



Skull base versus non-skull base meningioma surgery in the elderly

Torstein R. Meling^{1,2} · Michele Da Broi¹ · David Scheie³ · Eirik Helseth^{1,2}

Received: 4 March 2018 / Revised: 17 May 2018 / Accepted: 29 June 2018 / Published online: 5 July 2018
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Abstract

To compare outcomes after surgery for skull base meningiomas (SBMs) with non-skull base meningiomas (NSBMs) in the elderly. Overall, 128 consecutive patients ≥ 70 years of age with intracranial SBMs operated between 1990 and 2010 were compared to 193 consecutive patients ≥ 70 years of age with NSBMs operated within the same time period. Median age at surgery was 75.0 years (mean 75.7, range 70.0–92.4). Follow-up was complete with median 4.7 years (mean 5.5, range 0–19). The female-to-male ratio was 2.8 for SBMs and 1.3 for NSBMs ($p < 0.005$). The groups had similar preoperative KPS (median 80, range 20–100), but SBMs presented significantly more frequently with raised ICP (RR = 2.2, $p < 0.005$) and less frequently with seizures (RR = 0.6, $p < 0.05$). WHO I was significantly more frequent in SBMs ($p < 0.005$). Gross-total resection (GTR) was less frequent in SBMs (63 vs 82%) (RR = 2.1, $p < 0.0001$). SBMs were similar to NSBMs with respect to neurological outcome at 6–12 months, reoperations for hematomas, postoperative infections, and 30-day mortality. Retreatment rates and time to retreatments were also similar. There were no differences between the two groups with respect to risk of retreatment and overall survival (OS) at 5, 10, 15, and 20 years. In elderly patients with SBMs selected to surgical treatment, the risks of surgery, risk of retreatment, and OS were similar to NSBMs. Therefore, surgery for SBMs may be considered as safe as NSBMs in the elderly population.

Keywords Craniotomy · Intracranial tumor · Meningioma · Retreatment-free survival · Overall survival

Introduction

With the increase of life expectancy, the number of meningiomas identified in the elderly population has grown constantly over the last decades. The incidence of meningiomas increases with age and even among people over 80 years, the rate continues to be high (age-adjusted rate 52.28/100000) [46]. The availability of MRI and CT scan has contributed remarkably to increase the number of meningiomas detected in older patients. The prevalence of incidentally found meningiomas in patients 75 years of age or older is 1.6% [70]. Therefore, a larger number of asymptomatic or oligosymptomatic elderly patients are referred to neurosurgical departments, posing a

dilemma for neurosurgeons who must carefully weigh the treatment options.

At present, there is no common consensus regarding intracranial meningioma surgery in the elderly and the prognostic factors for surgical outcome remain rather controversial. Surgical excision of the tumor and its dural base attachment is the most common primary mode of management [18, 27]. However, considering the older patients' shorter residual life expectancy (RLE), subtotal resection (STR) with or without adjuvant radiotherapy (RT) may be a reasonable alternative to gross-total resection (GTR), especially for skull base meningiomas (SBM) [28]. Given the slow-growing nature of most intracranial meningiomas and the fact that intracranial meningiomas in older patients may have a slower growth rate compared to younger patients [28], one can even argue that the primary treatment option in SBMs in the elderly is watchful waiting.

Aggressive surgical treatment for intracranial meningiomas in older patients can increase morbidity and mortality [1, 5]. Other publications suggest that chronological age should not be considered a contraindication to surgery and that several other parameters should be taken into account, such as

✉ Torstein R. Meling
torsteinmeling@gmail.com

¹ Faculty of Medicine, University of Oslo, Oslo, Norway

² Department of Neurosurgery, Oslo University Hospital, N-0027 Oslo, Norway

³ Section of Neuropathology, Rigshospitalet, Copenhagen, Denmark

preoperative Karnofsky Performance Score (KPS), presenting symptoms, American Society of Anesthesiologists (ASA) class, and critical locations [31, 32, 45, 57, 64, 68]. However, should surgery be indicated, the treatment goal should be maximal safe tumor removal, taking the utmost care to avoid morbidity and mortality by preservation of cranial nerve functions, meticulous hemostasis, early mobilization, etc., in order to maintain a satisfactory quality of life after surgery.

Reported mortality rates after intracranial meningioma surgery in the elderly are highly variable, and conscientious patient selection is mandatory [5, 10, 19, 36]. Indeed, tumor location is of importance for surgical outcome, as well as for extent of resection (EOR) and for presenting symptoms and signs, and the role of skull base location as outcome predictor has been emphasized [7, 16, 19]. Skull base location is a negative factor in the SKALE prognostic score system [60], and given the relevance of meningioma location in younger patients [61, 62], the objective of this study is to analyze clinical outcomes, retreatment rates, retreatment-free survival (RFS), and overall survival (OS) in a consecutive series of older patients with SBM selected to surgery.

Materials and methods

Clinical setting

Oslo University Hospital (OUH) consists of two neurosurgical units (OUH-Rikshospitalet and OUH-Ullevaal) and is a tertiary referral center with a catchment area of approximately three million inhabitants (56% of the Norwegian population).

Patient cohort

A total of 321 consecutive elderly patients (≥ 70 years old) who underwent craniotomies for intracranial meningiomas between 1990 and 2010 were investigated. Clinical information was retrospectively reviewed using patients' medical and surgical records from 1990 to 2002, whereas patient data from 2003 to 2010 were prospectively collected. KPS [29] was assessed using clinical records of preoperative visits. The following variables were registered: gender, age, and presenting symptoms (seizures, increased intracranial pressure (ICP), and/or focal neurological deficits), tumor location, and Simpson grade of resection (SG) [65] postoperatively.

Tumor characteristics

The preoperative post-contrast imaging studies were reviewed to confirm tumor location, contrast enhancement, calcification,

and size of the tumors. The EOR was assessed using the SG scale. CT scans and MRIs were also reviewed to confirm degree of tumor removal. Each surgical case was approached attempting total tumor removal. The definition of SBM was based on Al-Mefty et al. [20] (Table 1), and thus, every intracranial meningioma located elsewhere was considered a non-skull base meningioma (NSBM).

Outcome

All patients underwent follow-up for the assessment of outcomes. Any re-operations for postoperative hematoma (extradural, subdural, intracerebral), reoperation for postoperative infection (extradural, subdural, intracerebral, or infected bone flap), and neurological outcome compared to preoperative status at 6–12 months postoperatively were recorded after surgery. Any retreatments for tumor recurrence by means of surgery, conventional fractionated RT, or stereotactic radiosurgery (SRS) were also recorded. The decision to retreat patients was done at the discretion of the treating physician. The primary endpoint of the study was OS for any cause of death, calculated from time of surgery to time of death or censoring. Risk of retreatment was calculated including all patients who were retreated because of recurrent meningioma, be it via craniotomy, fractionated RT, or SRS. Vital status (dead or alive) and time of death were obtained from the Norwegian

Table 1 Al Mefty's definition of skull base meningioma

Meningiomas of the anterior cranial base
Tuberculum sellae meningiomas
Olfactory groove meningiomas
Meningiomas of the orbital roof
Meningiomas of the middle cranial base
Meningiomas of the lateral and middle sphenoid wing
Meningiomas of the anterior clinoid
Meningiomas of the cavernous sinus
Meningiomas of the optic canal and orbit
Meningiomas of Meckel's cave
Cranio-orbital meningiomas
Meningiomas of the posterior clinoid and upper clivus
Meningiomas of the posterior cranial base
Clival meningiomas
Petroclival meningiomas
Sphenopetroclival meningiomas
Petrosal meningiomas
Anterior petrous meningiomas (petrous apex)
Posterior petrous meningiomas (CP angle)
Jugular foramen meningiomas
Tentorial meningiomas
Meningiomas of the temporal bone
Foramen magnum meningiomas

Population Registry (Folkeregisteret) on January 27, 2011. The surgical mortality was defined as death of any cause within 30 days of surgery [33].

Ethics

The study is 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 is not required by the Personal Data Act/Personal Health Data Filing System Act.

Statistics

Univariate statistics were calculated without assuming a Gaussian distribution using the Wilcoxon test when the variable was continuous. With categorical variables, univariate statistics were calculated using the Pearson chi-squared test. In ordinal variables, the proportional odds likelihood test was used. Survival curves were generated using the Kaplan Meier estimator, and the log-rank test was used to compare different survival curves. Relative risk ratios (RR) were calculated to estimate the strength of tumor location (SBM vs NSBM) and presenting symptoms, resection rates, neurological outcomes, and retreatment rates. The level of statistical significance was set at p value = 0.05. Descriptive statistics were reported as a median, mean, range, and 95% confidence interval (CI) if appropriate. JMP version 9 (SAS Institute Inc.) was used for all statistical analyses.

Results

Overall patient characteristics

We included in our study 321 patients ≥ 70 years with histologically verified intracranial meningiomas. Every patient underwent a craniotomy with resection and had complete follow-up from the day of surgery to the end of the study. Median follow-up was 4.7 years (mean 5.5 years, range 0–19 years) (Table 2).

Skull base vs non-skull base meningiomas

One-hundred and twenty-eight (40%) patients had SBM, while 193 (60%) had NSBM. The most common SBM locations were medial sphenoid wing ($n = 24$, 19%), tuberculum sellae/suprasellar ($n = 23$, 18%), and olfactory groove ($n = 22$, 17%), which had almost the same number of patients and represented 54% of the SBM in this series. The most common NSBM locations were convexity ($n = 111$, 58%) and parasagittal ($n = 48$, 25%) (Table 3). One patient with SBM had undergone 10 months preoperatively.

Table 2 Overall characteristics

	<i>n</i> (%)
Age	
70–79 years	272 (85%)
≥ 80 years	49 (15%)
Sex	
Male	119 (37%)
Female	202 (63%)
Preoperative KPS	
≥ 70	270 (84%)
< 70	51 (16%)
Presenting symptoms	
Asymptomatic	11 (3%)
Seizures	85 (26%)
Raised ICP	87 (27%)
Neurological deficits	229 (71%)
WHO grades	
WHO grade I	290 (90%)
WHO grade II	21 (7%)
WHO grade III	8 (3%)
Simpson grade	
Simpson grade I	133 (41%)
Simpson grade II	104 (32%)
Simpson grade III	18 (6%)
Simpson grade IV	62 (19%)
Simpson grade V	3 (1%)
Retreatment	
Any retreatment	19 (6%)
Surgery	12 (4%)
Fractionated RT	9 (3%)
Stereotactic RT	3 (1%)

Age

Median age at surgery was 75.0 years (mean 75.7 years, range 70.0–92.4 years). SBM patients were younger than those affected by NSBM (median age in SBMs 74.5 years vs NSBMs 81.3 years) ($p < 0.05$) (Table 4).

Sex

The female-to-male ratio was 2.8:1 in SBM, compared to 1.3:1 in NSBM (RR: 1.3, $p < 0.005$) (Table 4). The overall female-to-male ratio was 1.7:1 (Table 2).

Preoperative KPS

Regarding preoperative KPS, the two groups were similar (median 80 for both cohorts, range 20–100) (Table 4). Most patients had KPS ≥ 70 , and only 16% had lower KPS (Table 2).

Table 3 Tumor locations

	<i>n</i> (%)
Skull base	128 (40%)
Medial sphenoid wing	24 (19%)
Olfactory groove	23 (18%)
Lateral sphenoid wing	22 (17%)
Tentorium -intra	15 (12%)
Cerebellopontine angle	14 (11%)
Tuberculum sellae/suprasellar	10 (8%)
Petroclival	9 (7%)
Craniocervical junction/foramen magnum	5 (4%)
Tentorium-supra	4 (3%)
Middle fossa/Meckel's cave	1 (1%)
Cavernosus sinus	1 (1%)
Non-skull base	193 (60%)
Convexity	111 (58%)
Parasagittal	48 (25%)
Falx	32 (17%)
Intraventricular	2 (1%)

Presenting symptoms

Almost all patients in our cohort were symptomatic, with no difference between SBM and NSBM (SBMs 96% vs NSBMs 97%). With regard to presenting symptoms, SBMs had less often seizures (RR 0.6; $p < 0.05$), more often raised ICP (RR 2.2; $p < 0.005$), and no difference with respect to preoperative neurological deficits (SBMs 77% vs NSBMs 68%, $p = 0.09$) (Table 4).

WHO grades

The risk of higher-grade meningiomas was significantly lower for SBMs as compared to NSBMs (SBMs 2.3% vs NSBMs 13.5%) (RR 0.2; $p < 0.005$). In the SBM cohort, 123 patients (96.1%) had WHO I meningioma, and three patients (2.3%) had higher-grade lesions (WHO II or WHO III). Among NSBM patients, 167 patients (86.5%) were diagnosed with WHO I meningioma, while 26 patients (13.5%) had WHO II or III (Table 4).

Extent of resection

Patients with SBM underwent GTR (SG I and II) less frequently than those with NSBM (SBMs 63% vs NSBMs 81%). EOR by location was highly significant ($p < 0.0001$), and SBMs had a relative risk for STR (SG III, IV, and V) of 2.1 (Table 4).

Neurological outcome

Forty-seven patients (53%) with SBMs improved clinically over 6–12 months, 25 (28%) did not change, and 16 (18%)

were worsened. In the NSBM cohort, 88 patients (64%) were improved, 36 (26%) were unchanged, and 14 (10%) were worsened (Table 4). The minimal difference between the two groups reached no statistical significance ($p = 0.65$).

Complications

The postoperative infection rates (SBMs 1.6% vs NSBMs 3.6%) and postoperative hematoma rates (SBMs 7.0% vs NSBMs 4.1%) were not significantly different, despite the trends highlighted by our statistical analysis. Furthermore, the 30-day mortality rates (4.7% in both cohorts) were virtually the same (Table 4).

Retreatment

With respect to retreatment rate, ten (8%) cases with SBM were retreated. Five patients (4%) underwent surgery, five (4%) underwent fractionated RT, and two (2%) received SRS. In the NSBM group, nine patients (5%) underwent retreatment. Seven (4%) received surgery, four (2%) fractionated RT, and one (1%) SRS. Retreatments rates for recurrence at 6 months, 1 year, 2 years, and 5 years were 95.3, 92.2, 87.5, and 50.0% for SBMs, while they were 93.8, 91.7, 90.7, and 62.7% for NSBMs, respectively. The difference between the two groups was not significant (Table 4). The mean time from primary surgery to any retreatment was 5.1 ± 0.3 years for SBMs and 5.6 ± 0.4 years for NSBMs ($p = 0.38$).

Overall survival

OS rates at 5, 10, 15, and 20 years were 78, 50, 17, and 17% for SBMs and 82, 58, 19, and 11% for NSBMs, respectively. No significance was found between the two groups (Table 4, Fig. 1).

Discussion

In this study, 128 consecutive patients ≥ 70 years of age with intracranial SBMs were compared to 193 patients with NSBMs operated within the same time period in order to detect clinically relevant differences with regard to surgical outcome, retreatment rates, and OS. An age limit of ≥ 70 was chosen to define elderly patients as the current age of retirement is 67 years [44] but will be increased to 70 years shortly because the average life expectancy in Norway has increased by 2.3 years between 1990 and 2010 [58]. Therefore, we deemed 70 years of age to be a representative cutoff for our study's population. Secondly, many relevant published series have used the same age limit to distinguish older and younger subjects, facilitating direct comparisons [5, 9, 10, 51, 59].

Table 4 Skull base vs non-skull base

	Skull base <i>n</i> (%)	Non-skull base <i>n</i> (%)	<i>p</i> value
	128 (40%)	193 (60%)	
Age			
70–79 years	115 (90%)	157 (81%)	< 0.05
≥ 80 years	13 (10%)	36 (19%)	
Sex			
Male	34 (27%)	85 (44%)	< 0.005
Female	94 (63%)	108 (56%)	
Preoperative KPS			
100	2 (2%)	8 (4%)	NS
90	42 (33%)	52 (27%)	
80	39 (30%)	55 (29%)	
70	24 (19%)	48 (25%)	
< 70	21 (16%)	30 (16%)	
Presenting symptoms			
Asymptomatic	5 (4%)	6 (3%)	NS
Symptomatic	123 (96%)	187 (97%)	NS
Seizures	24 (19%)	61 (32%)	< 0.05
Raised ICP	47 (37%)	40 (21%)	< 0.005
Neurological deficit	98 (77%)	131 (68%)	NS
WHO grades			
WHO grade I	123 (96.1%)	167 (86.5%)	< 0.0005
WHO grade II + III	3 (2.3%)	26 (13.5%)	
Extent of resection			
Gross-total resection	80 (63%)	157 (81%)	< 0.0001
Subtotal resection	48 (37%)	35 (19%)	
Neurological outcome			
Improved	47 (53%)	88 (64%)	NS
Unchanged	25 (28%)	36 (26%)	
Worsened	16 (18%)	14 (10%)	
Complications			
Postoperative infection	2 (1.6%)	7 (3.6%)	NS
Postoperative hematoma	9 (7.0%)	8 (4.1%)	NS
30-Day mortality	6 (4.7%)	9 (4.7%)	NS
Retreatment			
Any retreatment	10 (8%)	9 (5%)	NS
Surgery	5 (3.9%)	7 (3.6%)	NS
Fractionated RT	5 (3.9%)	4 (2.1%)	NS
Stereotactic RT	2 (1.6%)	1 (0.5%)	NS
Retreatment-free survival			
6 months	95%	94%	NS
1 year	92%	92%	NS
2 years	88%	91%	NS
5 years	50%	63%	< 0.02
Overall survival			
5 years	78%	82%	NS
10 years	50%	58%	NS
15 years	17%	19%	NS
20 years	17%	11%	NS

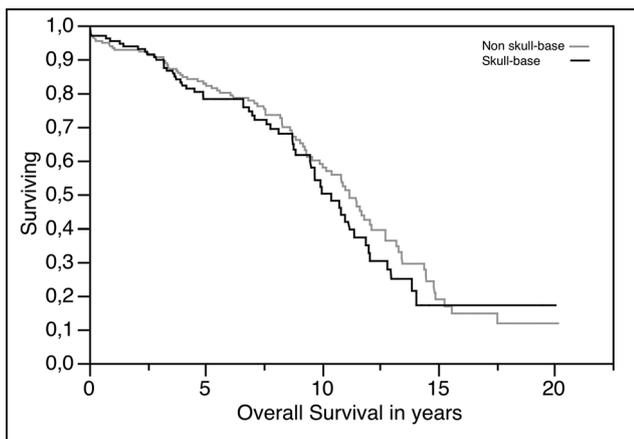


Fig. 1 Overall survival by meningioma location. The OS rates include mortality due to any cause and are not disease-specific survival. Given the advanced age of our study population, non-disease specific causes of death were most frequent

Age

The incidence of SBMs in our study was lower than that of NSBMs (SBMs 40% vs. NSBMs 60%) (Tables 3 and 4). Our results are in accordance with the majority of studies on intracranial meningiomas in the elderly, though the ratio is variable [1, 49, 68]. Noteworthy, the discrepancy was less important in series that also included the 60–70-years age class [16, 31, 64]. Buhl et al. [9] reported a minimal difference between SB and NSB location (52% vs. 48%). Conversely, authors who studied intracranial meningiomas in the ninth decade of life found higher ratios [19, 53, 60]. These findings probably reflect an underlying selection bias in surgical series, in that the threshold for surgical management of a SBM is higher than for a NSBM in the elderly. Indeed, the median age of our SBM group was significantly lower as compared to NSBM patients (median age in SBMs 74.5 vs NSBMs 81.3, $p < 0.05$). Our results are in line with the above-mentioned authors and are supported also by publications involving younger patients that show higher median ages among NSBM subjects [15, 27, 41, 62].

Sex

The overall female-to-male ratio in our cohort was 1.7:1 and is in line with series of elderly individuals [5, 11, 13], as well as with studies involving all age-classes [18, 27, 62, 67] (Table 2). However, the female-to-male ratio was 2.8:1 in SBMs and 1.3:1 in NSBMs ($p < 0.005$) (Table 4). Females had a RR of 1.6 of having a SBM. It is well known that meningiomas occur more often in women [71, 72], that this sex difference is larger in operated SBMs than in operated NSBMs [41, 50], and also larger in operated elderly patients [54]. With regard to gender as prognostic factor for outcome after surgery, Poon et al. [54] found female sex to be an

independent predictor for postoperative complications. However, our analysis does not confirm their results, and we found no correlation between sex and complications after surgery neither in SBM nor in NSBM groups.

Preoperative KPS

Regarding the preoperative KPS, there was no difference between SBMs and NSBMs (KPS ≥ 70 : 84% in both groups) (Table 4). This is in line with other series of elderly patients [11, 16, 19, 64]. However, KPS rates reported in prior studies vary considerably and this inconsistency mirrors presumably the heterogeneity of the series available in literature. For instance, more than half cohort of Proust et al. [55] had a KPS ≤ 70 , while the mean KPS was 59 according to Umansky et al. [68]. Other authors have described similar or lower KPS [1, 14, 32, 53].

Presenting symptoms

The vast majority of patients included in our study were symptomatic prior to surgery, and there was no significant difference between SBM and NSBM (SBMs 96% vs NSBMs 97%, $p = 0.70$). Presumably, our patients represent a subgroup of the elderly population with meningiomas, as most are asymptomatic and not offered treatment. According to Cornu et al. [16], surgery is not recommendable in older asymptomatic patients, and this philosophy is shared also by other authors [1, 9, 52]. Even though age per se is not a contraindication to surgery [10, 11, 64, 68], many publications suggest that surgical intervention in the elderly carries a higher morbidity and mortality risk for meningiomas [31, 51] and other brain tumors [33]. Evidence suggests that the key to success in meningioma surgery for the older patients is good patient selection [59]. Hence, the huge portion of symptomatic patients in our study, which is in accordance with a recent publication by Poon et al. [54], is probably ascribable to case selection.

In our cohort, seizures were significantly less frequent in patients with SBMs (SBMs 19% vs. NSBMs 32%, RR = 0.6, $p < 0.05$). Similarly, Poon et al. [54] found 13% seizures in NSB group and only 7% in SBMs. Reviewing the publications with the highest NSBM:SBM ratio, Djindjan et al. [21] (70% NSBMs) reported seizures in half of their patients, while D'Andrea et al. [19] (81% NSBMs) found seizures in 43% cases. On the contrary, in studies by Konglund et al. [31] (57% NSBMs) and Buhl et al. [9] (52% NSBMs), only 22 and 21%, respectively, had preoperative seizures. The trend described by these authors is in accordance with our findings. Our results are also supported by series comprising all age classes. In fact, Chen et al. [12] found NSBMs (OR = 2.13, $p < 0.005$) and advanced age (OR = 1.03 per year, $p < 0.005$) to be significant predictors of preoperative seizures.

Raised ICP was nearly twice as frequent in patients with SBM than in the NSBM group (SBMs 37% vs NSBMs 21%, RR = 2.2, $p < 0.005$). These results are in line with those reported by Poon et al. [54] and with a recent meta-analysis on supratentorial meningiomas by Englot et al. [22] who found a correlation between seizures and absence of headache, as well as seizures and NSBMs.

We found no significant difference between SBMs and NSBMs with regard to preoperative neurological deficits. This is somewhat surprising, but in most series of elderly patients, no peculiar trend is detectable for both neurological deficits and raised ICP and there are remarkable discrepancies among the authors. In fact, some of them are in accordance with our results with respect to preoperative neurological deficits [11, 14] and raised ICP [7, 16, 49, 54, 68], whereas others presented different findings [1, 9, 10, 13, 19, 32, 38]. Presumably, these differences are mostly due to patient selection for surgery.

WHO grading

SBMs had a lower risk of high-grade meningiomas (WHO II and WHO III) (SBMs 2.3% vs NSBMs 13.5%, RR = 0.2, $p < 0.0005$). These results confirm prior studies on younger [30, 62] and older patients [9, 11, 13]. Greater rates were described by Sacko et al. [60] who diagnosed 30 and 6.5% with WHO II and WHO III meningioma, respectively. With regard to higher-grade meningiomas in SB location, Nishizaki et al. [45] analyzed a series of 89 posterior fossa meningiomas and their results are paradoxically overlapping to our findings in NSBMs.

Extent of resection

With respect to EOR, GTR (SG I or SG II) was achieved in significantly fewer patients with SBM than NSBM (63 vs 81%; $p < 0.0001$) (Table 4), and the RR for STR (SG III–V) was 2.1 in SBMs. Our results (GTR 74%, STR 26%) are in line with the GTR rates reported in literature, which range from 72 to 100% [1, 8, 9, 11, 31, 53, 64, 68].

Regarding tumor location, total removal of the mass is generally easier to achieve in NSBMs and this relationship has been demonstrated in cohorts of both younger [41] and older patients, in which GTR rates for NSBMs range from 84 up to 97% [19, 31, 60, 68]. On the other hand, GTR rates for SBMs described by other authors tend to be lower [45, 54, 60] and are in accordance with the findings reported in the present study (GTR in SBMs 63%) (Table 4). However, attempting to achieve complete tumor removal in certain locations can lead to disastrous results regardless of age and some authors dissuade from aggressive surgery in the elderly [5, 11].

Complications to surgery

Quality of surgery is one of many factors that have an impact on OS, surgical mortality, and long-term clinical outcome. Rate of postoperative hematoma, rate of deep postoperative infection, and neurological deterioration after craniotomy are all well accepted indicators for quality of surgery [33]. Although some authors have correlated SB location with neurological outcome after surgery [1, 31], we did not find a significant difference between SBMs and NSBMs (Table 4). Our results are in accordance with Nishizaki et al. [45]. Indeed, according to the analysis carried out by Chen et al. [11], only preoperative KPS was significantly associated with postoperative KPS. Similar findings were reported also in cohorts that included younger patients. Indeed, Gousias et al. [25] found preoperative KPS to be the most powerful predictor of postoperative functional outcome with a hazard ratio of 35.8. Of note is that EOR was not an independent predictor of functional outcome [25]. Also, Cornu et al. [16] connected tumor location as well as low preoperative KPS and ASA score > 2 to poor outcome. Regarding neurological outcome 6 months after surgery in SBMs, 18% of our cases were worsened (Table 4). This is in line with Nishizaki et al. [45] and overlaps other series with elderly patients [7, 53, 57], but is more than twofold the rate reported by Roser et al. [59]. However, their cohort was likely tainted by selection bias. In fact, there were no significant changes in KPS after tumor resection, and surprisingly, the elderly had better outcome than younger subjects (worsened neurological outcome in elderly: 7 vs 12% in younger patients).

Postoperative hematomas are significant risk factors for surgical mortality for all brain tumors regardless histology [33]. Palmer et al. [48] identified meningioma as a risk factor for developing hemorrhage compared to intrinsic supratentorial tumors. Lassen et al. found no difference between intrinsic and extrinsic intracranial lesions, but age > 60 years was associated with increased odds of postoperative hematomas [33]. In the elderly, the rates reported for postoperative hematomas after meningioma surgery range between 3 and 20% [1, 8, 9, 11, 13, 16, 21, 23, 31, 32, 37, 60, 64, 68] (Table 5). In our cohort, 5.3% patients were reoperated for hematoma after craniotomy (mostly chronic subdural hematomas). Even though there was a trend towards SBMs having more postoperative hematomas (SBMs 7% vs NSBMs 4.1%), this did not translate into a significant result ($p = 0.26$) (Table 4).

The risk for postoperative infections is higher in meningiomas than in high-grade gliomas [33] and according to Roser et al. [59], this risk is even higher among the older cohorts for both wound and systemic infections. Postoperative infections cause prolonged hospitalization and higher costs. However, the impact of infection on long-term OS and neurological outcome is not as strong as for postoperative hemorrhage [33]. The rate of reoperation for deep infection after

Table 5 Mortality and complications in the literature

Author	Year	Cases	Age	30-Day mortality	Postoperative hematomas	Postoperative infections
Papo et al.	1983	50	≥ 65	45%	NG	NG
Djindjian et al.	1988	30	≥ 70	23.0%	10.0%	NG
Awad et al.	1989	25	≥ 70	8.0%	6.7%	4.0%
		50	61–70	6.0%		
Arienta et al.	1990	34	≥ 70	12.0%	12.0%	NG
Cornu et al.	1990	96	≥ 65	16.0%	15.0%	3.0%
Maurice-Williams et al.	1992	46	≥ 65	2.7%	20.0%	NG
Umansky et al.	1992	37	≥ 70	5.4%	8.1%	2.7%
Gijtenbeek et al.	1993	93	≥ 60	14.0%	NG	NG
Mastronardi et al.	1995	17	≥ 80	29.0%	NG	NG
Proust et al.	1997	39	≥ 70	7.6%	NG	NG
Black et al.	1998	57	≥ 65	1.8%	NG	NG
Lieu et al.	1998	36	≥ 65	11.1%	NG	NG
Pompili et al.	1998	37	≥ 75	10.8%	NG	NG
Buhl et al.	2000	66	≥ 70	7.6%	15.2%	NG
Bateman et al.	2005	2304	≥ 80	7.0%	NG	NG
			70–79	3.0%	NG	NG
Caroli et al.	2005	90	≥ 70	6.7%	NG	NG
D'Andrea et al.	2005	37	≥ 80	13.5%	NG	NG
Boviatsis et al.	2007	108	≥ 65	6.5%	7.4%	NG
Roser et al.	2007	43	≥ 70	0.0%	NG	NG
Sacko et al.	2007	74	≥ 80	0.0%	4.0%	1.4%
Cohen-Inbar et al.	2009	250	≥ 65	8.4%	3.0%	5.5%
Patil et al.	2009	258	≥ 70	12.0%	NG	NG
Grossman et al.	2011	5512	≥ 65	4.4%	NG	NG
Schul et al.	2011	164	≥ 65	3.7%	7.3%	1.2%
Konglund et al.	2012	54	≥ 60	5.6%	5.6%	1.9%
Konglund et al.	2013	51	≥ 80	3.9%	15.7%	3.9%
Poon et al.	2013	92	≥ 65	0.0%	NG	NG
Chen et al.	2015	86	≥ 65	1.2%	11.6%	5.8%
Present series	2018	321	≥ 70	4.7%	5.3%	2.8%

craniotomy for tumor is reported to be between 0.6 and 6.6% [33]. Reviewing only meningiomas in the elderly, the rate ranges from 1.2 and 5.8% [11, 13, 16, 31, 32, 60, 64, 68] (Table 5). In our series, 2.8% of the cases were complicated with a surgical site infection with no significant difference between SBMs and NSBMs ($p = 0.27$) (Table 4).

The 30-day mortality is extremely variable according to the literature and ranges from 0 to 45% [1, 2, 5, 7–11, 13, 16, 19, 21, 24, 26, 31, 32, 34, 36, 37, 49, 51, 53–55, 59, 60, 64, 68] (Table 5). In our series, 4.6% patients died (of any cause) within 1 month after craniotomy, and no significant difference was detected between SBMs and NSBMs (Table 4). Although many authors have found that advanced age carries a higher risk of mortality in meningiomas and other brain neoplasms [5, 31, 33, 51], the effect of tumor location in the elderly is less well documented. Indeed, some publications strongly support

our results [11, 45, 53], whereas others are more skeptical about surgery in SBMs in elderly patients [9, 16, 51, 55]. However, perioperative mortality rates may differ among different skull base locations. Considering the larger clinical series, olfactory groove meningiomas have rates between 1.0 and 8.9% [4, 42, 47, 66], whereas petroclival meningiomas and posterior fossa meningiomas have lower reported mortality rates (from 0 to 4%) [17, 35, 43, 56]. Sphenoid wing meningiomas, which were the most prevalent location in our cohort (medial and lateral sphenoid wing: 36%), have mortality rates of 0 and 1.1%, respectively, in two sizeable series [6, 63]. Hence, it is likely that the great number of sphenoid wing and olfactory groove meningiomas (36 and 18%, respectively) in our cohort has influenced our 30-day mortality rate for SBMs (Table 3). Reasonably, the same effect should be considered for complications after surgery, EOR, and risk of retreatment.

In a large, multicenter, population-based study of patients with meningiomas undergoing tumor resection, Bartek et al. [3] identified advanced age (≥ 70 years), long-lasting surgery (≥ 4 h), and poor functional status (KPS < 70) as independent predictors of severe postoperative complications. Sacko et al. [60] found tumor location to be a significant predictor of surgical outcome and included it in the SKALE prognostic score. However, the prognostic effectiveness of this score is unclear. It was validated by Konglund et al. [32] who compared it with three other scoring systems (CRGS, GSS, and CCI). Conversely, Schul et al. [64] found that both CRGS [10] and SKALE consist of significant and insignificant factors. According to their multivariate analysis, only ASA score and concomitant diseases were predictors of mortality. D'Andrea et al. [19] reported no significant correlation between location and mortality, even though in their series patients with SBMs were associated with higher morbidity.

Retreatments

In our study, the overall retreatment rate was 6% with no significant difference between the two groups (SBMs 8% vs NSBMs 5%, $p = 0.24$) (Table 4). Similar recurrence rates were reported by Sacko et al. [60] who reported 5.4% recurrence over a median follow-up period of 94 months and by other authors [10]. On the contrary, much higher recurrence rates were described by Cohen-Inbar et al. [13, 14] in two different meningioma series with long-term follow-up, respectively, 23.6 and 24.1%. Although the retreatment rate is not synonymous of recurrence rate, the two are comparable. We prefer to use retreatment rather than recurrence, since not every recurrence necessarily leads to retreatment. With regard to SB location, Nishizaki et al. [45] had 5.6% recurrence rate, which is slightly lower than our values, and even lower rates were attained by Roser et al. [59].

With respect to risk of retreatment, no significant difference was identified according to our analysis (Table 4). To our knowledge, this is the first study involving only elderly patients and addressing the clinical question whether SBMs are retreated more frequently compared to NSBMs. In a case series of 582 patients between 13 and 85 years of age, Savardekar et al. [61] compared the tumor progression patterns in SBM and NSBM. According to their analysis, tumor progression was significantly higher among patients with SBM within the first 10 years, while thereafter meningiomas at both locations paralleled each other. In particular, none of the factors considered, namely age, gender, EOR, tumor grade, and tumor location, affected the PFS after 10 years from surgery. Similar results were described recently in a large meningioma cohort, where RFS was significantly shorter among subjects with SBM compared to NSBMs [39]. In a recent publication, Gousias et al. [25] found tumor location and degree of resection to be independent predictors of PFS.

In particular, SG II doubled the risk of recurrence at 10 years compared to SG I in the overall series. Similar results were described by Scheitzach et al. [62]. In the present study, SB location had no significant impact on risk of retreatment (Table 4). Our findings may reflect the fact that intracranial meningiomas in the elderly seem to be a distinct clinical entity [59], and therefore, results from studies involving younger and pediatric patients may be not comparable with cohorts of older individuals.

Type of retreatment

With regard to the type of retreatment, 3.7% underwent a second operation to remove a recurrent tumor, while 2.8% were retreated with conventional fractionated RT and 0.9% with SRS (Table 4). There was no significant difference when patients were dichotomized by location, although a mild trend towards more RT and SRS in SBMs could be identified (conventional RT in SBMs 3.9% vs. NSBMs 2.1%, SRS in SBMs 1.6% vs. NSBMs 0.5%).

Overall survival

No significant difference was identified between SBM and NSBM with respect to the OS (Table 4; Fig. 1). It should be noted that the OS rates include mortality due to any cause and not only disease-specific survival (DSS). Given the advanced age of our study population, meningioma-specific causes played a minor role in the OS. Moreover, in cohorts of elderly subjects, the most relevant parameter to evaluate the safety of surgery is perioperative mortality. Indeed, in this cohort, no significant difference was detected between SB and NSB location with respect to 30-day mortality (4.7% in both groups) (Table 4).

Our OS rates are in accordance with case series involving younger patients [40, 69]; no comparison between SBMs and NSBMs in elderly patients with regard to OS has been previously reported. In the present study, 5-year OS for SBMs and NSBMs was 78 and 82%, respectively, (Table 4) and is in line with other rates reported in literature, which range between 73 and 81% [10, 14, 19, 57, 60]. Interestingly, despite higher rates of STR among patients with SBM (SBMs 37% vs NSBMs 19%), neither poorer functional outcome, higher retreatment rate, shorter RFS, nor reduced OS were found as compared to NSBM group (Table 4). Lastly, our results are supported by Gousias et al. [25] who found no relationship between SG and OS in a large cases series.

Conclusions

Elderly patients with SBMs did not have higher risk of retreatment nor poorer OS compared to those with NSBMs. Furthermore, SBMs did not have higher rates of postoperative

complications (infections or hematomas), neurological outcome, nor 30-day mortality. Hence, in the elderly SBM, surgery does not carry a higher risk of complications, mortality, or retreatment than in NSBMs.

Strengths and limitations of the study

The strengths of this study lie in the clinical setting, design, and follow-up. The data were restricted to one health center only (OUH), thereby reducing the possible confounding effect of differences in the access to health care services between health centers. Thus, we have avoided the selection bias inherently present in large multi-center studies. The two neurosurgical units performing these surgeries are within a geographically well-defined area. As the study includes all craniotomies performed for histologically verifiable meningiomas, there is no selection bias. All surgeries were performed within the same time period, thereby avoiding any “time bias” due to improvements in neurosurgical care during the study period. Our cohort represents the biggest series comparing SBMs with NSBMs in the elderly. The median follow-up was 4.7 years (range 0–19 years) and complete for all patients. The pre- and postoperative post-contrast imaging studies were reviewed to confirm tumor location and EOR. With respect to data quality, we only used endpoints that are easily verifiable (i.e., 30-day mortality, reoperation for hematomas, and reoperations for infections). Neurological status was trichotomized (unchanged, improved, or worsened) to reduce the subjectivity of the observers. Lastly, we focused our attention on RFS and retreatment rate in order to provide practical information to surgeons.

However, this study is not free from limitations. First of all, due to the retrospective nature of our analysis, there are limitations in terms of data collection inherent in such studies, despite data from 2003 being collected prospectively. For these reasons, data on indications for retreatment and postoperative RT were not available for every patient and thus excluded from our analysis. Furthermore, potential selection bias due to personal decision-making must be considered. Indeed, surgery may have not been offered to substantially older patients with SBMs, which could partially explain our different GTR rates among the two groups. Pathology review was not performed; so, the results are based on the original histopathology report and in accordance with the WHO criteria at the time of surgery. MIB-1 staining index or Ki67 was not available for the majority of the tumors, and this parameter was therefore excluded from the study. The WHO criteria changed during the study period. From 1990 to 2001, the tumors were classified as benign, atypical, or anaplastic. The present WHO-grading system for meningioma was implemented in 2001, which divides the tumors into grade I, II, and III. For this study, we reclassified the tumors operated before 2001 to the present WHO classification: benign = WHO grade I,

atypical = WHO grade II, and anaplastic = WHO grade III. Unfortunately, the retrospective chart review gave no reliable information regarding neurological deterioration, which is an indicator for quality of surgery. Only surgical mortality, the rate of postoperative hematoma and the rate of deep postoperative infection, which are well accepted indicators for quality of surgery, were used in this study.

Acknowledgements The authors would like to thank Bernt Filip Hasseleid MD, Andreas Mathisen MD, Andreas Hessen Schei MD, and Kristina M Ødegaard MD for their valuable contributions in collecting data for this manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval “All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.”

Informed consent For this type of study, formal consent is not required.

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