Intracranial Meningiomas in the Elderly

7

David B. Schul, Chochlidakis Nikos,
and Chirstianto B. Lumenta

7.1 Introduction

Meningioma represents the most frequent brain tumor in the elderly. The prevalence of the disease is difficult to define due to subclinical manifestation in large portion of the population [15]. Great amount of these tumors are discovered incidentally through cranial or spinal radiological exams due to other causes. Others are diagnosed only on autopsy. The increase in average lifespan and the more frequent and easy use of diagnostic neuroimaging have resulted in a larger quantity of lesions being detected in the aging population.

Due to its usually benign biological behavior, many of those tumors are being handled conservatively. In general meningiomas in elderly patients have been considered to have a more benign course than meningiomas in young patients. Annual growth rate seems to be higher in younger patients [43–45]. Kuratsu et al. [34] reported 49 % of asymptomatic meningiomas for patients older than 70 years. This is in contrast to 34 % under this age.

Furthermore, due to limited life expectancy as well as generally more significant concomitant diseases in the elderly, surgeons tend to be more conservative in the management of these patients. Dolecek et al., evaluating the Surveillance, Epidemiology and End Results (SEER) Program database for the year 2004–2011, could clearly demonstrate that patients older than 75 years were substantially less likely to receive any kind of treatment (surgery, surgery + radiotherapy, or radiotherapy alone).

D.B. Schul, MD (✉) • C. Nikos, MD • C.B. Lumenta, MD, PhD
Neurosurgical Department, Municipal Hospital Munich,
Teaching Hospital of the Technical University Munich,
Englschalkingerstrasse 77, 81925 Munich, Germany
e-mail: david.schul@klinikum-muenchen.de

M. Berhouma, P. Krolak-Salmon (eds.), *Brain and Spine Surgery in the Elderly*,
DOI 10.1007/978-3-319-40232-1_7

The enormous improvement of peri-, intra-, and postoperative management of neurosurgical patients in the last decades allows neurosurgeon to safely operate on many of those lesions. However, new technologies such as radiosurgery, gamma knife, and improvement of conventional beam radiation offer more therapeutic alternatives. Nevertheless, the diagnosis of meningioma in the elderly poses an ethical as well as medical decision difficulty on whether it should be treated and which treatment risk is acceptable.

The interest in defining better criteria for dealing with such patients is increasing. In the last 20 years, many authors have reported their treatment results. Most of them have tried to isolate different risk factors for adverse outcomes. Some of these authors suggested different grading scores in order to facilitate patients' selection [1, 9, 17, 18, 28, 36, 56]. Unfortunately their conclusions differ or even contradictory.

7.2 Epidemiology

According to the World Health Organization as published in its classification for nervous tumors [37], meningiomas account for about 24–30 % of all primary intracranial tumors in the USA. Its annual incidence rate is reported to be up to 13 per 100,000 habitants. The Central Brain Tumor Registry of the United States (CBTRUS) [47] collects data regarding malignant and nonmalignant brain tumors in the USA. It is the largest register providing statistical data on the population-based incidence of primary CNS tumors. In its last report on CNS tumors between 2008 and 2012, meningiomas were the most frequently reported histology with 36.4 % of all brain tumors. They were much more frequent in female and in American Africans. Meningiomas were also the most common nonmalignant brain and CNS tumor (53.4 %). The incidence of all brain and CNS tumors was highest among the age 85+ years, and from age 35 years, it was the most common histology diagnosed (Table 7.1). Meningiomas' incidence was increasing with age, and it dramatically increases after age 65 years. Age had a large effect on relative survival after diagnosis of malignant meningioma.

Yearly relative survival rates decrease with age. This decline is much more evident in the age group 75+ years. This might be the result of therapy, but it is probably due to average life expectancy in this group.

Reports from different world regions confirm the data reported in the USA [21, 22, 29, 59].

Table 7.1 Rates of average annual age-related incidence of meningioma among all primary CNS and brain tumors per 100,000 adjusted to age (CBTRUS) [47]

Age (years)	Rate
0–19	0.14
20–34	1.39
35–44	4.82
45–54	9.02
55–64	14.77
65–74	25.96
75–84	38.70
85+	51.31

7.3 Histology

Approximately 80–90 % of meningiomas are classified as benign (WHO grade I). Atypical meningiomas (WHO grade II) were reported to account for 5–15 % of meningiomas. Nevertheless, the current WHO classification from 2007 includes cerebral tumor invasion as one of the criteria for WHO grade II even in the absence of cellular atypia or anaplasia. Therefore, an increase in the diagnosis of grade II tumors has been reported [48, 54]. This diagnosis could newly account for up to 20–35 % [50, 62]. The remnant 0.8–2 % account for WHO grade III tumors.

Park et al. [48] tried to look at the influence of age on histological grading. In 1083 surgical cases of 1067 patients, they reported 91.8 %, 6.8 %, and 1.4 % WHO grades I, II, and III tumors, respectively. However, they evaluated patients treated between the years 1991 and 2006; hence, the portion of WHO grade II tumors might have been higher if they had used the 2007 WHO definition. Statistical analysis showed though higher incidence of the combined grades II/III meningiomas with respect to age. In patients older than 60 year, incidence of grades II/III combined was 11.9 % as compared to 6.9 % in younger patients. The relative distribution of histological subtypes within a WHO grade did not show any statistically significant difference related to age.

Other authors reported only statistically significant increase in incidence of grades I and II and decline of grade III tumors [24]. Yet, diagnostic confirmation through pathology was inversely correlated to age confirming the somehow more conservative therapy tendency in this age group.

Similar results were obtained in an epidemiological study using the CTBRUS data between the years 2004 and 2010 [33]. Likewise a linear growth of the incidence of all three grades was noticed with peak incidence in the age group 75–84 years followed by a drop-off in incidence in the >85 year group. This as well could be the result of a more conservative approach in extreme elderly patient, which would result in lack of pathological confirmation.

The pathophysiology of the apparent incidence increasing in grade II and eventually grade III meningiomas with age might be explained through the long period of time in which tumor progresses before it becomes clinically evident. This long period of time might be enough for tumor cells to gain atypias and anaplasias or for tumor to grow enough to invade brain parenchyma, which would pose a higher grade upon diagnosis.

7.4 Proposed Scores and Risk Factors for Adverse Outcome

Decision-making in this patient population is challenging both for caregiver and for patients and their relatives. Any offered treatment should follow a simple concept, namely, treatment's benefit far outweighs the risks of treatment or the risk of non-treatment. A simple numerical representation of risk prediction might be helpful for counseling patients and relatives, simplify therapy plan, and predict outcome. Incorporating a set of risk factors for adverse outcome seems to be more robust than depending on only one single factor.

Numerous publications tried to analyze different risk factors for adverse outcome in this patient's population [1, 2, 4–7, 14, 17–20, 23, 28, 31, 39–41, 46, 52, 55–57, 61]. Most of the studies consist in retrospective analysis of patient's outcome. Only three of them were prospective studies [9, 32, 49]. To date, no randomized study dealing with this issue was published. Published data in the literature regarding outcome of meningioma surgery in the aged population is controversial and inconsistent. A summary of papers published to date with the respective morbidity and mortality figures as well as identified risk factors for either morbidity or mortality is shown in Table 7.2.

Numerous single risk factors for adverse outcome (either morbidity or mortality) were proposed and are listed below:

1. Age
2. Sex (male/female)
3. Resection grade
4. Peritumoral edema
5. Tumor size
6. Tumor location (eloquence, vessels, skull base)
7. Preoperative neurological condition/deficit
8. Preoperative Karnofsky Performance Scale
9. Concomitant disease
10. ASA Score (American Society of Anesthesiologists Physical Status Classification System)
11. Diabetes mellitus
12. Hypertension
13. Pulmonary disease
14. Race
15. Smoking
16. Alcohol use
17. Disseminated cancer elsewhere
18. Histology
19. Emergency procedures
20. History of previous meningioma surgery
21. History of previous radiation

The most frequently identified single factors in the cited studies include age, sex (male/female), presence of peritumoral edema, tumor size and location, neurological condition and Karnofsky Performance score, as well as the presence of concomitant disease or higher ASA score.

It seems that general health condition (expressed as the presence of concomitant disease or higher ASA score) remains a constant risk factor in most of the studies. This probably correlates to advanced age too. The older the patient is, the higher is the risk to have more concomitant diseases. Schul et al. [57], analyzing single risk factors of two proposed grading scores, could show that when nonsignificant risk factors were stepwise omitted from further calculation, only the elements of ASA score and concomitant disease remained significant. Cohen-Inbar et al. [17, 18] proposing a novel scoring score based on analysis of different risk factors in 250

Table 7.2 Summary of published literature on meningioma surgery in the elderly

A. Description of patients' numbers, age cut-off, and reported morbidity/mortality							
Author	Year	No. pat.	Age cutoff (years)	Morbidity (%)	Mortality 30 days (%)	Mortality 90 days (%)	Mortality 1 year (%)
Djindjian et al.[a] [23]	1998	30	70	NA	23	37	NA
Awad et al. [2]	1989	25	70	52	8	8	NA
Arienta et al. [1]	1990	34	70	44	12	20	NA
Cornu et al. [19]	1990	96	65	43	16	NA	NA
Maurice Williams and Kitchen[a] [40]	1992	46	65	30	9	NA	NA
Umansky et al.[a] [61]	1992	37	70	40.5	5.4	NA	NA
McGrail and Ojemann[a] [41]	1994	56	70	11.3	3.6	NA	NA
Nishizaki et al. [46]	1994	78	70	13	NA	NA	NA
Mastronardi et al. [39]	1995	17	80	11.8	29	29	NA
Black et al. [5]	1998	57	65	15.8	1.8	NA	NA
Buhl et al.[a] [7]	2000	66	70	57.6	7.6	12	16
Caroli et al. [9]	2005	90	70	NA	6.7	7.8	15.6
D'Andrea et al. [20]	2005	37	80	2.7	10.8	13.5	13.5
Bateman et al. [4]	2005	2304	70	52.2	4	NA	NA
Boviatsis et al. [6]	2006	108	65	17,8	6,5	NA	NA
Sacko et al. [56]	2007	74	80	9.4	0	1.4	9.5
Rogne et al. [55]	2009	79	70	NA	2.5	NA	6
Cohen-Inbar et al. [17]	2010	250	65	NA	NA	8.4	NA
Patil et al. [49]	2010	258	70	29.8	12	NA	NA
Cohen-Inbar et al. [18]	2011	120	65	NA	NA	5.8	8.3
Grossman et al. [28]	2011	5717	65	17.5	3.2	NA	NA
Schul et al. [57]	2012	164	65	21	3.6	6.7	6.7
Konglund et al. [31]	2013	51	80	[b]	3.9	7.8	15.7
Konglund et al. [32]	2013	54	60	31.5	5.6	7.4	9.2
Poon et al. [52]	2013	92	65	69.6	0	2.2	4.3
Chen et al. [14]	2015	86	65	37.2	1.2	1.2	NA

(continued)

Table 7.2 (continued)

B. Description of investigated risk factors																			
	Risk factor identified for adverse outcome (morbidity and/or mortality)																		
Author	Age	Sex	Resection grade	Edema	Size	Tumor location	Neurological condition	KPS	Concomitant disease	ASA	Diabetes mellitus	Hypertension	Pulmonary disease	Race	Smoking	Alcohol abuse	Histology	Cancer	Surgery duration	Other
Djindjian et al.[a] [23]	y	NA	NA	y	n	NA	NA	y	NA	n	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Awad et al. [2]	y	NA	NA	NA	y	y	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Arienta et al. [1]	NA	NA	NA	y	y	y	NA	n	y	NA	y	NA	NA	NA	NA	NA	NA	NA	n	
Cornu et al. [19]	n	n	NA	n	n	y	y	y	y	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Maurice Williams and Kitchen[a] [40]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Umansky et al.[a] [61]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	n	
McGrail and Ojemann[a] [41]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Nishizaki et al. [46]	n	n	n	NA	NA	n	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	y	NA	
Mastronardi et al. [39]	NA	NA	NA	n	y	NA	NA	y	NA	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Black et al. [5]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Buhl et al.[a] [7]	n	NA	NA	y	y	y	NA	NA	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	y	
Caroli et al. [9]	n	y	NA	y	y	y	y	n	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
D'Andrea et al. [20]	NA	NA	NA	y	y	n	NA	y	NA	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Bateman et al. [4]	y	NA	NA	NA	NA	NA	NA	NA	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Boviatsis et al. [6]	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Sacko et al. [56]	NA	y	y	y	y	y	NA	n	NA	y	NA	NA	NA	NA	NA	NA	n	NA	NA	
Rogne et al. [55]	n	n	n	NA	NA	NA	NA	NA	[c]	n	NA	NA	NA	NA	NA	NA	n	NA	NA	PreOP ECOG[c]
Cohen-Inbar et al. [17]	y	y	n	y	NA	y	y	y	y	NA	NA	y	y	NA	NA	NA	NA	NA	NA	
Patil et al. [49]	y	NA	NA	NA	NA	y	NA	y[d]	NA	NA	NA	NA	NA	NA	NA	NA	NA	y	NA	
Cohen-Inbar et al. [18]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Grossman et al. [28]	y	n	NA	NA	NA	NA	NA	NA	NA[c]	NA	NA	NA	NA	y	NA	NA	y	NA	NA	CCS[c], Elective procedure
Schul et al. [57]	n	n	n	n	n	n	n	n	y	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Konglund et al. [31]	NA	y	NA	y	y	y	NA	y	NA	n	NA	NA	NA	NA	NA	NA	NA	NA	NA	

(continued)

Table 7.2 (continued)

B. Description of investigated risk factors																				
	Risk factor identified for adverse outcome (morbidity and/or mortality)																			
Author	Age	Sex	Resection grade	Edema	Size	Tumor location	Neurological condition	KPS	Concomitant disease	ASA	Diabetes mellitus	Hypertension	Pulmonary disease	Race	Smoking	Alcohol abuse	Histology	Cancer	Surgery duration	Other
Konglund et al. [32]	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Poon et al. [52]	y	y	n	NA	NA	y	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	n	NA	NA	Elective procedure
Chen et al. [14]	n	n	n	n	n	n	y	n	n	n	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Detailed figures on mortality from recent publication are presented in Table 7.8:
y yes, *n* no, *NA* not available
[a]No statistical tests were applied
[b]13.7 serious, 25.5 Infection, 15.7 neurological deficits
[c]CCG/ECOG are also an expression of concomitant disease
[d]Reported as functional dependency

elderly patients divided concomitant disease into three singular diseases, namely, diabetes mellitus, hypertension, and pulmonary disease. The consequence was that concomitant disease gained threefold strength in their score. Grossman et al. [28] performed a multi-institutional retrospective cohort analysis of the American Nationwide Inpatient Sample relating it to the Charlson Comorbidity Score (CCS) [10, 11, 13, 51]. They as well showed a strong correlation of outcome (mortality, postoperative morbidity, length of stay in the hospital, and consequently costs of treatment) with comorbidity.

Further risk factors that regard tumor characteristics as size, location, and edema might relate to neurological status and Karnofsky score. These factors are also frequently presented in different studies.

These results were confirmed in the retrospective report of a personal series of Sade and Lee, consisted in 300 analyzed patients. They also added previous surgery and history of radiation treatment to reported risk factors [36]. Poon et al. [53] reviewing 13 published studies between 2002 and 2012 reported that mortality was commonly associated with ASA score, peritumoral edema, and Karnofsky Performance score. Among the 11 factors they isolated, which were associated with mortality, five were related to preoperative status and comorbidities.

7.5 Scores

In light of different identified risk factors mentioned above, several authors proposed various scoring systems meant to provide prognostic value and help clinical decision-making and patient's counseling.

A summary of the proposed scores is shown in Tables 7.3, 7.4, 7.5, 7.6, and 7.7.

- *Clinical Radiological Grading System (CRGS)* [1, 9] Table 7.3
  This grading system was first introduced in 1990 in order to standardize surgical decision-making in elderly patients with intracranial meningiomas.

Table 7.3 Clinical–Radiological Grading System (CRGS) [1, 9]

	Score		
Factor	1	2	3
Size of lesion (cm)	6	4–6	<4
Neurological condition[a]	Unrecoverable	Progressive	No deficits
KPS score	≤50	60–80	90–100
Critical location[b]	Highly	Moderately	Not critical
Peritumoral edema[c]	Severe	Moderate	Absent
Concomitant disease(s)[d]	Decompensated	Compensated	Absent

[a]Unrecoverable deficits: deficits complete and stabilized (e.g., hemiplegia or amaurosis); progressive deficits: deficits incomplete or worsening (e.g., hemiparesis or impairment of visual acuity)
[b]A critical location is present if the tumor is attached to a primary vascular or nervous structure (such as the cranial base or an eloquent area)
[c]Peritumoral edema is classified as moderate (only peritumoral) and severe (with a shift of midline structures)
[d]Concomitant diseases were evaluated as being compensated (controlled by medical therapy) or decompensated (uncontrolled despite medical therapy)

Table 7.4 SKALE (sex, Karnofsky, ASA, location, edema) grading system

Factors	Score		
	0	2	4
Sex	M	F	–
Karnofsky score	≤50	60–70	≥80
ASA class	IV	III	I or II
Location	Critical Highly	Not critical Moderately	– Not critical
Edema	Severe	Moderate	No edema

In red: modified SKALE (mSKALE) [31, 56]

Table 7.5 The Geriatric Scoring System (GSS) [17, 18]

Admission parameter	1 point	2 points	3 points
Size	>5 cm	3–5 cm	<3 cm
Neurological deficit	Progressive	Stable severe	None, minor
Karnofsky Performance Scale	<50	60–80	90–100
Tumor location	Falcine, parasagittal Foramen magnum	Tentorial Posterior fossa jugular foramen	Convexity
			Intraventricular
			Sphenoid wing
			Tuberculum sellae cavernous sinus
			Optic nerve
Peritumoral edema	Severe	Mild	None
Diabetes mellitus	Not controlled	Medically controlled	None
Hypertension	Not controlled	Medically controlled	None
Pulmonary disease	Severe	Mild	None

It was based on a retrospective analysis of 46 patients (of whom 34 were surgically treated) with an age cutoff of 70 years. It incorporates six preoperative factors regarding patient's status and radiological tumor's characteristics, namely, size of lesion, neurological condition, KPS score, critical location, peritumoral edema, and the presence of concomitant disease. The resulting score 6–18 was found to reflect mortality at 3 months. The same group has validated their system in 2005 on a group of 90 patients, confirming that patients with a score > 10 were the best candidates for surgery.

Some critics were expressed regarding the composition of this grading system [56, 57]. Initially, the CRGS was developed based on a small database of 34

Table 7.6 Charlson Comorbidity Index/Score (CCS) [10, 13, 28]

Weight	Clinical condition
1	Myocardial infarction
	Congestive heart failure
	Peripheral vascular disease
	Dementia
	Uncomplicated diabetes mellitus
	Cerebrovascular disease
	Chronic lung disease
	Peptic ulcer disease
	Chronic liver disease
2	Hemiplegia
	Moderate or severe kidney disease
	Diabetes mellitus with complications
	Any malignancy (leukemia, lymphoma)
3	Moderate or severe liver disease
6	Metastatic tumor malignancy
	Acquired immune deficiency syndrome
Assigned weights for each condition the patient has. For example: congestive heart failure – 1 point; moderate kidney disease – 2 points. Total score – 3	

Weighting for age	
Age group (years)	Weight
0–49	0
50–59	1
60–69	2
70–79	3
80–89	4
90–99	5

Aged weight is added to clinical condition weight

patients. That put in question its statistical power. Furthermore, correlation between Karnofsky Performance Scale and mortality was not statistically significant. Nevertheless, the authors of CRGS choose to include it. In further validation work 15 years later [9], KPS remained statistically insignificant. The same work found a substantial correlation of outcome to sex. Still they were reluctant to add it into the scale arguing that it has been the first time such a correlation was described.

Schul et al. [57] confirmed the predictive ability of this scale for mortality and better clinical outcome expressed in the Glasgow Outcome Score. However, as for SKALE (see below), analysis of single components revealed a lack of significance for all components except of the presence of concomitant disease and the statistical strength of total score was similar to the single component "concomitant disease."

Table 7.7 CLASS Algorithmic Scale [36]

	Score				
Factors	−2	−1	0	+1	+2
Comorbidity	ASA 3	ASA 2	ASA 1		
Location	Complex	Moderate	Simple		
Age (years)	≥71	61–70	≤60		
Size (cm)			≤2	2.1–4	>4
Signs and symptoms			Asymptomatic	Mild symptoms Irreversible neurologic deficits	Severe symptoms Reversible neurologic deficits
Other		Prior radiotherapy and/or surgery		Radiographic progression	

- *Sex, Karnofsky, ASA, Location, Edema Score (SKALE)* [56] Table 7.4
  Sacko et al. introduced a new scoring system in 2007 based on a retrospective study of 74 patients 80 years and older. They tried to correlate mortality at 1-year following intracranial meningioma surgery. They could identify five risk factors: sex, preoperative Karnofsky Performance Scale, American Society of Anesthesiology Class, tumor location, and the presence of peritumoral edema. Resulting score could range from 0 to 16. A correlation was found between increased mortality at 1 year with score equal to or lower than 8. Konglund et al. [31] proposed a modification for this scale (mSKALE) based on their data of 51 patients. They could reproduce the results of Sacko et al. regarding total SKALE score and 1-year survival. Nevertheless, assessing single components they could not demonstrate the significance of ASA score and tumor location in the multivariate analysis (ASA score was significant in the univariate analysis). The original definition of tumor location had only two possibilities: critical and not critical which could obtain 0 or 2 points respectively. In the mSKALE location was adapted to the three variable systems as in CRGS, namely, location could be appointed to highly, moderately, and not critical with assigned scores of 0, 2, and 4, respectively.
  As Konglund et al. reported, the resulting mSKALE score was therefore skewed +2 points. A score of ≥8 could predict mortality at 1 year. Schul et al. [57] confirmed the utility of the SKALE score to predict mortality at 1 year. Yet, single component analysis showed significance only for ASA score with an odds ratio of 5.17 per point increase in ASA score. The authors concluded that both SKALE and CRGS might be simplified to one component without losing their predictive ability.
- *Geriatric Scoring System (GSS)* [17, 18] Table 7.5
  Cohen-Inbar et al. proposed the GSS in 2010 based on a study of 250 patients 65 years and older. The GSS includes the same parameters as the CRGS except for concomitant disease, which was substitute by three parameters, namely, the

presence of diabetes mellitus, hypertension, and pulmonary disease. Tumor size was defined slightly differently and tumor location was subdivided in more details. In this study, the authors found correlation between GSS score and survival at 3 months and 5 years. Higher GSS score was additionally significant for performance level at 5 years after surgery as well as time spent in intensive care unit and length of hospitalization. Konglund et al. could not confirm the data regarding survival in their study. Major critic for this scale was that concomitant disease was divided into three factors gaining threefold power. Furthermore, diabetes mellitus was not statistically investigated separately even though 70 % of the patients suffered from it.

- *Charlson Comorbidity Index/Score (CCS)* [10, 13, 28] Table 7.6
  The Charlson Comorbidity Index was originally designed to classify prognostic comorbidity in longitudinal studies in order to predict survival at 1 year. It has been used and validated in numerous studies, some of them in neurosurgical pathologies, in order to stratify patients according to comorbid conditions and overall survival [3, 10–12, 25, 26, 28, 35, 38, 42, 58].
  The CCS assigns a weight of 1, 2, 3, and 6 for different clinical conditions. It is calculated by summing the weights for each condition in patient's medical history. Regardless of whether the conditions are obtained in the contest of clinical care or outcome data, the CSS weight for each condition is identical. CSS scores can range from 0 to 15 and is adjusted for age.
  Grossman et al. [28] performed a multi-institutional retrospective cohort analysis of the American Nationwide Inpatient Sample relating it to the Charlson Comorbidity Index (CCS) [28]. They could confirm a strong correlation of outcome (mortality, postoperative morbidity, length of stay in the hospital, and consequently costs of treatment) with comorbidity.
  Konglund et al. [31] found that survival was improved by CCS ≤ 6, but it did not reach statistical significance ($p = 0.068$). It might be the consequence of the small patient's number ($n = 51$).
  Laor et al. [35] reporting on outcome in general surgery of elderly patients indicated that increased age was associated with a higher death rate after emergency surgery and with late deaths after elective surgery. A higher mean CCS was noted in early non-survivors after both elective and emergency surgery with a more significant effect of the preoperative CCS than chronological age for the prediction of late postoperative death.
  CCS seems to be effective prognostic tool in further neurosurgical pathologies as glioblastoma multiforme or traumatic spine injury [25, 42]. Although the CCS was not designed to predict perioperative mortality in surgical cohorts, it correlates with a greater risk than age for perioperative death in the elderly.
- *CLASS Algorithmic Scale* [36] Table 7.7
  This algorithm aimed to balance the risks and benefits of meningioma surgery. The purpose of this scale is to suggest physician about surgical treatment in incidental tumors. Unlike the previous scales, this system suggests a raw of risk factors (comorbidity defined by ASA score, tumor location, and patient age) and benefit factors (tumor size, neurologic signs). A score is assigned to each factor

as follows: risk factors are graded from −2 to 0, while benefit factors are graded from 0 to +2. A score of +1 was added to total score in the presence of radiographic progression and −1 for previous history of surgery and/or radiotherapy. Patients are then divided into CLASS I (total score of +1 or above), CLASS II (total score of 0 or −1), and CLASS III (total score of −2 or below).
The validity of this scale was tested by the authors showing that patients in CLASS group I should be offered surgery and those in CLASS group III should not be offered surgery. Patients in CLASS group II should be discussed with caution.
Major disadvantage of this scoring system is that location was only defined subjectively by the senior author and not based of defined criteria; therefore, it might not be transferred to other centers. Additionally, no other study had until now tested this scale; thus, its utility is questionable.

In summary, all systems have their utility and disadvantages when considering patients for surgery. It seems that patients' general conditions play a crucial role in defining prognosis. Tumors' characteristics as location, size, and peritumoral edema seem to have an important role as well. Patient's age seems to correlate with outcome although it is not an independent factor and usually older age is associated with different risk factors. Moreover, physicians might improve patient's likelihood for better outcome by improving the "dynamic" factors such as improving general condition or reduce edema. Unchangeable factors as age, sex, or tumor size contribute for risk assessment but are not disposed to changes.

These scoring systems do provide useful help for decision-making but should not be used as guidelines when treating these patients. Best approach is probably careful judgment of all different factors and an open discussion with patients and relatives.

7.6 Outcome

The most important aim of all studies is to improve future outcome by identifying risk factors and developing systems. This would allow improving patients' selection and advise other practitioners on the best way to choose. An imperative task would be to look at one's own outcomes and identify adverse as well as good results. The advances of medical technology make it hard to compare historical series. Furthermore, differences in study designs and size of patients' collectives contribute to a large difficulty in comparing these studies. Reported mortality and morbidity rates vary widely and are sometimes even contradictory. A summary of published rates is shown in Table 7.2.

- *Morbidity*
  The definition of morbidity and operative complication differs largely. Identifying postoperative morbidity is not an easy task. First of all, surgery of intracranial lesions runs the risk of neurological complication such as motor deficits, speech

deficits, neurocognitive impairment, etc. Some of these complications are only temporary and resolve within few days. Others take much longer and some are unfortunately permanent.

Reporting such results depend largely on subjective measures especially when most of the studies are retrospective.

Somewhat easier task is to report morphological complications as postoperative hemorrhage or CSF fistula. Such complications might be reported then as need or need-not surgery.

Further medical complications as pneumonia, urinary tract infections, cardiac decompensation, etc. are easy to register, but correlation with preoperative factors might be difficult to achieve.

Reported morbidity figures are therefore heterogeneously reported and range from 2.7 to 69.6 % (Table 7.2). Comparing this data is an almost impossible task. Poon et al. [53] summarized complications' relevant published data between the years 2002 and 2012. The overall incidence of complications was 20.1 % per patient (range 2.7–60.5 %). The percentage of complications being neurological in nature ranged from 42.5 to 100 %.

In different studies comparing young to elderly patients, the last had significantly higher complication rate [6, 49, 52]. Patil et al. reported that elderly were more likely to have one or more complications (29.8 % vs. 13.1 %, $p > 0.0001$). Poon et al. [52] described similar results with 69.6 % complications rate among older patients vs. 51.1 % ($p = 0.01$) among young patients.

- *Mortality*

  Since death is a definitive state, it can be assessed on a set time point (in hospital, 30 days, 3 months, or 1 year). Its documentation is a much easier task to achieve and report.

  Reported numbers vary between high figures in historical reports and much lower figures in recent ones. This might be explained due to better operative and perioperative technologies as well as stricter patient's selection in recent reports. Mortality rates at 30 days are reported to range between 29 and 0 % (Table 7.2). Further reports on 3, 6, and 12 months as well as 5-year mortality rates in addition to death cause are summarized in Table 7.8. One-year mortality rate range from 4.3 to 15.7 % seems to be similar to rates reported in the general population [8]. Five-year mortality rates are rarely reported. They seem to be elevated yet it might represent the expected span of life in aged people.

- *Quality of life*

  Important information concerning the utility of surgery in these patients is reported through several indicators for quality of life (as postoperative Karnofsky Performance Scale or the Glasgow Outcome Score). Other indicators such as hospital discharge information are important, not only to caregivers but also for politics and insurance companies when planning health resources.

  Schul et al. [57] reported an improvement of the median Karnofsky Performance Scale from 80 to 90 in the surviving patients suggesting benefit of surgery to most of the operated patients. These results were confirmed by other authors [9]. Rogne et al. reported an improvement of ECOG Performance score (Eastern

Table 7.8 Summary of mortality figures in the elderly in some of the reports from 2002 to 2013

	Mortality (%)					Cause of death (%)	
Author	In hospital	30 days	90 days	1 year	5 years	Surgery related	Non-surgery related
Poon et al. [52]	–	0	2.2	4.3	–	25	75
Chen et al. [14]	1.2	1.2	1.2	–	–	100	0
Konglund et al. [32]	–	5.6	7.4	9.2	–	74	26
Konglund et al. [31]	–	3.9	7.8	15.7	–	–	–
Schul et al. [57]	–	3.7	6.7	6.7	–	81.8	18.2
Grossman et al. [28]	3.2	–	–	–	–	–	–
Cohen-Inbar et al. [18]	–	–	5.8	8.3	88.3[a]	–	–
Patil et al. [49]	–	12	–	–	–	–	–
Cohen-Inbar et al. [17]	–	.	6.8	–	–	–	–
Rogne et al. [55]	–	2.5	–	6.3	26.6	–	–
Sacko et al. [56]	–	0	1.4	9.4	27	–	–
Boviatsis et al. [6]	6.5	–	–	–	–	–	–
D'Andrea et al. [20]	–	10.8	13.5	13.5	–	–	–
Caroli et al. [9]	–	6.7	7.8	15.6	–	25	75

Adapted from Poon et al. [53]

[a]No availability of the numbers of patient in whom 5-year survival data was available

Cooperative Oncology Group) following surgery [55]. In further study, Konglund et al. [32] found no significant overall change in the level of independence after surgery measured through KPS. Nevertheless, an improvement of the Mini Mental State Examination (MMSE) postoperatively was noticed. Further quality of life questionnaire analysis revealed better mean functional scores in physical and social aspects, yet poorer cognitive functioning (comparing to population-based data). Tucha et al. [60] in the only study published specifically on the effects of surgery on cognitive function in elderly patients with intracranial meningioma could not reveal any significant deterioration. They could find marked improvements in attentional and memory functions as well as in task processing speed.

- *Hospital recovery*
  Due to the prevalence of concomitant disease in aged patients, it is expectable that these patients would spend much longer time in hospital. Grossman et al. could confirm it by using the CCS. Each one-point increase in CCS was associated with significantly longer length of stay in hospital and consequently higher hospital charges [28]. Increasing in ASA score and the presence of concomitant disease were correlated to increasing length of stay [14]. A close correlation to length of stay in the ICU was also linked to preoperative condition as expressed in the preoperative Karnofsky Performance Scale [17]
  Comparing young to old patients revealed significantly longer hospital stay for elderly patients (17.4 ± 20.4 days vs. 9.1 ± 4.98 days). Furthermore, elderly patients were more prone to be discharged into a facility than young patients [52]. It might be safe to assume that the ability to rehabilitate aged patients into independent self-care, if needed, pose a big challenge and might be impossible task.

7.7 Radiotherapy

Despite the notable decrease in surgery related complications, surgery is often not feasible. Not operable tumors, patient to ill for a surgical intervention, incomplete resection or recurrence of tumor, and patient or surgeon's preference might require seeking alternative therapy option. To date, there is no available chemotherapeutic agent widely acceptable for the treatment of meningiomas.

At least to date, there are only two retrospective works dealing specifically with stereotactic radiotherapy in the elderly [27, 30]. Both report a similar radiologic local control rate and overall survival rates (Table 7.9).

Table 7.9 Summary of radiologic local control rates/progression-free survival and overall survival followed stereotactical radiotherapy

	Progression-free survival %				Overall survival %		
Author, year	1 year	3 years	5 years	10 years	1 year	3 years	5 years
Kaul et al., 2015 [30]	–	93.7	91.1	82	–	–	–
Fokas et al., 2014 [27]	98.3	98.3	94.7	–	95.8	92.0	79.0

Procedure-related complications were reported only as toxicity grades I and II in about 50 % of patients. These consisted in headaches, alopecia, fatigue, vertigo, cranial nerve deficits, memory impairment, pyramidal dysfunction, and hearing loss. No mortality was related directly to the procedure. Fokas et al. [27] reported 13.2 % mortality rate due to other causes not related to the procedure during the follow-up period (median 40 months).

Cohen-Inbar et al. [16] tried to test their proposed Geriatric Scoring System (GSS) Score onto meningioma patients treated radiosurgically. Despite this scoring system designed to evaluate risk in elderly patients, it was tested on all patients collectively (young and old). An age stratification and analysis has not been reported.

It seems that stereotactic-based radiotherapy is an effective and safe therapeutic modality for intracranial meningiomas in elderly patients. It is a valuable alternative treatment option and should be discussed interdisciplinary and with patients.

Conclusion

Recent works suggest acceptable outcomes following intracranial meningioma surgery and radiosurgery. Yet these results should be used with caution. To date, studies should be interpreted as at best level II (most of them are evidence level III).

Decision-making should be based on thorough discussion of all parameters discussed above. Further, treatment recommendation should be openly discussed with patient and his relatives, defining treatment's goals with careful evaluation of pro- and contraindications. Individual's preoperative status, comorbidities, and tumor characteristics should be taken into consideration.

Radiosurgery seems to be a valid alternative for the treatment of intracranial meningiomas in this patient's group. Multidisciplinary exhaustive discussion is strongly recommended.

References

1. Arienta C, Caroli M, Crotti F et al (1990) Treatment of intracranial meningiomas in patients over 70 years old. Acta Neurochir 107:47–55
2. Awad IA, Kalfas I, Hahn JF et al (1989) Intracranial meningiomas in the aged: surgical outcome in the era of computed tomography. Neurosurgery 24:557–560
3. Bar B, Hemphill JC 3rd (2011) Charlson comorbidity index adjustment in intracerebral hemorrhage. Stroke 42:2944–2946
4. Bateman BT, Pile-Spellman J, Gutin PH et al (2005) Meningioma resection in the elderly: nationwide inpatient sample, 1998–2002. Neurosurgery 57:866–872; discussion 866–872
5. Black P, Kathiresan S, Chung W (1998) Meningioma surgery in the elderly: a case–control study assessing morbidity and mortality. Acta Neurochir 140:1013–1016; discussion 1016–1017
6. Boviatsis EJ, Bouras TI, Kouyialis AT et al (2007) Impact of age on complications and outcome in meningioma surgery. Surg Neurol 68:407–411; discussion 411
7. Buhl R, Hasan A, Behnke A et al (2000) Results in the operative treatment of elderly patients with intracranial meningioma. Neurosurg Rev 23:25–29
8. Cahill KS, Claus EB (2011) Treatment and survival of patients with nonmalignant intracranial meningioma: results from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. Clinical article. J Neurosurg 115:259–267

9. Caroli M, Locatelli M, Prada F et al (2005) Surgery for intracranial meningiomas in the elderly: a clinical-radiological grading system as a predictor of outcome. J Neurosurg 102:290–294
10. Charlson M, Szatrowski TP, Peterson J et al (1994) Validation of a combined comorbidity index. J Clin Epidemiol 47:1245–1251
11. Charlson M, Wells MT, Ullman R et al (2014) The Charlson comorbidity index can be used prospectively to identify patients who will incur high future costs. PLoS One 9:e112479
12. Charlson ME, Charlson RE, Peterson JC et al (2008) The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. J Clin Epidemiol 61:1234–1240
13. Charlson ME, Pompei P, Ales KL et al (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40:373–383
14. Chen ZY, Zheng CH, Tang L et al (2015) Intracranial meningioma surgery in the elderly (over 65 years): prognostic factors and outcome. Acta Neurochir (Wien) 157:1549–1557; discussion 1557
15. Claus EB, Bondy ML, Schildkraut JM et al (2005) Epidemiology of intracranial meningioma. Neurosurgery 57:1088–1095; discussion 1088–1095
16. Cohen-Inbar O, Lee CC, Schlesinger D et al (2015) The Geriatric Scoring System (GSS) for risk stratification in meningioma patients as a predictor of outcome in patients treated with radiosurgery. World Neurosurg 87:431–438
17. Cohen-Inbar O, Soustiel JF, Zaaroor M (2010) Meningiomas in the elderly, the surgical benefit and a new scoring system. Acta Neurochir (Wien) 152:87–97; discussion 97
18. Cohen-Inbar O, Sviri GE, Soustiel JF et al (2011) The Geriatric Scoring System (GSS) in meningioma patients--validation. Acta Neurochir (Wien) 153:1501–1508; discussion 1508
19. Cornu P, Chatellier G, Dagreou F et al (1990) Intracranial meningiomas in elderly patients. Postoperative morbidity and mortality. Factors predictive of outcome. Acta Neurochir 102:98–102
20. D'andrea G, Roperto R, Caroli E et al (2005) Thirty-seven cases of intracranial meningiomas in the ninth decade of life: our experience and review of the literature. Neurosurgery 56:956–961; discussion 956–961
21. Das A, Chapman CA, Yap WM (2000) Histological subtypes of symptomatic central nervous system tumours in Singapore. J Neurol Neurosurg Psychiatry 68:372–374
22. Das A, Tang WY, Smith DR (2000) Meningiomas in Singapore: demographic and biological characteristics. J Neurooncol 47:153–160
23. Djindjian M, Caron JP, Athayde AA et al (1988) Intracranial meningiomas in the elderly (over 70 years old). A retrospective study of 30 surgical cases. Acta Neurochir 90:121–123
24. Dolecek TA, Dressler EV, Thakkar JP et al (2015) Epidemiology of meningiomas post-Public Law 107–206: The Benign Brain Tumor Cancer Registries Amendment Act. Cancer 121: 2400–2410
25. Ening G, Osterheld F, Capper D et al (2015) Charlson comorbidity index: an additional prognostic parameter for preoperative glioblastoma patient stratification. J Cancer Res Clin Oncol 141:1131–1137
26. Fiorentino A, Ricchetti F, Mazzola R et al (2015) Regarding Ening et al. Charlson comorbidity index: an additional prognostic parameter for preoperative glioblastoma patient stratification. J Cancer Res Clin Oncol 141:1139–1140
27. Fokas E, Henzel M, Surber G et al (2014) Stereotactic radiotherapy of benign meningioma in the elderly: clinical outcome and toxicity in 121 patients. Radiother Oncol J Eur Soc Ther Radiol Oncol 111:457–462
28. Grossman R, Mukherjee D, Chang DC et al (2011) Preoperative charlson comorbidity score predicts postoperative outcomes among older intracranial meningioma patients. World Neurosurg 75:279–285
29. Ibebuike K, Ouma J (2014) Demographic profile of patients diagnosed with intracranial meningiomas in two academic hospitals in Johannesburg, South Africa: a 12-month prospective study. Afr Health Sci 14:939–945

30. Kaul D, Budach V, Graaf L et al (2015) Outcome of elderly patients with meningioma after image-guided stereotactic radiotherapy: a study of 100 cases. Biomed Res Int 2015:868401
31. Konglund A, Rogne SG, Helseth E et al (2013) Meningioma surgery in the very old-validating prognostic scoring systems. Acta Neurochir (Wien) 155:2263–2271; discussion 2271
32. Konglund A, Rogne SG, Lund-Johansen M et al (2013) Outcome following surgery for intracranial meningiomas in the aging. Acta Neurol Scand 127:161–169
33. Kshettry VR, Ostrom QT, Kruchko C et al (2015) Descriptive epidemiology of World Health Organization grades II and III intracranial meningiomas in the United States. Neuro Oncol 17:1166–1173
34. Kuratsu J, Kochi M, Ushio Y (2000) Incidence and clinical features of asymptomatic meningiomas. J Neurosurg 92:766–770
35. Laor A, Tal S, Guller V et al (2016) The Charlson Comorbidity Index (CCI) as a mortality predictor after surgery in elderly patients. Am Surg 82:22–27
36. Lee JH (2008) Meningiomas: diagnosis, treatment, and outcome. Springer, London
37. Louis DN, Ohgaki H, Wiestler OD et al (2007) The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 114:97–109
38. Luber MP, Hollenberg JP, Williams-Russo P et al (2000) Diagnosis, treatment, comorbidity, and resource utilization of depressed patients in a general medical practice. Int J Psychiatry Med 30:1–13
39. Mastronardi L, Ferrante L, Qasho R et al (1995) Intracranial meningiomas in the 9th decade of life: a retrospective study of 17 surgical cases. Neurosurgery 36:270–274
40. Maurice-Williams RS, Kitchen ND (1992) Intracranial tumours in the elderly: the effect of age on the outcome of first time surgery for meningiomas. Br J Neurosurg 6:131–137
41. Mcgrail KM, Ojemann RG (1994) The surgical management of benign intracranial meningiomas and acoustic neuromas in patients 70 years of age and older. Surg Neurol 42:2–7
42. Menendez ME, Ring D, Harris MB et al (2015) Predicting in-hospital mortality in elderly patients with cervical spine fractures: a comparison of the charlson and elixhauser comorbidity measures. Spine 40:809–815
43. Nakamura M, Roser F, Michel J et al (2003) The natural history of incidental meningiomas. Neurosurgery 53:62–70; discussion 70–61
44. Nakamura M, Roser F, Michel J et al (2005) Volumetric analysis of the growth rate of incompletely resected intracranial meningiomas. Zentralbl Neurochir 66:17–23
45. Niiro M, Yatsushiro K, Nakamura K et al (2000) Natural history of elderly patients with asymptomatic meningiomas. J Neurol Neurosurg Psychiatry 68:25–28
46. Nishizaki T, Kamiryo T, Fujisawa H et al (1994) Prognostic implications of meningiomas in the elderly (over 70 years old) in the era of magnetic resonance imaging. Acta Neurochir 126:59–62
47. Ostrom QT, Gittleman H, Fulop J et al (2015) CBTRUS Statistical Report: primary brain and central nervous system tumors diagnosed in the United States in 2008–2012. Neuro Oncol 17:iv1–iv62
48. Park JS, Sade B, Oya S et al (2014) The influence of age on the histological grading of meningiomas. Neurosurg Rev 37:425–429; discussion 429
49. Patil GC, Veeravagu A, Lad SP et al (2010) Craniotomy for resection of meningioma in the elderly: a multicenter prospective analysis from the National Surgical Quality Improvement Program. J Neurol Neurusurg Psychiatry 81(5):502–505
50. Pearson BE, Markert JM, Fisher WS et al (2008) Hitting a moving target: evolution of a treatment paradigm for atypical meningiomas amid changing diagnostic criteria. Neurosurg Focus 24:E3
51. Peterson JC, Paget SA, Lachs MS et al (2012) The risk of comorbidity. Ann Rheum Dis 71:635–637
52. Poon MT, Fung LH, Pu JK et al (2013) Outcome comparison between younger and older patients undergoing intracranial meningioma resections. J Neurooncol 114:219–227
53. Poon MT, Fung LH, Pu JK et al (2014) Outcome of elderly patients undergoing intracranial meningioma resection–a systematic review and meta-analysis. Br J Neurosurg 28:303–309

54. Rogers L, Gilbert M, Vogelbaum MA (2010) Intracranial meningiomas of atypical (WHO grade II) histology. J Neurooncol 99:393–405
55. Rogne SG, Konglund A, Meling TR et al (2009) Intracranial tumor surgery in patients >70 years of age: is clinical practice worthwhile or futile? Acta Neurol Scand 120:288–294
56. Sacko O, Sesay M, Roux F-E et al (2007) Intracranial meningioma surgery in the ninth decade of life. Neurosurgery 61:950–954; discussion 955
57. Schul DB, Wolf S, Krammer MJ et al (2012) Meningioma surgery in the elderly: outcome and validation of 2 proposed grading score systems. Neurosurgery 70:555–565
58. Suidan RS, Leitao MM Jr, Zivanovic O et al (2015) Predictive value of the Age-Adjusted Charlson Comorbidity Index on perioperative complications and survival in patients undergoing primary debulking surgery for advanced epithelial ovarian cancer. Gynecol Oncol 138:246–251
59. Tamimi AF, Tamimi I, Abdelaziz M et al (2015) Epidemiology of malignant and non-malignant primary brain tumors in Jordan. Neuroepidemiology 45:100–108
60. Tucha O, Smely C, Lange KW (2001) Effects of surgery on cognitive functioning of elderly patients with intracranial meningioma. Br J Neurosurg 15:184–188
61. Umansky F, Ashkenazi E, Gertel M et al (1992) Surgical outcome in an elderly population with intracranial meningioma. J Neurol Neurosurg Psychiatry 55:481–485
62. Willis J, Smith C, Ironside JW et al (2005) The accuracy of meningioma grading: a 10-year retrospective audit. Neuropathol Appl Neurobiol 31:141–149