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Review of Current Evidence Regarding Surgery in Elderly Patients with Meningioma

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Abstract

The Japanese population features the highest rate of elderly individuals worldwide. Moreover, Japan has the highest number of computed tomography/magnetic resonance imaging devices in the world, which has led to an increase in the incidental detection of meningioma in healthy elderly patients. Many previous papers have discussed the risks and indications for surgery in this patient population, but available information remains insufficient, and the definition of "elderly" has not been standardized. This review tried to clarify the published evidence and challenges associated with elderly meningioma based on a search of the PubMed database using the terms "meningioma," "elderly," and "surgery" for English-language clinical studies and collected related papers published from 2000 to 2016. Twenty-four papers were reviewed and classified by definition of elderly age: over 60, 65, 70, and 80 years old. Six of seven papers that defined the elderly cutoff as over 65 years old were published after 2010, which suggested the consensus definition. Four preoperative grading scoring systems were described and associated with mortality. The 1-year and 5-year mortality rates ranged from 0% to 16.7% and from 7% to 27%, which were comparable with unselected cohorts. Review of risk factor analysis emphasized the importance of considering the preoperative status, presence of comorbidities, and optimum surgical timing during patient selection. Careful choice of patients can also lead to better quality of life. A prospective randomized study considering patient frailty should address the causes and prevention of complications.

Key words: meningioma, elderly, surgery, mortality, aged

Introduction

The populations of Organization for Economic Co-operation and Development (OECD) member countries worldwide are increasingly aging. In particular, the Japanese population contains the highest proportion of elderly individuals. The continued increase in this subpopulation will present unprecedented issues for human societies. Japan also has the highest life expectancy worldwide according to OECD health data,[1] and the Japanese Ministry of Health, Labour and Welfare predicts even greater healthy life expectancy in the future.

Meningioma is a common condition that accounts for more than one-third of all primary intracranial tumors.[2] Incidental detection of asymptomatic meningiomas has recently increased in the elderly Japanese population due to the increased life expectancy and more frequent use of diagnostic neuroimaging.[3] Currently, Japan had the highest number of computed tomography and magnetic resonance imaging devices in the OECD. Many studies have tried to evaluate the risks and indications of surgery in elderly patients with meningioma, but existing evidence is insufficient, and the definition of "elderly age" remains controversial.

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The present review tries to clarify the current evidence and address the known issues associated with meningioma in elderly individuals.

Definitions of elderly in the general population and society

The United Nations defines “aged people” as older than 60 years, whereas the World Health Organization (WHO) uses 65 years or older. In general, the “aging rate” is defined as the proportion of individuals aged 65 years or older in the total population; accordingly, “aging,” “aged,” and “super-aged” societies are defined as having aging rates of 7–14%, 14–21%, and 21% or more, respectively. The Japanese population recorded the lowest aging rate of 4.7% in 1935, and became super-aged with rates of 21.5% in 2007 and 26.0% in 2014, the highest in the world.

Natural history of meningioma in elderly patients

The natural history of incidentally found meningiomas is essential to understand for appropriate decision making regarding treatment, especially in the elderly. Several studies have investigated the behaviors of untreated meningiomas. For example, 47 asymptomatic patients were monitored with serial imaging which observed absolute annual growth rates of 0.03–2.62 cm^3/year (mean, 0.796 cm^3/year), with most tumors (66%) exhibiting a rate of less than 1 cm^3/year, and relative annual growth rates of 0.48–72.8% (mean, 14.6%).[4] The tumor doubling time ranged from 1.27 to 143.5 years (mean, 21.6 years). A moderate correlation was also observed between age and annual growth rates, with younger patients exhibiting a higher growth rate and shorter doubling time.[5] Retrospective analysis of 603 asymptomatic meningiomas concluded that approximately 63% of asymptomatic meningiomas did not exhibit tumor growth, and only 6% of all patients experienced symptoms for longer than 5 years.[6] Radical surgery in elderly patients with asymptomatic meningiomas is not reasonable and close attention must be paid to the manifestation of even minor symptoms. The timing of surgical decision making is very important in the elderly, because they have less recovery reserve capacity.

Several studies of the growth patterns of incidental meningiomas have calculated annual growth rates by determining the initial and final volumes during the follow-up period, assuming that these tumors grow exponentially.[4,7] Serial monitoring of the tumor volumes in 70 patients and regression analysis to analyze tumor growth found that 26 patients (37%) exhibited essentially no tumor growth, and 16 of the 44 patients with tumor growth showed an exponential growth pattern, 15 had a linear pattern, and 13 did not fit either pattern.[8] Investigation of 244 patients who harbored 273 incidental meningiomas found 2-mm or greater increase in maximum diameter in 120 tumors (44%) during a mean follow-up period of 3.8 years.[9] These studies found that predictive factors of tumor growth included younger age, absence of calcification, T2 signal hyperintensity, and peritumoral edema, whereas tumor location was not significantly predictive. Atypical meningiomas may grow exponentially, whereas benign meningiomas exhibit exponential, linear, or no growth.[10] Meningiomas may initially grow exponentially but then undergo a growth rate reduction, possibly due to changes in the available blood supply and progression of calcifications. However, the opposite may also occur, possibly consequent to the acquisition of new mutations that promote growth.

Literature review of surgery in elderly patients with meningioma

We searched the PubMed database using the terms “meningioma,” “elderly,” and “surgery” for English-language clinical studies and collected related papers published from 2000 to 2016 on 1st November 2016. We excluded case studies and review articles. We collected information regarding study characteristics (publication year, author, research period, country, research design, and sample size), patient characteristics (median, mean, and maximum age; sex; tumor location; tumor size or volume; preoperative condition, including rates of asymptomatic patients, of no neurological deficits, and of Karnofsky performance status [KPS] score more than 80, and preoperative American Society of Anesthesiologists [ASA][11] physical classification system; and WHO tumor grade), and treatment outcome characteristics (mortality [in-hospital, 1 and 3 months, and 1 and 5 years], cause of mortality, risk factors for death, complication [brain or general], and deterioration rate), as well as conclusive recommendations and comments. We contacted nearly all authors of reports that did not mention mortality via e-mail and received information from some authors.

Several classifications and clinical scoring systems used in these studies are explained below. The KPS,[12] a measure of preoperative function, has scores of 0–100: a score of 100 indicates full, independent performance; ≥80, normal level of activity; 50–70, living at home with assistance; and 0, death. The ASA system is used to assess a patient’s fitness for surgery, as follows: class I indicates good health; II, mild systemic disease; III, severe systemic disease; IV, severe, systemic, life-threatening disease; V, a moribund patient who is not expected to survive without surgery; and VI, a patient who has been declared brain dead and whose organs are being removed for donor purposes. Tumor location was defined as skull base for cases with skull base, posterior fossa, clinoid, or intraventricular tumors.

The SKALE[13] grading system comprises five statistically significant factors, sex, KPS, ASA, tumor location, and peritumoral edema, related to postoperative mortality after surgical treatment of intracranial meningiomas in patients in their ninth decade of life. The Geriatric Scoring System (GSS)[14,15] includes tumor size and location, neurological deficit, KPS, peritumoral edema, diabetes mellitus, hypertension, and pulmonary disease. The Charlson comorbidity score (CCS)[16] includes various comorbidities, each of which is assigned a score of 1, 2, 3, or 6 depending on the associated mortality risk. The Clinical Radiological Grading System (CRGS)[17] includes tumor size, neurological condition, KPS, tumor location, peritumoral edema, and concomitant disease(s).

Age classification of surgery in elderly patients with meningioma

Twenty-four papers were reviewed (Tables 1–3) and classified according to the definition of elderly age. These studies included a total of 9,987 patients evaluated from 1978 to 2013 for durations of 2–25 years. Women accounted for 66.0% with the exception of one study of the Veterans Affairs' Surgical Quality Improvement Program database (1.9% women), and mean age was 75.5 years (range, 60–92 years). The number of patients per study ranged from 21 to 5,717: 15 studies had fewer than 100 patients, 7 had 101–258 patients, and 2 had more than 2,000 patients. Three studies were prospective; all others were retrospective studies. Many papers published before 2010 reported both differences and similarities in the outcomes of young and elderly subjects, whereas authors tended to report the usefulness of preoperative clinical scoring systems, especially in patients over 65 years old, after 2010.

Four elderly age definition categories were determined: over 60, 65, 70, and 80 years old. The smallest category of two papers[18,19] defined elderly as aged over 60 years old and included 87 patients; skull base-related location rate of 44.5%, tumor size rate over 4 cm of 78.8%, KPS score over 80 of 88.9%, in-hospital mortality rate of 5.6%, deterioration rate of 31.5%, and brain and general complication rates of 33.5% and 11.2%, respectively. One study[18] evaluated preoperative assessments, KPS, the mini-mental state examination,[20] ASA, and SKALE scores, and concluded that meningioma surgery carries higher risks of mortality and morbidity in elderly patients, compared with intracranial tumor surgery in the general population. However, the authors noted that survivors exhibited improved cognitive function and acceptable quality of life (QOL), and the proportion of independent patients (according to KPS) did not decrease significantly.

The largest category of seven papers[14–16,21–24] defined elderly as age over 65 years old, and included a total of 6,607 patients (66.5% female). Six of the seven papers were published after 2010; one was published in 2007. All studies were retrospective. Mean skull base-related location rate was 26.2%, mean tumor size rate over 4 cm was 56.2%, mean asymptomatic or no neurological deficit rate was 24%, and mean KPS score over 80 was 50.1%. These patients had mean ASA class III and IV frequencies of 40.7% and 3.6%, respectively, and WHO tumor grade I, II, and III frequencies of 90.4%, 8.5%, and 1.2%, respectively. The mean in-hospital, 1-month, 3-month, 1-year, and 5-year mortality rates in this group were 2.7%, 3.9%, 5.5%, 5.8%, and 12.9%, respectively, and the surgical and general mortality rates were 7.0% and 1.2%, respectively. Several scoring systems were ultimately recommended for this age group.

Twelve papers[3,6,17,25–33] defined elderly as people aged over 70 years and included a total of 3,131 patients; 53.8% of whom were females (this category included the above-mentioned Veterans Affairs' Surgical Quality Improvement Program database study). Only three papers[31–33] were published after 2010 and three studies[17,31,32] were prospective. Ten papers[3,6,26–33] included some patients with surgically removed meningioma as a part of all age or other treatments. The mean skull base-related location rate was 49.9%, and two studies focused only on skull base[29] or cerebellopontine angle lesions.[27] The mean tumor size rate over 4 cm was 79.5%, mean asymptomatic or no neurological deficit rate was 45.7%, and mean KPS score over 80 was 90%. The mean ASA class I, II, III, and IV frequencies were 0%, 51.0%, 41.5%, and 7.4%, respectively, and the WHO tumor grade I, II, and III frequencies were 93.9%, 4.1%, and 4.0%, respectively (grade II and III cases were excluded from one study). The mean in-hospital, 1-month, 3-month, 1-year, and 5-year mortality rates were 2.0%, 4.3%, 5.0%, 8.7%, and 16.8%, respectively, and the rates of surgical and general mortality were 2.0% and 7.9%, respectively. The brain and general complication rates were 22.1 and 15.4%, respectively.

Finally, three papers[13,34,35] defined elderly as age over 80 years, and included 162 patients, of whom 63.6% were females. Only one[35] of the three papers was published after 2010. All studies were retrospective. Mean skull base-related location rate was 35%, mean tumor size rate over 5 cm was 48.7%, mean asymptomatic or no neurological deficit rate

Table 1 Summary of elderly patients with meningioma (age, tumor location, and size or volume)

Age Class (Years old)	Case no.	Year	Author	Research period	Country	Research design	No. of cases		Age (year)			Tumor location; skull-base related (%)	Tumor size or volume	
							Total	Female	Median	Mean	Maximum		≥ 4 cm in diameter (%)	≥ 40 ml (%)
60	1	2001	Tucha et al.[18]	–	Germany	Retro.	33	21	–	72.8	80	0	78.8	–
	2	2013	Konglund et al.[19]	2008–2009	Norway	Retro.	54	35	70	–	–	44.5	–	27.8
Total or mean							87	56	70	72.8	80	44.5	78.8	27.8
65	3	2007	Boviatsis et al.[21]	1989–2005	Greece	Retro.	108	71	–	–	–	–	–	–
	4	2010	Cohen-Inbar et al.[14]	1995–2005	Israel	Retro.	250	152	–	73	90	39.6	38 (≥ 5 cm)	–
	5	2011	Cohen-Inbar et al.[15]	2005–2010	Israel	Retro.	120	77	73	73	81	22.5	38.4 (≥ 5 cm)	–
	6	2011	Grossman et al.[16]	1998–2005	USA	Retro.	5717	3804	73.6	73	–	–	–	–
	7	2012	Schul et al.[22]	1995–2006	Germany	Retro.	164	125	–	72	87	42.7	53	–
	8	2015	Chen et al.[23]	2007–2013	China	Retro.	86	55	–	70	86	9.1	59.3	–
	9	2016	Brokinkel et al.[24]	1994–2009	Germany	Retro.	162	112	71	–	87	17	–	–
Total or mean							6607	4396	72.5	72.2	86.2	26.2	56.15	–
70	10	2000	Buhl et al.[25]	1991–1997	Germany	Retro.	66	43	–	75	86	7.6	–	–
	11	2000	Kuratsu et al.[3]	1989–1996	Japan	Retro.	30	–	–	–	–	–	–	–
	12	2005	Bateman et al.[26]	1998–2002	USA	Retro.	2304	1544	–	76.7	–	–	–	–
	13	2005	Nakamura et al.[27]	1978–2002	Germany	Retro.	21	–	–	73.8	84	100	–	–
	14	2005	Caroli et al.[17]	1999–2000	Italy	Pro.	90	60	74	74.2	92	30	91	–
	15	2005	Sonoda et al.[28]	1994–2003	Japan	Retro.	25	17	–	73.1	78	24	68	–
	16	2006	Yano et al.[6]	1989–2003	Japan	Retro.	54	–	–	–	–	–	–	–
	17	2007	Roser et al.[29]	2003–2004	Germany	Retro.	43	–	–	74.1	86	100	–	–

(*Continued*)

Table 1 (Continued)

Age Class (Years old)	Case no.	Year	Author	Research period	Country	Research design	No. of cases		Age (year)			Tumor location; skull-base related (%)	Tumor size or volume	
							Total	Female	Median	Mean	Maximum		≥ 4 cm in diameter (%)	≥ 40 ml (%)
	18	2009	Rogne et al.[30]	2003–2007	Norway	Retro.	79	–	–	–	–	–	–	–
	19	2010	Pirracchio et al.[31]	2003–2007	France	Pro.	46	–	–	–	–	43.5	–	–
	20	2010	Patil et al.[32]	1996–2006	USA	Pro.	258	5	–	–	89	44.2	–	–
	21	2015	Bartek et al.[33]	2007–2013	USA	Retro.	115	–	–	–	–	–	–	–
Total or mean							3131	–	74	74.5	85.8	49.9	79.5	–
80	22	2005	D'Andrea et al.[34]	1985–2002	Italy	Retro.	37	29	82	–	86	18.8	51.3 (> 5 cm)	–
	23	2007	Sacko et al.[13]	1990–2005	France	Retro.	74	47	85	82	90	35.2	46 (≥ 5 cm)	–
	24	2013	Konglund et al.[35]	2003–2013	Norway	Retro.	51	27	–	83.4	90	51	–	–
Total or mean							162	103	83.5	82.7	88.7	35	48.7 (≥ 5 cm)	–

Pro.: prospective, Retro.: retrospective.

Table 2 Summary of elderly patients with meningioma (symptom, KPS, ASA, pathology, and mortality)

Age Class	Case no.	Preoperative condition		ASA classification (%)				WHO grade (%)			Recurrence (%); year	Mortality (%)				
		Asymptomatic or no neurological deficit (%)	KPS ≥ 80 (%)	I	II	III	IV	I	II	III		In–hospital	1 M	3 M	1 Y	5 Y
60	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	2	–	88.9	5.7	54.7	37.7	1.9	94.4	3.7	–	–	5.6	5.6	7.4	9.3	–
Total or mean		–	88.9	5.7	54.7	37.7	1.9	94.4	3.7	–	–	5.6	5.6	7.4	9.3	–
65	3	–	–	–	–	–	–	–	–	–	–	6.5	–	–	–	–
	4	–	–	–	–	–	–	–	–	–	24.1; 5	–	–	6.8	–	–
	5	–	15	–	–	–	–	92.5	6.7	0.8	16.5; 5	0	–	5.8	13.7	16.2
	6	–	–	–	–	–	–	93.1	6.1		–	3.2	–	–	–	–
	7	4.9	70.1	3.7	31.1	60.4	4.8	87	12	1	–	–	3.7	6.7	6.7	–
	8	43	65.1	76.7		21	2.3	94.2	5.8	0	–	1.2	–	1.2	2.3	–
	9	–	–	–	–	–	–	85	12	3	11; 15.6	–	4	7	–	14
Total or mean		24.0	50.1	55.8		40.7	3.6	90.4	8.5	1.2	13.9; 8.5	2.7	3.9	5.5	7.6	15.1
70	10	–	–	–	–	–	–	92.5	4.5	3	–	–	7.6	12.1	16.7	–
	11	100	100	–	–	–	–	–	–	–	–	–	0	–	–	–
	12	–	–	–	–	–	–	–	–	–	–	4	–	–	–	–
	13	–	–	0	76.2	23.8	0	–	–	–	0; 5	0	0	0	4.8	–
	14	17	12 (≥ 90)	–	–	–	–	91.1	7.8	1.1	6.7; 8	–	6.7	7.8	15.6	–
	15	20	80	–	–	–	–	92	0	8	10; 2.8	4	4	–	–	–
	16	100	100	–	–	–	–	–	–	–	–	–	–	–	–	–
	17	–	–	0	67.4	32.5	0	100	excluded		4.6; 3	0	0	0	0	7
	18	–	–	–	–	–	–	–	–	–	–	–	2.5	–	6.3	26.6
	19	–	–	–	–	–	–	–	–	–	–	–	6.1	–	–	–
	20	–	–	0	9.3	68.2	22.1	–	–	–	–	–	12	–	–	–
	21	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Total or mean		45.7	90	0	51.0	41.5	7.4	93.9	4.1	4.0	5.2; 4.7	2	4.3	5.0	8.7	16.8
80	22	11	62	33	50	17	0	–	–	–	2.7; 4	–	10.8	13.5	16.2	24.3
	23	–	56.8 (≥ 60)	0	29.7	59.4	10.8	63.5	30	6.5	5.4; 7.7	0	0	1.4	9.4	27
	24	43.1	41.2	33.3		58.8	7.8	88.2	9.8	2	–	3.9	–	5.9	15.7	–
Total or mean		27.1	51.6	22.1	39.9	45.1	9.3	75.9	19.9	4.3	4.1; 5.9	2.0	5.4	6.9	13.8	25.7

ASA: American Society of Anesthesiologists, WHO: World Health Organization.

Table 3 Summary of elderly patients with meningioma (cause of mortality, risk factor, deterioration rate, and complications)

Age Class	Case no.	Cause of mortality (%)		Risk factors for death	Deterioration rate	Complication (%)		Conclusive recommendation	Comment
		Operative	General			Brain	General		
60	1	–	–	–	–	–	–	No cognitive deterioration	
	2	–	–	–	31.5	33.5	11.2	Elderly risk, KPS	SKALE
Total or mean		–	–		31.5	33.5	11.2		
65	3	–	–	–	17.8	13	15.8	Modified protocol	With all age
	4	8.4	–	Barthel Index, lung disease	–	–	–	GSS	–
	5	–	–	–	–	47.2	4.4	GSS	–
	6	–	–	Age, elective status	–	11	6.5	CCS	–
	7	5.5	1.2	SKALE	–	49.4	4.9	CRGS, SKALE	–
	8	–	–	Preoperative KPS	–	–	–	Preoperative KPS > 70	–
	9	–	–	–	–	–	–	Same as age–matched general population	–
Total or mean		7.0	1.2		–	–	–		
70	10	–	–	Recurrent meningioma	18.2	30.3	19.7	Risk of elderly recurrent meningioma	–
	11	–	–	–	–	23.3		Elderly risk of asymptomatic meningioma	With all age and conservative
	12	–	–	–	53.4	–	–	Elderly risk	With all age
	13	–	–	–	–	14.3	28.6	No elderly risk	With all age
	14	3.9	11.7	–	–	–	–	CRGS	–
	15	0	4	–	16	16	0	Multimodal strategy	With conservative
	16	–	–	–	9.3	11.1	5.6	Elderly risk of asymptomatic meningioma	With all age and conservative
	17	–	–	Decreased KPS	7	30.2	23.2	No elderly risk	With all age
	18	–	–	–	–	–	–	No elderly risk	With other tumors
	19	–	–	–	–	–	–	Low 1–year mortality	With other tumors
	20	–	–	–	–	29.8		Elderly risk, ASA	With all age
	21	–	–	–	–	–	–	Elderly risk, KPS, duration of operation, patient selection	With all age
Total or mean		2.0	7.9		20.8	22.1	15.4		
80	22	–	–	KPS < 70	–	2.7	–	KPS ≥ 70	–
	23	1.4	–	SKALE	–	6.8	2.7	SKALE score ≥ 8	–
	24	–	–	–	13.7	–	–	SKALE score	–
Total or mean		1.4	–		13.7	6.8	2.7		

ASA: American Society of Anesthesiologists, CCS: Charlson comorbidity score, CRGS: Clinical Radiological Grading System, GSS: Geriatric Scoring System, KPS: Karnofsky performance status, SKALE: sex, KPS, ASA, tumor location, and peritumoral edema.

was 27.1%, and mean KPS score over 80 was 51.6%. The mean ASA class I, II, III, and IV frequencies were 22.1%, 39.9%, 45.1%, and 9.3%, respectively, and the WHO tumor grade I, II, and III frequencies were 75.9%, 19.9%, and 4.3%, respectively. The mean in-hospital, 1-month, 3-month, 1-year, and 5-year mortality rates were 2%, 5.4%, 6.9%, 13.8%, and 25.7%, respectively, with surgical and general mortality rates of 7.0% and 1.2%, respectively. The authors of studies in this category concluded that the SKALE score was useful in this population.

Pathology and tumor recurrence

Thirteen of the 24 papers reported histological findings. Notably, more than 90% of patients in the over 60, 65, and 70-year-old groups had WHO grade I meningiomas; -whereas the over 80-year-old group had WHO grade I, II, and III frequencies of 75.9%, 19.9%, and 4.3%, respectively. Ten studies reported recurrence rates ranging from 0% to 24.1% during follow-up durations of 2.8–15.6 years (Table 2).

Tumor control after meningioma resection is apparently similar in elderly patients compared with younger patients. The 5-year disease recurrence rates in elderly patients were 0–24.1%, so not higher than the rates of 7–16%[36–38] reported for meningioma patients overall. However, elderly meningioma patients tended to have higher frequencies of WHO grade II or III tumors,[39] peaking in men aged 75–84 years and women aged 65–74 years according to the Central Brain Tumor Registry of the United States (CBTRUS),[39] and this factor presented the most serious follow-up challenge. Higher age is a significant prognostic factor in patients with atypical meningioma,[40] in agreement with other studies that identified older age as a significant risk for recurrence and shorter survival.[41–45] According to CBTRUS, the incidence of WHO grade II intracranial meningiomas increased from 0.28 to 0.30 between 2004 and 2010, representing an annual percent change of 3.6%.[39] The incidence of WHO grade II/III meningiomas was higher in women aged 35–64 years compared with males in the same age group, but was higher among men in the ≥ 75-year age group. Therefore, careful evaluation is essential in elderly male patients who may have grade II/III meningioma.

Mortality, complications, and grading systems

Cumulative mortality data are presented in Table 2. Twenty-one of 24 studies reported postoperative mortality. Overall, the reported in-hospital mortality rates ranged from 0% to 6.5%, and the rate ranges at 1 month, 3 months, 1 year, and 5 years were 0–10.8%, 0–13.5%, 0–16.7%, and 7–27%, respectively. No differences were found in in-hospital or 1- to 3-month mortality rates between the age categories, but the over 80-year-old category had higher rates of 1- and 5-year mortality (9.4–16.2% and 24.3–27%, respectively). No differences were found in the rates of operative and general mortality (Table 3), with respective ranges of 0–8.4% and 1.2–11.7%. The rate of operative mortality was only 1.4% in the oldest group. Six studies investigated statistical risk factors for death (Table 3) and identified Barthel index, lung disease, age, elective status, SKALE, preoperative KPS, and recurrent meningioma. The rates of neurological and general complications ranged from 2.7% to 49.4% and from 2.7% to 28.6%, respectively. The most commonly reported complications were postoperative hematoma, infection, and cerebrospinal fluid leakage.

The ASA physical classification system was most commonly used to assess preoperative physical status, with frequencies of class I, II, III, and IV ranging from 0% to 33%, 9.3% to 76.2%, 17% to 68.2%, and 0% to 22.1%, respectively. The worst preoperative ASA score resulted in the worst mortality rate at 1 month after surgery.[32] Four grading systems were used,[13–17,19,35,46] and the predictive and prognostic significances of these grading systems in each study are described in Table 4. The CRGS was evaluated in two studies,[17,22] and higher CRGS score was associated with lower 1-month mortality. Lower SKALE grading score was associated with a higher 1-year mortality rate.[13] CCS was found to correlate positively with in-hospital mortality and complication rates.[16] Higher scores on the GSS were associated with better outcomes, including lower mortality rates at different time points (1 month and 1, 3, and 5 years), reduced recurrence at 1 year, and better 5-year functional outcomes.[15] The SKALE and KPS scores were the most commonly identified risk factors of death in each age category, although deterioration rates differed among studies. The main conclusive recommendation in the 60- and 80-year-old categories was the usefulness of a scoring system, whereas the designation of elderly as a risk factor was recommended in the 70-year-old category.

All 4 grading systems mentioned in this review showed correlations with mortality; moreover, some were associated with other outcomes. The CRGS/GSS and CCS do not consider patient sex, which has been identified as prognostic in recent large series.[13,14] In contrast, SKALE does not incorporate tumor size or preoperative neurological deficits. The CRGS, SKALE, GSS, and CCS all consider comorbidities, whereas the latter does not incorporate the radiological features of the tumor. None of the

Table 4 Clinical scoring system for elderly patients with meningioma

	SKALE	CRGS	CCS	GSS
Score components				
Tumor size	−	+	−	+
Neurological condition	−	+	−	+
KPS	+	+	−	+
Tumor location	+	+	−	+
Peritumoral edema	+	+	−	+
Concomitant disease	−	+	+	(+)
Diabetes mellitus	−	−	+	+
Hypertension	−	−	+	+
Pulmonary disease	−	−	+	+
Other diseases	−	−	+	−
Sex	+	−	−	−
ASA classification	+	−	−	−
Known correlations				
Mortality	S	S	S	S
Complication	Not tested	Not tested	S	Not tested
Recurrence	Not tested	Not tested	Not tested	S
Function	Not tested	Not tested	Not tested	S

ASA: American Society of Anesthesiologists, CCS: Charlson comorbidity score, CRGS: Clinical Radiological Grading System, GSS: Geriatric Scoring System, KPS: Karnofsky performance status, S: significant association, SKALE: sex, KPS, ASA, tumor location, and peritumoral edema.

proposed methods consider radiological or physical changes over time. The predictive values of total CRGS and SKALE scores for 1-year mortality were confirmed in 2012 after intracranial meningioma surgery in patients aged 65 years or older,[22] but the statistical significance of all component elements were not reproduced. We note that neither system allows adjustment for age, but extending their use to younger age groups would not be difficult. The SKALE scoring system could be easily incorporated in daily clinical settings and could facilitate communication with and treatment of relevant patients.

Stereotactic radiosurgery and surgical timing in elderly patients with meningioma

Stereotactic radiosurgery (SRS) can be used to treat small- or medium-sized meningiomas, which yields long-term tumor control rates comparable with those of Simpson grade 1 resection.[47] SRS is associated with minimal procedure-related morbidities and is particularly suitable for tumors located in surgically less accessible locations, such as the skull base.[48,49] However, the indications for radiation therapy of asymptomatic elderly patients should be carefully considered because of the approximately 1% rate of possible malignant transformation.[50] SRS is usually not feasible for large-sized meningiomas, and surgical resection is preferred for immediate relief of the mass effect.[51] Clinical decision making is relatively straightforward for symptomatic lesions or those causing life-threatening mass effects. In contrast, minimally symptomatic meningiomas that are too large for SRS are more challenging, as unconsidered decisions for aggressive surgery may potentially jeopardize the patient's QOL, whereas delayed treatment could result in increased operative risks and suboptimal functional recovery. Therefore, the optimal surgical timing is most important for elderly patients with meningioma.

Surgical risk factors and indications in elderly patients with meningioma

Several recent large studies have suggested increasing age as a prognostic risk factor in patients indicated for intracranial meningioma surgery,[13,14,16,32,52] but clinical and functional status[13–16,18,32,34,53–55] and radiological features[13,17,25,32,53,54,56,57] are still more frequently recognized as risk factors. Moreover, female sex has been associated with better prognosis.[13,14,17] In addition, the risks of a wait-and-see strategy for elderly patients should not be underestimated, as the patient's medical condition is not likely to improve after diagnosis, and tumor-related mortality increases among patients who received conservative treatment compared with those who underwent resection.[56] It is unclear whether increasing age truly contributes to increased mortality in elderly patients with slow-growing meningiomas.

The present review observed 1-year mortality rates after meningioma resection of 0–16.7% among elderly patients with skull base-related location rate of approximately 45%, size over 4 cm rate of 60%, and asymptomatic rate of 30%, which was comparable with the range of 2–18% reported for unselected cohorts.[58–60] No excess 1-year mortality was found even among octogenarians (9.4–16.2%). Similarly, the 5-year mortality rates among elderly subjects (7–27%) were not higher than the rates reported for general populations (9–27%).[59–61] However, 5-year mortality rates of 24.3–27% among subjects over 80-year-old group might indicate less favorable long-term outcomes following meningioma resection. Both natural aging and altered physiological responses to surgery might have contributed to this observation, although uncertainty remains because of the incomparable cohorts and small cohort size.

Overall, we could not make direct comparisons because of variability in study design and found that among elderly patients, survival after meningioma resection is similar to that in the general population. Comparisons of median overall survival revealed no significant differences between older patients and the reported average life expectancy of the general German population of the same age.[24] In contrast, distinctly prolonged life expectancy after gross total removal might indicate that maximal safe tumor resection is also beneficial for elderly patients with thorough perioperative risk stratification and careful management.

Frailty and future directions in elderly patients with meningioma

One common theme uncovered during evaluations of frailty is increased vulnerability to stressors resulting from decreased physiological reserves,[62–64] which then increases the risk of adverse clinical consequences of these stressors.[65] Stressors can be classified as attributable to either acute or chronic illness, as well as to iatrogenic processes.[66] Several models have outlined the pathophysiology underlying the development and manifestation of frailty, but the two most commonly referenced models are the ''phenotype'' model[67] and the ''deficit'' model.[64] In the former, frailty manifests as ''declines in lean body mass, strength, endurance, balance, walking performance, and low activity,'' and assessments evaluate the presence of these features. In the latter model (e.g., Canadian Study of Health and Aging: CSHA), "summing the number of impairments" and clinical deficits, including a large range of symptoms from an inability to perform activities of daily living to mood disorders, can also determine frailty.

Regardless of the model used, healthcare practitioners should be mindful of the profound effects of exposure to stressors on the health statuses of patients deemed frail, as well as the potential associations with poor outcomes. For example, frail patients are at increased risk of adverse events such as delirium,[68] procedural complications, disability, mortality, morbidity, slowed recovery,[64,66] cardiovascular events, and increased length of hospital stay.[69]

Some studies suggest that the factors preceding frailty are introduced before a patient reaches old age[70]; as such, frailty could be considered a model of unsuccessful aging. Clinical Frailty Scale of CSHA was used to determine that 43.3% of patients in a cohort of 2,305 patients aged 65 years and older were classified as "vulnerable" or poorer.[64,65] Mortality was identified as a perioperative outcome associated with frailty.[62,71–77] However, no reports have discussed frailty among elderly surgical patients in the neurosurgical field. Additional evidence is needed in this area.

Future research should evaluate how frailty, once identified, could be modified with the intent to develop preventative strategies or minimize negative perioperative adverse events. Currently no single universal definition of frailty or standard assessment/scoring method is accepted.[78] Frailty is a multifactorial and complex health state representing the interplay among physiological, endocrine, genetic, inflammatory, and age-related factors. However, as age is a strong risk factor for frailty, perioperative clinicians must be knowledgeable about frailty, which is common among older adult patients and will become increasingly frequent as the population presenting for surgery continues to age. Frailty has also been associated with adverse perioperative outcomes among patients undergoing many types of surgical interventions regardless of the assessment method. Future research is needed to determine whether evaluation of frailty status should be included in routine perioperative care and whether the effects of frailty can be minimized.

Limitations

Larger-scale prospective studies that compare the outcomes of younger and older patients are needed to provide important information about clinical outcomes and risk factors. Details regarding patient selection, operative techniques, descriptions of complications, and causes of death should be standardized to allow meaningful comparisons. Studies that recruit only octogenarian patients would be valuable for decision making in this group of patients.

This review only included studies published between 2000 and 2016, so may have failed to draw from all available data. More recent studies might better reflect contemporary findings, given the rapid advances in surgical techniques in recent decades. We screened for studies that included subgroup analyses of elderly patients, but may have missed studies that did not specifically target the elderly. Therefore, a publication bias toward elderly cohorts with favorable outcomes at more resource-rich centers might have influenced our results. The included studies were heterogeneous, with few prospective studies. Furthermore, variations in the indications for surgery among centers may have contributed to the observed inconsistencies.

Conclusion

The current evidence indicates satisfactory surgical outcomes among elderly patients with intracranial meningiomas, although the risks of surgical complications necessitate careful decision making. This review of risk factor analysis emphasized the importance of considering the preoperative status, presence of comorbidities, and optimum surgical timing during patient selection. Future research and a prospective randomized study should address the causes and prevention of complications, as well as inter-racial differences. Furthermore, new indications for elderly patients with meningioma considering frailty are recommended.

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Conflicts of Interest Disclosure

The authors have no conflict of interest regarding this article.

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