Resection of meningiomas in octogenarians: a comparison with a younger geriatric population

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OBJECTIVE Intracranial meningiomas (ICMs) may be diagnosed in octogenarians. Since the lesions are rarely life-threatening, surgery is a questionable choice in this age group. The authors' aim in this study was to analyze factors associated with the extent of resection (EOR), overall survival (OS), and postoperative complications in octogenarians undergoing ICM surgery, by using a cohort of septuagenarians as a reference.

METHODS All patients ≥ 70 years of age who underwent surgery at Oslo University Hospital for an ICM between 1990 and 2010 were included in this study. Data on these cases were retrospectively (1990–2002) and prospectively (2003–2010) acquired from a databank belonging to Oslo University Hospital. All related preoperative imaging studies or reports (earlier cases) were reviewed to confirm tumor location, the presence of bone invasion, and the postoperative EOR.

RESULTS In this study, 49 octogenarians (29 females [59.2%], mean age 83.3 ± 2.5 years) were compared with 272 septuagenarians (173 females [63.6%], mean age 74.3 ± 2.7 years). Forty octogenarians (81.6%) and 217 septuagenarians (79.8%) underwent gross-total resection. Simpson grade IV resection was achieved in 9 octogenarians (18.4%) and 4 septuagenarians (1.4%), while Simpson grade V resection was obtained in 4 septuagenarians (1.4%). Postoperative complications were similar in both groups, and 4 octogenarians (8.2%) and 11 septuagenarians (4.1%) died within 30 days after surgery ($p = 0.25$). No octogenarian underwent adjuvant radiotherapy. The OS was 4.2 ± 2.8 years in the octogenarians and 5.8 ± 4.4 years in the septuagenarians ($p < 0.001$). Female sex (OR 0.36, 95% CI 0.14–0.93; $p = 0.03$) and a preoperative Karnofsky Performance Scale score ≥ 70 (OR 0.27, 95% CI 0.10–0.72; $p = 0.009$) were correlated to the OS.

CONCLUSIONS Octogenarians undergoing surgery for ICMs had an overall reduced OS compared to septuagenarians. However, the clinical relevance of this difference in OS is debatable and has to be put in perspective with expected survival without surgery. Data on symptoms upon admission, EOR, invasive tumor features, and postoperative complications in octogenarians are similar to those observed in septuagenarians. Therefore, the decision concerning whether surgery should be performed must be based on a case-by-case discussion, and surgery should not be immediately dismissed when it comes to ICMs in octogenarians.

<https://thejns.org/doi/abs/10.3171/2020.7.FOCUS20306>

KEYWORDS meningioma; elderly; overall survival; microsurgery; oncology

INTRACRANIAL meningiomas (ICMs) are mostly benign lesions representing approximately 30% to 40% of all primary tumors of the central nervous system.^{1,2} Given an aging population and greater availability of MRI, ICMs are increasingly diagnosed.³ In patients with growing and/or symptomatic meningiomas, resection is the preferred treatment option.¹ As most meningiomas affect patients

sometime between their fifth decade and the years following their retirement, it is not uncommon to diagnose ICMs in patients older than 80 years of age.^{4–6} The majority of Western countries define retirement age as beginning during the seventh decade. It is expected that a substantial proportion of patients between 70 and 79 years of age enjoy a more independent status than patients 80 years and

ABBREVIATIONS EOR = extent of resection; GTR = gross-total resection; ICM = intracranial meningioma; KPS = Karnofsky Performance Scale; OS = overall survival; OUH = Oslo University Hospital; RLE = residual life expectancy; WHO = World Health Organization.

SUBMITTED April 8, 2020. **ACCEPTED** July 17, 2020.

INCLUDE WHEN CITING DOI: 10.3171/2020.7.FOCUS20306.

older. In 2018, for example, about 1.5% of Swiss people 65–79 years of age were living in retirement homes, compared with 15.3% of octogenarians.⁷

Among several factors, continual advances in socio-medical care worldwide are allowing patients to live longer and stay in better shape.⁸ As a result, patients may enjoy several years of healthy autonomous as well as independent life after retirement. In parallel, technical and medical innovations in microsurgery and anesthesiology have had a tremendous impact on the surgical management of brain tumors,^{9–11} up to a point at which cranial surgery is considered even in patients of advanced ages.^{6,10,12–14} To do so, a thorough assessment of the benefit-to-risk ratio is of paramount importance, especially when it comes to ICM surgery in the elderly.

Regarding functional impairment, 1.9% of people 65–79 years of age were unable to carry out daily housework tasks, compared to 6.3% in octogenarians.⁷ Moreover, 1.8% of septuagenarians had difficulty taking care of themselves (showers, daily basic care) versus 5.3% of octogenarians. Last, 7.9% of people 65–79 years old reported difficulty with walking even short distances versus 15% of octogenarians.⁷ Consequently, 80 years of age seems to represent some kind of “functional threshold” observed in the geriatric population.

ICMs are often cured by surgery;^{11,14–16} they are rarely life-threatening but may have negative effects on function and may impair a patient’s quality of life.¹ This raises an important question regarding the appropriateness of surgery in the very elderly.¹⁷ Our aim was to analyze specific factors associated with the extent of resection (EOR), overall survival (OS), and postoperative complications in octogenarians (≥ 80 years old) undergoing craniotomies for ICMs, by comparing that group with a cohort of septuagenarians (70–79 years old) used as a reference.

Methods

Patient Cohorts

Data were retrospectively (1990–2002) and prospectively (2003–2010) acquired from a databank belonging to Oslo University Hospital (OUH) that covers approximately 3 million inhabitants, constituting up to 60% of the Norwegian population.

All patients 70 years or older who underwent surgical resection of an ICM at OUH during the study period were included. All related preoperative imaging studies or reports (earlier cases) were reviewed to confirm the tumor location, the presence of bone invasion, and the postoperative EOR.

The neurosurgical teams of OUH performed surgery in all patients included in the study. The EOR was assessed using the Simpson grading system,¹⁸ based on data from the surgical report in conjunction with postoperative imaging. Gross-total resection (GTR) was defined as Simpson grade I–III resection in accordance with the latest recommendations.^{1,10} Any cause of death was considered in the analysis of the OS.

The histopathological diagnosis and the World Health Organization (WHO) grading of ICMs were confirmed by a senior, experienced neuropathologist. The 2016 WHO

grading system was used to classify the histological characteristics of meningiomas. The WHO criteria changed during the study period. From 1990 to 2001, the tumors were classified as 1) benign, 2) atypical, or 3) anaplastic; later they were reclassified according to the 2016 WHO classification as 1) benign = WHO grade I, 2) atypical = WHO grade II, and 3) anaplastic = WHO grade III.

Ethics

The study was regulated by the Personal Data Act/Personal Health Data Filing System Act and approved by the Data Protection Official at OUH (2017/5204). Informed consent was not required according to the Personal Data Act/Personal Health Data Filing System Act.

Statistical Analysis

Statistical analysis was performed using R version 3.5.1 (<https://www.r-project.org>). Significance was set at $p = 0.05$. A multivariate analysis was performed using a linear generalized model approach. To do so, the variables considered were patient’s age, sex, preoperative Karnofsky Performance Scale (KPS) score, and clinical status as well as tumor location, WHO histopathological grade, and the presence of bone invasion. Also, the presence of a postoperative complication and the use of adjuvant radiation therapy were considered. Mean values are reported with standard deviations ($\pm$ SD).

Results

Baseline Demographics and Symptoms on Admission

Baseline demographics and symptoms on admission are summarized in Table 1. The demographic, radiological, surgical, and postoperative data obtained in the 49 patients allocated to the ≥ 80 years of age cohort (29 females [59.2%], mean age 83.3 ± 2.5 years) were compared to those in a reference cohort of 272 patients 70–79 years of age (173 females [63.6%], mean age 74.3 ± 2.7 years).

Regarding preoperative KPS scores and presenting symptoms on admission, the two subgroups were similar, despite the fact that the ≥ 80 years of age group displayed a tendency toward a reduced preoperative KPS score when compared to patients 70–79 years of age. However, this difference did not reach statistical significance (73.4 ± 44.6 vs 86 ± 34.7 , respectively; $p = 0.06$). In the ≥ 80 years of age cohort, 4 patients (8.2%) were asymptomatic on admission, 13 (26.5%) presented with seizures, 19 (38.8%) had intracranial hypertension, and 33 (67.3%) presented with a focal neurological deficit; similar numbers and proportions were found in the reference cohort (Table 1).

Tumor Characteristics

Baseline tumor characteristics are summarized in Table 1. In the ≥ 80 years of age cohort, the majority of patients (44 patients, 89.8%) harbored WHO grade I meningiomas, while 4 patients (8.2%) had WHO grade II and 1 patient (2.0%) had WHO grade III tumors. The following distribution of WHO grades was observed in the 70–79 years of age cohort: 248 patients (91.2%) with WHO grade I, 17 (6.2%) with WHO grade II, and seven (2.6%) with

TABLE 1. Baseline demographics and clinical, radiological, surgical, and outcome data in geriatric patients stratified by age group

	Patients ≥80 Yrs of Age		Patients 70–79 Yrs of Age		p Value
	n = 49	%	n = 272	%	
Baseline demographics & symptoms on admission					
Age in yrs, mean ± SD	83.3 ± 2.5		74.3 ± 2.7		
Sex					0.63
F	29	59.2	173	63.6	
M	20	40.8	99	36.4	
Preop KPS score, mean ± SD	73.4 ± 44.6		86 ± 34.7		0.06
Presenting symptom					
Asymptomatic	4	8.2	13	4.8	0.28
Seizures	13	26.5	85	31.2	0.61
ICH	19	38.8	86	31.6	0.33
Focal neurological deficit	33	67.3	161	59.2	0.34
Tumor characteristics					
WHO grade					0.82
I	44	89.8	248	91.2	
II	4	8.2	17	6.2	
III	1	2.0	7	2.6	
Skull base tumor	13	26.5	112	41.2	0.06
Bone invasion	6	12.2	46	16.9	0.53
Surgical outcome					
Simpson grade					0.87
I	20	40.8	104	38.2	
II	16	32.7	100	36.8	
III	4	8.2	13	4.8	
IV	9	18.4	51	18.8	
V	0	0	4	1.5	
GTR	40	81.6	217	79.8	0.80
Postop complications					
Hematoma	3	6.1	14	5.1	0.73
Infection	0	0.0	9	3.3	0.36
Neurological worsening	6	12.2	29	10.7	0.42
30-day mortality	4	8.2	11	4.0	0.25
Adjuvant radiotherapy	0	0	3	1.1	1
OS in yrs, mean ± SD	4.2 ± 2.8		5.8 ± 4.4		<0.001

GTR = gross-total resection as defined by the European Association for Neuro-Oncology (Simpson grades I–III); ICH = intracranial hypertension.

Boldface type indicates statistical significance.

WHO grade III. Skull base location was found in 13 patients (26.5%) ≥ 80 years of age and 112 patients (42.3%) 70–79 years of age ($p = 0.06$). The incidence of bone invasion was found to be similar between both cohorts (6 patients [12.2%] in the ≥ 80 years of age group vs 46 patients [16.9%] in the 70–79 years of age group).

Surgical Management

Data on surgical management of ICMs in both cohorts are shown in Table 1. GTR was achieved in 40 patients (81.6%) in the ≥ 80 years of age cohort and in 217 patients (79.8%) in the 70–79 years of age cohort. More specifically,

a Simpson grade I resection was achieved in 20 patients (40.8%) in the ≥ 80 years of age group and in 104 patients (38.2%) in the 70–79 years of age cohort, whereas Simpson grade IV was achieved in 9 patients (18.4%) in the ≥ 80 years of age cohort and in 51 patients (18.8%) in the 70–79 years of age cohort. No biopsies were performed in the ≥ 80 years of age cohort, while Simpson grade V resection was achieved in 4 patients (1.4%) in the 70–79 years of age cohort.

The occurrence of postoperative complications (hematoma, infection, and/or neurological worsening) was equally distributed between both groups. Four patients (8.2%)

TABLE 2. Predictive factors of overall survival in patients ≥ 80 years of age

	Overall Survival	
	OR (95% CI)	p Value
Female sex	0.36 (0.14–0.93)	0.03
Preop KPS score ≥ 70	0.27 (0.10–0.72)	0.009
WHO grade	1.45 (0.32–6.55)	0.63
Skull base location	1.47 (0.25–2.24)	0.61
Simpson grade	1.05 (0.67–1.66)	0.83
Postop hematoma	1.73 (0.18–16.69)	0.63
Postop radiation therapy	1.14 (0.22–5.89)	0.87

Boldface type indicates statistical significance.

in the ≥ 80 years of age cohort and 11 patients (4.0%) in the 70–79 years of age cohort died within 30 days after surgery ($p = 0.25$). In the ≥ 80 years of age group, no patient underwent adjuvant radiotherapy, whereas 3 patients (1.1%) in the 70–79 year of age cohort did so.

Overall Survival

The OS was 4.2 ± 2.8 years and 5.8 ± 4.4 years in the ≥ 80 and 70–79 years of age cohorts, respectively ($p < 0.001$) (Table 1).

Predictive Factors of Overall Survival

The predictive factors considered in the analysis are shown in Table 2. Among sex, preoperative KPS score ≥ 70 , WHO grade of tumor and Simpson grade of resection, skull base location of tumor, the occurrence of postoperative hematoma, and the use of postoperative radiation therapy, only female sex (OR 0.36, 95% CI 0.14–0.93; $p = 0.03$) and preoperative KPS score ≥ 70 (OR 0.27, 95% CI 0.10–0.72; $p = 0.009$) were correlated to the OS.

Discussion

In this single-center study, we provide data on geriatric patients divided into 49 octogenarians and 272 septuagenarians, showing that octogenarian patients did not display a higher incidence of complications or 30-day mortality after surgery for ICMs. The OS was the only statistically different variable between the two cohorts. To our knowledge, this is the first publication to assess such pre- and postoperative factors in octogenarians compared to septuagenarians.

Both groups shared similar characteristics in sex distribution, symptoms upon admission, bone invasion, EOR, postoperative complications, and adjuvant therapy. As previously reported, skull base ICMs were underrepresented in octogenarians (26.5% vs 42.3% in the 70–79 years of age cohort; $p = 0.06$), indicating that skull base ICMs are generally treated by surgery at younger ages,^{16,19–24} reflecting a selection bias.

As the incidence of postoperative complications and 30-day mortality were similar between the two groups, the slightly shorter OS for octogenarians (mean 1.6 years) is probably related to the age of the patients rather than

to the surgery or the pathology itself, since the OS was calculated regardless of the cause of death. This is of paramount importance, as it indicates that biology is the most determinant variable for survival and not the intervention per se. In this perspective, we support a surgical attitude toward meningiomas, even in octogenarians, as long as patients are carefully selected on the basis of their preoperative functional status and general condition.

The baseline KPS score on admission was slightly lower in the octogenarians than in the septuagenarians (mean KPS scores 73.4 ± 44.6 vs 86 ± 34.7 ; $p = 0.06$). The reason for this probably lies in stricter patient selection prior to surgery in the octogenarian group. There is potential for a dramatic effect of surgical intervention on functional status. Hence, only those octogenarians who experienced tumor-related impairment of functional status and who were otherwise in good shape to withstand surgery, as well as subsequent hospitalization, were treated surgically. Conversely, older patients who presented with preserved functional status and an incidental, asymptomatic ICM were probably not deemed good candidates for surgery. This assumption is also supported by previously reported data showing that elderly patients with surgically managed ICMs have a higher in-hospital mortality rate, higher rate of discharge to a facility other than home, and longer length of hospital stay.²⁵ However, one must keep in mind that stereotactic radiosurgery is a viable option for octogenarians and septuagenarians presenting with smaller meningiomas and medical contraindications to surgery.²⁶

The balance of risks should be carefully assessed, and only those patients with impaired functional status are likely to benefit from surgery. Furthermore, the KPS score can be influenced by chronic medical conditions or past surgical interventions, potentially impairing the patient's functional status; this is particularly true for the ≥ 80 years of age group, making it difficult to discern the impact of the ICM itself on the patient's KPS score. Unfortunately, we were not able to retrieve data on comorbidities in our cohort, which limits the analysis and elaboration of the frailty score.

Appropriateness of Surgical Management of ICMs in Octogenarians

Nowadays, neurosurgeons face an increasingly aging population on a daily basis. The surgical decision-making for octogenarians is challenging with respect to the benefit-to-risk assessment. This is particularly true for benign ICMs, which can be fully controlled by maximal surgical resection and appropriate follow-up. Unlike glioblastoma multiforme, ICMs do not dramatically reduce the life expectancy of patients, as long as appropriate management is applied.^{1,5,27} From the perspective of surgical risk assessment, our data show that octogenarians do not have higher incidences of postoperative hematomas, infection, or neurological worsening than septuagenarians. In addition, the 30-day mortality rate is comparable between groups. These data are in line with findings presented in previously published literature;^{4,6,12,28} therefore, ICM surgery should be considered for octogenarians as long as the tumor is accessible to surgery and the patient presents with some potential of recovery.

FIG. 1. Overall survival of patients ≥ 80 years old (dark gray) and of those between 70 and 79 years old (light gray). y.o. = years old.

Is It Worth It?

Residual life expectancy (RLE) should also be thoroughly considered when confronted with an octogenarian with a symptomatic ICM. The central questions are: 1) is the ICM likely to shorten the patient's life, and 2) can resection prevent this with an acceptable risk?

In 2010 (i.e., the final year of our study), the overall RLE in Norway for an 83-year-old (mean age of our octogenarian cohort) in the general population was 7.2 years (6.3 and 7.7 years for men and women, respectively).²⁹

Our data on OS are certainly limited; yet we are able to show a limited benefit regarding RLE following meningioma surgery in the ≥ 80 years of age group. As shown in Table 1 and Fig. 1, the OS of the octogenarians was a mean of 1.6 years shorter than that of the septuagenarians (4.2 ± 2.8 years vs 5.8 ± 4.4 years; $p < 0.001$). Despite the fact that the difference is statistically significant, its clinical relevance is debatable, since it has to be put in the perspective of expected survival in elderly patients without surgery. Unfortunately, we cannot provide a conclusion on this point, since only cases managed surgically were involved in this study.

Nevertheless, it is not possible to discriminate between excessive mortality due to the ICMs and age-related natural history, since we do not provide data on disease-specific mortality. The decision to operate or not must be based on a case-by-case discussion, relying on the surgeon's clinical judgment, the patient's potential for recovery, and the patient's involvement in the discussion.

Case selection in elderly patients may be difficult, especially in borderline situations (e.g., a patient with KPS score 60 and a right frontal convexity meningioma). Refining patient selection is therefore important. Konglund et al.⁶ reported on the usefulness of the SKALE score (based on sex, KPS score, American Society of Anesthesiologists class, location of tumor, and peritumoral edema grading

system) to reflect the mortality rate at 1 month and 1 year after surgery in 80- to 90-year-old patients presenting with symptomatic ICMs. Together with a thorough preoperative assessment, the SKALE score seems a useful and straightforward tool to select elderly patients for surgery.⁶ Other groups have assessed scores such as the Clinical-Radiological Grading System and the Geriatric Scoring System as well as prognostic factors for outcomes in the elderly.³⁰⁻³⁴ Notably, it was shown by Konglund and colleagues¹² that elderly patients, between 60 and 84 years of age, who underwent surgery for ICMs significantly improved in cognitive function after surgery. This is of paramount importance because a significant proportion of patients with ICMs present with impaired cognitive function upon admission.³⁵

Finally, our results show that the incidence of postoperative complications requiring repeated surgery in the ≥ 80 years of age cohort was similar to that observed in the 70-79 years of age cohort. In a recent study from Steinberger et al.,³⁶ age older than 80 years was an independent predictor for postoperative complications, increased 30-day mortality rate, and extended hospital length of stay. Similarly, Lassen et al.³⁷ reported a surgical mortality rate at 30 days of 2.3% and found that age ≥ 60 years was a risk factor in a cohort of 2630 patients who underwent craniotomies for intracranial tumors. In line with previously reported data from Steinberger et al.,³⁶ our results on 30-day mortality rates show an increase to 4.0% in septuagenarians, which was even higher (8.2%) in octogenarians. Together, these data illustrate the relationship between age and surgical mortality in patients with ICM.

Strengths and Limitations

Our dataset offers a comprehensive and very extended source of information on patients with ICMs with complete follow-up, since only one patient was lost during the study period, due to moving abroad. The clinical setting, the number of patients, and the length of follow-up (up to 21 years) are also strengths of our clinical study. All patients with a postoperative complication or disease recurrence were systematically referred again to our tertiary center. The data stem from one neurosurgical center with mostly homogeneous surgical practices. All patients in the specified age groups who harbored a histologically confirmed meningioma were included, which reduces selection bias.

The partial retrospective nature of data collection prior to 2003 is certainly a limitation. Grading of tumors was done according to two different WHO classifications, as mentioned in the *Methods*. Tumor size and molecular biomarkers of proliferation such as MIB-1 were not available due to the long period of data collection, which began in 1990. Despite being known factors influencing OS,³⁸ data on these factors are not available. Surgical and monitoring techniques evolved during the study period and probably also reflect on the OS. The difference in the proportions of Simpson grade IV surgeries in the octogenarians and septuagenarians (18.4% and 18.8%, respectively) possibly induced a bias in the survival results. Only patients undergoing surgery were included in the study; therefore, no data on observation, radiosurgery, or fractionated radiation therapy could be retrieved.

In terms of mortality, no disease-specific survival was registered. Therefore, no conclusion on ICM-related excessive mortality rate can be drawn on the basis of our data. Finally, the reported survival data are applicable to Norway. Although corroborated by US data from the Centers for Disease Control and Prevention, Norwegian data are probably not translatable to the rest of the world and, therefore, the RLE should be analyzed in other countries.

Conclusions

Our results suggest that the benefit of ICM surgery in octogenarians is limited with respect to OS, because we observed a reduced OS in this age cohort compared to data obtained in the 70–79 years of age cohort and compared to data available from the general population. However, data on symptoms upon admission, the EOR, invasive tumor features, and postoperative complications are similar to those observed in younger geriatric patients. As the disease-specific mortality rate of octogenarians who have been surgically treated for ICMs is still undetermined, the decision to operate or not must be based on a case-by-case discussion involving clinical judgment and patient adherence to the treatment. Therefore, surgery should not be immediately dismissed when confronted with a patient $\geq$ 80 years of age who harbors an ICM.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Corniola, Meling. Acquisition of data: Meling. Analysis and interpretation of data: Corniola, Meling. Drafting the article: Corniola, Meling. Critically revising the article: all authors. Reviewed submitted version of manuscript: Corniola, Meling. Approved the final version of the manuscript on behalf of all authors: Corniola. Statistical analysis: Lemée. Study supervision: Meling.

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