

## Original Research Article

# The efficacy of an endoscopic endonasal approach in the repair of cerebrospinal fluid fistula: a clinical analysis

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## ABSTRACT

**Background:** Cerebrospinal fluid (CSF) fistula is an abnormal CSF leakage due to bone and/or dural defect of the skull base and usually operated with endonasal endoscopic approach. The aim of this study was to determine the efficacy of an endonasal endoscopic approach in the repair of CSF leakage and to find the reasons of the recurrence of endoscopic procedure.

**Methods:** The medical records of 24 patients that presented with the diagnosis of cerebrospinal fluid fistula and who had undergone endonasal endoscopic repair surgery were reviewed retrospectively.

**Results:** 13 patients (54.2%) were found to have spontaneous CSF fistulas without any history of trauma, while 11 patients (45.8%) had posttraumatic CSF fistulas. The mean body mass index (BMI) of patients was 31.3 kg/m<sup>2</sup> (20.1-49.6). Nasal septal cartilage was used as a graft material in 19 patients (79%) while only fascia was used in 5 patients (21%). The evaluation of long-term results revealed recurrence in 4 patients (16.6%). Two of these patients required a second surgical repair.

**Conclusions:** An endoscopic endonasal approach is a safe method with less morbidity and a reliable outcome in the repair of CSF fistulas. The most important causative factors in the recurrence of endoscopic repair of CSF leak might be to have high BMI and not to use multilayered graft material for closure of fistula.

**Keywords:** Cerebrospinal fluid fistula, Rhinorrhea, Endoscopic endonasal surgery

## INTRODUCTION

Cerebrospinal fluid (CSF) fistula is an abnormal CSF leakage due to bone and/or dural defect that results in communication between the subarachnoid space and surrounding spaces like as paranasal sinuses and nasal cavity.<sup>1</sup> CSF fistulas are most commonly seen in the area between the anterior skull base and nasal cavity. Because, thin lamella of the bones and the dura that is very adherent to the bone in this region can be easily defected with any reason.<sup>2</sup>

A variety of situations could lead to the bone or/and dural defect and are classified as traumatic and non-traumatic

causes according to Har-El classification.<sup>3</sup> Non-traumatic fistulas include congenital, neoplastic, spontaneous or idiopathic. In older publications, accident-related trauma was the most common cause, however nowadays idiopathic-spontaneous causes are the most common cause of CSF fistulas.<sup>4</sup> Obesity has been shown as the most common cause of spontaneous CSF fistulas with percentage of 80%. The intracranial hypertension and elevated intracranial pressure are associated with spontaneous CSF with percentage of 40%.<sup>5</sup> The intracranial hypertension usually occurs in parallel with obesity and chronically elevated intracranial pressure may cause erosion and thinning in the lamellar bone of skull.<sup>6</sup>

Iatrogenic causes also have become more prominent in traumatic cases of CSF fistula development rather than accidents.<sup>4</sup> Within the last decade, the development of surgical techniques and improvement of optical devices<sup>7</sup> have provided the attention to skull base surgery. Usage of endoscope is increased among otolaryngologists and neurosurgeons and this typically may cause iatrogenic CSF fistulas.<sup>7</sup>

If not treated, CSF fistulas can lead to serious complications such as recurrent meningitis or unnecessary long-term medication use for rhinitis treatment.<sup>4</sup> Communication with the intracranial spaces may lead to meningitis or other intracranial complications that may be the first symptom of a CSF leakage.<sup>5</sup> Therefore, the treatment of CSF fistula is crucial.

In 1948 Dohlman used an extracranial approach for repair of CSF fistula for the first time. Then, in 1952 Hirsch introduced an intranasal sphenoid sinus approach. Later, in 1964, Varabec and Hallberg used an intranasal approach to the cribriform plate; however, the current method for endoscopic endonasal repair of CSF fistulas was first introduced in 1981 by Wigand.<sup>8</sup> The endonasal endoscopic method is a short procedure, which is much cheaper than other extracranial and intracranial surgeries and leads to less morbidity with a high success rate of repair.<sup>5,9</sup>

The purpose of this retrospective study is to determine the effectiveness of the endoscopic endonasal procedure in the treatment of CSF fistula and to find the reasons of the recurrence of endoscopic procedure. We evaluated 24 patients who underwent the endoscopic surgery and statistically compared the features of patients and operations for the determination of having recurrence.

## **METHODS**

This study was approved by Baskent university institutional review board and ethics committee (project no: K16/287).

In this study, the records of 24 patients of Baskent University Adana Training and Educational Hospital that were diagnosed with CSF fistula from December 2003-December 2016 and underwent endonasal endoscopic repair surgery were evaluated retrospectively. The patients' hospital records included patients' age, gender, symptoms, BMI, CT and/or MRI findings in the preoperative period, surgical method, graft material used in the surgery, fistula location and size, and postoperative medications.

### **Exclusion criteria**

The patients <16 years old, the patients with CSF and meningitis, the patients with CSF and the requirement of intensive care unit were all excluded from the study.

Besides these, all patients with CSF and treated in our clinic were included.

### **Preoperative evaluation**

Preoperative endoscopic evaluation was performed and detailed history was obtained for all patients admitted to the clinic because of rhinorrhea. The manifestation of clear fluid from the skull base with Valsalva maneuver during endoscopic examination was enough to accept the diagnosis of a defect. However, in patients that did not have this manifestation, the liquid coming from the nose was evaluated for  $\beta$ -2 transferrin.

All patients underwent high-resolution computed tomography (CT) and/or CT cisternography examination. In CT cisternography, the patient remained in knee-elbow position under fluoroscopy when entering into the subarachnoid space at L3-4. Then the patients were administered 10 ml of non-ionic contrast material (Omnipaque™, Opakim, Turkey) into the subarachnoid space and 1 mm CT sections were taken from the nasion until the dorsal sella was reached in the coronal plane. In CT cisternography, the direct visualization of the defect was done by a contrast agent passing through the defect, while indirect visualization was done by congestion of a contrast agent in the neighboring sinuses and both were considered positive for CSF fistula.

### **Surgical procedure**

Repair of CSF fistula was done with an endonasal endoscopic procedure under general anesthesia. Perioperative intravenous ceftriaxone was given as prophylaxis. A lumbar drain was placed after the application of general anesthesia. The intranasal mucosa was decongested prior the surgery. The areas from where the CSF could have leaked in the nasal mucosa were evaluated. Defects, particularly ones in the foveal ethmoidalis were visualized by anterior-posterior ethmoidectomy and positioning the middle turbinate laterally. The exploration of sphenoid sinus for defects was made after ethmoidectomy.

After the location of the bone and dural defect were determined, the area near these defects was cleaned of mucous debris and granulation tissue. Then, an approximately 2-3 mm space was created from the defect between the dura and bone for the graft, which would cover the defect from all sides. The graft was placed into the bone defect as inlay graft. In this situation, if surgeon decided that unilayer graft was insufficient than another graft material was placed on the bone defect as onlay graft. After the graft was placed, its surface was closed by using fibrin tissue adhesive glue and medializing the middle turbinate. Merosel buffer (cenefom, nasal packing; Longtek Scientific Co., LTD. the Netherlands) was placed into the passage between 3-5 days to keep the medialized turbinate in place.

### Postoperative care

After the surgery, prophylactic antibiotic was administered for about 5 days during the postoperative period. Lumbar drainage was set to be discharging 10-20 cc per hour and was taken out as soon as possible after a 5-day period. The information about postoperative follow-up by endoscopy, the success of the procedure and whether the revision surgery was performed were obtained from the patients' records.

The patients were statistically compared regarding BMI, insertion of LP set, etiology of fistula, and kind of graft material and technique of placement of graft. In this way, the causes of the recurrence and the effectiveness of endoscopic endonasal surgery could be evaluated objectively.

### Statistical analysis

All analyses were performed using statistical package for the social science (SPSS) 17.0. The chi-squared test was used with Fisher's exact test for statistical comparison between two groups. Significance level was set at  $p < 0.05$ .

## RESULTS

24 patients underwent endonasal endoscopic surgery due to CSF fistula. The successful result obtained in 20 patients; the evaluation of long-term results revealed recurrence in 4 patients (16.6%). Two of these patients required a second surgical repair.

The mean age was 43 years (17-66 years), 15 patients were females. Although all recurrent patients were female, there was no effect of being females on recurrence statistically ( $p > 0.05$ ). BMI of patients were recorded from their hospital charts and the mean BMI of all of patients was  $31 \pm 1.3$  (20-49)  $\text{kg/m}^2$ . When we compared recurrent and non-recurrent patients regarding BMI; in recurrence group, average BMI was  $35.0 \pm 6.2$   $\text{kg/m}^2$  and were clinically obese. However, these results have no importance statistically.

When patients were classified based on the etiology: 11 patients (45.8%) were found to have posttraumatic CSF fistulas, while 13 patients (54.2%) had spontaneous CSF fistulas without any history of trauma. Among 11 patients with posttraumatic CSF fistulas 6 patients (25%) had trauma-related CSF fistulas, while 5 patients (20.8%) had surgical trauma-related fistulas. Among recurrent patients, 2 patients had spontaneous reasons and one patient had trauma and one had iatrogenic fistula. There is no relationship statistically between recurrent and non-recurrent patients regarding etiology ( $p > 0.05$ ).

When we evaluated the patients, three patients had a history of meningitis prior to the diagnosis of CSF rhinorrhea and 5 patients had meningocele with CSF fistula. The effect of the present of meningocele on

recurrence was evaluated. Two of recurrent patients had meningocele and this was found statistically insignificant.

Patients were mostly diagnosed by evaluating the medical history followed by endoscopic and imaging examinations. In 16 patients (66.7%), right side and in 8 patients (33.3%) left side CSF leakage was present. These situation was not important statistically for occurrence of recurrence ( $p > 0.05$ ). Due to inability to observe the defects during the endoscopic imaging in 4 out of 13 patients with spontaneous CSF fistula,  $\beta 2$ -transferrin values were evaluated prior to the procedure and were found to be positive.

In two patients, the CSF fistulas that occurred during endoscopic sinus surgery were immediately noticed and repaired. In addition, CSF fistulas were detected on post-operative day 3 in two patients and were immediately repaired. The remaining 19 patients underwent CT cisternography and the presence of CSF fistulas was easily detected in these patients. In 9 patients (47.3%) the defect was shown directly by visualizing the passage of the contrast material through the bone defect (Figure 1), while in the remaining 10 patients (52.6%) the defect was shown indirectly via visualization of congestion of contrast material in the adjacent sinuses (Figure 2).



**Figure 1: The passage of the contrast material directly through the bone defect in a patient with spontaneous rhinorea.**



**Figure 2: Congestion of contrast material in the frontal sinus and fracture on upper side of frontal sinus in BT cisternography.**

Only in one patient (with spontaneous fistula) two fistulas were detected in the ethmoidalis fovea and cribriform plate. All other patients (23 patients, 95.2%) were determined to have fistula in one anatomical location. Among these patients; 5 patients had fistula in the superior wall of the sphenoid sinus (20.8%), 2 in the frontal sinus roof (8.3%), 8 in cribriform laminae (33.3%) and 9 in the fovea ethmoidalis (37.5%).

After determining the location of the fistula, the defect's diameter was observed and 9 patients (37.5%) were determined to have a major defect with  $\geq 10$  mm. The diameter of the defect was  $< 10$  mm in the remaining 15 patients (62.5%). In recurrent patients median diameter of fistula was 3.5 mm and we observed that there was no effect of the diameter of fistula defect on the recurrence growth ( $p > 0.05$ ).

In 19 patients (79%) the nasal septal cartilage was used as a graft material to close the fistula. Eight of them had only septal cartilage and other 11 had septal cartilage together with fascia (fascia lata in 8 patients and temporal fascia in 3 patients). In the remaining 5 patients (21%), only fascia or other smooth materials rather than cartilage were used. The effect of the usage of the septum cartilage on the prevention of recurrence was evaluated. The septal cartilage was used in two of recurrent patient and had no statistically significance. In operation, endoscopic closure of the defect with multilayer material were applied in 11 patients (45.8%) and closure with unilayer material was used in 13 patients (54.2 %). We observed that unilayer material for closure of the defect was used in 3 out of 4 recurrent patients (75%). However, this was not found as statistically significant.

After placing the graft, fibrin glue was used in all patients, a lumbar drainage kit was placed in 20 patients (83.3%) and drainage was provided for 5 postoperative days. Acetazolamide (Diazomide®, Sanofi Aventis, Turkey) was used 22 patients in postoperative period. The effect of these treatments for reduction of intracranial hypertension on the prevention of recurrence was also evaluated. All recurrent patients have given acetazolamide and 3 of them had LP drain. There was no effect of usage of acetazolamide or lumbar drain on the prevention of recurrence statistically ( $p > 0.05$ ).

The effect of etiological factor on the choice of graft and the placement of lumbar drain was also evaluated. In the group of patients with spontaneous CSF leak (13 patients), 7 patients operated with multilayered graft material and 12 patients followed by lumbar drain in postoperative period. Unfortunately, the significance of this information was not important regarding recurrence.

The evaluation of surgical results showed promising outcome in short term in all patients. The mean follow-up period for patients was  $48 \pm 7.8$  months (12-127 months). The patients were followed by nasal endoscopy.

The patients' features and surgical outcomes are summarized in Table 1.

**Table 1: Characteristics of the patients operated with endonasal endoscopic approach for CSF leaks.**

| Variables                               | Recurrent patients (n=4) | Non-recurrent patients (n=20) | P value |
|---|--------------------------|-------------------------------|---------|
| <b>Gender (F/M)</b>                     | 4/0                      | 11/9                          | NS      |
| <b>BMI (kg/m<sup>2</sup>) (mean±SD)</b> | 35±6.2                   | 30±1.1                        | NS      |
| <b>Etiology</b>                         |                          |                               |         |
| Trauma                                  | 1                        | 5                             | NS      |
| Spontaneous                             | 2                        | 11                            |         |
| Surgical                                | 1                        | 4                             |         |
| <b>Diameter, median</b>                 | 3.5 mm                   | 5 mm                          | NS      |
| <b>Fistula side (R/L)</b>               | 3/1                      | 13/7                          | NS      |
| <b>Symptom beginning time (days)</b>    |                          |                               |         |
| >7                                      | 4                        | 5                             | NS      |
| ≤7                                      | -                        | 15                            |         |
| <b>Graft</b>                            |                          |                               |         |
| Septum+                                 | 2                        | 17                            | NS      |
| Septum-                                 | 2                        | 3                             |         |
| Multilayered technique                  | 1                        | 10                            | NS      |
| <b>Meningocele</b>                      |                          |                               |         |
| +                                       | 2                        | 3                             | NS      |
| -                                       | 2                        | 17                            |         |
| <b>Acetazolamide</b>                    |                          |                               |         |
| +                                       | 4                        | 2                             | NS      |
| -                                       |                          | 18                            |         |

BMI: body mass index, F: female, M: male, R: right, L: left, LP: lumbar puncture, NS: non-significant.

**DISCUSSION**

Conservative medical treatment of CSF leaks includes absolute bed rest, antibiotics, putting a lumbar CSF drainage and administration of CSF production reducing drugs such as acetazolamide.<sup>10</sup> This treatment can lead to the development of spontaneous fibrosis, which in turn can help to achieve recovery in some cases.<sup>10</sup> However, the fibrosis-induced improvement before complete closure of the fistula defect still have risk of infection through the fistula region.<sup>5,11</sup> Conservative medical treatment also causes high hospital cost and more length of stay in the hospital.<sup>11</sup>

In endonasal endoscopic CSF fistula repairs, the two most important factors are the choice of graft material and the creation of suitable space to position the graft in the defect. The different surgical techniques can be applied in this procedure.<sup>9-12</sup> One of the most efficient techniques was placing the graft in an underlying position in the area where the dura was lifted for approximately

0.5 mm near the fistula in the section of the bone defect. This was called underlay or inlay technique in that graft was facing the dura to ensure good adhesion.<sup>11,12</sup> In the other technique, the fistula's surroundings that was facing the nasal area and near the section of the bone defect, was cleaned from granulated tissue and a free graft or pedicle flap was placed directly in position on the defect.<sup>9,10</sup> This was called onlay or outlay technique.<sup>10</sup> The combined use of both methods is also a preferred method of treatment called as multilayered closure of CSF fistula.<sup>13</sup>

Various different grafts have been reported in CSF fistula repair.<sup>9-12</sup> Many graft material options such as temporalis fascia, fascia lata, muscle, mucoperichondrium, cartilage, bone and synthetic dural materials can be used with many different techniques. Fascia lata have been used in this study with 9 patients and as a multilayered closure with septal cartilage in eight patients. The reasons of selection of the fascia lata were to be free graft, easy to obtain, thick and be shaped easily.<sup>11</sup> In our study, septal cartilage was used in 19 patients and 11 of them had multilayered closure technique (septum and another fascia). The reasons of the common use of septal cartilage is that it is inside the surgical area and therefore easy to obtain. Actually, our study was suggested that the important step in the prevention of recurrence was usage of multilayered closure rather than choose of graft material. In our study, 3 out of 4 patients with recurrence had operated with unilayer graft and two of them operated again. This suggestion was supported by Gore et al and Eryilmaz et al.<sup>13,14</sup> They reached a 100% success rate in multilayered endoscopic closure of CSF fistulas with minimal morbidity even in large defects and high-flow leaks.

The application of fibrin glue on the CSF fistula after the bone defect was closed with graft material is a frequently preferred.<sup>10-12</sup> The fibrin glue was used also in our cases. There are some studies in the literature that reported using fat tissue instead of fibrin glue suggesting that it provides the same stability.<sup>2</sup> Here, the important point is to provide optimum adhesion of the graft to the dura and this adhesion takes place after approximately 1 week, according to some studies.<sup>15</sup> Although fibrin glue was used in all patients in this study, the necessity of this procedure is debated and needs prospective studies.

In the literature, it was reported that after a CSF fistula repair, lumbar puncture (LP) drainage was preferred in 67% of the cases.<sup>4</sup> The LP drainage is usually preferred in cases with large bone defects, concomitant encephalocele and high intracranial pressure; however the benefit of LP drainage has not been definitively shown.<sup>4,5,11</sup> One randomized study of CSF fistula repairs has showed that usage of LP drainage does not significantly decrease the recurrence postoperatively.<sup>16</sup> The danger of moving the underlying graft due to a vacuum effect may be also possible.<sup>5</sup> In our study, the LP drainage was placed in 20 out of 24 patients (83.3%) during the surgery. The reason for this high percentage of usage might be the fact that our study mostly consisted of trauma patients and also

due to the cooperation of with brain surgeons during the evaluation of the patients in our hospital. Although the effectiveness was not shown thus far, intermittent LP drainage with/without acetazolamide reduce pressure and prevent graft from the high pressure especially in the patients of CSF fistulas with concomitant intracranial hypertension.<sup>17</sup> Actually LP drain allows us as a surgeon feeling more confident with the operation. However, in our study we did not see significant relationship between LP drain and prevention of the recurrence.

In this retrospective study, the reasons of recurrence of endonasal endoscopic repair of CSF fistula were analyzed. Many reasons of the recurrence in the literature such as the gender, the position and diameter of fistula, reason of fistula, the kind of graft materials, the usage of T-cell, acetazolamide and lumbar drainage kit and BMI of the patients were analyzed. We did not find any statistically difference between recurrent and non-recurrent patients regarding all about these reasons. However, we only realized that in the recurrent group (n=4) and in the patient with second surgery (n=2), the multilayered closure technique did not be preferred and most patients in the recurrent groups have near the obesity border (average BMI: 35.0±6.2 kg/m<sup>2</sup>).

In this study, we also aimed to determine the efficacy of the endonasal procedure. The endoscopic endonasal method may have rare complications such as meningitis, hematoma and anosmia.<sup>11,17</sup> Multi-analysis studies have shown a fairly high success rate.<sup>4,5</sup> The most common causes of failure of the endoscopic method are inability to identify the location of the defect, presence of a second defect, graft shift, insufficient closure of the graft defect, in compliance of the patients in the postoperative period and poor wound healing.<sup>2,10</sup> We did not see any complication in our patients except recurrence. In our study, this method was successful in 20 out of 24 patients (83.3%), while recurrence was observed in 4 patients (16.7%). Two of those 4 patients responded to the conservative treatment and therefore two patients required a second surgery. This second surgery was also performed endonasally by using an endoscope with a successful outcome without the need for the intracranial method. The literature showed that in most of the patients that required a second surgery, the procedure was performed by using an endonasal endoscopic method.<sup>2,11</sup> The combined (endonasal+intracranial) method was used in very few recurrent cases, while the use of an intracranial method alone was rarely preferred even in cases of recurrence.<sup>10</sup>

## CONCLUSION

In conclusion, with the widespread of endoscopic sinus surgery, the endoscopic endonasal approach is a safe method with less morbidity and a reliable outcome in the repair of CSF fistulas. The most important factors in the recurrence of endoscopic repair of CSF leak might be to have high BMI and not to use multilayered graft material

for closure of fistula. These results must be confirmed with huge series of patients with multicenter studies.

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