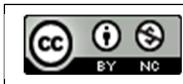


Original article

Comparative retrospective study of post operative CSF leak in endoscopic endonasal transsphenoidal pituitary surgery with and without fibrin glue

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ABSTRACT

Aim: Comparative Retrospective study of post operative in Endoscopic endonasal transsphenoidal pituitary surgery without and with fibrin glue.

Materials and Methods: A retrospective study was done at the Department of Neurosurgery of MGH with the approval of the institutional ethics committee. The study comprised all patients who was planned for surgical removal of pituitary adenoma using Endoscopic endonasal transsphenoidal approach. We gathered data about the demographic and clinical features of patients, the percentage of cerebrospinal fluid leakage post surgery, and the specific surgical method used for repairing the leakage.

Results: The average age at the time of surgery was 51.23±6.32 years. Postoperative cerebrospinal fluid (CSF) leakage was reported in 52 individuals, representing 12.25% of all cases. Micro and macro adenoma was reported in 6.55% and 93.45% of the subjects respectively. High and low flow leakage was reported in 13.95% and 86.05% of the subjects respectively. Mortality was found in 1.14% of the subjects.

Conclusion: Fibrin glue repair treatments are commonly used and effective methods for treating cerebrospinal fluid (CSF) leakage via the nose during endoscopic endonasal transsphenoidal operations. Every patient's treatment plan should be customized to suit their individual requirements.

Keywords: CSF, Endoscopic endonasal transsphenoidal, fibrin glue

Introduction:

The endoscopic endonasal transsphenoidal approach was first used in the latter part of the 20th century as a surgical method for extracting pituitary tumors.¹ Since then, it has been a popular method for eliminating sellar and parasellar lesions, as well as for restoring the skull base. Advancements in optics and high-resolution technology have enhanced the effectiveness of results, making it the favored method for surgeons compared to the transcranial approach² endoscopic endonasal transsphenoidal approach offers a safe and effective route to the tumor location, leading to reduced levels of damage or sickness. However, the excision of the tumor during the therapy may result in a significant and well recognized problem / complication due to archer known as cerebrospinal

fluid (CSF) leakage. This issue necessitates prompt therapeutic intervention.³

The main treatment is surgery for pituitary adenoma. Currently, the direct endonasal transsphenoidal method is becoming used. An endoscope has many advantages over a microscope, such as providing a clearer and enlarged picture from different perspectives, and enabling more comprehensive tumor removal by virtue of the light's close closeness to the target region. Nevertheless, it necessitates the use of endoscopic equipment and expertise in maneuvering tissues inside constricted pathways.⁴⁻⁷ However, the surgical excision of the tumor may result in a significant and well recognized complication known as cerebrospinal fluid (CSF) leakage, needs prompt attention and treatment.

Various techniques are available for skull-base reconstruction, however there is currently no universally accepted protocol for reconstructing the skull base after the excision of pituitary tumors utilizing endoscopic transnasal transsphenoidal

(ETNTS) operations. The surgical restoration of the skull base and repair of the cerebrospinal fluid (CSF) leak need an individualized strategy that is adapted to the particular conditions of each patient.

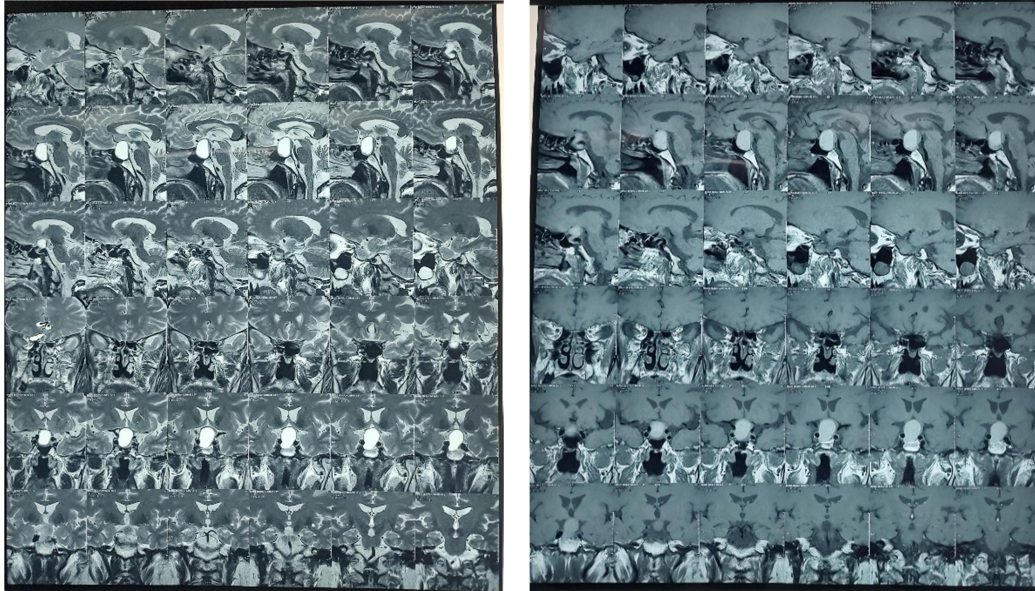


Figure 1 – MRI Brain showing Pituitary macroadenoma/apoplexy
i) T2WI sagittal section and coronal section (sellar cuts) ii) T2WI sagittal section



Figure 2- Instruments used in ETNTS (like endoscope)

Cerebrospinal fluid (CSF) leaks during endonasal transsphenoidal pituitary surgery (TNTS) is a recognized postoperative complication. The fibrin glue usage in these surgical procedures is intended to effectively close the dural lesions and minimize the likelihood of cerebrospinal fluid (CSF) leaking. Below is a comparison of cerebrospinal fluid (CSF) leak after surgery, with and without the use of fibrin glue:

Without Fibrin Glue:

Increased susceptibility to CSF leak: Surgeries performed without the use of fibrin glue may have

a greater likelihood of experiencing CSF leaks. This is because it is more challenging to effectively seal dural lesions simply by suturing or other traditional techniques.

Enhanced postoperative surveillance: Patients may need heightened monitoring after surgery to detect indications of cerebrospinal fluid (CSF) leakage, such as transparent nasal discharge, headache, or symptoms of meningitis.

Potential for revision surgery: If cerebrospinal fluid (CSF) leaks develop, patients may need to have revision surgery to fix the leak. This may result in a

longer recovery period and higher healthcare expenses.

Untreated cerebrospinal fluid (CSF) leaks provide an elevated risk of consequences, including meningitis, brain infections, and delayed wound healing.

With Fibrin Glue:

Minimized risk of cerebrospinal fluid (CSF) leak: The use of fibrin glue may enhance the sealing of dural defects, hence decreasing the likelihood of CSF leaking after surgery.

Fibrin glue facilitates hemostasis and serves as a framework for tissue regeneration, hence possibly accelerating wound healing and reducing the likelihood of infection.

Fibrin glue is a topical biological adhesive, the effect of which imitates the final stages of coagulation. The glue consists of a solution of concentrated human fibrinogen which is activated by the addition of bovine thrombin and calcium

chloride. The resultant clot aids haemostasis and tissue sealing and is completely absorbed during wound healing without foreign body reaction or extensive fibrosis. The haemostatic and adhesive properties of fibrin glue can be employed in virtually every surgical specialty.

Reduced hospitalization duration: Administering fibrin glue during surgery to patients may lead to shorter hospital stays and faster recovery due to a decreased occurrence of cerebrospinal fluid leaks.

Reduced need for revision surgery: The fibrin glue use may diminish the probability of needing further surgery to correct cerebrospinal fluid (CSF) leaks, thereby saving patients from extra treatments and the accompanying hazards. In summary, the application of fibrin glue in endonasal transsphenoidal pituitary surgery can significantly decrease the incidence of postoperative CSF leaks, leading to improved patient outcomes and reduced healthcare burden.

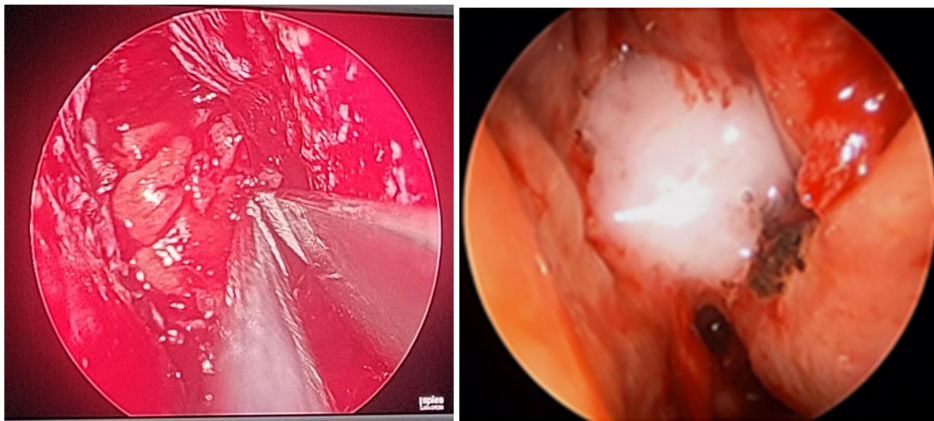


Figure 3– showing repair of sellar floor with i) using autologous fat graft followed by ii) application of fibrin glue

Aim and Objectives:

- a. To evaluate the CSF leakage postoperatively in Endonasal Transsphenoidal pituitary surgery with fibrin glue.
- b. To evaluate the CSF leakage postoperatively in Endonasal Transsphenoidal pituitary surgery without fibrin glue.
- c. To compare the CSF leak post operatively in Endonasal Transsphenoidal pituitary surgery without and with fibrin glue.

Materials and Methods:

A retrospective study was undertaken at the Department of Neurosurgery at MGMH, with the

approval of the institutional ethics committee. The study comprised all patients who had received surgical removal of pituitary adenoma (functional/non functional) using endoscopic endonasal transsphenoidal approach. The research did not include patients who were diagnosed with small tumor nodules in the metastatic diseases medical therapy. We gathered data about patient characteristics, the percentage of cerebrospinal fluid leakage after surgery, and the specific technique used for repair. An analytical investigation was carried out on various techniques of closing the sellar region and the accompanying medications prescribed for distinct situations. Probable risk factors for post-operative

cerebrospinal fluid (CSF) rhinorrhea were analyzed.

Prior to and during the injection of Gadolinium-based contrast agent, all patients received radiological assessment utilizing 3 Tesla magnetic resonance imaging (MRI). The tumor was classified as either a macroadenoma (more than 10 mm) or a microadenoma (less than 10 mm), based on its largest size. The lesions were classified as either exclusively situated in the sellar area, positioned above the sellar region (suprasellar), or next to the sellar region (parasellar). For each case, a CT scan of paranasal sinuses with nose was conducted to assess the anatomical composition of the nasal septum and paranasal sinuses.

CSF leakage repair techniques:

An anesthesiologist performed the Valsalva procedure to ascertain the presence of intra-operative leaks. If we identified intra-operative cerebrospinal fluid (CSF) leakage, our typical approach included first verifying the presence of an arachnoid leak and then addressing this by one of the following methods. If the tear in the arachnoid membrane is of a small size and the rate of cerebrospinal fluid (CSF) with flow leak, a small

piece of fat coated with Surgicel was inserted in the sella area and then covered with fibrin glue. Next, the sphenoid sinus was filled with Gelfoam in order to provide support. If the tear in the arachnoid membrane was significant and the rate of cerebrospinal fluid (CSF) flow is high, fat obtained from the lateral aspect of the thigh of the patient, and was shaped into a dumbbell configuration & inserted into the damaged area. The fat graft was subsequently coated with fibrin glue. Some patients underwent external cerebrospinal fluid (CSF) lumbar drainage for a duration of 2 to 4 days.

Statistical analysis:

The probability of cerebrospinal fluid (CSF) leakage was compared using SPSS software version 24. The findings are shown as the mean value with the standard error of the mean indicated as a range. A significance level of $P < 0.05$ is considered statistically significant.

Observation:

This study includes a group of 424 people, of which 278 were males and 146 females. The mean age at the time of procedure was 51.23 ± 6.32 years (table 1).

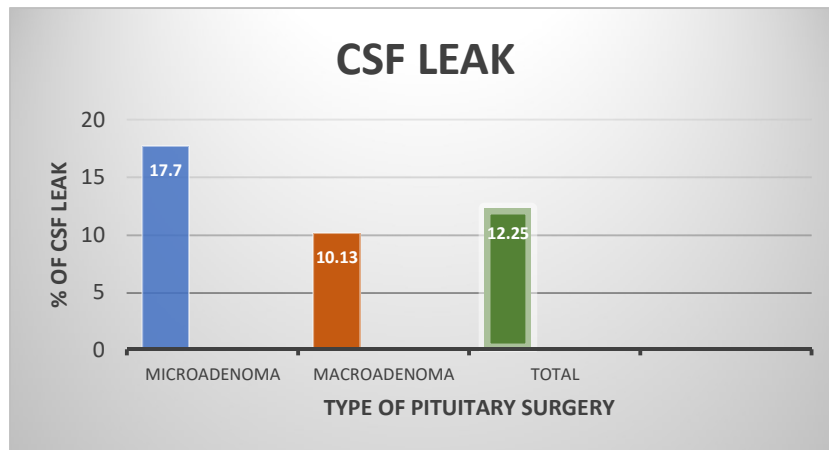
Table 1: Gender and age of the patients

Variables	N=424	%
Gender		
Male	278	65.56
Female	146	34.43
Age		
Below 30	31	7.12
30-50	229	54.13
50-70	118	27.64
Above 70	46	11.11

Micro and macro adenoma was reported in 27.83 and 72.16% of the subjects respectively. Postoperative cerebrospinal fluid (CSF) leakage was reported in 98 individuals, representing 12.25% of all cases. CSF leakage was found more in micro adenoma as compared to macro adenoma (table 2).

Table 2: Prevalence of post operative CSF leakage

Type of Adenoma	N	%	CSF leakage	%
Microadenoma	118	27.83	21	17.70
Macroadenoma	306	72.16	31	10.13
Total	424	100	52	12.25



No association was found between male and female as well as different age groups w.r.t. CSF leakage (table 3).

Table 3: Gender and age of the patients

Variables	CSF leakage =52	%	P-value
Gender			
Male	44	83.72	0.15
Female	8	16.28	
Age (in years)			
Below 30	1	2.33	0.21
30-50	36	69.77	
50-70	11	20.93	
Above 70	4	9.30	

Table 4 displays the mean values of several hormones. The mean values for GH, PRL, CORTISOL, T3, T4, TSH, FSH, LH, TESTOSTERONE, and HBA1C are 0.030 ± 0.02 , 12.45 ± 2.54 , 8.66 ± 1.11 , 3.58 ± 0.79 , 3.11 ± 0.75 , 3.44 ± 0.32 , 5.45 ± 1.08 , 4.58 ± 0.87 , 4.87 ± 0.94 , and 6.98 ± 0.79 , respectively.

Table 4: Mean of the hormones and co-morbidities

Hormones	Mean	Sd
GH	0.030	.02
PRL	12.45	2.54
CORTISOL	8.66	1.11
T3	3.58	0.79
T4	3.11	0.75
TSH	3.44	0.32
FSH	5.45	1.08
LH	4.58	0.87
TESTOSTERONE	4.87	0.94
HBA1C	6.98	0.79
Co-morbidities	N	%
Diabetes	68	15.95
Hypertension	88	20.79

Table 5: Leakage

Leakage	CSF Leakage (N=52)	Percentage
High Flow	7	13.95
Low Flow	45	86.05

Table 6: Lumbar drain according to CSF leakage

Lumbar drain	CSF Leakage=52	%
Yes	42	81.40
No	10	18.60

Table 6 shows CSF leakage in 42(81.40%) subjects.

Table 7: Mortality among the study subjects

Mortality	N=424	%
Yes	5	1.14
No	419	98.86

Mortality was found in 1.14% of the subjects (table 7).

Discussion:

The first transsphenoidal surgery (1907-1909) were conducted with the external rhinotomy incisions developed by Schloffer, Kocher and von Eiselsberg.⁸ Later on, the sublabial transseptal, transcolumellar procedur and endonasal transseptal, were introduced. Nevertheless, these operations still included the potential for complications such as lip and tooth numbness, septal perforation, and the formation of crusts. Prior to the 1960s, a major obstacle in performing sella procedures was the insufficient capacity to effectively light and see the operative site. During this period, Hardy invented the direct transsphenoidal approach, using an operating microscope, which significantly enhanced surgical visibility and gained widespread acceptance. The device's remarkable luminosity and magnification facilitated the effectual removal of pituitary tumors without causing significant disruption in anatomy. The employment of rigid endoscopes in sinus surgery provided the foundation for their use in pituitary surgery.⁹ Jankowski (1992) was the first to give an early account of the endoscopic transnasal technique, which was subsequently made famous by Jho et al.^{10,11} The transsphenoidal midline route has emerged as the established method for accessing the pituitary gland, and the endoscope is a recent technological advancement that provides a broader panoramic field of view. Endonasal endoscopic surgery, with its boundless potential, offers a novel

option for treating pituitary adenoma.¹² Several studies support the use of this technique, as it provides better visualisation, magnification, more thorough tumour removal, and a lower rate of complications compared to the conventional microscopic technique. This suggests that it is a minimally invasive procedure, as it preserves the septal and nasal architecture to the maximum extent possible.^{12,13} The fundamental premise for comprehending and effectively attaining favourable outcomes with these procedures lies in the intimate cooperation of a highly skilled otolaryngologist specialising in FESS surgery and a proficient neurosurgeon with expertise in transsphenoidal pituitary surgery.¹⁴

We conducted a study including 424 individuals who had Endonasal transsphenoidal pituitary tumor excision for the removal of their pituitary adenoma. Postoperative cerebrospinal fluid (CSF) leakage was reported in 52 individuals, representing 12.25% of all case in this study which is approximately similar to the rate reported in prior published data (11.5%).¹⁵ When there are recurrent instances of a cerebrospinal fluid (CSF) leak with severity levels II and III, a more sophisticated closure procedure is required. This entails using the Hadad flap technique and the gasket strategy, which includes strengthening the area of the leak with septal cartilage. No problems, such as hemorrhage or infection, were seen in the donor

locations, namely the thigh, for the extraction of fat.¹⁶

Patients with preoperative grade 0 CSF leak did not exhibit any postoperative CSF leak, which is a noteworthy finding. Postoperatively, individuals who did not have an intraoperative cerebrospinal fluid (CSF) leak did not exhibit any CSF leakage, which contradicts the findings reported in the literature.¹⁷

Furthermore, our investigation shown that using just fat for the intraoperative repair of grade I cerebrospinal fluid (CSF) leaks was effective in preventing any postoperative leaks. This approach proved to be more effective than the excessive repairs reported in the literature, such as the multilayer technique or dural graft repair.¹⁸

The incidence of cerebrospinal fluid (CSF) fistulas during surgery is greater, with rates ranging from 18.1% to 53.2%.¹⁹ Moreover, the current study's 12.25% rate aligns with the findings of these prior investigations. Shiley et al. found that patients who have an intra-operative cerebrospinal fluid (CSF) fistula are six times more likely to have a CSF fistula post-operatively. To ensure accurate identification of dural lesions, it is important to use careful haemostasis techniques and utilise the Valsalva manoeuvre and Trendelenburg position.^{20,21}

Tamasauskas et al. found that patients with growth hormone-producing adenomas had higher rates of post-operative CSF fistula²², while Shiley et al. concluded higher CSF fistula rates in patients with non-adenomatous disease such as craniopharyngioma.¹⁹

Nishioka et al. conducted a retrospective analysis of 200 consecutive instances of TSS for sellar lesions and found that intra-op CSF leaking occurred in 19.0% of the cases.²⁰ Patients who had previously had transsphenoidal surgery (TSS), radiation, or both, had a considerably higher chance of developing cerebrospinal fluid (CSF) leakage after their operation. Prior studies have identified macroadenomas, especially those with suprasellar extension, as well as the need for repeat transsphenoidal surgery, intra-operative leaks, and

increased body mass index as factors that might predict the occurrence of post-operative cerebrospinal fluid (CSF) rhinorrhea^{23,24}. When a cerebrospinal fluid (CSF) leak develops during or after surgery, the main method of restoration involves using grafts from the patient's own body (autologous grafts), such as fascia lata, or a pedicled nasoseptal flap.^{25,26} Presutti et al. recommended prompt surgical intervention once the patient's overall health permits, after the detection of cerebrospinal fluid (CSF) leakage and identification of the specific location of the leak using diagnostic evaluations. The researchers determined that the clinical presentation and examination of the nasal passages using an endoscope in a medical college and hospital setting were crucial for assessing potential cerebrospinal fluid leakage. There is a need for future studies that are randomized and controlled in order to determine the best method and timeframe for surgically repairing cerebrospinal fluid (CSF) rhinorrhea.²⁷ According to Couldwell et al., there were 0 cases of postoperative CSF leakage via the nose if there was no leakage during the operation to remove a pituitary tumour through the nose. However, it is worth noting that post-operative cerebrospinal fluid (CSF) rhinorrhea may develop, even in cases where there was no leaking during the surgery, although this is uncommon.²⁸

Conclusion:

Postoperative cerebrospinal fluid (CSF) leakage was reported in 52 individuals, representing 12.25% of all cases. Micro and macro adenoma was reported in 6.55% and 93.45% of the subjects respectively. High and low flow leakage was reported in 13.95% and 86.05% of the subjects respectively. Mortality was found in 1.14% of the subjects. Fibrin glue repair therapies are widely used and effective methods for treating cerebrospinal fluid (CSF) leakage via the nose following endoscopic transnasal transsphenoidal operations. It is important to customize the treatment approach for each patient according to their individual requirements.

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