

Comparative Efficacy of Craniotomy Versus Endoscopic Approaches for Pituitary Adenoma Resection

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Abstract: Pituitary adenomas are the most common tumors of the brain, and surgical treatment has evolved from transcranial craniotomy to an endoscopic endonasal transsphenoidal approach. The aim of this study was to make a comparative analysis of the surgical, hormonal, visual, and safety outcomes between craniotomy and endoscopic endonasal resection in a consecutive cohort of 103 patients with pituitary adenoma. A cross-sectional analysis study was performed to analyze 103 patients undergoing resection of pituitary adenoma, of which 44 patients had transcranial craniotomy and 59 patients had endoscopic endonasal transsphenoidal surgery. Demographic and tumor characteristics, surgical parameters, extent of resection, hormonal and visual results, and postoperative complications. The endoscopic group had significantly smaller tumors and smaller Knops grades at baseline, shorter operative time, less blood loss, shorter hospital stay, and fewer admissions to the ICU. Endoscopic surgery also resulted in the achievement of gross total resection more often compared with open surgery (71.2% vs. 50.0%), and this was an independent predictor of gross total resection. The same was true for the rates for hormonal remission and improvement in visual function, with the endoscopic group showing higher rates of these outcomes than the craniotomy group, although these are not statistically significant. Complication rates were also broadly similar between groups but were numerically higher in the endoscopic group (2.6% for CSF leak, 1.1% for epistaxis) and higher in the craniotomy group (2.0% for hypopituitarism, 2.6% for hematoma), though the latter were not statistically significant. This study demonstrated that the endoscopic endonasal approach was superior in terms of peri-operative efficiency and resection rates in the appropriate selection of tumors, and craniotomy still had a place in the management of larger, more invasive tumors.

Keywords: Pituitary Adenoma; Craniotomy; Endoscopic Endonasal Surgery; Transsphenoidal Surgery; and Gross Total Resection.

INTRODUCTION

Pituitary adenomas make up a significant portion of intracranial tumors detected in both surgical series and incidental imaging and may be asymptomatic microadenomas or large, invasive macroadenomas, which present with mass effect, visual compromise, and hormonal dysfunction [Müller, H. L. *et al.*, 2019; Bal, E. *et al.*, 2016; Zacharia, B. E. *et al.*, 2012].

The surgical management is to ensure maximal safe resection, alleviate optic apparatus compression, and normalize hormonal hypersecretion (if present), and maintain or restore normal pituitary function while keeping the perioperative morbidity to a minimum [Tang, B. *et al.*, 2018; Müller, H. L. *et al.*, 2017; Bao, Y. *et al.*, 2016]. The most common surgical approach to tumors that extended beyond the limits of the sella was transcranial craniotomy, performed usually through one of the corridors, namely the pterional or subfrontal corridor [Dhandapani, S. *et al.*, 2017; Agam, M. S. *et al.*, 2018].

Over the last 20 years, the endoscopic endonasal transsphenoidal approach has greatly transformed the surgical treatment of pituitary disease [Akbari,

H. *et al.*, 2018] by being able to visualize the sellar and parasellar anatomy with a high degree of detail through a minimally invasive corridor [Almutairi, R. D. *et al.*, 2018].

The endoscopic approach has been growing in use for tumors that were once thought to be candidates for open transcranial surgery, such as selected macroadenomas with suprasellar extension [Barkhoudarian, G. *et al.*, 2019].

It is noted that the endoscopic approach may be used in the right tumors for gross total resection with equivalent or better results, in addition to fewer operative complications and a shorter hospital stay [Broersen, L. H. *et al.*, 2018].

PATIENTS & METHODS

This is a cross-sectional study of a group of patients who had surgical resection of Pituitary adenoma at a tertiary neurosurgical referral center in Baghdad, Iraq. The surgical database for the department was used to identify consecutive patients who fulfilled eligibility criteria, and their records were reviewed for demographic,

radiological, and operative, and outcome data. Finally, 103 patients were included.

In patients, both transcranial craniotomy (n = 44, mainly pterional and subfrontal) and endoscopic endonasal transsphenoidal resection (n = 59) were performed. The surgical approach was chosen preoperatively as per the standard clinical decision-making process of the neurosurgical team based on a number of clinical factors including the size of the tumor, suprasellar and parasellar extension, Knosp grade, involvement of the cavernous sinus, sphenoid sinus anatomy, and previous surgical history.

The inclusion criteria were adult patients with a histologically proven pituitary adenoma who had been successfully treated with primary surgical resection and had at least 12 months of follow-up after surgery. Patients who underwent any recurrent surgery on an already operated sella, pituitary carcinoma, non-adenomatous sellar lesions (craniopharyngioma, Rathke cleft cyst), or who had incomplete follow-up data were excluded.

Baseline characteristics were age, sex, tumor size on the pre-treatment magnetic resonance imaging (MRI), Knosp grade, functioning versus non-functioning adenoma, and headache and visual field deficit. Operative variables were operative time, estimated blood loss, requirement for blood transfusion during operation, requirement for postoperative intensive care unit (ICU) admission, and total hospital length of stay. Extent of resection was defined as gross total or subtotal resection based on postoperative contrast-

enhanced magnetic resonance imaging done within three months after the surgery, hormonal remission defined according to the standard consensus biochemical criteria for the respective hormone axis, visual improvement defined as improvement on formal perimetry at the end of 12 months, complications including CSF leakage, postoperative hematoma, meningitis, new hypopituitarism, thirty-day mortality, diabetes insipidus, gross total or subtotal resection, and tumour recurrence or regrowth at 12 months imaging, respectively.

Multivariate logistic regression was carried out with gross total resection as the dependent binary outcome, and surgical approach, tumor size larger than 3 centimeters, Knosp grade 3–4, cavernous sinus invasion, and functioning adenoma status as independent predictors, with the results shown as adjusted odds ratios (AOR) with 95% confidence intervals (CI). Throughout, statistical significance is determined by a 2-tailed p-value of <0.05. The analyses were organized according to the usual procedures in statistical software, SPSS (Version 26.0).

RESULTS

The total of 103 patients included were treated by transcranial craniotomy (44, 42.7%) or endoscopic endonasal transsphenoidal resection (59, 57.3%). Baseline demographic and clinical parameters of both groups are summarized in Table 1. The endoscopic group showed significantly smaller tumour sizes and the distribution of the Knops Grades.

Table 1: Outlines the clinical and demographic features in the 103 patients.

Variable	Craniotomy (n=44)	Endoscopic (n=59)	p-value
Age, years (mean ± SD)	46.8 ± 11.4	44.2 ± 10.9	0.212
Male sex, n (%)	24 (54.5%)	29 (49.2%)	0.583
Female sex, n (%)	20 (45.5%)	30 (50.8%)	—
Tumor size, cm, median (IQR)	3.2 (2.6–4.1)	2.1 (1.6–2.8)	<0.001
Knosp grade 0–2, n (%)	14 (31.8%)	47 (79.7%)	<0.001
Knosp grade 3–4, n (%)	30 (68.2%)	12 (20.3%)	—
Functioning adenoma, n (%)	18 (40.9%)	26 (44.1%)	0.741
Non-functioning adenoma, n (%)	26 (59.1%)	33 (55.9%)	—
Visual field deficit at presentation, n (%)	32 (72.7%)	31 (52.5%)	0.039
Headache, n (%)	27 (61.4%)	30 (50.8%)	0.281

Table 2 shows the operative and perioperative parameters. The endoscopic group had significantly lower operating times, estimated blood loss, and intensive care unit admission rates, as well as lower rates of intraoperative transfusion, than the craniotomy group (all p<0.05). The rates

of intraoperative transfusion, intensive care unit admission, and estimated blood loss, and the operating times were significantly lower in the endoscopic group than in the craniotomy group (all p<0.05).

Table 2. Determining the hospitalization outcomes of 103 patients.

Variable	Craniotomy (n=44)	Endoscopic (n=59)	p-value
Operative time, min (mean $\pm$ SD)	245.6 $\pm$ 52.3	168.4 $\pm$ 38.7	<0.001
Estimated blood loss, mL, median (IQR)	420 (300–600)	150 (100–250)	<0.001
Length of hospital stay, days, median (IQR)	8 (6–11)	4 (3–6)	<0.001
ICU admission, n (%)	19 (43.2%)	9 (15.3%)	0.002
Intraoperative blood transfusion, n (%)	12 (27.3%)	4 (6.8%)	0.005

Extent of resection and clinical outcomes are shown in Table 3. There were 71.2% of the endoscopic group and 50.0% of the craniotomy group that underwent gross total resection. The endoscopic group had a higher rate of gross total resection (71.2%) than the craniotomy group (50.0%). In the first group of patients (those with

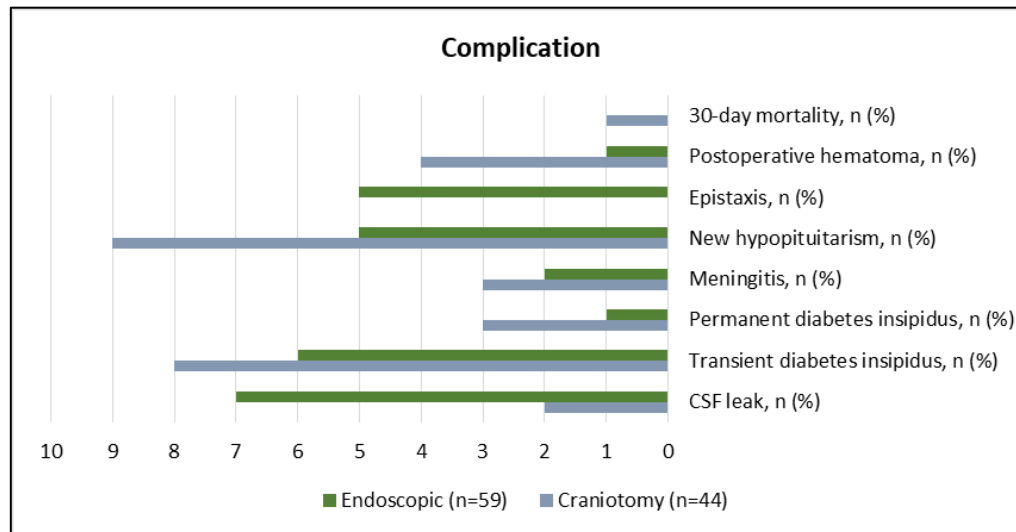
functioning adenoma), hormonal remission occurred more often in the endoscopic group (76.9% versus 50.0%), and in the second group (patients with a visual field defect), visual improvement was more frequent in the endoscopic group (87.1% versus 62.5%).

Table 3: Extent of resection and clinical outcomes of 103 patients

Variable	Craniotomy	Endoscopic	p-value
Gross total resection, n (%) (n=44 / n=59)	22 (50.0%)	42 (71.2%)	0.024
Subtotal resection, n (%)	22 (50.0%)	17 (28.8%)	—
Hormonal remission among functioning adenomas (n=18 / n=26)	9 (50.0%)	20 (76.9%)	0.048
Visual improvement among those with deficit (n=32 / n=31)	20 (62.5%)	27 (87.1%)	0.020
Recurrence at 12-month follow-up, n (%)	5 (11.4%)	4 (6.8%)	0.435

Figure 1 shows the summary of postoperative complications. The overall complication rates were similar in both groups. The endoscopic group had a higher number of cerebrospinal fluid leaks and

epistaxis, and the craniotomy group had a higher number of new hypopituitarism and postoperative hematoma, although this was not statistically significant.

**Figure 1:** summary of postoperative complications

A multivariate logistic regression model was set up to determine independent predictors of gross total resection while controlling for differences between groups at baseline. Following multivariate logistic regression analysis, which adjusted for tumor size ($p < 0.001$), Knosp grade ($p = 0.016$), cavernous sinus invasion ($p = 0.026$), and functional status ($p = 0.001$), the endoscopic approach continued to be independently associated with a higher likelihood of gross total resection (adjusted OR

2.86, 95% CI 1.18–6.94, $p = 0.020$). A tumor size > 3 cm, Knosp grade 3–4 and cavernous sinus invasion were each separately associated with a decreased gross total resection rate.

DISCUSSION

The operative time, amount of blood loss, hospital stay, and number of patients admitted to the intensive care unit were significantly shorter for the patients receiving endoscopic endonasal

transsphenoidal resection, while gross total resection, hormonal remission, and visual improvement rates were significantly higher.

Additionally, a definite endoscopic approach-gross total resection correlation remained even after multivariate correction for tumor size, Knosp grade, and cavernous sinus invasion [Burke, W. T. et al., 2019; Bander, E. D. et al., 2017; Jimenez, A. E. et al., 2022].

The studies suggested that tumor size, cavernous sinus invasion, and Knosp grade were all independent negative predictors for gross total resection for both surgical approaches [Kong, D. S. et al., 2018; Sigler, A. C. et al., 2017].

The complication profile seen from both groups is similar to what is often reported in the Chinese literature [Algattas, H. et al., 2020; McCoul, E. D. et al., 2014; Hadad, G. et al., 2006; Mou, J. et al., 2019], and is higher in number, but not significantly different, for cerebrospinal fluid leakage and epistaxis, both of these complications being related to the challenges of endonasal surgery of the skull base.

The rate of new hypopituitarism and postoperative hematoma within the craniotomy group was higher, which may be related to the extent of dissection of the pituitary gland and its surrounding structures in the transcranial approach of larger or more difficult tumors [Page, M. J. et al., 2021; Giammattei, L. et al., 2020].

The lack of statistically significant differences between the techniques in most of the categories of complications may be due to either a true similarity in the safety of the techniques used or because of overall small sample size and limited statistical power for a single-center cohort to detect differences in relatively infrequent events.

CONCLUSION

Endoscopic endonasal transsphenoidal resection of pituitary adenoma in this comparative cohort of 103 patients was found to be linked to a lower rate of operative morbidity, higher gross total resection rate, higher hormonal remission rate, and visual recovery rate after accounting for baseline tumor factors. The overall incidence of complications was similar between approaches.

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