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Transnasal Transsphenoidal versus Transcranial Surgery for Resection of Sellar Lesions; A National Database Analysis

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ABSTRACT

AIM: To present a national database analysis comparing transnasal transsphenoidal (TNTS) and transcranial (TC) approaches in sellar lesion management.

MATERIAL and METHODS: We analyzed the National Surgical Quality Improvement Program (NSQIP) database by TNTS and TC CPT codes from 2014-2018. Outcome measures included perioperative complications, surgical complications, reoperation within 30 days, readmission, and death. Statistical comparisons were made using Wilcoxon rank-sum test in STATA.

RESULTS: A total of 488 procedures were identified (232 TC; 256 TNTS). Baseline demographics were comparable between groups. Patients undergoing craniotomy were more likely to have DVT or PE (8 vs 2 patients, $p=0.042$) and stroke (11 vs 0 patients, $p<0.001$). TC approach was associated with longer hospital length-of-stay (6.1 vs 4.2 days, $p<0.001$), 30-day readmission (15.8% vs 7.1%), and death (2.6% vs 0.4%, $p=0.042$). Craniotomy was more likely to be performed in nonelective cases (26.3% vs 12.6%, $p<0.001$), however the difference in complication rates was driven by elective cases.

CONCLUSION: We found that the TC approach to the sella was associated with higher rates of complications and greater mortality than the TNTS approach. The TC approach was also more likely to be performed in nonelective cases, but the difference in morbidity and mortality was driven by elective cases. Further study is warranted to identify lesion characteristics that may influence choice of approach and outcomes.

KEYWORDS: Sellar mass, Pituitary surgery, Transnasal transsphenoidal, Transcranial

ABBREVIATIONS: TNTS: Transnasal transsphenoidal, TC: Transcranial, CPT: Current procedural terminology, DVT: Deep vein thrombosis, PE: Pulmonary embolism, ACS: American college of surgeons, NSQIP: National surgical quality improvement program, IRB: Institutional review board, ASA: American society of anesthesiologist, DVT: Deep vein thrombosis, PE: Pulmonary embolism, UTI: Urinary tract infection, MI: Myocardial infarction, LOS: Length of stay, RVU: Relative value units, STROBE: Strengthening the reporting of observational studies in epidemiology, CSF: Cerebrospinal fluid, ENT: Ear, nose, and throat

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■ INTRODUCTION

Both transnasal transsphenoidal (TNTS) and transcranial (TC) interventions are viable surgical approaches for resection of sellar lesions. Each possess relative advantages and limitations. Technological advances such as high-resolution noninvasive imaging, endoscopic visualization, microneurosurgery, frameless stereotactic neuronavigation, color Doppler ultrasonography, real-time intraoperative magnetic resonance imaging and neuromonitoring have dramatically increased the effectiveness and decreased the morbidity and mortality of TNTS surgery. These advancements have helped the TNTS approach become effectively the standard of care for small lesions limited to the sella. TNTS techniques are increasingly applied to a wide range of anatomic zones extending beyond the sella to include the clivus, anterior fossa, suprasellar cistern and third ventricle.

Despite the technical advances that fostered the proliferation of TNTS surgery, this approach still has its limitations. In particular, masses that extend beyond its defined operative corridors can be difficult to visualize and expose. In these cases, TC approaches may provide certain advantages, albeit at the cost of potentially higher procedural morbidity and limited access to more caudal structures within the sella. Furthermore, TNTS surgery is often performed with the assistance of an otolaryngology-trained approach surgeon, a resource which may not be available at smaller, community-based medical centers.

There are multiple confounding factors that obfuscate any comparison of these two techniques. For this reason, there is significant disagreement in the literature regarding the outcome and complication profile of TNTS versus TC surgery. This motivated a national database analysis, with the goal of quantifying these metrics and providing greater clarity for surgeons and patients.

■ MATERIAL and METHODS

The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database was used for this study's analysis. The ACS NSQIP database collects patient data from 700 participating medical centers including demographics, preoperative risk factors, laboratory values, intraoperative variables and 30-day postoperative outcomes. This repository is also publicly accessible and all patient data is deidentified. For these reasons, this study did not require Institutional Review Board (IRB) approval.

A query for patients undergoing pituitary mass resection in 2014–2018 was conducted by relevant Current Procedure Technology (CPT) codes. The results were filtered by code for craniotomy for pituitary mass resection (CPT 61546) and transsphenoidal approach for pituitary mass resection (CPT 62165). Holistic global codes were used in lieu of more nuanced codes to maintain the homogeneity of the population. The bundled transsphenoidal approach to sellar region code came into use in 2014 and the last year of available data was 2018, thereby driving the date range.

Baseline demographics queried were age, sex, diabetes status, smoking status, use of hypertensive medication, use of steroids pre-operatively, ASA class, and whether the surgery was classified as elective. Complications included pneumonia, reintubation, deep vein thrombosis (DVT) or pulmonary embolism (PE), renal insufficiency, urinary tract infection (UTI), stroke, myocardial infarction (MI), bleeding complication, and shock or sepsis. Outcome measures included reoperation within 30 days, hospital length of stay, readmission within 30 days and death. Average work relative value units (RVUs) for each CPT code were also collected.

Statistical comparisons between demographics, complications, and outcomes were made using Wilcoxon rank-sum test in STATA. A logistic regression model was used to compare outcomes between TNTS and TC approaches stratified by nonelective vs elective cases. Average RVUs were compared using a two-sample z-test. A p-value of less than 0.05 was considered statistically significant.

Study design and manuscript preparation were performed in accordance with STROBE guidelines (4).

■ RESULTS

A total of 488 procedures were identified (232 TC; 256 TNTS). No patients in this cohort underwent both procedures. Baseline demographics were comparable between groups (Table I). Craniotomy was more likely to be performed in nonelective cases (26.3% vs 12.6%, $p < 0.001$).

Across all patients the complication rate was 14.1% (Table II). The overall complication rate was higher in TC compared with TNTS surgery (20.7% vs 8.2%, $p < 0.001$). Patients undergoing craniotomy were more likely to have DVT or PE (8 vs 2 patients, $p = 0.042$) and stroke (11 vs 0 patients, $p < 0.001$).

The TC approach was associated with longer hospital length-of-stay (6.1 vs 4.2 days, $p < 0.001$), 30-day readmission (15.8% vs 7.1%, $p = 0.007$) and death (2.6% vs 0.4%, $p = 0.042$) (Table III). Mean operative time was 251 minutes (std dev 133 mins) for TC and 197 minutes (std dev 115 mins) for TNTS ($p < 0.001$). The average work RVU was high for TC (33.6, 95% CI 33.4 – 33.7) than TNTS (17.8, 95% CI 17.7 – 18.0) ($p < 0.001$). No differences were observed in rates of perioperative pneumonia, reintubation, renal insufficiency, UTI, MI, bleeding complication, shock/sepsis or 30-day return to OR.

The finding that craniotomy was more common in nonelective cases motivated a secondary analysis in which outcomes were stratified by nonelective vs elective. This demonstrated that for elective cases ($n = 387$), craniotomy was associated with significantly increased risk of any complication, return to OR, 30-day readmission, or death (OR 2.69, $p < 0.001$; 95% CI 1.555–4.645) compared to TNTS. For nonelective cases ($n = 92$), craniotomy was not associated with a statistical difference in risk of any complication, return to OR, 30-day readmission, or death (OR 1.38, $p = 0.501$; 95% CI 0.541–3.513).

Table I: Baseline Demographic Factors and Medical Comorbidities

Demographic and risk factors	All patients (n=490)	TC (n=232)	TNTS (n=256)	p-value
Age, years (mean)	52.7	53.6	51.9	0.261
Male, proportion (%)	47.4	48.7	45.9	0.533
Diabetes, n (%)	99 (20.2)	47 (20.2)	52 (20.3)	0.988
Smoking, n (%)	91 (18.6)	46 (19.4)	45 (17.6)	0.605
HTN medication, n (%)	207 (42.2)	105 (45.3)	101 (39.5)	0.195
Pre-operative steroids use, n (%)	65 (13.3)	36 (15.5)	29 (11.3)	0.174
ASA Class 3 or 4, n (%)	307 (62.8)	143 (61.9)	163 (63.7)	0.687
Elective surgery, n (%)	389 (80.9)	171 (73.7)	216 (87.5)	<0.001

HTN: Hypertension, **ASA:** American Society of Anesthesiologist.

Table II: Complications Associated with TNTS vs TC Surgery

Complications	All (n=490)	TC (n=232)	TNTS (n=256)	p-value
Pneumonia, n (%)	6 (1.2)	4 (1.7)	2 (0.8)	0.345
Reintubation, n (%)	10 (2.0)	6 (2.6)	4 (1.6)	0.426
DVT or PE, n (%)	10 (2.0)	8 (3.4)	2 (0.8)	0.042
Renal insufficiency, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
UTI, n (%)	8 (1.6)	4 (1.7)	4 (1.6)	0.888
Stroke, n (%)	11 (2.2)	11 (4.7)	0 (0.0)	<0.001
MI, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Bleeding complication, n (%)	15 (3.1)	10 (4.3)	5 (2.0)	0.132
Shock or sepsis, n (%)	9 (1.8)	5 (2.2)	4 (1.6)	0.627
Overall, n (%)	69 (14.1)	48 (20.7)	21 (8.2)	<0.001

TNTS: Transnasal transsphenoidal, **TC:** transcranial, **DVT:** deep vein thrombosis, **PE:** pulmonary embolism, **NA:** not available, **UTI:** urinary tract infection, **MI:** myocardial infarction.

Table III: Outcomes of TC vs TNTS Surgery

Outcomes	All (n=490)	TC (n=232)	TNTS (n=256)	p-value
30-day return to operating room, n (%)	32 (6.5)	19 (8.2)	13 (5.1)	0.166
Hospital length of stay, days (mean)	5.1	6.1	4.2	<0.001
30-day readmission, n (%)	46 (11.7)	31 (15.8)	14 (7.1)	0.007
Death, n (%)	7 (1.4)	6 (2.6)	1 (0.4)	0.042

TC: Transcranial, **TNTS:** transnasal transsphenoidal.

■ DISCUSSION

This database analysis uncovered important and significant differences between TC and TNTS approaches to the parasellar region. TC surgery is associated with a higher rate of DVT/PE, MI, overall complications, hospital LOS, 30-day readmission and death. The increased complication profile of

TC surgery is consistent with institutional series demonstrating higher rates of pituitary dysfunction (8), and worsened visual outcomes (17) in TC approaches when compared with TNTS.

Of note, multiple authors have described a higher rate of cranial nerve injuries in the TNTS cohort (9). Unsurprisingly, TNTS surgery is also associated with more olfactory nerve

disturbances (17). These represent a form of morbidity which is likely not captured by database reporting. Additionally, an increased cerebrospinal (CSF) leak rate in TNTS compared with TC surgery is a common observation (7,9,17). There is significant heterogeneity in reported rates of CSF leak following TNTS surgery, but a rough estimate provided by the CRANIAL Consortium is 5% in standard transsphenoidal approaches and 20% in expanded endoscopic endonasal surgery (3). CSF rhinorrhea after pituitary surgery is also a known predictor of increased LOS (6,14,15). However, we found that TNTS patients overall have a shorter LOS despite presumably experiencing increased rates of CSF leakage.

Though baseline characteristics of all patients undergoing these procedures in this cohort were similar, the TC approach was more likely to be performed in nonelective cases. This may have to do with the availability of an ENT co-surgeon, or lack thereof, which could force surgeons to perform a TC approach. Interestingly, the difference in complications and outcomes between approaches is driven solely by elective cases. This suggests that in emergent cases, such as apoplexy causing optic nerve compression, either approach may suffice. Conversely, for elective cases the complication profile strongly favors TNTS surgery.

This analysis also demonstrated that the TC approach was associated with a higher work RVU and longer operative time than TNTS. The difference in work RVU is likely a function of the reimbursement structure dictated by the Centers for Medicare and Medicaid, as the baseline work RVU for TC resection (CPT code 61546) is 69.65 compared with 45.73 for TNTS (CPT code 62165) (11). However, these findings suggest there may be underlying differences between the TNTS vs TC cohorts in terms of case complexity or other comorbid factors not captured by the demographic variables encoded in the NSQIP database.

Lastly, a database study limits the ability to assess the reasoning behind choice of approach, such as the size of the mass or the extent of invasion. We recognize that this limitation could introduce selection bias, and delineating rationales for approaches is a prospective area of future study to eliminate this bias. The characteristics of the lesion itself could provide insight into the differences in complications and outcomes. Nonetheless, the TC approach fared worse in this study in terms of stroke, DVT or PE, hospital LOS, 30-day readmission and death. Whether this is a consequence of the more complex nature of these cases cannot be determined from this dataset but is important to consider.

Additional limitations include the minimal granularity of the database, which does not provide information regarding factors such as tumor size, pathology, tertiary vs non-tertiary care centers, endocrinologic outcomes, adjuvant radiotherapy, Hardy classification/Knosp score or the use of endoscopic vs microscopic technique for the TNTS approach. It is also worth noting that there are many variations of the TNTS approach which include the expanded endoscopic endonasal approach (2) staged transsphenoidal surgeries (13), simultaneous “above and below” surgery combining an endonasal transsphenoidal approach with a transcranial

resection (1,5,10), and combined transsphenoidal and transcranial endoscopic approach via supraorbital keyhole (12,16). Each of these individual techniques carries a unique complication profile. However, this dataset does not allow us to quantify the impact of specific techniques on the overall outcome measures associated with TC vs TNTS resection. Furthermore, the dataset used (NSQIP) is limited to the most recent available data at the time of study initiation. Further research using more recent datasets could shed additional light on differences in these approaches.

■ CONCLUSION

We found that the TC approach to the sella was associated with a higher rate of complications and greater mortality than the TNTS approach. The TC approach was also more likely to be performed in nonelective cases, however the difference in morbidity and mortality was driven by elective cases. While these findings are limited by lack of granularity in terms of lesion characteristics and specific aspects of the surgical approach, they suggest that TNTS surgery may possess certain advantages over TC approach to the sella. Further study is warranted to identify lesion characteristics that may influence choice of approach and outcomes.

Declarations

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

Ethical statement: The repository is publicly accessible and all patient data is deidentified. For these reasons, this study did not require Institutional Review Board (IRB) approval.

AUTHORSHIP CONTRIBUTION

Study conception and design: DM

Data collection: AR

Analysis and interpretation of results: AR

Draft manuscript preparation: DM, BO

Critical revision of the article: DM, BO

Other (study supervision, fundings, materials, etc...): OS

All authors (DN, BO, AR, MG, OS) reviewed the results and approved the final version of the manuscript.

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