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# Outcomes of transnasal endoscopic repair of cerebrospinal fluid leaks: a prospective cohort study

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## Abstract

**Background:** Although cerebrospinal fluid (CSF) leak repair of the anterior and middle skull base defect by endonasal endoscopic surgery (EES) presents one of the more difficult challenges, it has shown high success rates with less morbidity. Our objective is to evaluate the outcomes of transnasal endoscopic repair of CSF leak regarding success rate, impact on olfaction, and sinonasal function.

**Methods:** A prospective cohort study was conducted to evaluate the CSF leak repair outcomes related to the site, size of the defect, surgical techniques, and the materials that been used through Smell Identification Test (SIT), 22-item Sino-Nasal Outcome Test (SNOT-22), Perioperative Sinus Endoscopy score (POSE), and Lund-MackKay Scoring (LM) of CT scan.

**Results:** Twenty-one patients were enrolled in the study; 12 out of 21 were females with a higher prevalence of traumatic causes of 61.9%. Different techniques and materials were used for the repair with a success rate recorded at 90.5% after the first closure attempt. The mean standard deviation (SD) scores postoperatively (after 6 months) was markedly decreased in SNOT 22 with mean (SD)  $5.55 \pm 3.6$ , slightly increase in POSE (mean  $\pm$  SD =  $0.43 \pm 0.6$ ), and slightly decrease in SIT (mean  $\pm$  SD =  $10.31 \pm 4.7$ ) and LM (mean  $\pm$  SD =  $0.57 \pm 0.7$ ).

**Conclusion:** Transnasal endoscopic CSF leak repair is an effective technique for skull base defect closure with a high success rate and no valuable morbidity to sinonasal function other than mild hyposmia in patients where nasoseptal (NSF) and septal flap have been used.

**Trial registration:** The study was approved by the institutional review board and ethics committee of (The Arab Board of Health Specializations) with order no. (453) on 1 April 2018.

**Keywords:** Cerebrospinal fluid (CSF), CSF leak repair, Nasoseptal flap (NSF), Sinonasal function

## Background

Cerebrospinal fluid (CSF) leak occurs as a consequence of communication between the subarachnoid space and the upper aerodigestive tract due to a breakdown of the layers of the arachnoid membrane, dura mater, the

bony skull base, and the nasal mucosa. Patients with CSF leaks may have a spectrum of presentation, ranging from clear nasal discharge and headaches to potential life-threatening symptoms such as mental status changes, meningitis, or brain abscess which make the defect closure warranted [1, 2].

Different approaches have been described to achieve the surgical repair of CSF leaks at the anterior skull base includes; trans-cranial through a bifrontal craniotomy, extracranially through an external ethmoidectomy or frontal sinusotomy, and transnasally with microscopic or

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endoscopic visualization. In 1926, Dandy described the transcranial approach through a frontal craniotomy with a success rate of 60% to 80% and the advantages of direct visualization, treating any concomitant brain injury, and the opportunity to use a vascularized flap to cover the defect site [3–5]. Later on, in 1948, Dohlman introduced the first extracranial approach using a naso-orbital incision, and then subsequently, others developed a variety of endonasal approaches. In the last four decades with the advent of the rod lens rigid endoscope and the development of instruments tailored to transnasal endoscopic technique, endoscopic closure has revolutionized the management of cerebrospinal fluid (CSF) rhinorrhea due to its less morbidity and better closure rate. Endoscopic sinus surgery (ESS) provided direct short-cut access to the anterior and middle skull base without traversing any neurovascular structures [3, 6–9].

Although not enough articles exist that documented the preference and the effectiveness of utilizing specific material or technique over another in CSF leak repair, free grafts have been preferred to vascularized flaps for small defects repair because of technical ease of manipulation and obviation of the potential for contraction with healing [10, 11]. However, recent interest in closing large defects associated with skull base surgery has a favored pedicled flap, the bone or cartilage grafts are helpful in medium-sized defects. Scaring is incited by mucosal stripping with some evidence supporting the use of fibrin glue to reinforce and makes the repair denser [12, 13]. For the aforementioned reasons, we undertook this study and focused on the interpretation of the outcomes and sinonasal effectiveness of the endoscopic transnasal CSF leaks repair using different techniques and materials for the repair.

## Methods

A prospective cohort study was conducted at the Department of Otolaryngology-Head & Neck Surgery (Sulaymaniyah Teaching Hospital, College of Medicine, University of Sulaymaniyah, Kurdistan Region, Iraq) in a period between April 2018 and March 2019. The study was approved by the institutional review board and ethics committee of (The Arab Board of Health Specializations with order no. 453/2018). After informed consent, all patients who were clinically and intraoperatively confirmed to have CSF leaks from anterior, middle, and posterior cranial fossa who had failed conservative treatment were included in the study. Patients with CSF rhinorrhea secondary to leak from the mastoid region, malignant tumors invaded skull base, and patients with impaired sinonasal function were excluded from this study. Evaluation of the effectiveness of the transnasal endoscopic CSF leak repair and the impacts on the sinonasal function

especially olfaction, related to the site, size of the leak, materials, and surgical techniques that have been used for the repair had been done through: Smell Identification Test (SIT) 16 sniffing sticks were applied pre- and postoperatively at 1, 3, and 6 months. A sinonasal function was evaluated pre- and postoperatively, subjectively using the 22-item Sino-Nasal Outcome Test (SNOT-22) and objectively by the Perioperative Sinus Endoscopy score (POSE) and Lund-MacKay Scoring of CT scan.

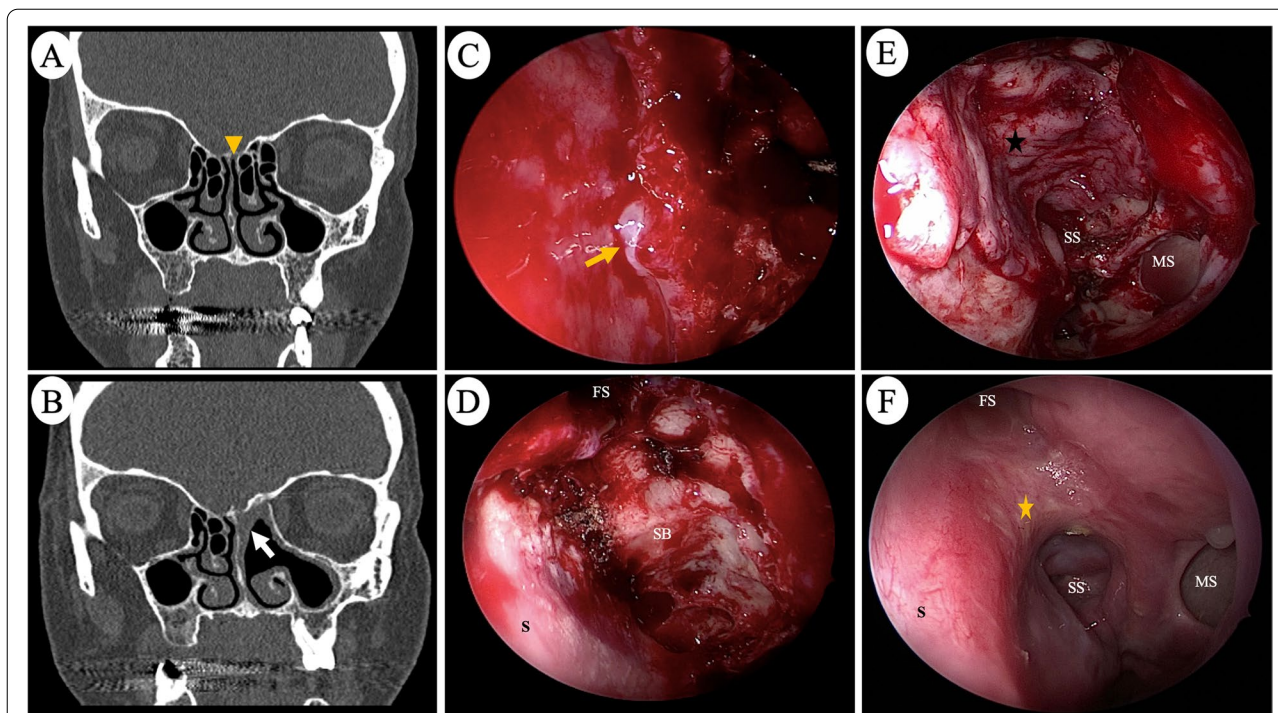
## Statistical analysis

All data was collected and statistically analyzed using Friedman and Wilcoxon signed rank tests by (SPSS Version 25) where *P*-value was considered statistically significant if it is  $\leq 0.05$  and highly significant if  $P < 0.0001$ .

## Surgical technique

Different techniques and materials are adopted in the endoscopic transnasal repair, starting with complete or partial trimming of the middle turbinate (MT) to get better access and visualization and then proceed with ordinary functional endoscopic sinus surgery (FESS) steps, and the intraoperative identification of the leak site has been done.

Once the encephalocele exists, downgrading in size to the stalk by using bipolar cauterization was performed, and then the mucosa is completely stripped away from the defect site for at least 5 mm in all directions. The bony projections near the defect were drilled out and regularized for better graft placement and taken up by the bed of the leak site. Overlay, multilayer, and gasket seal techniques were performed harvesting either grafts or flaps or combined as follows: grafts (MT, nasal floor mucoperiosteum's, septal cartilage, and fascia lata) and flaps (NSF and anterior ethmoid artery-based septal flaps). Overlay technique harvested graft or flap were adopted for the small defects  $< 1 \text{ cm}^2$  or when there is no space for undermining the cranial part of the defect medially, especially in the defects located far medially in the lateral lamella (LL) and cribriform plate (CP) respectively as shown in Fig. 1. In multilayer and gasket seal techniques, both graft and flap were mostly utilized simultaneously to address defects with either of the following criteria:  $> 1 \text{ cm}^2$ , multiple, high-pressure leaks, and in revision cases. In the multilayer technique, undermining the dura from the bony margins is the cornerstone of the technique, and the fascia lata was harvested and used as the first and the second layers. The graft was measured to be 1/3 larger than the defect diameter, so there will be at least 5 mm of the graft to insert into the space between brain tissue and dura ("underlay") as the first layer. The second layer will be the same size as the first one and located as extradural intracranial



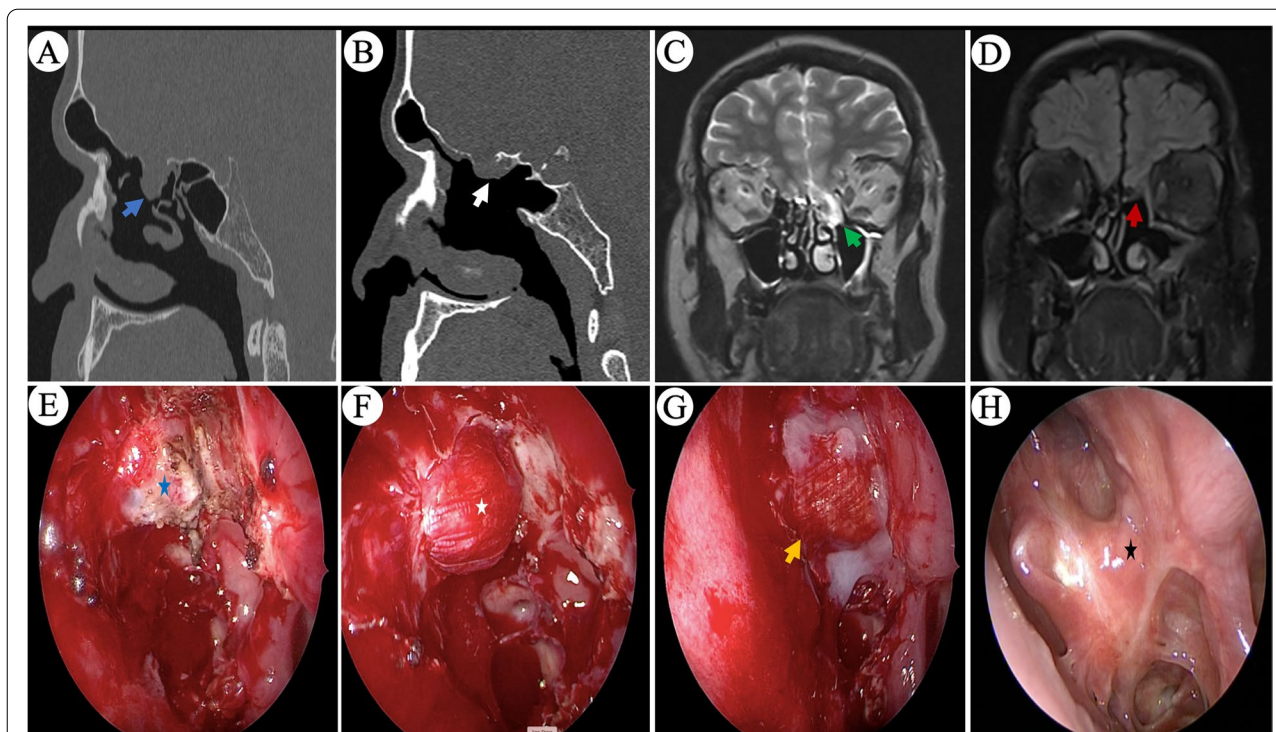
**Fig. 1** Illustrate overlay technique. **A** Pre-operative CT coronal view showing the possible defect site at the left olfactory cleft where denoted by yellow arrowhead. **B** Postoperative CT scan coronal view noted the defect sealed and marked by white arrow. **C** Intra-operative endoscopic image showing the defect site marked with yellow arrow. **D** Intra-operative endoscopic image showing the prepared skull base area denuded of the mucosa and drilled out bony margins. **E** Intraoperative endoscopic image of draped middle turbine mucoperiosteum as overlay graft denoted by black asterisk. **F** Postoperative endoscopic image showing the defect repaired and marked by yellow asterisk. SS (sphenoid sinus), MS (maxillary sinus), FS (frontal sinus), S (nasal septum), SB (skull base)

(“interlay”), and a third layer (“overlay”) using either flap or graft according to availability of tissue was placed on the nasal surface supported by fibrin glue, surgecil, gel-foam, and merocele as shown in Figs. 2 and 3. Whenever the effective epidural detachment is challenging and a leak is at the high-pressure area like lateral recess and clivus, the Gasket seal technique is preferred.

**Postoperative care**

All patients have been kept on strict bed rest with the head of the bed elevated to 15° for 5 days. This short period of inactivity will facilitate the healing process and avoid any sudden pressure changes or Valsalva maneuvers that may significantly elevate the intracranial pressure (ICP) and compromise the reconstruction. Soft diet and antitussives are important adjuncts to minimize ICP spikes during this crucial period. The patient is carefully daily observed for any signs of CSF leakage in the bed rest position. Broad-spectrum intravenous antibiotics (ceftriaxone vial in a dose of 50–100 mg per kg + metronidazole bottles 500 mg three times daily) are continued for 5 days and then changed to oral one for further 10 days. Acetazolamide

(ACTZ) is a carbonic anhydrase inhibitor that has the ability to decrease CSF production, dosage range from 250 mg two to four times a day for 4 weeks along with replacement of potassium and bicarbonate to maintain normal electrolyte values. Advise using saline sprays twice daily for 6 to 8 weeks. Patients stay in the hospital till the nasal tampon (Merocele) is removed (on the fourth or fifth day); once the packs were removed, an endoscopic examination is done to get the first look after the surgery. Discharge the patient to home with instructions minimizing their daily activity like weight lifting, upstairs, sex, avoid constipation by eating rich fiber diet, and avoid blowing their nose. The activity restrictions are lifted based on the endoscopic examination rather than a rigid timeline. Patients are seen in the office 7 days after surgery, conservative debridement limited to suctioning of mucus or debris in the dependent sinuses to maintain patency has been done. Debridement of the skull base reconstruction commences 4 weeks after surgery and continues until all healing has taken place. Patients were advised for monthly visits till 6 months for endoscopic examination and assessment to ensure the success of the



**Fig. 2** Demonstrate a multilayer technique utilizing fascia lata and middle turbinate grafts. **A** Preoperative CT scan image (sagittal view) shows a defect marked by blue arrow. **B** Postoperative CT scan image (sagittal view) shows the repair site marked by white arrow. **C** T2-weighted MRI (coronal view), green arrow denoted the skull base defect site at level of posterior ethmoid sinuses. **D** Postoperative T2 flair MRI (coronal view) shows the repair site marked by red arrow. **E** Intraoperative endoscopic image shows the defect site marked by blue asterisk. **F** First layer (inlay) of the repair using fascia lata marked by white asterisk. **H** Second layer using fascia lata as (overlay) sealed with fibrin glue marked with yellow arrow. **G** Six months postoperative endoscopic image shows the healed defect site denoted by black asterisk

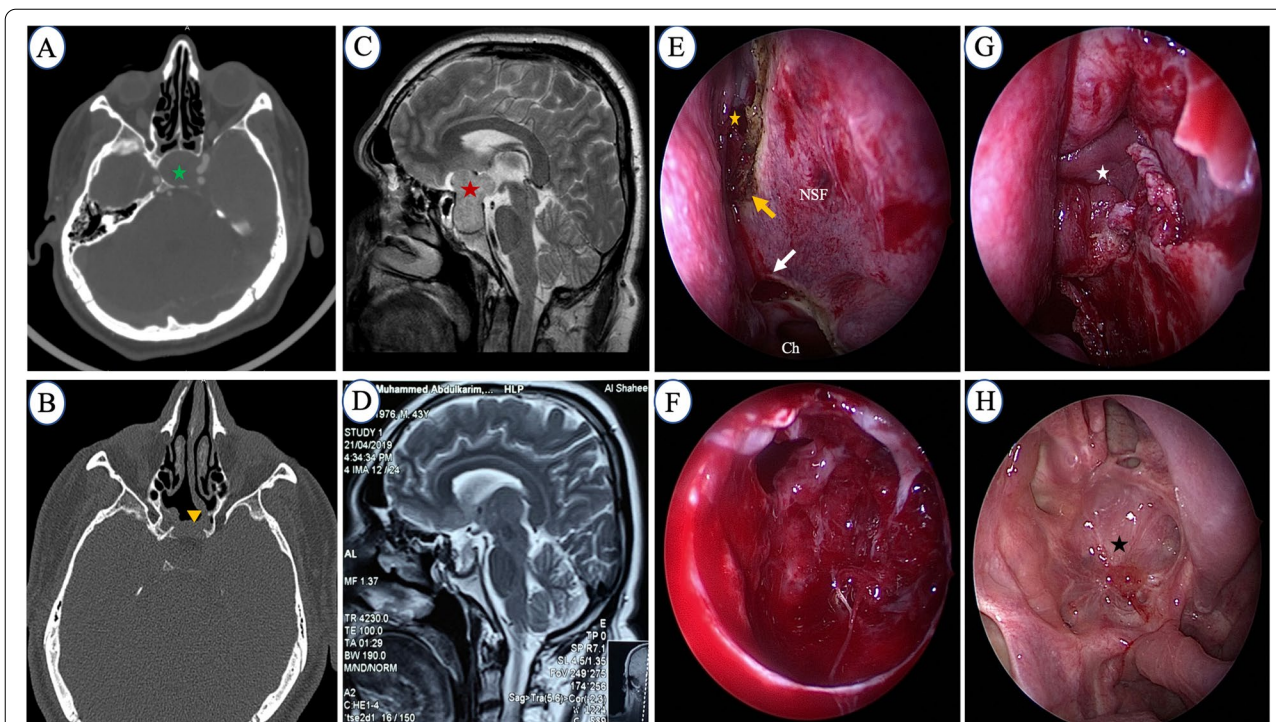
reconstruction and continued patency of the adjacent sinuses.

## Results

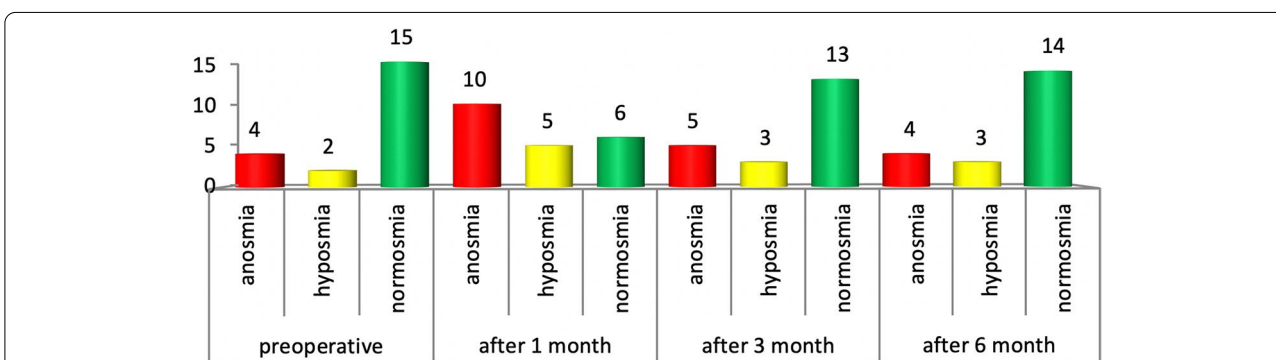
Twenty-one patients were enrolled in the current study; all underwent transnasal endoscopic repair of CSF leak; data demonstrated 12 females (57.1%) and 9 males (42.9%), and patient ages ranged from 16 to 62 years with a mean of 39 years. The collected data of our patients regarding the cause, site, size of the defects, material, and the techniques were used for the repair were distributed and demonstrated in Table 1 as follows. The cause was *traumatic* in origin in 13 (61.9%) patients (incidental in 11 (84.6%) patients and accidental in two (15.4%) patients) and *non-traumatic* (spontaneous) in 8 (38.1%) patients, 6 of them with high body mass index (BMI) more than 25 kg/m<sup>2</sup> with a mean of 29.01. The site of the leak was located preoperatively through high-resolution CT scan and T2-weighted MRI images with and without flair with a specificity reaching 90% and was noted in the sphenoid sinus (SS), cribriform plate (CP), fovea ethmoidalis (FE), and lateral lamella (LL) in the frequency of 11 (52.4%), 6 (28.6%), 2 (9.5%), and 2 (9.5%)

patients respectively. The size of the leak was less than 1 cm<sup>2</sup> in 16 (76.2%) patients; however, 5 (23.8%) patients were more than 1 cm<sup>2</sup>. Combined reconstruction material (fascia lata graft and nasoseptal flap) was the choice for the defect closure in 12 (57.1%) patients, 5 (23.8%) patients by mucoperiosteal of the middle turbinate, 2 patients (9.5%) by fascia lata, and in other 2 patients (9.5%), a pedicled septal flap was utilized. Multilayer, overlay, and gasket seal techniques were adopted in 10 (47.61%), 7 (33.33%), and 4 (19.04%) patients respectively. Laterality was distributed as follows: 7 patients on the right side, 4 patients on the left side, and the rest 10 patients in diaphragma sellae (both sides).

Generally, the success vs failure rate was (90.5%/9.5%) after the first closure attempt, and it was 100% after the second attempt. A higher success rate (100%) was reported in the cases with a leak from the sphenoid sinus and fovea with a size more than 1 cm<sup>2</sup>, where multilayer or gasket seal technique was chosen and utilizing both graft and flap at the same session, while the least success rate was with the leak from lateral lamella (50%) using overlay technique 71.4%. In this study, the mean  $\pm$  standard deviation (SD) of SNOT 22, POSE, SIT, and LM scores for the



**Fig. 3** Transnasal paraseptal transsphenoidal hypophysectomy with skull base reconstruction by multilayer technique using (fascia lata graft and NSF). **A** CT scan image (axial view) showing the isodense opacity filling the sphenoid sinus bilaterally marked with green asterisk. **B** Six months postoperative CT scan (axial view) showing resected pathology with reconstructed skull base defect which denoted with yellow arrowhead. **C** T2-weighted MRI (sagittal view) showing a large pathology filling the sella with a suprasellar extension denoted by red asterisk. **D** Six months postoperative T2-weighted MRI (sagittal view) shows resected pathology with reconstructed skull base. **E** Nasoseptal flap (NSF) pedicle with superior incision marked by yellow arrow and inferior incision marked with white arrow, sphenoidotomy denoted by yellow asterisk. **F** Endoscopic image showing the sellar and suprasellar areas free of the tumor. **G** Harvested NSF draped as third outer layer in the reconstruction. **H** Six months postoperative endoscopic image showing posterior part of the nasal cavity illustrating posterior septectomy, reconstructed skull base defect with NSF showing complete mucosalization which denoted with a black asterisk



**Fig. 4** The Smell Identification Test (SIT) at pre-operative and 1, 3, and 6 months post-operatively

patients pre-operatively was  $17.74 \pm 11.51$ ,  $0.21 \pm 0.54$ ,  $10.47 \pm 4.17$ , and  $1.38 \pm 0.82$  respectively; however, post-operatively (after 6 months), the score was markedly decreased in SNOT 22 with (mean  $\pm$  SD =  $5.55 \pm 3.6$ ), slightly decrease in SIT (mean  $\pm$  SD =  $10.31 \pm 4.7$ ) and LM (mean  $\pm$  SD =  $0.57 \pm 0.7$ ), and slightly increase in

POSE (mean  $\pm$  SD =  $0.43 \pm 0.59$ ). There was a significant difference between pre/postoperative scores in all parameters through the 3 postoperative readings after 1, 3, and 6 months collectively as follows: SNOT 22, POSE, and SIT were  $P=0.001$  and LM  $P=0.003$  as shown in Table 2 and Fig. 4.

**Table 1** Illustrate the success and failure rate according site, size of leak, surgical technique, and material of repair

Studies variables	No.	Success rate (%)	Failure rate (%)
Site of leak			
Sphenoid	11	100	0
Cribriiform plate	6	83.3	16.7
Lateral lamella	2	50	50
Fovea ethmoidalis	2	100	0
Size of leak			
< 1 cm <sup>2</sup>	16	87.5	12.5
> 1 cm <sup>2</sup>	5	100	0
Surgical technique			
Multilayer	10	100	0
Overlay	7	71.4	28.6
Gasket seal	4	100	0
Material of repair			
Combined	11	100	0
Graft	6	83.3	16.7
Flap	4	75	25

Our study results' analysis demonstrated in Tables 3 and 4 showed a decrease in the SNOT 22 mean scores after 6 months postoperatively in relation to all study variables (site, size, technique, and material of the repair) and statistically was significant in patients with a leak size <1cm<sup>2</sup>, utilizing multilayer or overlay techniques with grafts or combined materials as follows:

**Table 2** Friedman test showed differences between ranks of measured dependent variables according to some measured variables and the time of measurements

	No.	Mean	Std. deviation	Mean rank	P value
<b>SNOT 22</b>					
Preoperative	21	17.74	11.510	3.33	0.001
After 1 month	21	17.14	9.931	3.24	
After 3 months	21	9.33	4.351	2.21	
After 6 months	21	5.55	3.640	1.21	
<b>POSE</b>					
Preoperative	21	0.21	0.538	1.57	0.001
After 1 month	21	2.643	1.4675	3.71	
After 3 months	21	1.810	1.9201	2.90	
After 6 months	21	0.43	.598	1.81	
<b>SIT</b>					
Preoperative	21	10.476	4.1728	2.90	0.001
After 1 month	21	7.81	4.226	1.57	
After 3 months	21	9.286	4.4541	2.33	
After 6 months	21	10.31	4.689	3.19	
<b>LM</b>					
Preoperative	21	1.38	0.820	9.63	0.003
After 6 months	21	0.57	0.746	8.50	

0.002, 0.021, 0.028, 0.046, and 0.009 respectively. POSE mean scores 6 months postoperatively noted an increase in most of the study variables except those with a leak size > 1 cm<sup>2</sup> located at the FE, and the only remarkable increase was depicted in the POSE mean score of the LL leak group with a P-value = 0.0317. The mean of the SIT scores after 6 months postoperatively noted variable records. It showed a non-significant decrease in a group of patients with a leak size < 1 cm<sup>2</sup> wherein flap was utilized for the reconstruction and increased the score in most of the other variables with significant records in a leak size > 1 cm<sup>2</sup> repaired by graft material with a significant P-value of 0.042. LM mean score revealed a decrease in the mean of 6 months postoperatively for all study variables with a significant difference in groups of patients with a leak in SS < 1 cm<sup>2</sup>, reconstructed with multilayer technique and utilizing combined materials with a P-value as follows: 0.02, 0.012, 0.018, and 0.005 respectively.

The correlation of the aforementioned parameters (SNOT 22, POSE, SIT, and LM) with the studied variables (site, size, technique, and material of the repair) at the same time revealed that sinonasal function was more affected in CSF leak repair cases with a leak size < 1 cm<sup>2</sup>, utilizing multilayer or overlay techniques with grafts or combined materials, and leak site at LL and SS where the SIT and LM specifically were more affected respectively.

**Discussion**

Nowadays, endoscopic endonasal repair of CSF rhinorrhea becomes the preferred option for the repair of CSF rhinorrhea getting an advantage over the open approach that there are less morbidity and mortality, with preservation of the nasal functions [14].

CSF leaks are classically categorized according to the cause into traumatic and non-traumatic types. Traumatic leaks are more common, and it is noted either after accidental skull base fracture or incidental during sinus and skull base surgery. Non-traumatic leaks presented as spontaneous or congenital variety and may be secondary to skull base tumors causing skull base erosion. In CSF leaks, the patient occasionally presented with undetermined cause and was identified as idiopathic type [1, 3].

Although several studies series have shown equally distributed patients through both groups with increased prevalence of incidental CSF leak [15, 16], our study noted that 61.9% of the cases listed within the traumatic group with a higher prevalence of incidental type, and it is enforced by Sharma et al. [1] (61%) and Kljajic et al. [17] findings. Contradict to literature reports that show traumatic leaks were more common than non-traumatic, others like Virk [18] reported 2/3 of patients with spontaneous CSF leak.

**Table 3** Wilcoxon signed rank test showed differences between ranks of SNOT 22, POSE, SIT, and LM scores according to some studied variables (site and size of the leaks) and time of measurements (preoperative and 6 months after operation)

Site of the leak (pre- and 6 months post-operative)																
Parameters	CP (N=6/6)			SS (N=11/11)			LL (N=2/2)			FE (N=2/2)						
	M	SD	MR	P value	M	SD	MR	P value	M	SD	MR	P value				
SNOT22	18.08/8.58	13.455/4.477	4.38/1.75	0.141	15.27/13.09	9.519/7.006	5.56/7.17	0.305	17.50/5.00	4.950/0.00	1.50/0.00	0.180	30.50/5.00	20.50/2.82	1.50/0.00	0.180
POSE	0.08/0.33	0.204/0.816	1.00/2.00	0.655	0.18/0.55	0.603/0.522	3.50/3.50	0.102	0.00/0.50	0.0/0.707	0.00/1.00	0.031	1.00/0.00	0.707/0.00	1.50/0.00	0.180
SIT	11.58/9.92	2.2004/5.142	4.25/2.17	0.786	11.7/12.2	2.57/2.20	6.75/5.57	0.589	6.500/6.00	9.1924/8.485	1.00/0.00	0.317	4.000/5.00	5.656/7.071	.00/1.00	0.317
LM	0.92/0.50	0.917/0.548	1.67/1.33	0.257	1.4/0.55	0.789/0.934	5.56/5.00	0.020	1.75/0.50	0.354/0.707	1.50/0.00	0.180	1.75/0.50	0.354/0.707	1.50/0.00	0.180
Size of the leak (pre- and 6 months postoperative)																
Parameters	< 1cm <sup>2</sup> (N=16/16) (Pre and 6M. Post-operative)			> 1cm <sup>2</sup> (N=5/5)												
	M	SD	MR	P value	M	SD	MR	P value								
SNOT22	17.15/5.71	12.93/4.07	8.73/3.25	0.002	10.5/12.5	1.9/1.58	3.50/1.00	0.078								
POSE	0.062/0.375	0.17/0.62	1.5/5.00	0.06	0.7/0.6	0.97/0.54	3.00/2.00	0.705								
SIT	10.47/9.62	4.71/5.15	8.00/5.83	0.458	10.5/12.5	1.9/1.58	0.0/3.00	0.042								
LM	1.37/0.56	0.763/0.813	7.67/6.5	0.012	1.4/0.6	1.08/0.54	2.5/0.00	0.066								

**Table 4** Wilcoxon signed rank test showed differences between ranks of SNOT 22, POSE, SIT, and LM scores according to some studied variables (surgical technique and material of the repair) and time of measurements (preoperative and 6 months after operation)

Surgical technique (pre- and 6 months post-operative)		Gasket seal (N=4/4)		Multilayer (N= 10/10)		Overlay (N= 7/7)		P value	
Parameters	M	SD	MR	M	SD	M	SD	MR	P value
SNOT22	21.00/5.50	8.246/1.732	2.50/0.00	15.20/4.60	13.011/4.033	19.50/6.93	11.500/3.813	4.50/1.00	0.028
POSE	0.50/0.75	1.0/0.50	2.00/2.00	0.20/0.50	0.483/0.707	0.07/0.14	0.189/0.378	1.00/2.00	0.655
SIT	11.125/13.13	1.4930/0.854	.00/2.50	10.45/10.4	4.6335/4.298	10.143/8.5	4.9305/6.007	3.17/2.75	0.588
LM	1.13/0.50	1.031/0.577	2.00/0.00	1.65/0.60	0.626/0.966	1.14/0.57	0.945/0.535	3.13/2.20	0.176
Material of the repair (pre- and 6 months post-operative)		Flap (N=4/4)		Graft (6/6)		P value			
Parameters	M	SD	MR	M	SD	M	SD	MR	P value
SNOT22	18.27/5.18	12.571/3.65	5.89/2.00	14.50/6.50	8.660/3.786	18.92/5.58	12.579/4.079	20.00/1.00	0.046
POSE	0.23/0.64	0.607/0.674	2.50/4.60	0.13/0.25	0.250/0.50	0.25/0.17	0.612/0.408	2.00/1.00	0.655
SIT	10.273/11.0	4.0272/4.15	7.00/5.13	13.25/9.00	1.8484/6.37	6.42/9.92	3.584/5.142	.00/3.00	0.042
LM	1.32/0.27	0.751/0.467	5.50/0.00	1.88/1.25	0.629/1.258	1.17/0.67	1.033/0.516	2.67/2.00	0.273



The considerable variability in the literature regarding the prevalence of leak cause, which shifted from accidental to incidental traumatic one, is due to decreasing the incidence of the direct head trauma as a result of better road safety measures and increasing the trend of the endoscopic sinus and skull base surgery with different levels of training. High BMI is noted in our patients with non-traumatic leaks which explains their incidence, and it is harmonized with the increasing risk of the occurrence of non-traumatic rhinorrhea within a Western population because of increasing BMI [1, 15].

Kljajic et al. [17] reported that male patients outnumbered female ones in the group of traumatic CSF leaks while most of the patients with spontaneous CSF leak are females which is supported by Seth et al. [19], and our study results were 84.6% and 87.5% respectively.

In contrast to several studies [8, 20–25], there were documentations that the leak site is more evident in the fovea, LL, and CP; our series reported uneven distribution of fistula site, and it is noticeably more seen in the sphenoid sinus in 52.4% of patients where it is in harmony with Zweig et al. [3] series which were recorded in 37%. This is explained by including incidental leaks during transnasal trans-sphenoidal pituitary surgery in the study when the arachnoid membrane inadvertently breached especially in large macroadenoma or tumors with supra-sellar extension. Localization of the site of leak preoperatively utilizing endoscopic examination, CT, and MRI images is a paramount step in the repair process. Although intraoperative documentation of the leak site using intrathecal fluorescein was advocated by many authors that enforced the diagnosis, especially where the site of the leak was difficult to identify, its use is still controversial due to possible neurological complications [9, 26]. In our series, CT scan and MRI (with flair T2 sequence) imaging used detected even small defect with a high sensitivity which reached 90%, and in difficult unclear fistula asking the anesthetic for intraoperative Valsalva maneuver, significantly, it optimized the identification of the exact leak site.

Our series showed that the leak size was  $< 1\text{cm}^2$  in 16 cases (76.2%) and  $> 1\text{cm}^2$  in 5 cases (23.8%); however, Zaroni et al. [25] detected 47.4% size of leak less than  $1\text{cm}^2$  and 52.6% more than  $1\text{cm}^2$ ; this study outlined that it is not the defect size “per se” that makes the reconstruction complex as even when addressing a very small fistula, and using more sophisticated than simple overlay technique may be warranted.

Zaroni et al. [25] and Majhi et al. [27] were identical to the current study in the success rate after the second attempt (100%). Gilat et al. [28] published a prospective study of 10 years of experience with endoscopic surgical repair of CSF rhinorrhea (1996–2006), showing a lower success rate (83% at first attempt and 91% at second).

Clarifications in surgical technique and increasing experience have contributed to ameliorating success rates over the years.

There is no directly proportional link between the defect size and the increased risk of failure when dealing with the anterior cranial base. This is documented in our series and coincides with Zweig et al. [3] and Zaroni et al. [25] reports; although it is a small group in comparison to the Zaroni series, only two out of twenty-one cases failed after primary closure, where both of them presented with a defect size  $< 1\text{cm}^2$  and located at the olfactory cleft. The first one was a 45-year-old lady with a high BMI ( $29.4\text{kg/m}^2$ ); anterior ethmoid artery-based septal flap was tailored for the defect, re-leak was noted on the second postoperative day, and then a revision surgery was done using multilayer technique. The second case was a 50-year-old male with no risk factors like high BMI where overlay technique was used, leak was noted on 9th postoperative day, the revision surgery been done, and a septal flap adapted to seal the defect.

Throughout the literature, the choice of the techniques and materials used for CSF leak repair appears to depend on surgical experience and skills their familiarities with the repair materials. This was well clarified by Weber et al. [29] who used both free grafts and vascularized flaps, with on-lay and underlay techniques, and noted a success rate of 100% from primary surgery.

Regardless of the site and the size of the defect, the key to a successful repair depends on a wide exposure of the defect site with removing the surrounding mucosa and making a bare bone to allow the graft to firmly adhere to the skull base [3, 25]. This concept was disagreed by some authors who discussed the factors that implicated in the primary closure failure and advocated the choice of the material and the technique according to the size and the site of the leak which contradicts most literature records. Burns et al. [30] recommended in their article for closing a defect in the cribriform plate and fovea ethmoidalis, choosing a free mucosal defect for small defect  $< 0.5\text{cm}^2$ , and advocated a composite graft with rigid support from the turbinate bone or septal cartilage to close the larger defect.

Although the most probable causes of primary leak repair failure in our series are contributing factors like high BMI and early mobilization of the patients, the technical error with a primitive surgical experience is a possible fact. Other valuable possibilities include multiple leak sites which are not recognized primarily, an area of a bony defect with dural dehiscence which opened on the repair of the primary leak site, and comorbidities like a chronic cough [3, 25].

Yet, the long-term impact of anterior and middle skull base CSF leak repair on sinonasal quality of life (QOL),

endoscopic, olfaction, and radiographic outcomes remains incompletely defined. Although several studies have looked at components of this question, to our knowledge, this is one of the few prospective studies to examine long-term overall and subdomain SNOT-22, POSE, SIT, and LMS scores in patients undergoing endoscopic CSF leak repair surgery that compared pre- and post-operative scores in the same patients.

Nasal function was evaluated subjectively by SNOT-22, which is focused on sinonasal function and quality of life. The SNOT-22 questionnaire is a patient-reported outcome measure developed for use in chronic rhinosinusitis (CRS). It is a modification of a pre-existing instrument, the SNOT-20, which itself is a modification of the 31-question Rhinosinusitis Outcome Measure (RSOM-31) [24]. Regarding the current study, we obtained 100% compliance with SNOT-22 questionnaire completion at pre-/post-operative periods in three intervals, giving us a robust dataset.

Generally, there were significant differences between pre-/post-operative periods in three intervals collectively with a  $P$ -value = 0.001, besides that significant differences were noted with the size defect < 1 cm<sup>2</sup>, repair done by overlay or multilayer techniques, and were graft or combined materials (graft and flap in the same session) utilized with ( $P$  = 0.002, 0.0028, 0.0021, 0.046, 0.009) respectively; however, there were no significant differences regarding the site of the leak (cribriform plate, sphenoid, lateral lamella, and fovea) with  $P$  = 0.141, 0.305, 0.180, and 0.180 subsequently. The finding was up to the expectation for the score of a 1-month follow-up. However, the 1-month score was transiently worse than the pre-surgical level due to nasal edema and crust formation post-operatively.

Riley et al. [31] conducted prospective case series examining adult patients undergoing endoscopic anterior skull base (EASB) surgery with NSF reconstruction; there were no statistically significant differences that were noted between the mean overall pre- and postoperative SNOT-22 scores. SNOT-22 scores improved in 58.7%, deteriorated in 37.0%, and stayed the same at 4.3%. Deterioration in SNOT-22 scores was greater in younger vs. older patients with  $P$  = 0.010.

Jallesi et al. [32] evaluated the impact of NSF elevation on sinonasal quality of life (QOL) in patients with pituitary adenomas who underwent endoscopic endonasal trans-sphenoidal approach (EETSA) and noticed no significant inter-group differences in the mean SNOT-22, 9Q, and sense of taste/smell scores in preoperative and all postoperative assessments. Within each group, a significant improvement of SNOT-22 and 9Q scores was noted after 12 months of surgery compared to preoperative data, and this harmonized with our data interpretations.

Objectively, the POSE score generally was significant with  $P$  = 0.001; a transient upturn in the score after 1 month was noticed as a result of crust and polypoidal changes at the site of repair which was a part of the healing process. And it significantly noted when the leak was in the lateral lamella with  $P$  = 0.0317. However, the size of the leak, surgical techniques, and material used showed no significant difference in the score; this means meticulous repairing, satisfying follow-up, and superb healing process.

Olfaction was subjectively assessed by SIT score; generally, the mean decreased after 1 and 3 months postoperative but retained back to normal values and improved after 6 months postoperative with a significant difference  $P$  = 0.001 when compared preoperative with the three postoperative periods collectively. Moreover, when SIT score was applied to four groups, it showed improvement in the olfaction in the group of the patient with defect size > 1 cm<sup>2</sup> and utilizing the graft (in both, the mean increase after 6 months postoperatively) with significant differences  $P$  = 0.042 for both. Our study proved that the site of the leak and techniques that were used did not affect the olfaction and showed no significant differences, but olfaction was worse when repair was done by a flap (which was either nasoseptal or anterior ethmoidal artery-based pedicle flaps) due to the healing process and crust formation, especially at the site of harvesting flap.

Many authors study the effect of elevation of nasoseptal Hadad's or rescue flap on olfaction and showed different results. Sowerby et al. [33] published a prospective study of 22 patients. A unilateral middle-turbinate-sacrificing approach was used, with partial ipsilateral superior turbinate resection and routine cold elevation of an ipsilateral nasoseptal rescue flap. NSF was used in 4 patients. UPSIT scores showed preservation of objective olfactory function ( $34.8 \pm 2.3 \rightarrow 35.1 \pm 3.0$ ;  $p$  = 0.37). No significant change in UPSIT was seen in the 4 patients undergoing NSF, which coincides with our records. On the other side, Tam et al. [34] published a single-blinded, randomized controlled trial of 20 patients. The treatment group had the elevation of a Hadad-Bassagasteguy nasoseptal flap (NSF) with cutting mode monopolar electrocautery, with the control group having no flap elevation. In the NSF group, UPSIT declined by 19.7% ( $38.2$  to  $30.7$ ,  $p$  < 0.001), compared to a 9.1% decrease in the control group ( $37.3$  to  $33.9$ ,  $p$  < 0.001). The difference between the 2 groups was statistically significant ( $p$  < 0.001). The study was adequately powered to detect a clinically significant difference of 10% in UPSIT scores. Due to the significant heterogeneity in study design, the use of different tests of olfactory function, and variable surgical approaches, further meta-analysis was not feasible. The

aforementioned articles showed that in the absence of using NSF or septal flap for reconstruction in the skull base defect, the resection of other normal nasal structures as part of the extended endoscopic approach is a potential factor in olfactory impairment because of a wide distribution of the olfactory epithelium over a 2-cm<sup>2</sup> area, covering the superior nasal septum, cribriform plate, or olfactory cleft and the superior aspect of apposing lateral nasal wall at the level of the common lamina which constitutes the origin of the middle, superior, and supreme turbinate [35].

Lastly, generally, the LM score affirmed the improvement in a score by decreasing the mean at 6 months postoperative when compared with preoperative, with a significant difference  $P=0.003$ . LM according to the site of leak showed a mean decrease overall sites and was highly significant with a  $P=0.020$  in sphenoid sinus leak where 9 out of 11 cases decreased in the score, but it was not significant in cribriform, lateral lamella, and fovea with  $P=0.257$ , 0.18, and 0.18 respectively. These findings were attributed to no interference with other sinuses other than sphenoid sinus which were mostly pituitary surgeries performed with a meticulous repair which has been done on the sphenoid defect. Also, LM enforced in groups which were isolated according to the size of the leak, surgical technique, and material used shows the mean decrease overall after 6 months when compared to preoperative with significant differences when the size less is than 1cm<sup>2</sup>, and repair was done with multilayer technique and by utilizing combined material (graft and flap) with  $P=0.012$ , 0.018, and 0.005 respectively.

Ashraf et al. [36] attempted to study this staging system to determine what score should be considered an incidentally normal range. They concluded that an LM score of 3 or less was most likely normal, above 6 was most likely pathological, and 4–5 indeterminate; in the current study, all shows score 3 or less; this means within the normal range in pre-/postoperatively, and it is noticed that there is no any mucosal thickness in the frontal sinus. Longdon et al. [37] published a prospective study that included 55 patients who underwent advanced endoscopic skull base surgery, which showed a significant difference with the mean total LMS being  $0.63 \pm 1.2$  (range 0–4). After 3 and 12 months, postoperatively, the mean scores were  $3.5 \pm 3.8$  ( $P<0.05$ ) and  $2.0 \pm 2.5$  ( $P<0.05$ ) respectively, and patients who needed NSF for reconstruction had a greater Lund-Mackay score ( $P<0.05$ ). Deconde et al. [38] published a retrospective study, examined the consequences of partial middle turbinate resection, maxillary antrostomy, and nasoseptal flap harvest in skull base surgery, and noticed that the mean difference in pre-/postoperative LM score for the right anterior ethmoid sinus was significantly different from the

left-sided  $P=0.002$ . The difference in the frontal sinuses approach was not significant with a  $P$ -value=0.0625.

Generally speaking, postsurgical sinonasal dysfunction almost always has a cause, which is not just related to anatomical alteration. The mucosal stripping, middle turbinate resection, and the design of the nasoseptal flap have not been well addressed are common causes. Avoidance of mucosal stripping will decrease the chance of intranasal adhesion, which might trap the mucous clearance and impair sinonasal function even with using nasal irrigation. Although middle turbinate resection rarely affects olfaction, anterior stump lateralization after its resection is not uncommon and might cause frontal sinus outflow obstruction and end in secondary rhinosinusitis. However, in the harvesting of the nasoseptal flap, following the lateral nasal wall common lamina landmark which is parallel to the superior olfactory strip (SOS) area can provide a low morbidity approach while maintaining reconstruction options [39, 40]. The aforementioned facts suggest that a combination of minimizing mucosal trauma and respecting the olfactory-bearing areas of the nasal cavity are likely to ensure minimal impact on sinonasal function and olfaction.

#### Limitation of the study

Although the aim of the current study is to describe our experience to repair CSF leak in a prospective fashion, many limitations come into view which is as follows: a limited number of the studies cases, make statistical findings of the leak site, especially at LL and FE non-significant, and prevent multivariate analysis of the surgical failure cases. Moreover, the duration of the follow-up is limited which may not predict the recurrence rate. This report is, however, sufficient to provide useful information about this disease entity, technique, and material used for the repair.

#### Conclusion

From the current study, we found that using a multilayer or gasket seal technique utilizing both graft and flap at the same session for a defect size of more than 1 cm<sup>2</sup> had a more successful rate and favorable outcomes. Olfactory hypofunction was noted especially after harvesting NSF or septal flap, for that the probability of postoperative hyposmia or anosmia should be discussed with patients who underwent endoscopic surgery of CSF rhinorrhea. Many considerations can be made to decrease the risk of unintended damage to olfactory mucosa through regular cleaning and resurfacing of the septal donor site to improve re-mucosalization, and using cold knife incision other than monopolar cauterization in harvesting the flap is preferred. The limited number of investigated patients identified in this article highlights

the need for further research with specific areas of focus which should include clarification of the role of the level of surgical experience on the success rate.

#### Abbreviations

CSF: Cerebrospinal fluid; EES: Endonasal endoscopic surgery; SIT: Smell Identification Test; SNOT-22: 22-item Sino-Nasal Outcome Test; POSE: Perioperative Sinus Endoscopy score; LM: Lund-MacKay; NSF: Nasoseptal flap; BMI: Body mass index; SD: Standard deviation; MT: Middle turbinate; FESS: Functional endoscopic sinus surgery; ICP: Intracranial pressure; ACTZ: Acetazolamide; SS: Sphenoid sinus; CP: Cribriform plate; FE: Fovea ethmoidalis; LL: Lateral lamella; RSOM- 31: 31-question Rhinosinusitis Outcome Measure; EASB: Endoscopic anterior skull base surgery; QOL: Sinonasal quality of life; EETSA: Endoscopic endonasal trans-sphenoidal approach; UPSIT: University of Pennsylvania Smell Identification Test; SOS: Superior olfactory strip.

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#### Authors' contributions

MIB; Concept, Initiate the study design, and outline and writing introduction of the manuscript. DS; collect and analyze the patient data regarding pre and postoperative sinonasal symptoms, the material used in the repair, and the surgical outcome of the repair, and a major contributor in the writing of the manuscript. SH; collect, arrange the references, and editing, revising linguistic errors of the manuscript. AS; reviews the manuscript, arrange the tables, and figures. PC; a major contributor in revising all sections of the manuscript. All authors read and approved the final manuscript.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the institutional review board and ethics committee of (Arab Board of Health Specializations with order no. 453/2018). After informed consent, all patients were clinically and intraoperatively confirmed to have CSF leaks from anterior, middle, and posterior cranial fossa who had failed conservative treatment were included in the study.

##### Consent for publication

Written informed consent for publication was obtained.

##### Competing interests

The authors declare that they have no competing interests.

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