



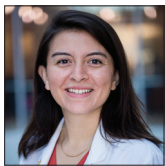
Original Article

Outcomes of infratentorial cranial surgery for tumor resection in older patients: An analysis of the National Surgical Quality Improvement Program

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ABSTRACT

Background: Poorer outcomes for infratentorial tumor resection have been reported. There is a lack of large multicenter analyses describing infratentorial surgery outcomes in older patients. We characterized outcomes in patients aged ≥ 65 years undergoing infratentorial cranial surgery.

Methods: The National Surgical Quality Improvement Project database was queried from 2012 to 2018 for patients ≥ 18 years undergoing elective infratentorial cranial surgery for tumor resection. Patients were grouped into 65–74 years, ≥ 75 years, and 18–64 years cohorts. Multivariable regressions compared outcome measures.

Results: Of 2212 patients, 28.3% were ≥ 65 years, of whom 24.8% were ≥ 75 years. Both older subpopulations had worse American Society of Anesthesiologists classification compared to controls ($P < 0.01$) and more comorbidities. Patients 65–74 and ≥ 75 years had higher rates of major complication (adjusted odds ratio [aOR] = 1.77, 95% CI = 1.13–2.79 and aOR = 3.44, 95% CI = 1.96–6.02, respectively), prolonged length of stay (LOS) (aOR = 1.89, 95% CI = 1.15–3.12 and aOR = 3.00, 95% CI = 1.65–5.44, respectively), and were more likely to be discharged to a location other than home (aOR = 2.43, 95% CI = 1.73–3.4 and aOR = 3.41, 95% CI = 2.18–5.33, respectively) relative to controls. Patients ≥ 75 had higher rates of readmission (aOR = 1.86, 95% CI = 1.13–3.08) and mortality (aOR = 3.28, 95% CI = 1.21–8.89) at 30 days.

Conclusion: Patients ≥ 65 years experienced more complications, prolonged LOS, and were less often discharged home than adults < 65 years. Patients ≥ 75 years had higher rates of 30-day readmission and mortality. There is a need for careful preoperative optimization in older patients undergoing infratentorial tumor cranial surgery.

Keywords: Brain tumor, Cranial, Elderly, Infratentorial, Meningioma

INTRODUCTION

Central nervous system tumors are associated with high morbidity and mortality and accounted for an estimated 79,718 deaths in the United States between 2012 and 2016.^[30] Brain tumors can be broadly classified as primary or metastatic. While metastatic lesions are almost exclusively intra-axial, primary tumors may be further classified into intra-axial or extra-axial lesions

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based on location of origin inside or outside of the brain parenchyma. The average annual age-adjusted incidence of primary brain tumors in the United States is approximately 23.41/100,000 individuals.^[31] Nonmalignant primary brain tumors are more common than primary malignant tumors. Meningiomas account for the majority of nonmalignant primary brain tumors when cerebellopontine angle tumors, such as vestibular schwannoma, are excluded, as we have done here.^[31] The most common primary malignant brain tumor is glioblastoma, accounting for 48.3% of primary malignant brain tumors.^[31] The 5-year survival rate for primary malignant brain tumors of all types is approximately 29.1%, indicating particularly high morbidity and mortality for these lesions.^[5] Brain metastases are 5–10 times more common than primary brain tumors, occurring in as many as 24% of cancer patients.^[26,34]

Several small, single-institution studies comparing the outcomes of surgical resection for supratentorial and infratentorial brain tumors suggest poorer outcomes in infratentorial neurosurgery; for metastases, elevated risk of local meningeal disease is one reason.^[11,15,17,22] In addition, older age has been previously associated with poorer outcomes, overall survival, and progression-free survival in primary intra-axial low-grade tumors.^[4,10] However, most studies suggest that intra-axial tumor resection in older patients is safe in well-selected patients.^[16,18,19] Similarly, age has been correlated with poorer outcomes in meningiomas in the absence of careful consideration of preoperative medical risk factors that may disproportionately affect older patient populations.^[6,9,11,13,21,23,29] Several case series have reported age as an important prognostic factor for infratentorial tumor outcomes.^[1,3,23] This literature highlights the importance of considering medical comorbidities, age, tumor location, and surgical approach when treating older infratentorial tumor patients.

Although outcomes of infratentorial tumor resection in older populations have been studied, these studies were primarily small, single-center case series; the need remains for large multicenter analyses to compare outcomes for older (>65-years-old) versus younger (<65-years-old) patient populations. We used the National Surgical Quality Improvement Project (NSQIP) database to study 30-day postoperative outcomes in older patients undergoing infratentorial neurosurgery for definitive resection of intrinsic or metastatic tumors and meningiomas.

MATERIALS AND METHODS

Data source

We queried the American College of Surgeons National Surgical Quality Improvement Program Participant Use Data File (ACS-NSQIP PUF; NSQIP) for patients who

underwent surgery from 2012 through 2018. NSQIP contains deidentified, prospectively collected inpatient and outpatient multicenter data on demographics, comorbidities, intraoperative variables, and 30-day postoperative outcomes. The Institutional Review Board reviewed the study and deemed it exempt from continuing review (#1466665).

Study population

We identified patients aged 18 years or older undergoing elective cranial surgery for infratentorial tumors, including brain metastases, primary intrinsic brain tumors, or meningioma. Cranial surgery patients were selected through a combination of Current Procedural Terminology (CPT) and postoperative International Classification of Disease (ICD) codes [Supplementary Table 1]. Specificity beyond gliomas for the intrinsic tumors is not provided by the ICD and CPT coding systems [Supplemental Table 1] and NSQIP does not supply more granular detail. We excluded patients who underwent surgery for a tumor located wholly in the cerebellopontine angle (that is, vestibular schwannomas), since patients with these tumors are a homogeneous, but different population, one we will study separately.

The American Society of Anesthesiologists (ASA) Physical Status Classification System was used to classify patients' preoperative risk.^[14] Patients who underwent elective surgery and those with ASA Class <5 were included in our analysis. Furthermore, elective surgery patients were only included if they arrived from home on the day of surgery.^[24,28] We excluded patients who were pregnant or in the puerperium period, those who received preoperative blood transfusions, and those with an infection present at the time of surgery. Finally, we excluded patients with hospital stays <2 days [Figure 1]. These criteria were collectively implemented to select a cohesive population of patients across age categories who were medically optimized for elective neurosurgery according to baseline characteristics.

Age categorization

Patients were first grouped into a cohort aged 65 or older and a control cohort aged 18–64 years. As a secondary comparison, the older population was subdivided into those aged 65–74 years and those aged 75 years or older.

Study outcomes

Inpatient and 30-day outcomes were considered. Inpatient outcomes included prolonged length of stay (LOS) and disposition other than home at discharge. Minor and major complications were analyzed during inpatient hospitalization and at 30 days [Supplementary Table 2]. Thirty-day outcomes included readmission, reoperation, and mortality.

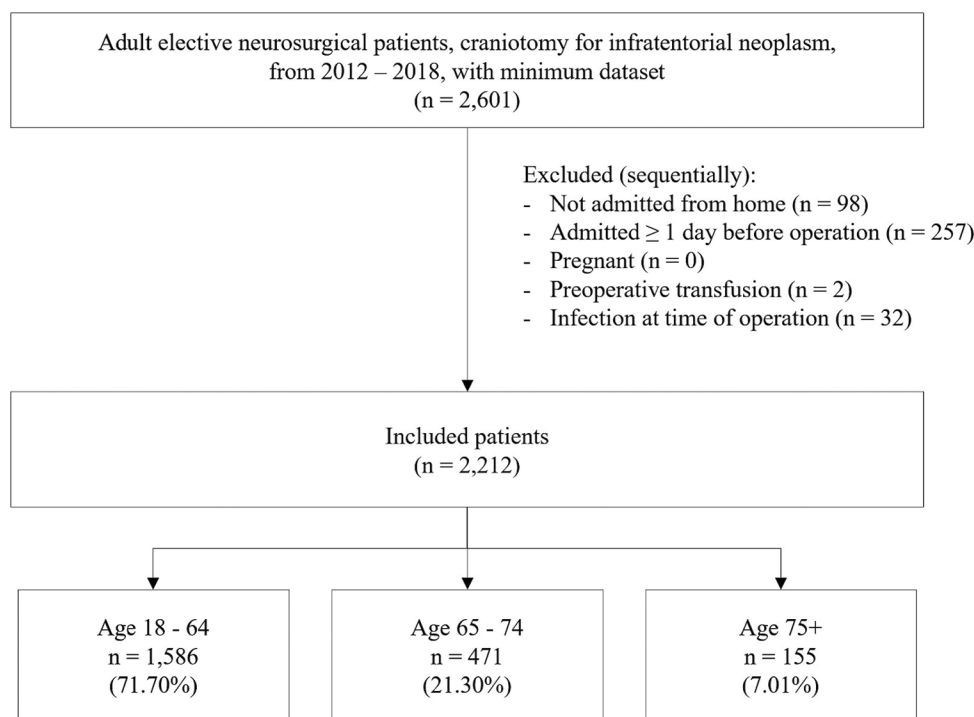


Figure 1: Population selection (age in years).

Statistical methods

Stata statistical software, version 16 (StataCorp LP, College Station, Texas), was used for data management and statistical analyses. We compared patient demographics, comorbidities, and intraoperative variables between older and control cohorts using Pearson's χ^2 for categorical variables and Student's *t*-test for continuous variables [Table 1]. Multivariate logistic regression was performed for all covariates with an incidence $\geq 1\%$ to assess the relationship between age category and each outcome. All three age categories were adjusted for ASA class, functional status, comorbidities, and operative duration. Patients with metastases possessed, by definition, "disseminated cancer," so this NSQIP comorbidity was excluded from all regressions to prevent overlap in patients with a metastasis and to prevent repeat counting. All outcome regressions were assessed for goodness-of-fit using Pearson χ^2 and all were found to be significant ($P < 0.05$). In addition, all receiver operator curves (ROCs) were evaluated and area under the ROC curve ranged from 63% to 86%. No attempt was made to optimize the models for predictive power using stepwise regression or other methods. For all analyses, $P \leq 0.05$ was considered statistically significant.

RESULTS

We identified 2212 eligible adult patients who underwent elective craniotomy for infratentorial neoplasm from 2012 through 2018. Of these patients, 28.3% were ≥ 65 years

($n = 626$) and, of those patients, 75.2% were aged 65–74 years ($n = 471$) and 24.8% were aged 75 years or older ($n = 155$). When comparing each older subpopulation to the control group, patients aged 65–74 years and those aged 75 years or older both had increased distributions of patients in higher ASA categories (both $P < 0.001$) and were more likely to be functionally dependent compared to the control cohort (65–74 years old, $P = 0.029$; 75+ years old, $P < 0.001$). Both older subpopulations were also more likely to have diabetes, dyspnea, history of chronic obstructive pulmonary disease (COPD), hypertension, and disseminated cancer compared to patients 18–65 years. In addition, both older populations had an increased distribution of metastatic disease or meningioma tumor type compared to controls ($P < 0.01$) [Table 1]. There was an overall decreasing trend in rate of intrinsic brain tumors with increasing age [Figure 2].

We performed multivariate regression to evaluate the effect of older age (≥ 65 years), age 65–74 years, and age 75 years or older on outcome measures relative to the control population [Table 2]. After adjustment, patients aged 65–74 years had statistically significant increased risk of prolonged LOS (adjusted odds ratio [aOR] = 1.89, 95% CI = 1.15–3.12), major complication (aOR = 1.77, 95% CI = 1.13–2.79), and disposition other than home (aOR = 2.43, 95% CI = 1.73–3.4; $P < 0.001$) compared to the control group. Patients aged 75 years or older were more likely to have prolonged LOS (aOR = 3.00, 95% CI = 1.65–5.44, $P < 0.001$), minor complication (aOR = 3.37, 95% CI = 1.65–6.89, $P = 0.001$),

Table 1: Demographic and clinical features of the populations of interest by age group.

Characteristic	Age 18–64 Y n=1586 (71.70%)	Age 65–74 Y n=471 (21.30%)	P-value	Age 75+Y n=155 (7.01%)	P-value
Mean age, years (SD)	47.47 (12.23)	68.98 (2.76)	---	78.61 (3.73)	---
Gender, male (%)	583 (36.76)	205 (43.52)	0.008	66 (42.58)	0.152
Race, not-White (%)	165 (13.89)	32 (8.72)	0.009	12 (10.71)	0.349
BMI (%)			0.273		<0.001
<18.5	24 (1.53)	4 (0.85)		1 (0.65)	
18.5–25.0	478 (30.39)	137 (29.27)		45 (29.41)	
25.1–30.0	482 (30.64)	163 (34.83)		72 (47.06)	
>30.0	589 (37.44)	164 (35.04)		35 (22.88)	
ASA classification (%)			<0.001		<0.001
1 and 2	618 (38.97)	89 (18.90)		22 (14.19)	
3	858 (54.10)	323 (68.58)		111 (71.61)	
4	110 (6.94)	59 (12.53)		22 (14.19)	
Tumor type (%)			<0.001		0.001
Intrinsic brain tumor	718 (45.27)	137 (29.09)		48 (30.9)	
Meningioma	536 (33.80)	170 (36.09)		60 (38.71)	
Metastatic disease	332 (20.93)	164 (34.82)		47 (30.32)	
Functionally dependent (%)	20 (1.27)	15 (3.18)	0.005	8 (5.16)	<0.001
Comorbidities (%)					
Diabetes	125 (7.8)	81 (17.20)	<0.001	31 (20.00)	<0.001
Smoker	295 (18.60)	69 (14.65)	0.049	10 (6.45)	<0.001
Obese BMI >30	589 (37.44)	164 (35.04)	0.344	35 (22.88)	<0.001
Dyspnea	53 (3.34%)	28 (5.9)	0.011	17 (10.97)	<0.001
History of COPD	39 (2.46)	42 (8.92)	<0.001	16 (10.3)	<0.001
Ascites	0 (0.00)	0 (0.00)	---	0 (0.00)	---
History of CHF	1 (0.06)	3 (0.64)	---	0 (0.00)	---
Hypertension	422 (26.61)	252 (53.50)	<0.001	114 (73.55)	<0.001
Renal failure	1 (0.06)	0 (0.00)	---	0 (0.00)	---
Dialysis	5 (0.32)	1 (0.21)	---	0 (0.00)	---
Disseminated cancer	325 (20.49)	152 (32.27)	<0.001	45 (29.03)	0.013
Chronic steroid use	259 (16.33)	87 (18.47)	0.275	31 (20.00)	0.242
Significant weight loss	21 (1.32)	12 (2.55)	0.063	5 (3.23)	0.062
Bleeding disorder	16 (1.01)	9 (1.9)	0.117	4 (2.5)	---
Mean operative time, min (SD)	253.64 (148.04)	236.76 (141.52)	0.028	212.83 (113.01)	0.001

*Comparisons made with each older patient age group against the 18–64 years old (baseline) group. †Y: Years, ASA: American Society of Anesthesiologists, BMI: Body mass index, SD: Standard deviation. ‡Student's *t*-test used to compare continuous variables and Pearson's χ^2 used to compare categorical variables. §No statistical comparison made as age was used to stratify patients. ¶Group sizes inadequate to calculate χ^2 statistic, which requires ≥ 5 /group

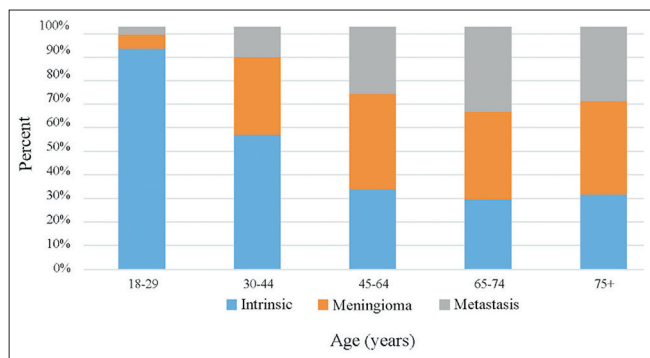


Figure 2: Infratentorial tumor type distribution by age *Age, in years, at index surgery.

major complication (aOR = 3.44, 95% CI = 1.96–6.02, $P < 0.001$), disposition other than home (aOR = 3.41, 95% CI = 2.18–5.33, $P < 0.001$), 30-day readmission (aOR = 1.86, 95% CI = 1.13–3.08), and 30-day mortality [Figure 3] (aOR = 3.28, 95% CI = 1.21–8.89) compared to the control group. No overt collection of two or more comorbidities appeared to be combinatorial drivers of suboptimal outcomes (data not shown).

DISCUSSION

This study reinforces and extends prior reports of poorer outcomes in patients undergoing infratentorial tumor neurosurgery.^[11,15,17,22] In particular, older age exacerbates

Table 2: Adjusted odds ratios for multivariate analyses and outcomes of interest*.

Outcome	Age 18–64 Y		Age 65–74 Y			Age 75+Y			
	Incidence (%)	Incidence (%)	aOR	95% CI	P-value	Incidence (%)	aOR	95% CI	P-value
Prolonged LOS	10.40	17.62	1.89	1.15–3.12	0.013	19.35	3.00	1.65–5.44	<0.001
Minor complication	3.03	5.73	1.45	0.77–2.74	0.254	9.68	3.37	1.65–6.89	0.001
Major complication	6.18	11.46	1.77	1.13–2.79	0.013	16.77	3.44	1.96–6.02	<0.001
Any complication	8.07	15.07	1.80	1.20–2.68	0.004	21.94	3.39	2.06–5.57	<0.001
Discharged not to home	11.31	23.61	2.43	1.73–3.4	<0.001	30.67	3.41	2.18–5.33	<0.001
30-day readmission	9.97	14.01	1.31	0.9–1.91	0.157	17.42	1.86	1.13–3.08	0.015
30-day return to the OR	5.23	5.94	1.45	0.85–2.46	0.169	7.10	1.83	0.86–3.88	0.114
30-day mortality	1.07	3.18	1.88	0.78–4.49	0.158	6.45	3.28	1.21–8.89	0.019

*Full model including all variables incident >1% in control and each respective population and significantly imbalanced between groups ($P < 0.05$) in Table 1. [†]Prolonged LOS = $\geq 90^{\text{th}}$ percentile for the entire population. [‡]Y: Years, aOR: Adjusted odds ratio, CI: Confidence interval, LOS: Length of stay, OR: Operating room

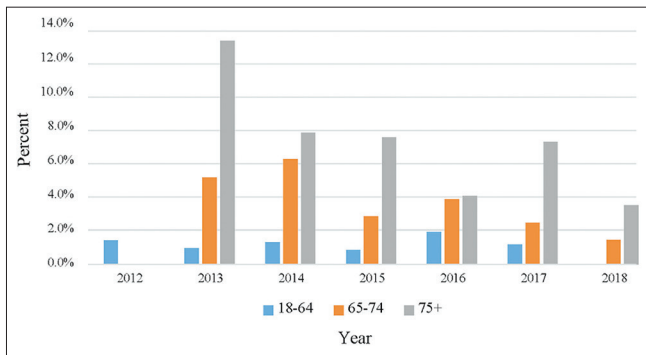


Figure 3: Infratentorial 30-day mortality by age from 2012-2018. *Age, in years, at index surgery.

poorer outcomes in this population. In particular, the ≥ 65 years patient cohort had higher rates of both major and minor complications and prolonged LOS than those reported in prior studies, which used results showing lower rates of poor outcome compared to the present study to conclude that tumor resection in older patient populations is safe in carefully selected patients.^[16,18,19] Our results reinforce the need for careful consideration and preoperative optimization of medical comorbidities and other risk factors more prevalent among older patients.^[2,33] It is also notable that many of these prior studies were conducted on patients with glioblastoma alone. Due to the high rate of mortality of glioblastoma, undergoing craniotomy for maximal safe resection confers a survival advantage that may outweigh the risks of surgery in many older patients.^[25] Thus, older glioblastoma patients may represent a unique cohort where the benefits of surgery may more often outweigh the

risks.^[28] In contrast, the infratentorial tumor population may represent a distinct cohort of brain tumor patients with unique risks related to location, more independent of tumor type. Our data demonstrating worse outcomes for older patients compared to younger patients across meningioma, metastatic, and intrinsic infratentorial lesions may support this hypothesis; however, prospective brain tumor registries or randomized trials, with more granular tumor subtype and surgical decision-making data, may be better suited to study these important questions.

From a technical standpoint, one of the most notable differences between performing supratentorial and infratentorial tumor craniotomy is patient positioning during surgery and the proximity of crucial brainstem and cranial nerve structures and functions. While in supratentorial cranial surgery, the patient is typically supine, infratentorial surgery often requires the patient to be in prone or a rotated, lateral position. Prone positioning poses intraoperative challenges in patients with comorbidities such as increasing degrees of elevated BMI and without or with concomitant sleep apnea. Older individuals may not tolerate this position as well as younger or healthier patients; Deiner *et al.* found patients aged 68 years or older to be twice as likely to experience cerebral desaturation in the prone position compared the supine position, even after adjusting for increased prone surgery duration.^[12] Furthermore, higher rates of diabetes, previous surgery or radiation, and natural changes in suboccipital cutaneous and subcutaneous tissues with age may partially explain higher rates of wound complications in the older, infratentorial tumor patient population.^[7,8,27] NSQIP, regrettably, does not

flag the reason(s) for readmission or reoperation specifically. Additional studies are needed to investigate possible explanations.

Our study found patients ≥ 65 years to be less likely to be discharged to home, more likely to be readmitted within 30 days, and more likely to have died by 30 days compared to those < 65 years. These findings present possible opportunities for the use of novel institutional quality improvement initiatives to enhance outcomes for older neurosurgical populations who may be disproportionately affected. Implementing programs such as home health aides and nurse visits for more vulnerable neurosurgical patients may mitigate the number of patients who are unable to be discharged home due to lack of support. In addition, such strategies may reduce the rate of readmissions by ensuring patients receive more structured care. With an aging population in the United States and a looming, disproportionate increase in adults aged ≥ 65 years through 2030,^[32] it is important to develop and improve systems of care for these populations. The findings in the present study highlight a need for presurgical optimization, and, potentially, novel postoperative support mechanisms for older patients undergoing infratentorial cranial surgery.

One of the limitations of the present study is the use of a national database with a relatively short (30-day) follow-up period. The absence of detailed, individual demographics, and social determinants of health factors in the NSQIP database further limits study of the effects of factors in the patients' home, social, and socioeconomic environments that may impact outcomes. Social and economic factors, physical environment, and health behaviors have been shown to account for 40%, 10%, and 30% of an individual's health outcomes, respectively, while direct clinical care factors (i.e., access and quality of care) cumulatively account for only 20%.^[20] In addition, analyses demonstrated a high correlation between disseminated cancer comorbidity and the metastatic cancer group. To adjust for this association, we excluded the disseminated cancer comorbidity variable from all analyses across age groups, which may influence results that we cannot determine from NSQIP. Finally, due to the relatively small number of patients aged 75 years or older in the intrinsic, metastatic, and meningioma tumor groups, we were unable to adjust for tumor type across all age categories. This may be in part due to a decreased number of patients aged 75 years or older who chose to undergo operation for infratentorial tumors due to risk or comorbidities. Nevertheless, there is a need for closer examination of infratentorial tumor patient outcomes for individual tumor types in light of differences in outcomes independent of age across intrinsic, metastatic, and meningioma lesions.

CONCLUSION

Patients aged 65 years or older experienced higher rates of complications, prolonged LOS, and were less likely

to be discharged home compared to the control cohort (aged 64 years or younger). The sub-population of patients aged 75 years or older experienced higher rates of 30-day readmission and mortality compared to the control group, as well. These findings highlight a need for preoperative optimization in older patients undergoing infratentorial tumor cranial surgery and for systems and processes peri- and postoperatively to enhance support for these patients.

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Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY TABLE

Supplementary Table 1: Diagnosis and procedure codes utilized for patient selection from NSQIP.

Tumor category	Diagnosis codes	Procedure codes
Intrinsic	ICD-9: 191.xx, 225.0, 237.5, 239.6 ICD-10: C71.xx, D33.0 – D33.2, D43.0 – D43.2	CPT: 61518, 61520,
Metastatic	ICD-9: 198.3 ICD-10: C79.30 – C79.32	61526, and 61530
Meningioma	ICD-9: 192.1, 192.3, 225.2, 225.4, 237.6 ICD-10: C70.0, C70.1, C70.9, D32.0, D32.1, D32.9, D42.0, D42.1, D42.9	CPT: 61519

*ICD-9 and ICD-10: International Classification of Disease Codes ninth and tenth edition respectively, CPT: Current procedural terminology

Supplementary Table 2: Listing of minor and major complications.

Minor complications	Major complications
Superficial surgical site infection, urinary tract infection, deep venous thrombosis/ thrombophlebitis, and <i>C. difficile</i> infection	Deep incisional surgical site infection, organ or space surgical site infection, sepsis, septic shock, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, more than 48-h postoperative ventilator-assisted respiration, progressive renal insufficiency, acute renal failure, cardiovascular accident with neurological deficit, coma of more than 24 h, peripheral nerve injury, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, graft, and prosthesis or flap failure