning and intraoperative image guidance. Skull base defect could be found in 14 cases by CT scan, while the other seven cases underwent MRI scan and found increased signal intensity in paranasal sinus on T2-weighted sequences (Fig. 2).

CANS was routinely used in SCSFR transnasal endoscopic surgery. Device setup times for each patient were recorded with a maximum of 13 min and a minimum of
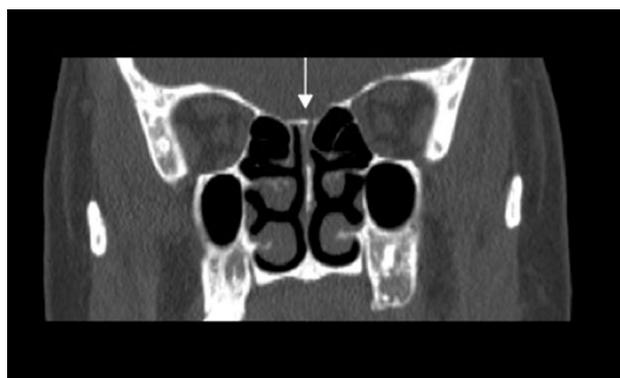


**Fig.2** Coronal CT scan: the white arrow indicates the skull base defect located at left cribriform plate

5 min (mean: 7 min). Based on the transferred multislice CT scans and multiplanar reformatted images, the DigiPointeur® Surgical Navigation System was able to display the position of the tip of the surgical instrument (aspirator) relative to the position of anatomical landmarks with less than 1.5 mm. After preoperative registration, no loosening of headset had been happened during surgery.

Intraoperatively, the skull base defects were found most frequently on the ethmoid roof in 12 cases (57.1%), followed by the cribriform plate in seven cases (33.3%), and sphenoid sinus in two cases (9.5%) (Fig. 3). One patient was also identified with a meningoencephalocele in the roof of the sphenoid sinus. The size of the skull base defect was < 5 mm in 13 cases, 5 mm ~ 10 mm in six cases and two cases involved defects of ≥ 10 mm. The graft materials were chosen based on the size of the defect. Small leaks were packed with thigh muscle with dumbbell-shaped technique and an overlay of fascia lata, and large leaks were packed with turbinate graft first, and then reinforced by fascia lata.

CSF rhinorrhea ceased postoperatively in all patients, yielding a success rate of 100%. The mean follow-up period was 15 months (range: 11–24 months). One patient complained about hyposmia postoperatively, and this symptom mostly improved after medication for nerve nutrition.

**Table 1** Demographics

| | |
|---|---|
| Patients, $n$ | 21 |
| Mean age $\pm$ SD, year | $51.0 \pm 9.8$ |
| Mean BMI $\pm$ SD, Kg/m$^2$ | $27.2 \pm 1.6$ |
| Sex, $n$ | |
| Male | 3 |
| Female | 18 |
| Mean duration of CSF rhinorrhea $\pm$ SD, weeks | $9.8 \pm 5.9$ |
| Accompanied chronic disease | |
| Type II diabetes | 1 |
| Hypertension | 7 |
| Hypertension with Diabetes | 4 |

*BMI* body mass index, *CSF* cerebrospinal fluid



**Fig.3** Location of SCSFR in our series

# Discussion

SCSFR occurs in the absence of trauma, surgery, tumor, or other inciting event. SCSFR is a rare pathology and has long been underdiagnosed. In our report, SCSFR accounted for 22.8% of all CSF rhinorrhea. SCSFR often result from skull base dehiscence and bony erosion from sinonasal and intracranial lesions. The etiology of SCSFR is not completely understood. SCSFR occurs with chronically skull base attenuation, which has been related to elevated intracranial pressure, more commonly seen in females who are middle-aged and overweight, and eventually leads to bony dehiscence, dural exposure, dural rupture and CSF leak [12–14]. Recent studies have demonstrated a significant correlation between obesity and attenuation of the anterior, lateral, and squamosal skull base bone [15, 16]. In our series, SCSFR occurred in patients who were mostly middle-aged, female, and overweight, which was mirrored in previous studies. Studies have demonstrated that patients with SCSFR have an elevated body mass index [17]. It is believed that SCSFR through the skull base are secondary to an inadequate resorption of CSF in arachnoid villi, leading to chronic intracranial hypertension. Elevated pressure and chronic CSF pulsations result in weakening of the thin parts of the skull base and lead to CSF leak when arachnoid membrane ruptures and /or to meningoencephaloceles [18].

The most common symptom in this series was unilateral clear nasal rhinorrhea. The symptoms of SCSFR are similar with rhinitis, thus it's easily to be misdiagnosed in early period. In our study, all patients had a history of treatment in other hospital, diagnosed as allergic, acute, or chronic rhinitis, and no obvious relief of symptoms was achieved by conservative rhinitis medical treatment. Clinical suspicion of SCSFR should prompt immediate nasal fluid evaluation, radiologic analysis and surgical consultation. This syndrome places patients at an increased risk of developing bacterial meningitis, which carries a high mortality rate [19].

The least invasive confirmatory tests for CSF rhinorrhea are the presence of $\beta_2$ transferrin and glucose concentration in the nasal discharge, which are sensitive and specific for CSF and perilymph fluids [20]. $\beta_2$ transferrin immunofixation is currently the gold standard for diagnosing CSF rhinorrhea, and has been noted to have a sensitivity of 100% and a specificity of 71% for detection of CSF leaks [21]. In our study, we confirmed the nasal drainage as CSF using these two tests.

Using techniques to precisely localize the leak site before surgery plays a key role in managing CSF rhinorrhea and facilitating a successful surgical repair. Localization of the CSF leak may be accomplished by nasal endoscopy, although this technique is typically insufficient, especially in those cases with intermittent or low-volume flow. In four cases of obvious leaks in our study, visualization of clear pulsatile fluid discharge could be found by rigid nasal endoscopy. Imaging studies are indispensable in localizing the site of the CSF leak and in providing adequate insight for presurgical planning and guidance. With thin 1 mm cuts of coronal section, a CT scan is helpful in detecting bony defects. High solution CT scan has an overall sensitivity of 70% in detecting bony dehiscence [22]. False-negative results can occur in patients with small bony defects, while false-positive results can occur from volume averaging. The more recent studies described the use of combined CT and MRI and the literature quotes a sensitivity of detecting CSF leak of 97% using this modality [23]. In our report, skull base defect could be found in 14 cases (67%) by CT scan, while the other seven cases underwent MRI scan and found increased signal intensity in paranasal sinus using T2-weighted sequences. There are also reports mentioned CT cisternography (CTC) which involves scanning the sinonasal cavities after intrathecal administration of about 8–10 mL of non-ionic iodinated contrast and placing the patient prone in Trendelenburg position for about 5 min, for craniad migration of contrast to achieve optimal cisternal opacification [24, 25]. The study is positive when there is contrast pooling. The sensitivity of CTC ranges between 85–92% in patients with active leak and 40% in those with inactive leak [26]. The disadvantages of CTC include: low sensitivity in patients with inactive/intermittent leaks, increased radiation dose due to multiple scans, the invasive procedure of administering contrast-enhanced agent through lumbar puncture carries the risk of brain hernia and allergic reaction. After we weighed the pros and cons, we had not used CTC as routine radiology study in SCSFR cases. Intrathecal injected fluorescein also helps to detect the lesion of CSF leaks. A lumbar puncture is needed, followed by nasal endoscopy for inspection of fluid to confirm and detect the site of CSF leaks. Potential side effects include cardiac arrhythmias, seizures, headaches, and cranial nerve defects [27]. Intrathecal injected fluorescein is an off-label use for diagnosis of the location of CSF leak according to FDA, thus its not licensed for this use by ethics committee in our institute.

Surgical repair of the skull base defect include transnasal endoscopic approach and open approaches. Open approaches are associated with intracerebral hemorrhage, cerebral edema, frontal lobe deficits, lengthened hospital stay, anosmia, and higher recurrence rates than the endoscopic approach. Therefore, repair of CSF rhinorrhea has evolved from requiring an open craniotomy approach to a minimally invasive endoscopic procedure [27]. Rigid endoscopes provide surgeon with excellent viewing capabilities.

However in transnasal endoscopic surgery, the paranasal sinuses border vital structures such as orbit and intracranial contents, serious complications may occur; lacrimal dysfunction due to injury of the lacrimal drainage system, ocular motility dysfunction, injury to the optical nerve, orbital hematoma, damage to brain issue or vessels have been reported [28]. Thus, over the past three decades, CANS was employed by otolaryngologists to enhance surgeon confidence, allow more thorough surgical dissections and possibly reduce the complication rate of endoscopic sinus surgery. The first CANS used in rhinology was developed in 1980 in Aachen, Germany by Klimek and coworkers [29]. In 2002, the American Academy of otolaryngology-Head and Neck Surgery endorsed the use of CANS for seven indications, which included CSF rhinorrhea or conditions where there is a skull base defect. In our series, CANS (The DigiPointeur® Surgical Navigation System) was routinely used in all SCSFR surgery procedure. This system uses an electromagnetic localization technique that provides a high level of precision with a reduced field. The navigation function includes two stages: preoperatively, the lesion area is located and surgical approach is determined according to the three-dimension model; intraoperatively, the position of the surgical instruments were localized in real-time, meanwhile current surgical approach and various parameters (angle, depth, etc.) can be observed, thus to avoid possible hurt to danger zone and reach the target lesion in the shortest time. In CSF rhinorrhea surgery procedure, when the skull base defect is close to the optic nerve or internal carotid artery (sphenoid sinus), locating of the defect is relatively difficult, CANS can play a role in safely guiding of the anatomical structure, helping the surgeon to avoid damage to the internal carotid artery and optic nerve.

There is considerable variability in the literature with regards to the grafts used for skull base defect repairs, and their success. Graft materials for repair include autologous and alloplastic materials. Autologous materials are typically used in the reconstruction of CSF leaks, which include turbinate grafts, nasoseptal mucosal grafts and flaps, cartilage grafts, fascia lata [30–32]. The choice of graft materials depends on the size of the defect and also relies on surgeons' favor. Fascia, mucosal grafts are used for watertightness because of their high collagen levels while cartilage and bone can act as rigid buttresses. It is, however, difficult to draw any conclusions with regards to success rates with different materials. Multitude of reconstructive techniques have also been described in the literature including sandwich grafts, three layer closure, overlay and underlay technique; however, there is a paucity of data delineating success rates by reconstructive method for patients with SCSFR [27, 33]. In our study, thigh muscle with fascia lata was used in small defects and middle turbinate graft with fascia lata was used in large defects. It was worth noting that the graft materials were stuck outside the leak during transnasal endoscopic surgery in conditional way. We considered that the pulsation of CSF put pressure on the graft materials continuously, thus might cause recurrence. So we modified the technique based on our experience. In small leaks, we did not simply attach the graft materials to the defects; instead, the thigh muscle was dumbbell-shaped herniated into the bony defect and with an overlay of fascia lata. Larger defects were packed with the anterior part of middle turbinate, reinforced by fascia lata. Then, fibrin glue was injected to the defect area to reinforce the graft materials. During the follow-up period, no failure of SCSFR repair has been occurred.

## Conclusion

SCSFR is rarely seen in clinical practice and more commonly seen in females who are middle-aged and overweight. The most common symptom is unilateral clear nasal rhinorrhea, exacerbated by bending over, thus it's easily to be misdiagnosed when the clinical symptoms are not typical. The combination of biochemical assay with radiologic studies is typically required to confirm a diagnosis of SCSFR and guide management. Endoscopic repair of SCSFR with assistance of CANS is safe and effective. The choice of graft materials depends on the size of the defect and also relies on surgeons' favor. Ideal surgical outcomes were achieved using thigh muscle dumbbell-shaped herniated into small defects and middle turbinate graft reinforced with muscle fascia packed into large defects.

## Compliance with ethical standards

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