Predictors of Severe Complications in Intracranial Meningioma Surgery: A Population-Based Multicenter Study

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■ OBJECTIVE: **To investigate predictors of complications after intracranial meningioma resection using a standardized reporting system for adverse events.**

■ METHODS: **A retrospective review was conducted in a Scandinavian population—based cohort of 979 adult operations for intracranial meningioma performed at 3 neurosurgical centers with population-based referral between January 1, 2007, and June 30, 2013. Possible predictors of severe complications were identified and analyzed in univariable analyses. Variables with a P value < 0.10 were included in a multivariable model.**

■ RESULTS: **Severe complications were observed in 68 (7%) operations. Univariable analyses identified patient age >70 years ($P < 0.001$), male sex ($P = 0.03$), Charlson Comorbidity Index >1 ($P = 0.02$), Simpson grade >3 ($P = 0.03$), Karnofsky performance scale score <70 ($P < 0.001$), and duration of surgery >4 hours ($P < 0.001$) as significant predictors of severe complications. Age >70 (odds ratio = 2.5, $P < 0.01$), duration of surgery >4 hours (odds ratio = 3.2, $P < 0.001$), and Karnofsky performance scale score <70 (odds ratio = 2.5, $P < 0.01$) were independent predictors of severe complications in the multivariable regression analysis.**

■ CONCLUSIONS: **Severe complications after meningioma resection are more encountered often in elderly patients (>70 years old), dependent patients (Karnofsky performance scale score <70), and patients who underwent longer lasting surgery (>4 hours). Patient selection, including careful consideration of the individual risk-benefit ratio, is important in improving the safety of intracranial meningioma resection.**

INTRODUCTION

Intracranial meningiomas represent 30% of all primary intracranial tumors (31). As the oldest segment of the population continues to increase along with increased use of magnetic resonance imaging (MRI), the incidence of intracranial meningiomas is expected to increase (17, 29). In patients with a growing or symptomatic meningioma, craniotomy with tumor resection is usually the first-line treatment. Although surgical resection offers a potential cure and preservation or even improvement of neurologic function, it is associated with morbidity and mortality (10, 19). A standardized way of reporting adverse events was introduced for neurosurgical procedures in recent years (16). For meningioma surgery, standardized reports on complications are so far lacking. Most studies on complications and adverse events after meningioma surgery are single-institution series spanning previous decades with limited external validity and questionable relevance to contemporary microneurosurgical approaches. The results from these studies are varied and conflicting, possibly secondary to the patient selection, study length, and methodology (4, 10, 13, 20, 22, 30). Nevertheless, old age and reduced functional status have often been

Key words
- Charlson Comorbidity Index
- Complications
- Ibanez classification
- Karnofsky performance scale
- Meningioma
- Outcome

Abbreviations and Acronyms
CI: Confidence interval
KPS: Karnofsky performance score
MRI: Magnetic resonance imaging
OR: Odds ratio

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mentioned as predisposing factors to poor outcome after intracranial meningioma surgery (23). In this retrospective, population-based, multicenter study, we explored frequencies and predictors of severe complications occurring within 30 days after intracranial meningioma surgery using a standardized reporting form of adverse events.

MATERIALS AND METHODS

The Regional Committee for Medical and Health Research Ethics in Central Norway and the Regional Ethics Committee in Stockholm, Sweden, approved the study protocol.

Patients

All adult patients (≥18 years old) with a histologically confirmed meningioma treated with craniotomy and tumor resection in the period between January 1, 2007, and June 30, 2013, were eligible for inclusion. Patients operated with a transsphenoidal approach and patients undergoing biopsy only were excluded.

Patients from a consecutive population-based cohort at 3 neurosurgical departments were included. Statistics Norway and Statistics Sweden were used to estimate the mean population of the catchment areas of the hospitals in the study period. The study centers were University Hospital of North Norway ($n = 466,699$; 14% of study total [Statistics Norway]), St. Olavs University Hospital representing Central Norway ($n = 673,874$; 21% of study total [Statistics Norway]), and Karolinska University Hospital representing the greater Stockholm area and Gotland ($n = 2,129,919$; 65% of study total [Statistics Sweden]). The Scandinavian public health care system with regional neurosurgical centers and strict regional referral practice limits the possibility of referral bias and ensures a representative population-based study.

Treatment Characteristics

All patients were evaluated with contrast-enhanced MRI before surgery unless contraindicated. Steroids were administered to selected patients with tumor edema verified by preoperative MRI. Prophylactic anticonvulsants were not routinely administered. Tumor resection was performed using standard microneurosurgical techniques with additional frameless neuronavigation, intraoperative ultrasound, and electrophysiologic monitoring if deemed necessary. At Karolinska University Hospital in Sweden, cloxacillin 2 g was administered before surgery; cefalotin 2 g was the antibiotic of choice at both Norwegian neurosurgical centers.

Study Variables

Data were collected from electronic patient charts. Patient characteristics and preoperative status including Charlson Comorbidity Index (6) and Karnofsky performance scale (KPS) score (27) were registered. Tumor characteristics included location (falcine/parasagittal, convexity, sphenoid wing, olfactory/planum/sella, and infratentorial/other); duration of surgery as a marker of surgical difficulty grouped into <2 hours, 2–4 hours, and >4 hours; histopathologic grading (21); and Simpson grade of resection (28). Adverse events within 30 days were classified according to Ibanez et al. as follows: grade I, any non–life-threatening deviation from normal postoperative course treated without invasive procedures; grade II, complications requiring invasive management such as surgical, endoscopic, and endovascular procedures; grade III, life-threatening adverse events requiring treatment in an intensive care unit, subdivided into IIIa, complications involving single-organ failure, and IIIb, complications involving multiorgan failure; and grade IV, deaths as a result of complications (16).

Statistical Analysis

Outcome was classified in 2 clinically relevant subgroups: 1) patients with no or nonsevere complications (Ibanez grade I–II); 2) patients with major complications (Ibanez grade III–IV). We used quantile-quantile plots to test whether data were normally distributed. Categorical variables were assessed with χ^2 test. Univariable analyses included screening of all gathered outcome predictors, with age as a continuous variable, whereas all other predictors were categorical. Outcome predictors with a P value ≤ 0.1 were included in a final multivariable regression model. To test if the model was robust, the variables were also analyzed with full information (i.e., no categorization). $P \leq 0.05$ was considered statistically significant. We used SPSS for Windows version 18.0 (SPSS, Inc., Chicago, Illinois, USA) to analyze data.

RESULTS

We identified 979 operations with craniotomy and resection of intracranial meningioma performed during the study period. There were 123 operations (13%) performed at University Hospital of Northern Norway, 230 operations (23%) performed at St. Olavs University Hospital, and 626 (64%) operations performed at Karolinska University Hospital. The difference between expected proportion of caseload compared with the actual caseload was not significant ($P = 0.93$). Crude incidence rates of craniotomy and meningioma resection were 4.1/100,000/year at University Hospital of North Norway, 5.3/100,000/year at St. Olavs University Hospital, and 4.5/100,000/year Karolinska University Hospital.

Patient Characteristics

Mean patient age was 57.1 years ± 12.5, and 675 (69%) patients were female. In 911 (93%) operations, patients experienced no or nonsevere complications (Ibanez grade I–II); in 68 (7%) operations, patients experienced severe complications or death (Ibanez grade III–IV). There was no difference in severe complications between centers (7%, 4%, and 8%, $P = 0.18$). The overall 30-day mortality was 6 of 979 (0.6 %), and 4 of 6 deaths were due to surgical complications. Baseline and treatment characteristics for the 2 complications groups are presented and compared in Table 1. Patients with severe complications were older, were more often men, had more comorbidities, had lower functional status, more often underwent subtotal resection, and underwent longer duration surgery.

Ordinal variables may be difficult to interpret in multivariable analyses because each step may not be uniform; we used age >70 years and duration of surgery >4 hours as categorical variables because there were marked differences in the proportion between groups (Table 1). As seen in Figure 1, the independent predictors for experiencing severe complications were age >70 years ($P \leq 0.01$, odds ratio [OR] = 2.5, 95% confidence interval [CI] = 1.3–4.6), duration of surgery >4 hours ($P < 0.001$, OR = 3.2,

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