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Olfactory changes after endonasal endoscopic cerebrospinal fluid fistula repair: long-term outcomes

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Abstract

Objective. This study aimed to evaluate odour measurements after endoscopic repair of cerebrospinal fluid fistulas.

Method. Demographic characteristics, cerebrospinal fluid leak location, surgical procedure, aetiology and smell test results were retrospectively reviewed.

Results. A total of 27 patients were included. The mean age was 43.52 years. The aetiology was spontaneous in 13 patients (48.1 per cent) and traumatic in 14 patients (51.9 per cent). The skull base defect was at the cribriform plate in 15 patients (55.6 per cent), the frontal sinus posterior wall in 4 patients (14.8 per cent), the sphenoid sinus posterior wall in 4 patients (14.8 per cent), around the anterior ethmoid artery in 2 patients (7.4 per cent), at the ethmoid roof in 1 patient (3.7 per cent) and at the sphenoid sinus posterolateral wall in 1 patient (3.7 per cent). After the comparison of pre-operative and post-operative values in identification, discrimination and threshold categories, a statistically significant difference was seen only in the threshold category ($p = 0.014$).

Conclusion. The results demonstrated that endoscopic repair of cerebrospinal fluid leak is safe in terms of olfactory functions.

Introduction

Having a normal olfactory function is vital to protect against hazardous and toxic substances, and it also has an effect on gustatory functions.[1,2] Some studies have shown that quality of life is affected when sense of smell is impaired.[3] Any nasal surgery, such as septoplasty or endoscopic sinus surgery, negatively or positively affects olfactory functions.[1,4] In patients with chronic rhinosinusitis and nasal polyps, nasal surgery may help to improve smell sensation when nasal obstruction is fixed and mucosal oedema is removed. Nevertheless, it may cause transient or permanent hyposmia or anosmia when the olfactory neuroepithelium is damaged because of surgical trauma.[5]

Cerebrospinal fluid (CSF) fistula is described as a CSF leakage through a bony skull base defect, causing a connection between the nasal cavity and subarachnoid space. It can be congenital, spontaneous, traumatic (including iatrogenic injury), or caused by inflammatory and tumoral diseases.[5] It may occur in any site of the anterior skull base but is usually detected at the level of the cribriform plate, ethmoid roof, sphenoid sinus and (less commonly) the posterior wall of the frontal sinus.

The incidence of the defect sites and sizes may differ according to the aetiology.[5] Open traditional surgical approaches cause more morbidity and more damage to olfactory fibres. The currently preferred approach, rather than traditional external approaches, is the minimally invasive endonasal endoscopic approach, which is an effective and safe method for management of CSF leaks. Needing revision surgery is more common in spontaneous CSF leaks because they have higher recurrence rates (25–87 per cent) compared with others (less than 10 per cent), which means an increased risk of olfactory damage caused by surgical trauma.[4,5]

Understanding olfactory anatomy is crucial in order to limit the damage after endoscopic surgery.[6] Olfactory neuroepithelium distributes vertically from the cribriform plate, medially onto the area that is 1–2 cm superior to the septum, laterally to the middle and superior turbinate, and expands to the face of the sphenoid posteriorly.[6,7] Because of the close relationship between the olfactory epithelium, olfactory fibres and skull base, endonasal endoscopic repair of CSF leak comes with an increased risk of damage to the olfactory epithelium. Harvesting Hadad-Bassagasteguy flap[8] also presents a risk of damaging the olfactory nerve, depending on the size, level of the superior margin and the instruments used for harvesting it.[1,9] We therefore investigated the olfactory outcomes of patients who had undergone endoscopic endonasal repair for CSF leak. We believe this is the first study that evaluates the olfactory outcomes following endonasal repair of spontaneous or traumatic CSF fistula and the effects of other surgical factors, such as reconstruction materials, cause of the leak and area of the leak on olfactory functions.

Main Article

Dr H Basak takes responsibility for the integrity of the content of the paper

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Materials and methods

Study design

The medical records of patients who had endoscopic endonasal surgery for CSF fistula at a single tertiary referral centre from 2017 to 2019 were reviewed. The demographic characteristics, CSF leak location, surgical procedure details, aetiology and odour measurement results, including identification, discrimination, and threshold, were noted from the medical records of the patients.

Inclusion and exclusion criteria

All patients who experienced endoscopic skull base repair for CSF fistula were included in the study. All surgical procedures were performed by an experienced skull base revision surgeon; patients with other sinonasal co-morbidities (such as nasal polyposis, chronic rhinosinusitis and tumoral diseases) were excluded. In addition, none of the patients included had neurodegenerative diseases such as Alzheimer's or Parkinson's disease, so there was no need for exclusion.

Surgical procedure

All surgical procedures were performed under general anaesthesia. Additionally, 5 per cent sodium fluorescein (0.1 ml per 10 kg body weight, maximum 0.5 ml, intrathecally, lumbar site) were applied immediately after intubation to all patients as a part of our CSF leak closure protocol. Intra-operatively, after single-sided maxillary antrostomy was completed, a Draf 2a procedure and total sphenoethmoidectomy were performed regardless of where the defect was in order to detect concomitant skull base defects as a result of high intracranial pressure or multiple fractures. A Draf 3 procedure was performed for frontal sinus posterior wall defects to provide adequate access and drainage of the sinus. If the location of the skull base defect was in the sphenoid sinus, a large sphenoidotomy with removal of superior turbinate and sinus mucosa was performed. In all cases, middle turbinate resection was performed for the best visualisation and exposition of the skull base defect. In some cases, middle turbinate mucosa was used for reconstruction (Table 1).

Sinonasal mucosa in and around sinuses and the skull base were removed to prevent any mucocele formation after reconstruction. All mucosa around the area of the defect at the cribriform plate were removed as well. Blue light with a yellow filter on the endoscope was used to detect the leak site, and a secure corridor was created for the instrumentation when the surgery was performed. If needed, a pedicled nasoseptal flap was prepared using electrocautery with an upper incision maximum of 1 cm near to olfactory mucosa. An extradural multilayer repair with the combination of synthetic dura graft, fascia lata graft, middle concha mucosa, adipose tissue or pedicled nasoseptal flap was performed according to the size and location of the defect. Fibrin tissue glue (Tisseel, Baxter Healthcare, Deerfield, USA) was applied right after no leak was detected in the last control through a fluorescein filter. The surgery was complete after the nasal package was placed for three days.

Odour measurements

Odour measurements were performed on the day of hospital admission and one year post-operatively, using the 'Extended Sniffin Sticks' test (Olfasense, Kiel, Germany) by performing tests on the side of the skull base defect. This test enables odour assessment in identification, discrimination and threshold categories. In this study, we identified three groups as improved, stable and worsened, depending on whether there was one point difference in pre-operative and post-operative scores.

Results

Statistical analysis

The data were analysed using SPSS® statistical software (version 27.0) with a 95 per cent confidence interval. The descriptive statistics were presented as mean ± standard deviation for the numerical variables and were presented as number of cases (percentage) for the categorical variables. Normality hypotheses were tested with the Kolmogorov–Smirnov and Shapiro–Wilks tests. Double-group comparisons of the normally distributed continuous variables were tested using the Mann–Whitney U test. Comparisons of pre- and post-operative variables were tested using the paired sample t-test. Comparisons of numeric variables and more than two categories were performed using Kruskal–Wallis test. Univariate data analysis was performed using a 2×3 table and compared using Fisher's exact test. A result of $p < 0.05$ was considered to be statistically significant.

A total of 27 patients comprising 20 females (74.1 per cent) and 7 males (25.9 per cent) were included in the study. The mean age was 43.52 years (minimum: 20; maximum: 75; standard deviation: 13.62 years). The aetiology for CSF rhinorrhoea was spontaneous in 13 patients (48.1 per cent) and traumatic in 14 patients (51.9 per cent). The skull base defect was at the cribriform plate in 15 patients (55.6 per cent), the frontal sinus posterior wall in 4 patients (14.8 per cent), the sphenoid sinus posterior wall in 4 patients (14.8 per cent), around the anterior ethmoid artery in 2 patients (7.4 per cent), the ethmoid roof in 1 patient (3.7 per cent) and the sphenoid sinus posterolateral wall in 1 patient (3.7 per cent). A pedicled nasoseptal flap was performed for closure of defects in 19 patients (70.4 per cent; Table 1). No septal perforation was observed during follow ups. The success rate of CSF leak closure was 100 per cent. All patients had symptoms such as nasal obstruction, crusting, swelling of the face and reduced smell at the surgical site. The descriptive statistics and the differences of pre-operative and post-operative first-year test values are summarised in Table 2. Figure 1 displays case-by-case numerical differences in odour identification, discrimination and threshold categories of the patients.

After comparing pre-operative and post-operative values in identification, discrimination and threshold categories, we detected a statistical difference only in the threshold category ($p = 0.014$). A weak difference was also observed in the identification category, even if it was not statistically significant ($p = 0.064$, Table 2). Self-assessment of olfaction scores was lower than objective test scores in most patients, and there was improvement in symptoms in subjective assessment of olfaction when comparing pre-operative and post-operative results.

Aetiology of CSF leak and smell results did not show a significant correlation, but there was a slight difference ($p = 0.049$) showing lower but not significant test scores in patients with traumatic aetiologies. There was no difference between closure method and test results; however, although not

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Table 1. Demographic and clinicopathological features of the patients

Patient number	Age (years)	Gender	Aetiology	Location of defect	Reconstruction method	Draf procedure
1	36	Female	Traumatic	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
2	36	Female	Spontaneous	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
3	52	Female	Traumatic	Cribriform plate	Dura graft + nasoseptal flap + middle turbinate mucosa	Draf 2a
4	60	Female	Spontaneous	Cribriform plate	Dura graft + nasoseptal flap + middle turbinate mucosa	Draf 2a
5	29	Female	Spontaneous	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
6	45	Female	Traumatic	Cribriform plate	Dura graft + middle turbinate mucosa	Draf 2a
7	40	Female	Spontaneous	Cribriform plate	Fat + dura graft + nasoseptal flap	Draf 2a
8	47	Female	Spontaneous	Cribriform plate	Fat + fascia lata + nasoseptal flap	Draf 2a
9	53	Female	Spontaneous	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
10	57	Female	Traumatic	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
11	25	Female	Spontaneous	Cribriform plate	Dura graft + nasoseptal flap	Draf 2a
12	38	Female	Spontaneous	Cribriform plate	Fat + dura graft + nasoseptal flap	Draf 2a
13	44	Female	Traumatic	Cribriform plate	Fat + dura graft + nasoseptal flap	Draf 2a
14	51	Female	Spontaneous	Cribriform plate	Fat + fascia lata + nasoseptal flap	Draf 2a
15	28	Male	Traumatic	Cribriform plate	Middle turbinate mucosa	Draf 2a
16	62	Male	Spontaneous	Frontal sinus posterior wall	Fat + dura graft	Draf 3
17	20	Male	Traumatic	Frontal sinus posterior wall	Fat + fascia lata + nasoseptal flap	Draf 3
18	37	Male	Traumatic	Frontal sinus posterior wall	Fat + fascia lata	Draf 3
19	46	Female	Traumatic	Frontal sinus posterior wall	Fat + fascia lata	Draf 3
20	66	Female	Traumatic	Sphenoid sinus posterior wall	Fascia lata + nasoseptal flap	Draf 2a
21	75	Female	Traumatic	Sphenoid sinus posterior wall	Fat + fascia lata	Draf 2a
22	47	Female	Spontaneous	Sphenoid sinus posterior wall	Fat + fascia lata	Draf 2a
23	45	Male	Spontaneous	Sphenoid sinus posterior wall	Fat + fascia lata + nasoseptal flap	Draf 2a
24	22	Male	Traumatic	Around anterior ethmoid artery	Fat + fascia lata + nasoseptal flap	Draf 2a
25	33	Female	Spontaneous	Around anterior ethmoid artery	Middle turbinate mucosa	Draf 2a
26	32	Male	Traumatic	Ethmoid roof	Fat + fascia lata + nasoseptal flap	Draf 2a
27	49	Female	Traumatic	Sphenoid sinus posterolateral wall	Dura graft + nasoseptal flap	Draf 2a

statistically significant, the cases that used nasoseptal flap had worse scores in odour discrimination and threshold (Tables 3, 4 and 5).

The smelling status of the patients was allocated as improved, stable or worsened in each smell test category, and the distribution of differences in all such categories were statistically significant ($p < 0.001$). Tables 3, 4 and 5 summarise the relationship between age, gender, aetiology, use of pedicled flap and smelling status in odour identification, discrimination and threshold, respectively. In all these categories, a weak difference was found between spontaneous and traumatic cases regarding odour discrimination ($p = 0.049$).

Discussion

In this study, we investigated the self-assessment and odour measurements of patients who underwent endoscopic endonasal repair of CSF leak. Patients complained of a worse sense of smell in the early post-operative period. We also recommended nasal cleaning to the patients in the first month after the surgery. However, we believe an assessment in this period was not optimal because of crusting, oedema and obstruction. We detected an increase in odour thresholds of the patients in the first year, when compared with pre-operative status, after CSF leak closure (mean: 5.05 *vs* 6.58; $p = 0.014$). We also determined that the spontaneous cases got worse in odour discrimination than the traumatic cases (7 of 13 *vs* 2 of 14 patients respectively, $p = 0.049$). This result may be caused by the fact that the defect was at the cribriform plate in most of our cases with spontaneous CSF fistula. This is where the olfactory fibres are located, and during the surgery, the cauterisation of fibre and damaging of the mucosa for reconstructive purposes may play a role. Thus, even the head trauma itself can be one of the reasons for the smell loss. Moreover, olfactory neural regeneration occurring over time may cause better outcomes in such cases, even if olfactory training was performed.[10] Nevertheless, this study's results indicated that endoscopic endonasal repair of CSF leak is safe in regard to the preservation of olfaction, although the pre-operative scores differ slightly.

Olfaction is at the centre of our daily lives and plays a critical role in detecting hazards, taste function, sexuality and

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Table 2. Statistical results of smelling test variables

Variable	Mean score	Minimum score	Maximum score	Standard deviation	*P*-value
Pre-operative identification	6.33	0	12	3.50	0.064
Post-operative identification	7.07	2	11	2.67	
Difference in identification	−0.74	−4	4	1.99	
Pre-operative discrimination	6.15	3	11	1.81	0.505
Post-operative discrimination	5.89	2	11	2.40	
Difference in discrimination	0.25	−3	4	1.99	
Pre-operative threshold	5.05	0	15.25	3.97	0.014*
Post-operative threshold	6.58	1	15.25	3.83	
Difference in threshold	−1.52	−12	1	3.01	

*Statistically significant value

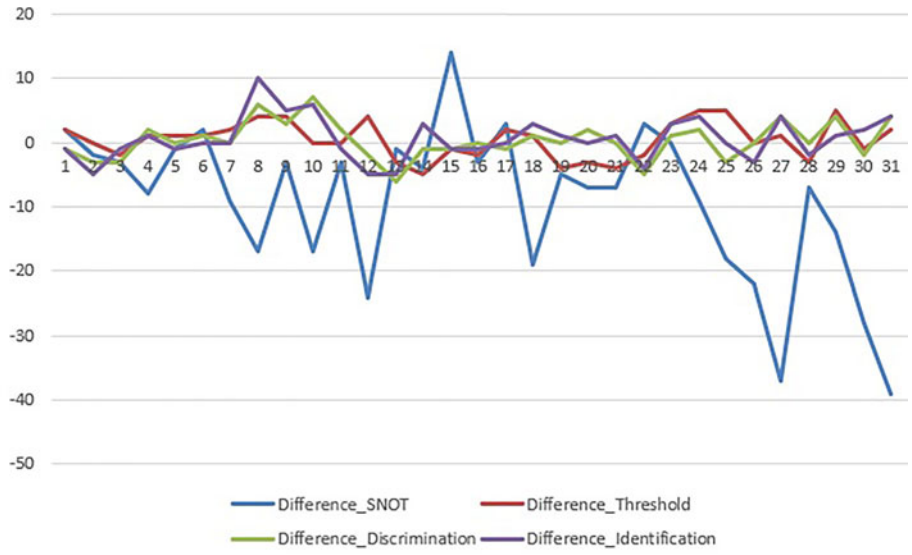

Fig. 1. Case by case basis numerical differences in odour identification, discrimination and threshold categories of the patients. The skull base defect was at the cribriform plate in patients numbered 1–15, at the frontal sinus posterior wall in patients numbered 16–19, at the sphenoid sinus posterior wall in patients numbered 20–23, around the anterior ethmoid artery in patients numbered 24 and 25, at the ethmoid roof in patient numbered 26 and at the sphenoid sinus posterolateral wall in patient number 27.

emotions.[11] In addition to preventing fatal complications from CSF leaks, preserving olfaction may be one of the goals of endoscopic CSF leak repair and any skull base surgery.[9] We believe this is the first study that evaluates olfactory outcomes of patients with CSF fistula and the effects of other surgical factors such as reconstruction materials, cause of the leak and area of the leak on olfactory functions.

Nasal surgery is a balance in regard to olfactory function as it can include both improvement and worsening of function. Improvement is possible when a nasal obstruction is fixed[12] or inflammatory pathologies, such as chronic rhinosinusitis and nasal polyposis, are removed.[13] However, smell loss may occur when olfactory fibres are damaged or vascular supply is disrupted.[6,14] Endoscopic skull base reconstruction is a complex surgery that comprises sinus surgery, turbinate resection, flap harvesting and other procedures. Its close proximity to olfactory structures means more damage risk during surgery.

Some studies have investigated the olfactory outcomes of endonasal surgery.[9,15] Most have focused on sellar or parasellar lesions comparing microscopic and endoscopic approaches or flap harvesting techniques.[9,15] Zhu *et al.*[9] found that a decrease in the incidence of olfaction was 36.88 per cent (52 of 141 patients) in the microscopic approach and 18.48 per cent (39 of 211 patients) in the endoscopic approach in their meta-analysis ($p < 0.01$). They also concluded that rescue flaps may be preferred to pedicled nasoseptal flaps and that harvesting flap was unfavourable for olfaction. In our study, although it is not statistically significant, worsening in olfactory function was more common in the pedicled nasoseptal flap harvesting group (Tables 3, 4 and 5). Kim *et al.*[1] suggested that using a cold knife for making a superior border incision may reduce olfactory damage during harvesting of nasoseptal flaps. In contrast, Puccinelli *et al.*[6] stated that the cold knife and electrocautery group had similar pre-operative and post-operative 3rd and 12th month scores using the University of Pennsylvania Smell Identification Test (32.8 *vs* 32.4, $p = 0.80$; 33.1 *vs* 33, $p = 0.96$, and 33.6 *vs* 33.3, $p = 0.84$, respectively). In this study, we used electrocautery in all cases, and the comparison with and without flap harvesting showed no statistical difference. However, we detected a decrease in odour discrimination and threshold in cases that used a nasoseptal flap (Tables 3, 4 and 5).

The turbinates play a key role in nasal resistance and arranging airflow in the nasal cavity.[7] Therefore, most surgeons prefer to resect the middle turbinate to have better exposure. However, the effect of middle turbinate resection on olfaction

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Table 3. Relationship between identification scores and age, gender, aetiology and use of pedicled nasoseptal flap

Variable	Odour identification			
	Improved (*n* (%))	Stable (*n* (%))	Worsened (*n* (%))	*P*-value
Age				
– ≤40	9 (50)	0 (0)	3 (42.9)	0.578
– >40	9 (50)	2 (100)	4 (57.1)	
Gender				
– Female	12 (66.7)	2 (100)	6 (85.7)	0.797
– Male	6 (33.3)	0 (0)	1 (14.3)	
Aetiology				
– Spontaneous	9 (50)	1 (50)	3 (42.9)	1.000
– Traumatic	9 (50)	1 (50)	4 (57.1)	
Use of pedicled flap				
– No	5 (27.8)	0 (0)	3 (42.9)	0.662
– Yes	13 (72.2)	2 (100)	4 (57.1)	

Table 4. Relationship between discrimination scores and age, gender, aetiology and use of pedicled nasoseptal flap

Variable	Odour discrimination			
	Improved (*n* (%))	Stable (*n* (%))	Worsened (*n* (%))	*P*-value
Age				
– ≤40	3 (30)	4 (50)	5 (55.6)	0.621
– >40	7 (70)	4 (50)	4 (44.4)	
Gender				
– Female	7 (70)	5 (62.5)	8 (88.9)	0.552
– Male	3 (30)	3 (32.5)	1 (11.1)	
Aetiology				
– Spontaneous	2 (20)	4 (50)	7 (77.8)	0.049*
– Traumatic	8 (80)	4 (50)	2 (22.2)	
Use of pedicled flap				
– No	5 (50)	2 (25)	1 (11.1)	0.186
– Yes	5 (50)	6 (75)	8 (88.9)	

*Statistically significant value

Table 5. Relationship between threshold scores and age, gender, aetiology and use of pedicled nasoseptal flap

Variable	Odour threshold			
	Improved (*n* (%))	Stable (*n* (%))	Worsened (*n* (%))	*P*-value
Age				
– ≤40 – >40	5 (33.3) 10 (66.7)	5 (55.6) 4 (44.1)	2 (66.7) 1 (33.3)	0.456
Gender				
– Female	12 (80)	7 (77.8)	1 (33.3)	0.298
– Male	3 (20)	2 (22.2)	2 (66.7)	
Aetiology				
– Spontaneous	8 (53.3)	3 (33.3)	2 (66.7)	0.542
– Traumatic	7 (46.7)	6 (66.7)	1 (33.3)	
Use of pedicled flap				
– No	4 (26.7)	4 (44.4)	0 (0)	0.504
– Yes	11 (73.3)	5 (55.6)	3 (100)	

is controversial. Nyquist *et al.*[16] suggested that the middle turbinate may be preserved to have a better sinonasal function in sellar or parasellar skull base surgery. Conversely, some studies[1,17] have argued that there is no effect of the middle turbinate resection on olfactory functions. Similarly, we had to resect the middle turbinate in all of the cases in the current study, and we concluded that resecting the middle turbinate is safe and has no effect on olfactory functions if performed properly.

We believe that this is the first study on the topic of odour measurements after endoscopic repair of CSF fistula, although it has some limitations. The current study is retrospective with a small number of patients. This is a small study population because CSF leak without any other sinonasal co-morbidities is not a common situation. Moreover, complete olfactory testing takes a long time, and patient cooperation is crucial. We described worsening or improving odour perception as a point difference between pre-and post-operative values, but another chosen level may affect the results. Further studies on the topic will be useful because endoscopic repair of CSF fistula is rare. Another weakness of this study is with regard to the use of fibrin tissue glue because we used it regularly in all of our CSF leak closure cases, and it was impossible for us to make a comparison between using tissue glue and not using it.

- Sense of smell is closely related to quality of life of patients
- Every nasal surgery has a damage risk for olfactory functions
- The relationship between endoscopic repair of cerebrospinal fluid (CSF) leak and olfaction has not been investigated yet
- This study detected an increase in odour thresholds of the patients in the first year after CSF leak closure compared with pre-operative status
- There is a weak correlation between the aetiology and test results; spontaneous cases got worse in odour discrimination than traumatic cases
- The results of this study suggest that endoscopic endonasal repair of CSF leaks are safe regarding the preservation of olfaction

Conclusion

Our results suggest that complaints as a result of olfactory changes after anterior skull base CSF repair decrease during the first year after surgery. There was a weak correlation between the aetiology and test results, and in that aspect we believe that surgical trauma has more effect than the cause of CSF leak on olfactory functions, and any closure methods will have similar results in long-term follow up. Multivariate analysis, including aetiology, location, use of flap and flap harvesting technique with larger populations is needed to confirm our results.

Competing interests. None declared

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