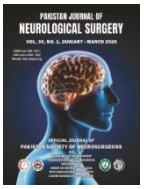

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Original Research

Safety and CSF Leak Outcomes After Endoscopic Endonasal Resection of Giant Pituitary Adenomas Without Nasoseptal Flap

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ABSTRACT

Objective: The study aimed to assess the risk of CSF leakage without the use of Nasoseptal flap elevations (NSFE) as compared to the standard practices of endoscopic endonasal approach (EEA) and multilayer graft reconstruction.

Materials & Methods: A retrospective review of EEA surgeries performed with multilayer graft repair in patients with per op CSF Leak but not with the NSFE, between June 2018 and February 2023, with a follow-up at one and three months. A proforma mentioning perioperative, preoperative, pre-operative, and follow-up data regarding CSF leak, intervention, and investigation was used. Descriptive statistical analysis was done.

Results: We collected data for 175 patients (70 male and 105 female). Mean age was 40 yrs. Mean tumor size in diameter was 45mm.CSF leakage in NSFE ranged from one to five percent in the literature, owing to the size. Similarly, due to large tumor sizes, there were 54/175 (30.86%) patients with CSF leak postoperatively. These 54 cases underwent multilayer graft reconstruction during the same surgery. Total CSF leaks were 8/175(4.57%) on follow-ups. Five patients out of these eight improved with conservative management (lumbar drain and puncture). Two patients had to go for surgery immediately postoperatively, and one had a follow-up. Redosurgery accounted for 3/175(1.71%). There were no invasive nasal complications as in NSFE.

Conclusion: Even with giant macro adenomas, EEA with multilayer graft reconstruction gave equally effective results as compared to the landmark considered treatment option, controlling CSF leak, and the NSFE.

Keywords: Nasoseptal Flap Elevation, Pituitary Neoplasms, Macro adenomas, Cerebrospinal Fluid, Multilayer Graft reconstruction, Transsphenoidal surgery, Endoscopic Endonasal.

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INTRODUCTION

Giant macroadenomas are of size greater than 40mm in diameter and have an aggressive nature with parasellar and extrasellar involvement, and are mostly non-functional.[1] EEA provides a less invasive approach with lesser postoperative morbidity and complications as compared to open techniques.[2] But one of the major risk factors of morbidity with EEA has been CSF leak and its associated complications, like meningitis.[3] Surgeons must be prepared to address these risks promptly and effectively to ensure patient safety and a successful outcome. CSF leakage is relatively lower when skull base reconstruction is adopted as a norm after endonasal excision in endonasal surgeries, particularly pituitary tumors of large sizes and extensions in the literature.[4] Conventionally, different NSFE techniques have been adopted since their inception in 2006 by Hadad Bassagasteguy (HB flap) to reduce CSF leakage.[5] NSF are modified pedicled flaps based on the nasoseptal artery, a branch of the posterior septal artery and modified flaps techniques are used by adding the nasal floor and inferior meatus mucosa, inferior turbinate mucosa, or entire lateral nasal wall mucosa at the sellar or skull base defective wall that heals owing to its vascularized supply and seals off CSF leakage and is being hailed as the ultimate solution for CSF leakage complication, post EEA.[6] However, many studies and a major meta-analysis puts overall prevalence of CSF leak around 3.2% (95% CI, 2.5-4.2%) and with pituitary excision around 3.4% with increased risk in patients with increased size, extension and cavernous sinus invasion (OR 3.0, 95% CI 1.1-8.7), making overall prevalence of CSF leak after endo nasal excision in adults to 3.4-4%.[7] But after various multilayer grafts reconstruction immediately per op, this number is the same.[8] It is even less, around 0.8% in some experience sharing analysis in which they formed an algorithm in a lower middle-income country like Iran, to define when to do a reconstruction per op, but only after transsphenoidal excision of small pituitary adenomas.[9] In multiple retrospective meta-analyses, the number is the same, around 2.6%, even in a 1000-plus case series.[10] Multilayer graft reconstruction might involve a layer of fat, fascia, and some kind of glue closing the gap. The CSF leakage rates after NSFE range from hailing it as having none in the earlier mentioned retrospective studies, and comes around to 2-3% in macro adenomas with high-flow CSF leaks.[6,11] And to around 3.3%-4% even with modified vascular NSF in some studies.[12] There are also reported complications, including Septal perforation, mucocele formation (5.3%), prolonged skull base crusting, etc., with NSFE.[12] An Australian prospective cohort study sought to identify changes in quality of life after utilizing the NSF for skull base reconstruction, showing increased otalgia and hyposmia in some studies, too, compared to the controls.[13,6] Other studies have suggested persistent mild hyposmia for as long as six months postoperatively. There is also partial necrosis of the NSF, causing around 5% increase risk of CSF leakage.[14] So, NSFE could be more invasive, requires more resources and expertise.

In Pakistan, no such specific study regarding CSF leak rates after endoscopic excision of Giant pituitary adenomas has been done to the best of our knowledge, searching the literature. However, there are certain retrospective studies in Punjab Institute of Neurosciences (PINS) (Lahore), Liaquat University (Karachi), which study different outcomes after endonasal excision and quantify the success rate of total excision of pituitary microadenomas to 90 percent.[15,16] In a retrospective review in a tertiary teaching care setup in Peshawar, Pakistan, endoscopic excision of macroadenomas showed 61% success rate and 90 percent in micro adenomas excision, even with their limited resources and only a 6.1% leak rate.[17] In another study, a CSF rhinorrhea repair retrospective study shows a 90 percent leak control rate in the same center, PINS, Lahore, using endonasal multilayer graft reconstruction.[18] Same principles can be applied for EEA and multilayer

graft reconstructions to study the alleged superiority of NSFE versus other techniques, including the need for multilayer grafts, which needs to be studied.

MATERIALS AND METHODS

It is a Retrospective Cross-sectional study, set in the Department of Neurosurgery, Punjab Institute of Neurosciences (PINS), Lahore, Pakistan. The duration of the study was five years (June 2018 and Feb 2023) with at least two follow-ups at 1 month and 3rd month. Follow-up MRI at 3 months.

Sample size was calculated using the Cochran equation:

$N = Z^2 pq/e^2$

Here e2 $=(p1-p0)^{2,}$ or called proportion.

p0=3 (average NSF proportion CSF leak taken from multiple studies mentioned in the introduction).[7,11,12] p1 =3.5 (average CSF leak after EEA with graft).[4,9,15]

Using the above formula, taking proportion as 0.5, Confidence interval(Z) as 80%, and precision level as +-5%(q). The sample size was calculated as 165 for better retrospective comparison. Ten patients were taken in addition to the amount for follow-up losses.

Inclusion Criteria

Patients clinically and radiologically diagnosed with giant pituitary adenomas. Age ranged from 18 to 65 years. No patient had previous surgery or CSF leak. With at least one month of follow-up.

Exclusion Criteria

Patients who had previous treatment with Bromocriptine. Recurrent Pituitary Adenomas. Sellar pathology other than pituitary adenoma. Tumors that needed two-step operations.

Data Collection Procedure

Operational Definitions

a) *CSF Leak*

The operational definition of CSF here will be taken as visual, clear watery fluid discharge from **the operative site** per op or via nose after surgery or in follow-up that is observed through Halo sign or head tilt sign and further confirmed through investigations like CT and MRI cisternography if needed. Chemical and expensive analysis is not considered here, considering lower-middle-income resources (β-2 transferrin is not easily available in our country). Per op leakage was considered according to CSF Leak grades after Valsalva, per op, as per the literature.[19] (as in Table 1).

b) Proposed technique for enhancing safety

During the Sellar floor reconstruction (as in Figure 1 below), per op CSF discharge was noted from the excised area after Valsalva, after hemostasis securing, and excision. If there was even a minute amount of CSF leakage suspicion or a large defect, as was the case with giant pituitary adenomas, then per op, basal skull reconstruction was done with **Multilayer graft reconstruction**. In a low-flow CSF leak, fat graft is strengthened with a layer of fascia and then BioGlue on top. In high flow leaks per op, the Gasket technique was used for reconstruction involving the use of a fascia lata, onlay graft that is countersunk into the skull base defect with a rigid buttress to create a watertight seal against the bony margins of the defect, and then glue was used.[20] Nasal packing (bismuth iodoform paraffin paste packing) was done and kept per op for a minimum of 48-72 hours. Surgicell (oxidized cellulose) / Spongostone (absorbable hemostatic gelatin sponge) layers were used for hemostasis and enhancing the effectiveness of the graft.

c) CSF leaks (post op)

Low Flow CSF: leaks were considered as a minute amount (only a few drops after a few minutes) of CSF leak that can be treated with conservative or lumbar drains.

High Flow CSF: Leaks amounted to a type of leak that had a high amount (like a partially open tap) of CSF leak, even on a simple head tilt test that usually warrants intervention or surgical repair.

d) Procedure

The exact steps varied from procedure to procedure, depending upon the size, location, and surgeon's preference. After informed consent, the patient was given general anesthesia, positioned supine on the operating table, with the head immobilized on a headrest, and an elevated and slightly extended neck with the help of shoulder rolls. After painting and draping and inserting pyodine-soaked gauzes in the nasal cavity, the surgeon used an endoscope to visualize the nostrils, and decongestants and local anesthesia were applied to the mucosa. The endoscope was inserted. Middle and inferior turbinate pushed aside, according to the extent of the tumor, the sellar basal region of the skull or sphenoid sinus may be opened to access the pituitary gland. Bony pieces of the sphenoid or sellar floor are kept aside for the Gasket technique if needed. Tumor was usually dissected using specialized instruments, cauterization, suction, and dissection techniques, and its removal from the sella turcica and associated areas according to its extent. These basic principles of EEA are used along with the proposed safety technique mentioned above. If some part of the tumor cannot be resected, it is termed a subtotal excision (mostly in cases of higher grade than KNOSP grade 2). KNOSP grading higher than grade 2 (tumor extends between the intercarotid line and the lateral tangent), which is based on MRI coronal images that define lateral invasion of the tumor into the cavernous sinus. It was not considered in detail as higher grades required two-step surgeries (endoscopic plus transcranial). In grade 1, the tumor extends between the medial tangent and the intercarotid line, and in grade 3 cavernous innervation.[21] Near total excision is achieved in other cases owing to the size.

Total CSF Leak

Only the patients with **postoperative CSF leak,** either high or low flow, will be considered as the total no of CSF leaks, which would require some kind of intervention.

Data Collection Method

A retrospective review of 175 patients maintained a database containing details of endoscopic endonasal operations performed by the senior authors here on giant adenoma patients after endonasal excision with or without multilayer fascial graft repair in patients with per op Cerebrospinal fluid (CSF) leak, but not with NSFE, from months between June 2018 to February 2023. Retrospectively reviewed 175 patients who were diagnosed with giant adenomas (>40 mm diameter) at the Punjab Institute of Neurosciences, Lahore, between June 2018 and Feb 2023, with at least two 2 follow ups at one month or at the third month and one year as per need in a lower-middle-income country. The data was collected using Proforma of prospectively maintained database mentioning per op, pre op observations, relevant history, per op observations including CSF leaks, graft reconstruction done, follow op observations like CSF leak, high or low flow, conservative management, intervention needed, hospital stay days, discharge condition, type of intervention post leak(if undergone), investigations like CT, MRI, if needed. Follow-up MRI usually at 3 months. Calculators from https://www.socscistatistics.com, SPSS (version 26, IBM Corp.) were used to analyze the descriptive statistics.

Follow-up: Patients visited the outpatient department with at least two mandatory follow-ups at one month and then at the third month after the operation, and were counseled to contact in between and then followed according to need. The follow-up observations were noted on the prospectively maintained Performa, mentioning name, age, gender, hospital number, size of tumor,

different hormonal levels, per op leak or not according to grades in operational definitions, type of sellar reconstruction and its details, follow-up leak rate at one month, third month, and other follow-ups. Size in postoperative MRI at 3 months. Intervention was done in case of CSF leak. Any complications encountered and hospital stay.

Ethical Approval: The srudy was approved by the ethical review committee of PINS (No.1781/IRB/PINS/Approval/2024).

RESULTS

Age and Gender Distribution: A total of 175 patients with giant pituitary adenomas were included in the study. The mean age was 40 ± 9.6 years (range: 20–60 years). There were 70 males (40%) and 105 females (60%).

Size of Tumors: The mean tumor diameter was 45 ± 5.1 mm. Most tumors measured 40–45 mm (128/175, 73.1%), followed by 46–50 mm in 20 patients (11.4%), 51–55 mm in 16 patients (9.1%), and ≥56 mm in 11 patients (6.3%).

Baseline Hormonal concentration: Approximately 20% of patients had near-normal hormonal profiles. The majority (~75%) exhibited varying degrees of hypopituitarism, predominantly involving cortisol and thyroid axes, while <5% demonstrated hyperfunctioning adenomas. Most were non-functioning adenomas.

Resection: Post-operative MRI at 3 months demonstrated >80% tumor resection in approximately 80% of cases. Subtotal resection was primarily observed in tumors with lateral extension and higher KNOSP grades.

CSF Leakage: CSF leakage is summarized as: (per op leak and post op leak were considered different as per definitions) (As in Tables 1-4).

Follow-up of patients with a mean duration of 3 months showed no follow-up CSF leakage cases, even those managed with conservative treatment. Only one patient had a CSF leak after 2 months on follow-up and had to undergo repair in a redo surgery. This patient didn't have any per op CSF leak.

Visual Symptoms: There was 30% visual symptoms improvement in three months in most cases with visual problems (S.D 95%) in our study in patients who had some sort of visual issues (50 percent owing to large size). Most patients

Table 1: *CSF LEAK per operatively (n=175. Per op leakage is only considered here for per op reconstruction details, according to CSF Leak graded after Valsalva, as per literature[19].*

Per op leaks	Patients n%: (S.D 95%)	Reconstruction Done and Discussion
Grade 0 – no leak	121/175 (69.14%)	Only hemostatic agents used Surgicell(oxidized cellulose), and spongostone(absorbable hemostatic gelatin sponge) filling the dead space + nasal packing(bismuth iodoform paraffin paste packing bipp) leaks in follow-up of patients 1/121 (0.01%)-grade 1 leaks patients with per op leak = 54
Grade 1 – weeping leak	19/175 (10.85%)	Fat +- In-lay fascia lata + overlay fascia lata + Glue(Fibrin glue)/sealant + nasal packing. (bipp) 19/54 (35.18%) grade 1-per op leak percentages
Grade 2 – moderate leak, visible defect	15/175 (8.57%)	Fat +- IN-lay fascia lata + overlay fascia lata + Glue/sealant + nasal packing(bipp). 15/54(27.78%)-grade 2-per op leak
Grade 3- large defect, high flow leak	20/175 (11.42%)	Gasket technique(fat +inlay fascia + then bone graft + onlay fascia)[19] + Glue /Sealant + Nasal Packing (bipp) 20/54(37.03%)-grade 3-per op leak

Table 2: *CSF Leak total summary (Total Patients n=175).*

CSF Leak frequencies	No. of Patients Incidence and Percentages (S.D = 95%)	Comments and Discussion
Peroperative leak	54/175 (30.86%)	All had some form of reconstruction per op apart from NSFE.
Postoperative leak(including follow op patients)/ total CSF leak	8/175(4.57%)	Patients who had immediate postoperative CSF leaks were 7. Two were managed with intermittent lumbar puncture, and 3 with lumbar drains postoperatively. 2 had high-flow leaks, repaired immediately. One of the patients who had no per op leak came with a low-flow CSF leak in 2 months of follow-up. He underwent elective surgery. The total number became 8 with the redo surgery.
Conservatively management with leak days	5/8 (71%) (average 3-5 days settled S.D 95%)	All 5 had low-flow leaks.2 managed with intermittent lumber punctures. 3 settled with lumber drain. (5+-2 days increase in average hospital stay for the patients that needed to be intervened on or had these complications)
Redo surgery	3/8 (37.5%) 3/175 (1.71%)-total redo freq	Out of the 8 leaks, 2 high-flow leaks were immediate post-initial operation. Only 1 had no per op leak and no reconstruction per op. He had redo surgery when presented with a low-volume flow CSF leak in 2 months of follow-up.
Intervention(lumbar puncture) or lumbar drain	5/8 (62.5%) 5/175 (2.8%)	All low-flow CSF leaks. Lumber drain = 3/5(0.6%) ,L.P = 2/5 (0.4%)

involved had prolonged disease duration owing to socioeconomic status, lack of awareness regarding the disease, as well as prolonged morbidity before coming to us for definitive treatment; hence, the reason for decreased visual improvements, and most complications involved were wound and postoperative infection.

Size of Tumors and Management: Total Redo surgeries included 3/8 patients. These cases were found to have had a KNOSP grade 3 or higher. Two of these patients had high-flow CSF leak postoperatively and were operated on immediately, and the other one had had a low-flow CSF leak on follow-up. Lumber drains were done in 6/8 patients. And all these intervention cases had an average tumor size greater than >45 mm and had an extended extension, i.e., KNOSP grade two and above. The findings suggest that reconstructive procedures after endoscopic endonasal resection have the same CSF leakage rate as compared to NSFE in the literature, and a case can be made that it is associated with tumor extent and size, causing greater manipulation of the cistern and tissue, causing high-pressure leaks (Figure 1-2).

Statistical Analysis: The Chi-square analysis demonstrated a significant association between perioperative and postoperative CSF leak ($p<0.05$). The Wilcoxon test revealed a correlation between paired CSF leak and whole resection, as well as

Table 3: *Post-operative CSF Leak and Management.*

Variable	n (%)
Total post-op CSF leaks	8 (4.57%)
Low-flow leaks	6
High-flow leaks	2
Conservative management (L.P)	5 (62.5%)
Redo surgery	3 (37.5%)
Overall redo surgery rate	3/175 (1.71%)
Additional hospital stays (days)	5 ± 2

Table 4: *Statistical Analysis of Factors Associated with CSF Leak.*

Comparison	Statistical Test	Result	p-value
Per-op vs Post-op CSF leak	Chi-square	Significant association	<0.05
Tumor size vs Post-op CSF leak	Mann–Whitney U	Larger tumors associated	<0.01
Tumor size vs CSF leak	Pearson correlation	Positive correlation	<0.05

multilayer graft reconstruction with CSF leak rate. However, Pearson correlation analysis further showed a positive correlation between tumor diameter and CSF leak occurrence ($p < 0.05$). KNOSP grading above 2 patients was not made part of or considered pre op as they normally required 2-step surgeries, and KNOSP grading was not considered in greater detail in retrospective analysis. The Mann–Whitney U test revealed that patients who developed post-operative CSF leak had significantly larger tumors compared with those without leaks ($p < 0.01$) (Table 3).

Table 5: *Post-operative Complications and Outcomes.*

Complication	n (%)
Meningitis	5 (2.8%)
Transient diabetes insipidus	4 (2.3%)
Visual improvement (3–6 months)	~30%
Hyposmia	0
Septal perforation	0
Mucocele	0
Mortality	1 (0.6%)

DISCUSSION

In our study, the patients with macro adenomas, including both males and females, underwent tumor resection without NSFE. Giant pituitary tumors were mostly non-functioning tumors. EEA with multilayer reconstruction has around the same CSF leak rates as NSFE in even a UK multi-center pilot study, also involving pituitary Giant adenomas, 3.8%.[22,8] The results range from 1 to 5 in smaller studies with smaller samples.[12] And even to 7% and even more with complications like high flow CSF leak to around 5.7%.[23] With increased flap necrosis risk, the CSF leak rate increases.[14] The CSF leak rate also increases due to extensive involvement of the cavernous sinus or bone with NSFE.[11] The results are comparable to our findings below.

As compared to these previous studies, our study showed a marked reduction in total CSF leak that had to be intervened on (n=8/175, 4.57%). This Percentage is comparable to nearly 5 %, which is equal to CSF leak frequencies needing intervention in most studies available. Overall, many studies and a major meta-analysis put overall prevalence of CSF leak around 3.2% (95% CI, 2.5-4.2%) and with pituitary excision around 3.5% with increased risk in patients with increased size, extension and cavernous sinus invasion (OR 3.0, 95% CI 1.1-8.7), making overall prevalence of CSF leak after endo nasal excision in adults to 3.5-5.5%.[7] No separate leak rates for giant adenomas are present definitively in the literature.

With NSFE, this number is around 1-3 percent in the literature. Some studies hail it as having no CSF leak in small retrospective studies.[6] It comes around to 2-3% in macro adenomas with high-flow CSF leaks.[11] And to around 3.3%-4%, even with modified NSFE in some studies.[12] In Endoscopic reconstruction, different multilayer graft reconstruction techniques showed the result.[8] It is even less, around 0.8% in some experienced centers, e.g., in an analysis in which they formed an algorithm in a lower middle-income country like Iran, to define when to do a reconstruction per op after EEA of small pituitary adenomas.[9] And even so, in multiple retrospective meta-analyses, the number is the same, around 2.6%, even in a 1000-plus case series.[10] In a review study of Hannan et al., we can see that even in different studies, NSFE has the same leak rate, if not more.[7,11,12,24] It ranged from 2% in an article

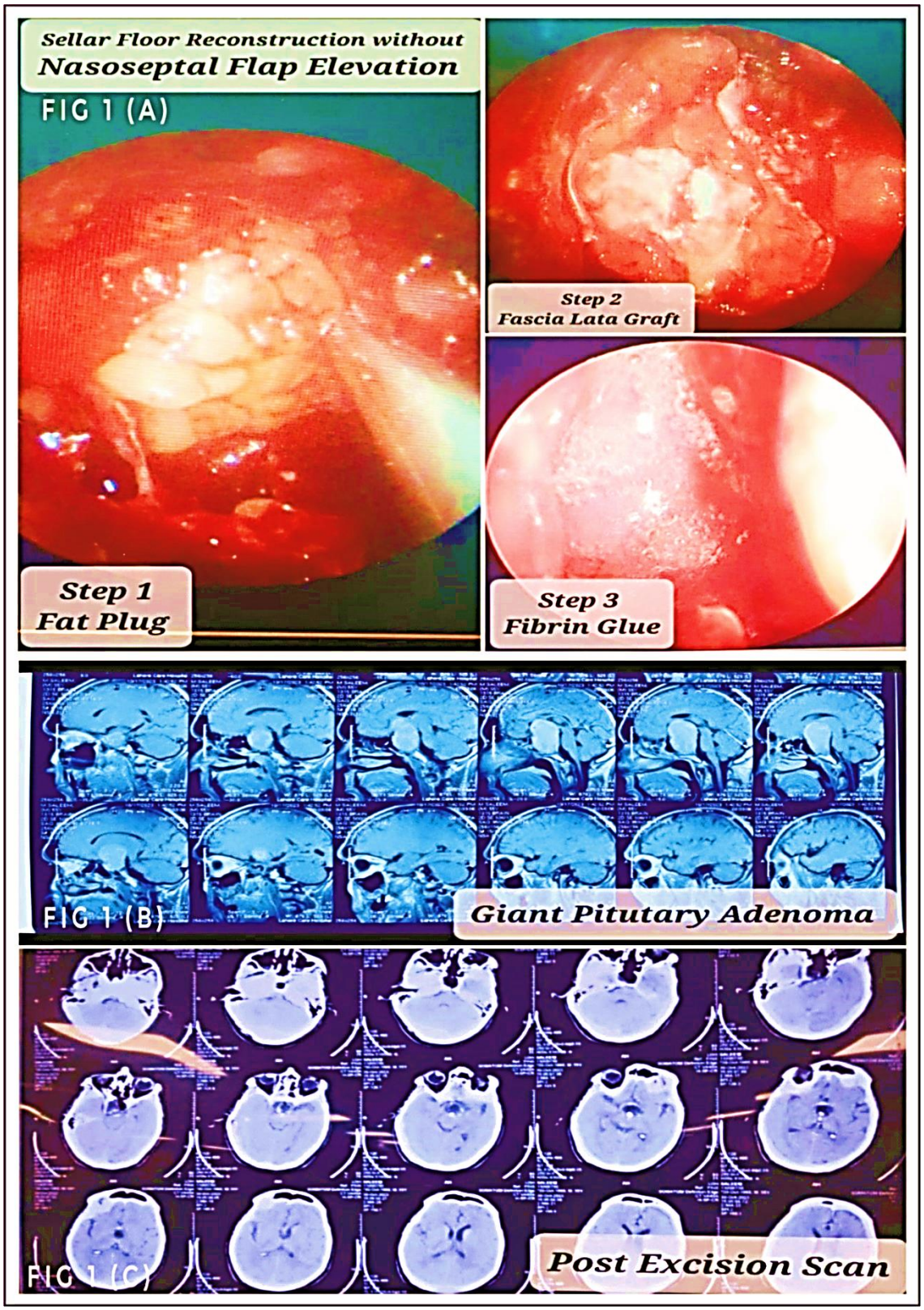

Figure 1(a): *Sellar Floor Reconstruction without Nasoseptal Flap Elevation after Excision of Giant Pituitary Adenoma above.* **Figure 1(b):** *MRI Brain of the same patient pre op below.* **Fig 1(c):** *Postoperative CT brain of the same patient. (Scans shared with the patient's consent).*

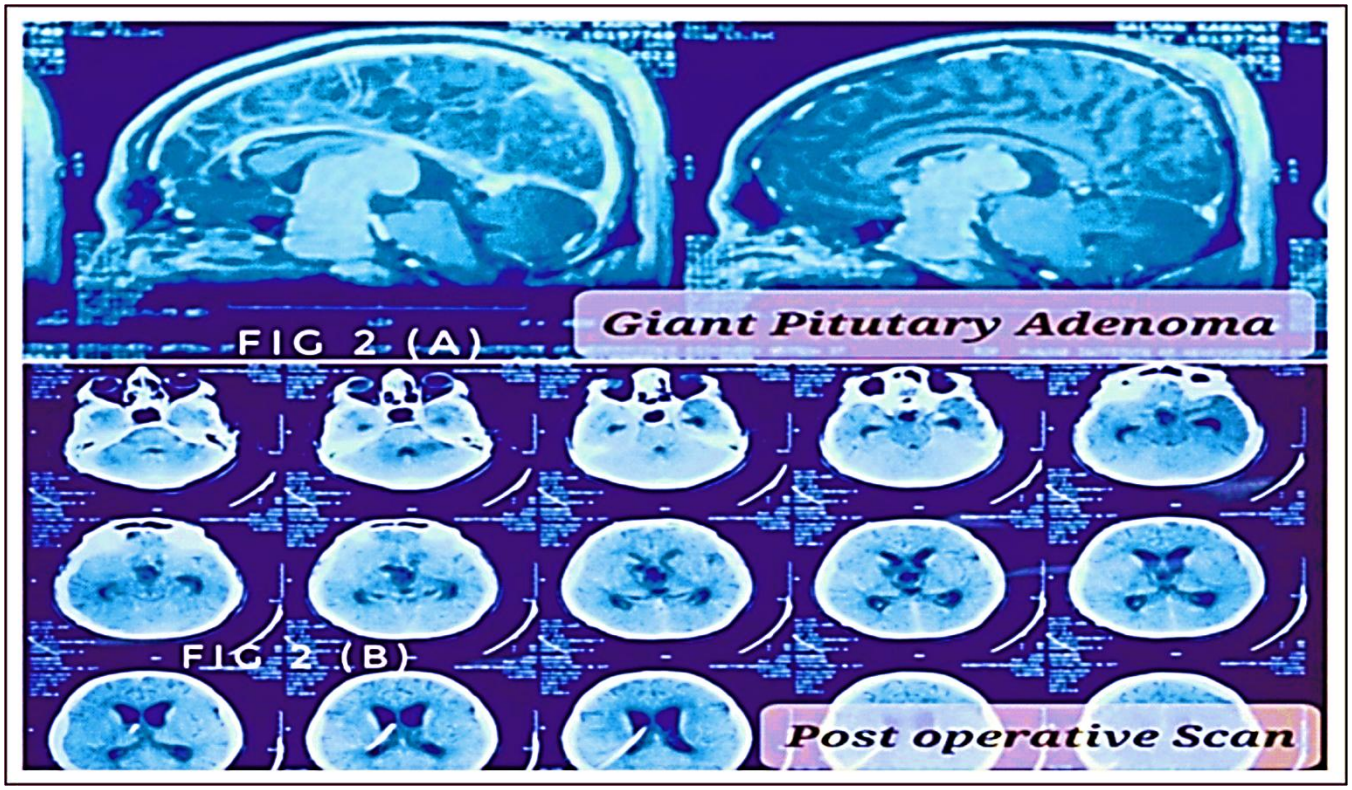

Figure 2(a): *Endoscopic Transsphenoidal Excision of Giant Pituitary Adenoma. Preoperative & Postoperative Images. MRI Brain above.* **Fig. 2 (b):** *Postoperative CT below. (Sharing with consent).*

having 44 cases, Hadad et al., using NSFE, to 8% CSF leak rate in Kassam et al., with 55 cases, to 2.1% CSF leak in Thorp et al., with 144 cases, and more recently, 4.3% leak was found in Conger et al, 2019 study with 88 cases.[24] Even in proper retrospective analysis, the leak rates still fall in the average range with our endoscopic repair technique. The management of CSF leak and its management is summarized in Tables 1-4. Low flow CSF leakage was around 6 (n=6/175). One of them that had no per op leak came with a low-flow CSF leak in two months and high flow (n=2/175). Of the 5 patients that had low flow leak postoperatively, two were managed with intermittent lumbar puncture, and three settled with lumbar drain. The two high-flow leak postoperatively needed immediate redo surgery. One had a graft placed, while the other had no perioperative CSF leak and had no repair done during the first surgery. Hence, the leak can be justified. Therefore, the total CSF leak that had to be intervened was (n=8/175,4.57%). This Percentage is comparable to or nearly equal to CSF leak frequencies needing intervention in most studies available.

The standard endonasal endoscopic skull reconstruction techniques after tumor excision were utilized per op as mentioned in operational definitions, after CSF leakage. It can be observed as shown in Fig. 1. Fat, Fascia, both together and alone, along with Bio glue, for affording patients or when glue was intended in O.T stocks, as not to charge the patients a lot, keeping in view the resources and feasibility according to the scenarios in our setup.

However, the leak rates were lower as all had multilayer graft reconstruction done. Those that had leaks were due to their large sizes greater than 45mm (S.D 95%).

Out of the 54/175 (30.86%) per op leak

patients, all of them had multilayer reconstruction done. (As shown in Figure 1). MRI and post-treatment CT are also shown in Figures 1 and 2. Nearly 80% of the cases had a complete resection done on repeat MRIs. No cases with leak were subtotal resections, but no apparent link can be made.

Patients with at least two follow-ups at one month and the third month were kept in the study, then followed yearly as needed. However, nine patients didn't come on yearly follow-up, most likely due to not being able to come from other provinces for some, and unknown reasons for others, but were included in the study as a minimum of two follow-ups were included (even though we had a 10 patient margin). All had no CSF leak postoperatively.

Our results are comparable when compared to the fact that even in low resources only 4.57 percent of the post operative patients had to have a definite intervention (surgery or lumber drain) rest of the patients settled on their own and conservative management, indicating that traditional endoscopic reconstruction techniques give the same CSF leak rate in our centre as NSFE as compared to the literature in different studies discussed.[8,10,12,24]

COMPLICATIONS

Meningitis occurred in 5/175(2.8%) patients (one with redo surgery and two with lumbar drains and two postoperatively). One developed a month into follow-up, and the other after redo surgery, unfortunately. One of them remained under-treated owing to being from remote areas and socioeconomic status. This follow-up patient died of secondary insults, sepsis, and DIC post meningitis despite best efforts when he came to us. The average increase in hospital days was 15+-5 days from the normal 3-5 days postoperatively of meningitis patients. All culture results were bacterial. Four patients were treated for diabetes insipidus postoperatively, and the condition was transient in nature. It settled after a 1- 2-day dose of desmopressin 0.1mg tablet 12 hourly. The eight patients who had CSF leak, their ICU /HDU stay was 8-10 days (S.D 95%). Only two patients had redo surgery for resection for recurrence, as the suprasellar tumor shifted down on postoperative MRI on follow-ups. No patients had hyposmia, no patient had any mucosal crusting, mucocele, or other bone issues, as NSFE was not done (Table 4).

LIMITATIONS

It was a single-center retrospective study with a minimum of two, at one month, then at the third month, and then at one-year intervals. Nine patients were lost to yearly follow-up but were included. KNOSP grades higher than two were not included in the study.CSF leak could not be confirmed on **chemical analysis** (beta transferrin tests, etc.) owing to the unavailability of these tests. **Unspecific tests** could have had an impact on making the leak rate appear higher than it really is. Surgical preference bias can have an effect on overall results.

CONCLUSION

NSFE seems like a landmark treatment option in literature in controlling CSF leak rates, but with giant pituitary adenomas, classical endonasal excision followed by multilayer grafting techniques can give equally comparable results to NSFE CSF leak rates, as presented in the literature. There is an added benefit of not having NSFE-related complications like anosmia, mucocele, crusting, etc. Simple multigraft reconstruction is equally comparable to prevent CSF leak after excision of giant pituitary adenomas, necessitating further research for improved patient outcome, even without NSFE.

Recommendation: Our study has laid the basis for further research and experimental studies.

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Additional Information:

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Ethical Review Board Approval: Approval was obtained from the IRB committee of Punjab Institute of Neurosciences (PINS). (No.1781/IRB/PINS/Approval/2024).

Human Subjects: Consent was obtained from all patients/participants in this study.

Conflicts of Interest: None.

Data Availability Statement: For data sharing, interested researchers can contact the corresponding authors

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Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Khawar Anwar	1. Study design and methodology, supervision, quality assurance.
2.	Sumira Kiran, Madikh Hameed, and Khawar Anwar	2. Paper writing and critical review.
3.	Madikh Hameed, Manal Khan, and Kaleem Iftikhar.	3. Data collection and calculations.
4.	Zubair Mustafa Khan, Sumira Kiran, and Madikh Hameed	4. Analysis of data and interpretation of results.
5.	Manal Khan, Khawar Anwar, and Madikh Hameed	5. Literature review and referencing.
6.	Kaleem Iftikhar and Zubair Mustafa Khan.	6. Editing and quality insurer.