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Study Protocol

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Comparing the efficacy of endoscopic endonasal versus microscopic transsphenoidal approach for the management of sellar and suprasellar tumors: a systematic review and meta-analysis protocol

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Abstract

Managing sellar and suprasellar tumors is challenging due to their diverse origins and proximity to critical structures. The transsphenoidal surgical approach has become the preferred method, evolving from transcranial attempts to reduce morbidity. Microscopic transsphenoidal techniques have been refined over time, with endoscopic endonasal surgery emerging as a significant advancement. Due to the multifaceted nature of these approaches, the complexities of the pathology and the paucity of data from specific regions, understanding the prevalence, characteristics and management outcomes of sellar and suprasellar tumors is crucial for informing healthcare practices and resource allocation. This study aims to collate evidence-based insights into the efficacy of the endoscopic endonasal approach compared with the microscopic transsphenoidal approach as a surgical intervention for sellar and suprasellar tumors, following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines for 2020. To source pertinent information, we will rely on four primary central databases: PubMed, EMBASE, SCOPUS and the Cochrane Central Register of Controlled Trials. The primary outcome measure will be the surgical outcome's effectiveness in achieving tumor resection and preserving pituitary function. The study protocol is duly registered with the International Prospective Register of Systematic Reviews (PROSPERO), with no requirement for ethical approval as it exclusively relies on previously published research. We aim to publish our findings in scientific journals and present the abstract at conferences to guide clinical practice. PROSPERO Registration Number: CRD42023461972: available via https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023461972.

INTRODUCTION

Sellar and suprasellar masses are space-occupying lesions arising from the pituitary gland or surrounding structures [1]. Depending on their size, extent, consistency and function, patients with sellar and suprasellar tumors may be present with different clinical features, including symptoms of mass effects such as headaches or vision loss and features of hormonal dysfunction [2, 3]. While several studies have reported on the epidemiological features of sellar and suprasellar tumors from Europe and North America, no information has been provided on the epidemiology of sellar and suprasellar tumors from the Middle East and North African region, except small studies describing the experiences of tertiary referral centers [2].

Despite their common location, sellar and suprasellar tumors are highly diverse lesions with multiple origins. These tumors can be congenital lesions, such as lipomas, Rathkes' cleft (pars intermedia) cysts, arachnoid cysts and hamartomas, or they can develop from any of the surrounding structures, resulting in pituitary adenomas, meningiomas, craniopharyngiomas, chordoma, optic nerve gliomas, among others [1, 4]. Non-neoplastic lesions, such as cavernous malformations, fibrous dysplasia, and inflammatory lesions, such as sarcoidosis, are also present here, and

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tumors from distant sites are found in the form of metastases in both the pituitary and cavernous sinuses [4]. This extraordinary diversity can complicate the management of cases with these tumors due to the myriad pathologies that occur. To further complicate the treatment of sellar and suprasellar tumors, there are numerous critical structures in this region, including the pituitary gland, critical vessels and several cranial nerves. Avoiding injury to these important structures is a key component of treatment planning [4, 5].

The principles of surgical treatment of sellar and suprasellar tumors are to relieve mass effects, normalize pituitary hypersecretion, preserve or restore normal pituitary function, prevent tumor recurrence, and provide tissue for pathological and scientific study. Over the past century, the transsphenoidal approach has become the approach of choice for neurosurgeons [6]. Transsphenoidal approaches to the sellar were preceded by transcranial surgical attempts to get access to the region. However, the morbidity of these transcranial approaches catalyzed the development of extracranial approaches to the Sella [6, 7]. Since its introduction, the microscopic transsphenoidal approach has undergone several modifications: the sublabial approach has given way to primary endonasal techniques, which have become more and more direct; frameless stereotaxy was routinely applied; and the corridors accessible through the transsphenoidal approach have been expanded, and, as discussed elsewhere, the endoscope has dramatically expanded the transsphenoidal surgeon's armamentarium [7]. These are skull base approaches in which the exposure of the broad bone, microsurgical techniques, and microdissection are in the foreground. Endoscopic endonasal surgery is a two-surgeon, three-hand or four-hand procedure. One surgeon can operate the endoscope using this method, while the other performs bimanual work at depth. [14] The benefit is the endoscope's flexible mobility in the surgical field, notably absent with a fixed holding device. The second surgeon may occasionally use a third instrument to aid in the dissection; however, they often irrigate frequently to keep the lens and operative field clean. [8, 13]. The endoscopic endonasal transsphenoidal approach is an established technique for resectioning a variety of benign sellar and suprasellar lesions, mostly pituitary adenomas, since first reported in the 90s [9–12]. It has clear advantages over the microscopic approach, such as a superior close-up view of the relevant anatomy and tumor-glandular interface, an increased working angle and an improved panoramic view within the surgical field [8, 9].

STUDY AIMS

We aim to compare the surgical approaches (endoscopic endonasal versus microscopic transsphenoidal) and analyze their impact on patient-reported quality-of-life outcomes among patients with sellar and suprasellar tumors who underwent surgical intervention.

PICO FRAMEWORK

Participant: patients with sellar and suprasellar tumors.

Intervention: endoscopic endonasal approach.

Comparison: microsurgical transsphenoidal excision.

Outcome: tumor reduction.

Research question: Does the endoscopic endonasal approach have better efficacy in terms of surgical outcomes (tumor removal/reduction, duration of surgery, hospital stay, recovery period, postoperative complications) compared with microscopic transsphenoidal surgery in treating patients with sellar and suprasellar tumors?

OUTCOMES

Primary outcomes

- Surgical outcomes (proportion of cases achieving complete and partial tumor removal and operative time);
- Frequency of postoperative complications;
- Hospital stay duration;
- Recovery rate;
- Patient-reported outcomes, including self-reported quality of life postoperatively.

Secondary outcomes

- Tumor recurrence rates;
- Long-term follow-up.

METHODS

The authors will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline 2020. Four databases will be used for systematic search: PubMed, EMBASE, Scopus and Cochrane Central Register of Controlled Trials. The search strategy is as follows:

Databases	Search Strategy
PubMed	(endoscopic endonasal OR endoscopic endonasal approach) AND (microscopic transsphenoidal surgery) AND (sellar tumor OR suprasellar tumor OR pituitary adenoma OR benign pituitary adenoma OR microadenoma OR macroadenoma OR giant adenoma)
EMBASE	(endoscopic endonasal:ab,ti,kw OR endoscopic endonasal approach:ab,ti,kw) AND (microscopic transsphenoidal surgery:ab,ti,kw) AND (sellar tumor:ab,ti,kw OR suprasellar tumor:ab,ti,kw OR pituitary adenoma:ab,ti,kw OR benign pituitary adenoma:ab,ti,kw OR microadenoma:ab,ti,kw OR macroadenoma:ab,ti,kw OR giant adenoma:ab,ti,kw)
Scopus	All fields: (endoscopic endonasal OR endoscopic endonasal approach) AND (microscopic transsphenoidal surgery) AND (sellar tumor OR suprasellar tumor OR pituitary adenoma OR benign pituitary adenoma OR microadenoma OR macroadenoma OR giant adenoma)
Cochrane Library	Title-abstract-keywords:(endoscopic endonasal OR endoscopic endonasal approach) AND (microscopic transsphenoidal surgery) AND (sellar tumor OR suprasellar tumor OR pituitary adenoma OR benign pituitary adenoma OR microadenoma OR macroadenoma OR giant adenoma)

INCLUSION CRITERIA

A study will be included if it meets the following criteria:

(i) Studies that compared the efficacy of the endoscopic endonasal approach and microscopic transsphenoidal surgery among patients with sellar and suprasellar tumors;
(ii) Studies involving adults and pediatrics;
(iii) Studies written in English, and study design of randomized controlled trials and cohort studies.

The **Exclusion Criteria** include review articles and case reports.

DATA ANALYSIS

The data will be presented in graphical and tabular forms, offering a numerical summary and a descriptive narrative. We will identify commonalities, such as studies that include endoscopic endonasal approach and microsurgical transsphenoidal excision, and synthesize and present the findings using qualitative and quantitative approaches. The effect estimates will be reported employing random-effect models. We will employ funnel plots and conduct Egger's tests to assess publication bias.

Statistical analysis will be performed using IBM SPSS. I^2 statistics will be used to assess the heterogeneity of the study. I^2 statistic is more outstanding than 50%, which is statistically significant. $P < 0.05$ is considered statistically significant.

QUALITY EVALUATION AND DATA EXTRACTION

After reviewing a random selection of the articles that meet the inclusion criteria, a consensus will be made on the precise data to extract. The following data will be extracted, including authors' name, publication year, age, sex, sample size, type of tumor (sellar or suprasellar tumor), type of intervention (surgery or stereotactic radiosurgery), follow-up period and Karnofsky performance status.

Two independent reviewers (T.T. and J.O.I.D.) will screen titles and abstracts using Rayyan. Papers that fulfill the inclusion criteria will be further assessed by evaluating the full text. The ambiguous decision of whether or not to include or exclude the papers will be solved through discussion with the senior author. Two co-authors will extract the data for each eligible study independently, while a third-party author will resolve the conflicts if needed.

Data Charting will be done using Google Sheets (Google, Mountain View, CA, USA) to ensure homogeneous data extraction by all reviewers. The following data from the eligible studies will be extracted:

- Author and name of study;
- Year of publication;
- Country of origin;
- Study population and sample size;
- Intervention type and comparator;
- Duration of intervention if present;
- Overall survival and progression-free survival;
- Inclusion criteria;
- Follow-up for the outcome(s) in days;
- Clinical outcomes and measures, as listed below;
- The proportion of cases achieving complete and partial tumor removal;
- Operative time;
- Frequency of surgical-related complications;
- Hospital stay duration and recovery rate;
- Self-reported quality of life;
- Tumor recurrence rates.

The process will be documented and presented via a PRISMA flow diagram.

RISK OF BIAS (QUALITY) ASSESSMENT

Two independent reviewers will evaluate within-and across-study bias for each outcome and rate the evidence certainty using the Grade of Recommendations Assessment, Development, and Evaluation. Consensus will be reached through discussion with a third reviewer for conflict resolution if needed. The Newcastle-Ottawa Scale (NOS) will be used to evaluate the quality of the observational study. In contrast, The Cochrane Collaboration risk-of-bias tool will be used to evaluate the RCT. Only studies with a score of NOS ≥ 4 will be considered low ROB and included for review and meta-analysis.

SUBGROUP ANALYSIS

We will conduct a sub-group analysis to explore potential outcome variations based on specific tumor characteristics. We aim to investigate whether the tumor size, location and histological type influence the relative effectiveness of the two surgical approaches.

Tumor size

Based on preoperative imaging measurements, we will categorize cases into small, medium and large tumors. Our analysis aims to determine whether one surgical approach has a more favorable outcome for specific tumor sizes.

Tumor location

We will classify cases into purely sellar, purely suprasellar, and combined sellar and suprasellar tumors. This analysis seeks to determine the efficacy of Endoscopic Endonasal Approach (EEA) and Microscopic Transsphenoidal Surgery (MTS) based on tumor location within the sellar and suprasellar regions.

Histological type

We will stratify cases histologically, including pituitary adenomas and other rare histologies, to identify whether the tumor types influenced the surgical approach's efficacy regarding resection rates, complications and overall patient outcomes.

MEASUREMENT OF EFFECT

We will analyze data from the EEA and MTS groups. The odds ratio will assess the association between each group and the treatment outcome. Sub-group analysis will be performed if data homogeneity allows. Chi-square tests, Fisher's exact tests and Logistic regression models will be employed to compare the outcomes between the EEA and MTS groups. For continuous, numerical and categorical variables, we will compute the mean difference or standard mean difference. Additionally, multivariate analyses will be conducted to control for potential confounding factors, such as tumor size, location and patient characteristics.

Study limitations

Despite our rigorous approach to this systematic review, it is crucial to acknowledge the limitations of this study. Language limitations could exclude non-English studies. Due to the inherent biases between studies that will be reviewed, this may affect our analysis.

Ethical consideration

This study does not involve human subjects, so no ethical approval is needed.

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None declared.

CONFLICT OF INTEREST STATEMENT

None declared.

AUTHORS' CONTRIBUTIONS

T.T., J.O.I.D., N.M. and G.B. contributed significantly to the protocol and provided their inputs. J.O.I.D. developed the methodology and wrote the abstract. T.T., J.O.I.D., N.M. and G.B. wrote the manuscript. All authors proofread and edited it. Finally, this review was approved as the final version of the protocol for publication through a unanimous decision.

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