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Multivariate risk factor analysis and literature review of postoperative deterioration in Karnofsky Performance Scale score in elderly patients with skull base meningioma

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OBJECTIVE Elderly patients are particularly at risk for severe morbidity following surgery. Among the various risk factors, age and skull base location of meningioma are known to be poor prognostic factors in meningioma surgery. The authors conducted this study to analyze significant preoperative risk factors in elderly patients with skull base meningioma.

METHODS A total of 265 elderly patients (≥ 65 years old) with meningioma were surgically treated at the authors' institute and affiliated hospitals between 2000 and 2016, and these cases were reviewed. Among them, 57 patients with skull base meningioma were evaluated. Among the various risk factors, the authors analyzed age, sex, Karnofsky Performance Scale (KPS) score, American Society of Anesthesiologists score, and tumor size, location, and pathology. Body mass index (BMI) and serum albumin were investigated as the frailty factors. The authors also reviewed 11 surgical studies of elderly patients ≥ 60 years old with meningioma.

RESULTS The mean age was 72.4 ± 5.7 years, and 42 patients were female (73.6%). The mean size of meningioma was 36.6 ± 14.8 mm at the maximum diameter, and the mean follow-up period was 31.1 ± 31.5 months. (The continuous variables are expressed as the mean ± SD.) Histopathological investigation revealed a higher incidence (71.9%) of WHO Grade I. The rates of deterioration after surgery, at 3 months, and at 1 year were 33.3%, 37.3%, and 39.1%, respectively. Univariate analysis revealed location, preoperative KPS score, BMI level 2, and serum albumin level ($p = 0.010$, 0.017, 0.0012, and 0.0019, respectively) to be poor prognostic factors. Multivariate analysis revealed that location ($p = 0.038$) and BMI ($p = 0.035$) were risk factors for KPS score deterioration immediately after surgery. According to the 11 papers reviewed, the median rate (25th–75th percentile) of skull base–related location was 43.5% (39.6–47.75); for asymptomatic status the mean was 24%; and for mortality at 3 months and 1 year the medians were 6.3% (0.7–7.1) and 8% (4.8–9.4), respectively.

CONCLUSION Careful preoperative assessment based on the frailty concept was essential for better outcome in elderly patients with skull base meningioma. The BMI is appropriate as a quantitative factor for measure of frailty, particularly in elderly individuals with skull base meningioma. Further prospective randomized controlled trials are necessary to validate frailty as a preoperative risk factor. Not only patient selection but also surgical timing was an important factor.

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KEY WORDS elderly; skull base; meningioma; surgery; frailty; outcome

Meningioma, a neoplastic growth originating from meningothelial cells embedded in the meninges, is the second most common primary brain tumor and accounts for 13%–26% of primary intracranial tumors.[7,43] Based on the site of origin, meningiomas can be broadly classified as skull base and non–skull base meningiomas—and skull base meningiomas constitute approximately 30% of all intracranial meningiomas.[13] Skull base location is a known poor prognostic factor in meningioma surgery and is an important determinant in

ABBREVIATIONS ASA = American Society of Anesthesiologists; BMI = body mass index; KPS = Karnofsky Performance Scale.

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treatment strategy and further clinical course.[27,28] Despite astounding improvements in microsurgical technique and treatment strategy, the difficulty in approaching the tumor, presence of vital neurovascular structures at the skull base, narrow surgical corridor with difficulty in obtaining total resection of the tumor, longer operative time, and greater volume of blood loss all render skull base location as a surgical challenge.[5,24,27] The relatively large size of the meningioma results in neurovascular compression and infiltration, which are common at the skull base, and impede the total resection and may require further adjuvant treatment, adding to the complications.

According to the revised WHO classification of 2016, the lifetime risk of developing meningioma is 1%, and the incidence increases with age. The incidence rate progressively increases from 4.9/100,000 in the 45- to 54-year age group to 7.9/100,000 and 12.8/100,000 in the 55- to 64-year and the ≥ 65-year age groups, respectively.[9] With the increase in life expectancy and more frequent use of advanced diagnostic neuroimaging, the detection and prevalence of symptomatic and asymptomatic meningioma in the elderly is increasing as well.[30]

Several studies have evaluated preoperative risk factors in the elderly, including preoperative neurological status, American Society of Anesthesiologists (ASA) score, and tumor characteristics in association with surgical outcome. Frailty, an indicator of functional and physiological vulnerability in the elderly, exhibits a dose-response relationship with poor survival.[22] One model defines frailty as a phenotype of clinical syndromes, whereas the other defines it as a cumulative deficit composed of multiple symptoms, signs, disease, and disabilities.[10,22] Sheehan et al. have reported a positive association between body mass index (BMI) (i.e., obesity) and frailty.[41] Very few studies have considered obesity and high BMI as a risk factor for meningioma incidence.[1,26,35,44] Furthermore, Michaud et al. have reported a positive association of meningioma with BMI that is better than other anthropometric measures.[26] However, the association of BMI with frailty and postoperative deterioration reported by these authors has not been clearly elucidated. The concept of frailty has, moreover, not been properly studied in association with the surgical outcome in elderly patients with skull base meningioma.

In this study, we aimed to retrospectively analyze significant preoperative risk factors in elderly patients with skull base meningioma, taking the concept of frailty in terms of BMI and serum albumin as a risk factor for an adverse outcome following surgery.

Methods

Patient Population

This study was conducted after receiving approval from the institutional review board of Hiroshima University, which waived the need for informed consent because of the opt-out method. We retrospectively reviewed a total of 265 elderly patients (≥ 65 years) with meningioma who underwent resection at our institute and other affiliated hospitals between 2000 and 2016. Among these, 57 patients (21.5%) had skull base meningioma and were evaluated in detail.

Of the 57 skull-base meningiomas (42 in female and 15 in male patients) locations were as follows: 17 at the posterior fossa, 3 at the foramen magnum, 9 tentorial, 1 falcotentorial, 9 petroclival, 1 petrous, 4 intraventricular, 7 at the olfactory groove, 5 frontobasal, and 1 at the orbital fossa. All cases were histopathologically confirmed as meningioma.

Preoperative Risk Factors

Risk factors for meningioma have been extensively studied, and these include patient-related, tumor-related, and treatment-related factors. Among the various risk factors, we analyzed age, sex, preoperative Karnofsky Performance Scale (KPS) score, ASA class, and tumor size, location, and pathological type as preoperative risk factors. The BMI and serum albumin were investigated as the frailty factors in elderly patients.

Postoperative Outcome

The postoperative outcome was assessed based on the postoperative KPS score at the following intervals: immediately postoperatively and at 3 months and 1 year following surgery. Postoperative deterioration was defined as any decline in postoperative KPS score compared to the preoperative KPS score. Similarly, postoperative complications were categorized as brain and other systemic complications.

Histopathological Study

Tumor specimens were obtained in all cases after total (Simpson grades I and II) or subtotal (Simpson grades III–V) resection and fixed in formalin, and then embedded in paraffin blocks. Representative slides were stained with H & E reagent and then histologically diagnosed and graded according to WHO criteria.

Review of Literature on Elderly Patients With Meningioma

We searched the PubMed database using the search words "meningioma", "skull-base", "elderly", and "surgery" for clinical studies published in English. First, the abstracts of all the articles found with these search words were reviewed and, if considered relevant, a full text of the article was found and reviewed. References from those articles were also reviewed. All case studies and review articles were excluded. Twenty-four clinical studies were finally selected and reviewed, and those with no information regarding skull base location were excluded. Studies in which skull base meningiomas constituted ≥ 33% were selected. Finally, 11 clinical studies were included for a literature review, and information was collected and categorized to include study characteristics (author, year, and sample size), patient characteristics (mean, median, and maximum age; sex; tumor size, location, and pathology; KPS score; and ASA grading), and treatment outcome (mortality rate at 1 and 3 months and at 1 and 5 years).

Statistical Analysis

All the statistical analyses were performed using JMP (Pro 13 software, SAS Institute). The factors analyzed as

potential preoperative risk factors included age, sex, preoperative KPS score, ASA class, tumor size and pathology, BMI, and serum albumin. Based on various risk factors, patients were classified to assess the influence of these factors on surgical outcome, as follows: 1) KPS score (≥ 80 and ≤ 70); 2) preoperative ASA class (class I–V); 3) preoperative BMI (< 18.5 kg/m^2, BMI level 1; 18.5–25 kg/m^2, BMI level 2; and > 25 kg/m^2, BMI level 3); 4) preoperative serum albumin (< 3.5 g/dl and 3.5–5.0 g/dl); 5) extent of resection (Simpson grade I–V); and 6) histopathological grade (WHO grade I–IV). Four of the patients did not have complete information regarding preoperative BMI and 6 patients had no information regarding preoperative serum albumin level, and these patients were excluded from those particular studies. The treatment outcome was measured by the improvement or deterioration of the postoperative KPS score immediately after surgery, at 1 and 3 months, and at 1 and 5 years. One patient had no information regarding extent of resection, and was excluded from treatment outcome studies.

The continuous variables in our patients are expressed as the mean ± SD. Multivariate analyses with logistic regression modeling of specific risk factors was performed to assess the influence of these factors. The continuous variables from the literature review were expressed as the median and as the 25th to 75th percentile, and were compared using the Mann-Whitney U-test, and the discrete variables were compared using the chi-square test or Fisher's exact test. All the values with $p < 0.05$ were considered significant.

Results

Patient Characteristics

The patient and tumor characteristics are summarized in Table 1. The skull base location in elderly (≥ 65 years) patients with meningioma comprised 21.5% of individuals (57/265). The mean age of the 57 patients with skull base meningioma was 72.4 ± 5.7 years (median 71 years, range 65–85 years), with 42 women and a female/male ratio of 2.8:1. Preoperative KPS score was ≤ 70 in only 17.5% (10/57) of patients. For preoperative ASA classifications, 57.9% of patients were class II, 28.1% were class I, 12.3% were class III, and only 1 patient (1.8%) was ASA class V. For BMI scores, 73.6% of patients had normal weight (BMI level 2) and only 3.8% were underweight (BMI level 1), whereas 22.6% were overweight (BMI level 3). Last, 23.5% of elderly patients had hypoalbuminemia (serum albumin level of < 3.5 g/dl), whereas the rest had a normal level.

Tumor Characteristics

The mean size of the meningiomas was 36.6 ± 14.8 mm (median 35 mm, range 11–86 mm) at the maximum diameter. The mean follow-up period was 31.1 ± 31.5 months (range 1–122 months); 2 patients were lost to follow-up. Histopathologically, meningioma at the skull base location showed relatively higher incidence (71.9%) of WHO Grade I meningioma, with 22.8% and 5.3% of Grade II and Grade III meningiomas, respectively.

TABLE 1. Summary of characteristics in 57 patients with skull base meningiomas

Variable	Value
Patient characteristics	
No. of patients (F/M)	57 (42/15)
F/M ratio	2.8:1
Age	
Mean age ± SD (range) in yrs	72.4 ± 5.7 (65–85)
Median age	71
Preop KPS score; n (%)	
≥80	47 (82.5%)
≤70	10 (17.5%)
Mean KPS score ± SD/median KPS score (IQR)	85.09 ± 14.9/90 (80–90)
Preop ASA class; n (%)	
Class I	16 (28.1%)
Class II	33 (57.9%)
Class III	7 (12.3%)
Class IV	0 (0%)
Class V	1 (1.8%)
Preop BMI; n (%)	
Level 1, <18.5 kg/m^2	2 (3.8%)
Level 2, 18.5–25 kg/m^2	39 (73.6%)
Level 3, >25 kg/m^2	12 (22.6%)
Mean BMI ± SD/median BMI (IQR)	21.2 ± 6.6/21.8 (20.2–24)
Preop SA; n (%)	
<3.5 g/dl	12 (23.5%)
3.5–5.0 g/dl	39 (76.5%)
Mean SA ± SD/median SA (IQR)	3.5 ± 1.34/4 (3.3–4.3)
Tumor characteristics	
Mean size ± SD at the maximum diameter (range) in mm	36.6 ± 14.8 (11–86)
Extent of resection—Simpson grade; n (%)	
Grade I	4 (7.1%)
Grade II	23 (41.1%)
Grade III	6 (10.7%)
Grade IV	23 (41.1%)
Grade V	0 (0%)
Histopathology—WHO grade; n (%)	
Grade I	41 (71.9%)
Grade II	13 (22.8%)
Grade III	3 (5.3%)
Follow-up period	
Mean ± SD in mos	31.1 ± 31.5
Range in mos	1–122

IQR = interquartile range; SA = serum albumin.

Surgery and Postoperative Outcome

Gross-total resection (Simpson grades I and II) was obtained in 48.2% of patients, whereas 51.8% patients received subtotal resection (Simpson grades III and IV),

TABLE 2. Details of patients with immediate severe postoperative brain complications

Case No.	Age (yrs)/ Sex	Location	Size Max (mm)	KPS Score		ASA	BMI	Albumin	Simpson Grade	WHO Grade	Complications
				Preop	Postop						
1	65/F	Petroclival	32	80	70	2	18	2.2	IV	III	CN palsy
2	65/F	Posterior fossa	43	100	90	1	21	3.8	IV	I	CN palsy
3	66/F	Tentorial	36	60	40	2	21.6	—	IV	II	Cerebral infarction
4	67/F	Petroclival	32	70	60	1	21	3.7	IV	I	CN palsy
5	69/F	Posterior fossa	30.0	60	50	3	30.1	4.2	II	I	CN palsy
6	70/F	Posterior fossa	34.0	90	80	2	18.6	4.6	IV	I	Other
7	70/F	Tentorial	45	70	0	2	23.47	4.7	IV	III	Death
8	73/F	Intraventricular	40	90	80	1	20	4.6	I	I	Cerebral infarction
9	73/M	Petroclival	29	100	80	1	25.6	4.2	IV	I	CN palsy
10	75/M	Tentorial	35	90	70	5	19	3.2	IV	II	Cerebral infarction
11	75/F	Tentorial	40	80	60	2	24	3.3	IV	II	CN palsy
12	76/F	Falcotentorial	35	80	60	2	19	2.6	IV	III	Dementia
13	78/F	Foramen magnum	23	90	80	2	21	4.0	IV	I	CN palsy

CN = cranial nerve; max = maximum.

with a majority of that subgroup (41.1%) receiving grade IV resection. Postoperative deterioration was defined as the deterioration in the KPS score. A total of 19 patients (33.3%) had deterioration in the KPS score immediately following surgery, and an additional 5 patients had deterioration at 3 months postsurgery, whereas 2 patients had recovered from initial deterioration at 3 months postsurgery. There was 1 (1.8%) in-hospital death related to surgical procedure in our study. Details regarding the patients with severe brain complications (excluding patients with other systemic complications) are shown in Table 2.

Among the 19 patients with postoperative complications, the most common one was cranial nerve palsy (36.8%), followed by cerebral infarction (15.8%). One patient with falcotentorial meningioma had cognitive impairment following surgery. The mean size of the tumor in the patients with complications was 38.6 ± 13.7 mm and the posterior fossa was the most common tumor location (36.9%). Most of these patients (78.9%) with complications received subtotal resection (Simpson grades III and IV resection) and harbored WHO grade I tumors (68.4%).

TABLE 3. Univariate analysis of various prognostic factors

Prognostic Factors	p Value
Age	0.053
Sex	0.601
Location	0.010*
Size	0.163
Preop KPS score	0.017*
ASA grade	0.227
BMI level 2	0.0012*
SA	0.0019*

* $p < 0.05$.

Risk Factor Analysis

To evaluate the prognostic value of various preoperative risk factors, the postoperative outcome was defined as good outcome or postoperative deterioration based on the KPS score calculated pre- and postoperatively, and postoperative deterioration was defined as decrease in postoperative KPS score compared with the preoperative score.

Patients were stratified for risk factor assessment based on BMI, which was classified as levels 1–3. Univariate analysis showed location of meningioma ($p = 0.010$), preoperative KPS score ($p = 0.017$), BMI ($p = 0.0012$), and serum albumin ($p = 0.0019$) to be the risk factors for poor outcome following surgery (Table 3). Both the OR analysis and multivariate analyses were performed to evaluate the significance of each factor in relation to KPS score deterioration immediately following surgery (Tables 4 and 5).

Multivariate logistic regression analysis showed location and BMI (level 2) as the risk factors for KPS deterioration immediately following surgery ($p = 0.042$ for frontobasal vs petroclival, $p = 0.038$ for frontobasal vs posterior fossa, and $p = 0.035$ for BMI level 2) (Table 4).

Analysis of the OR showed tumor location (petroclival and posterior fossa vs frontobasal [$p = 0.042$ for petroclival and 0.038 for posterior fossa comparison]; OR 2029.5 and 392.8, respectively) and BMI (level 2 vs level 3 [$p = 0.035$]; OR 93.8) to be the risk factors for poor outcome and KPS score deterioration immediately following surgery (Table 5), whereas age, sex, tumor size, and ASA status were nonsignificant.

Literature Review and Comparison With Our Study Results

The 11 reports in the literature that we reviewed are summarized in Table 6. The articles were categorized based on the definition of elderly age as follows: 1) ≥ 60 years; 2) ≥ 65 years; 3) ≥ 70 years; 4) ≥ 75 years; and 5)

TABLE 4. Multivariate analysis of preoperative risk factors causing deterioration of KPS score immediately following surgery

Prognostic Factors	p Value
Age	0.66
Sex	0.61
Location of meningioma*	0.038 & 0.042†
Size of meningioma	0.91
Preop KPS score	0.77
Preop ASA grade	0.99
BMI	0.035†
SA	0.99

* The locations compared were frontobasal versus posterior fossa, and frontobasal versus petroclival, respectively.
† $p < 0.05$.

TABLE 5. Odds ratio analysis of preoperative risk factors causing deterioration of KPS score immediately following surgery

Risk Factors			p	95% CI	
Location 1	Location 2	OR	Value	Lower	Upper
Frontobasal	Petroclival	2029.5	0.042*	1.31	3,144,639.9
Frontobasal	Posterior fossa	392.8	0.038*	1.38	111,509.4
BMI category I	BMI category II				
Level 3	Level 2	93.8	0.035*	1.39	6,347.4

* $p < 0.05$.

≥ 80 years. A comparison of our study results with the literature is shown in Table 7. The total number of patients included in these studies was 1150, with 517 females (44.9%), whereas 73.68% were females in our study. The median age of elderly meningioma patients was 73.4 years (25th–75th percentile: 71–78 years), which was almost the same as the median age in our study (71 years). The median percentage of patients with skull base meningioma was 43.5% (25th–75th percentile: 39.6–47.75) in the literature, whereas our study exclusively included elderly patients with skull base meningioma (i.e., 100% in our study had skull base meningioma).

The median percentage of patients with tumor size ≥ 4 cm was 52.1% in the literature, which was comparable with our study result of 42.1%. Similarly, 82.5% of our patients had a preoperative KPS score of ≥ 80, whereas it was found in only 56.8% (median) of patients in the literature review. Also, 53.1% of patients had ASA class ≥ 3 in the literature, compared to 14.1% in our study. Most of the elderly patients (median 88.2%) had WHO grade I meningioma, which was seen in 71.93% of our patients.

The mean in-hospital mortality rate in the literature review was 1.9%, and it was 1.8% (1/57) in our study. The median mortality rates (25th–75th percentile) at 1 month, 3 months, and 1 year in the literature review were 5.6% (0–12), 6.3% (0.7–7.1), and 8% (4.8–9.4), respectively.

Discussion

Several studies have suggested advanced age as a risk factor for adverse postoperative outcome in patients who undergo intracranial meningioma surgery. In addition to increasing age, other recognized risk factors are sex, preoperative clinical and neurological status, and tumor characteristics. Very few studies have evaluated the frailty factors in association with postoperative outcome in intracranial meningioma surgery, and none have reported the association of frailty factors with skull base meningioma surgery in the elderly. Our study results show that careful preoperative assessment of elderly patients with skull base meningioma, including frailty factors (i.e., BMI), is essential for better postoperative outcome.

Meningioma, in the elderly, mostly presents as a slow-growing, asymptomatic, benign incidental tumor; these patients are offered conservative observation and follow-up, with surgical treatment being reserved for clinically symptomatic tumors.[19,42] In skull base meningioma, however, rapid growth rates and neurological deficits, even in small tumors, and biologically different characteristics of meningioma in surgically treated elderly patients favor resection as the mainstay of treatment, in addition to radiotherapy and radiosurgery for high-grade and residual tumors.[38,45] Elderly patients in particular, however, are at increased risk of severe morbidity and mortality following surgery. Several previous studies have reported increased morbidity and mortality in elderly compared with younger patients.[6,25] Poon et al., in their meta-analysis of the effects of surgery in the elderly, have reported an overall rate of complications ranging from 2.7% to 29.8% and an overall incidence of complications ranging from 3% to 61%.[33] However, some comparative studies have reported no association of age with postoperative outcome in elderly patients with skull base meningioma.[38] Our study results also show no significant association of age with postoperative outcome in elderly patients who underwent skull base meningioma surgery, which is consistent with the findings of a recent study by Yamamoto et al.[45]

Many previous studies report the high risk of mortality and morbidity and poor overall outcomes associated with radical skull base surgical strategies in elderly patients. On the contrary, Roser et al., have reported that even a radical skull base strategy does not significantly contribute to surgical morbidity in elderly patients with skull base meningioma.[38] Other studies have attributed postoperative complications in skull base meningioma surgery to direct surgical manipulation and approach, including nerve manipulation and brain retraction, postoperative brain edema, and cerebral infarction, and also the experience of the surgeon and the institute, regardless of the patient's age.[45] In the present study, our results showed that posterior fossa location of meningioma and preoperative KPS score are significant risk factors for poor postsurgical outcome, which is consistent with other studies. These findings can be explained by the technical difficulty, strong brain retraction and cranial nerve manipulation, and subtotal excision (grades III and IV resection in 78.9%) associated with skull base location, and poor neurological status associated with low preoperative KPS score, which showed limited recovery. The preoperative patient and neurological status and tumor-related neurological deficits

TABLE 6. Summary of published reports of elderly patients with skull base meningiomas

				Age (yrs)			Tumor Size (%)		Preop Condition (%)		ASA Class (%)				WHO Grade (%)			Mortality (%)				
Authors & Year	No. of Cases	F (%)	Elderly (yrs)*	Mean	Med	TL/SB (%)	≥4 cm (dia)	≥40 ml	Asymp	KPS Score ≥80	I	II	III	IV/V	I	II	III	In-Hospital	1 Mo	3 Mos	1 Yr	5 Yrs
Cornu et al., 1990	96	60	65	70	NR	40	52.1	NR	NR	52.1	21.9	50	28.1	NR	NR	NR	NR	NR	16	8.6	NR	NR
Gijtenbeek et al., 1993	93	66	60	67	NR	33	63.6	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	14	NR	NR	NR
Nakamura et al., 2005	21	NR	70	73.8	NR	100	NR	NR	NR	NR	0	76.2	23.8	0	NR	NR	NR	0	0	0	4.8	NR
Roser et al., 2007	43	NR	70	74.1	NR	100	NR	NR	NR	NR	0	67.4	32.5	0	100	Excluded		0	0	0	0	7
Sacko et al., 2007	74	47	80	82	85	35.2	46	NR	NR	56.8	0	29.7	59.4	10.8	63.5	30	6.5	0	0	1.4	9.4	27
Cohen-Inbar et al., 2010	250	152	65	73	NR	39.6	38	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	6.8	NR	NR
Pirracchio et al., 2010	46	NR	70	NR	NR	43.5	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	6.1	NR	NR	NR
Patil et al., 2010	258	5	70	NR	NR	44.2	NR	NR	NR	NR	0	9.3	68.2	22.1	NR	NR	NR	NR	12	NR	NR	NR
Grossman et al., 2011	164	125	65	72	NR	42.7	53	NR	4.9	70.1	3.7	31.1	60.4	4.8	87	12	1	NR	3.7	6.7	6.7	NR
Konglund et al., 2013[20]	54	35	60	NR	70	44.5	NR	27.8	NR	88.9	5.7	54.7	37.7	1.9	94.4	3.7	NR	5.6	5.6	7.4	9.3	NR
Konglund et al., 2013[21]	51	27	80	83.4	NR	51	NR	NR	43.1	41.2	33.3		58.8	7.8	88.2	9.8	2	3.9	NR	5.9	15.7	NR
Present study†	57	73.7	65	72.4	71	100	42.1	NR	0	82.5	28.1	57.9	12.3	1.8	71.9	22.8	5.3	1.8	0	0	0	0
Total or mean	1150	517	NA	74.41	77.5	52.15	50.54	27.8	24	61.8	8.08	45.5	46.1	6.78	86.6	13.9	3.2	1.9	6.38	4.6	7.65	17
SD	NA	NA	NA	5.6	NA	24.14	9.45	NA	NA	18.4	12.61	23.4	17.4	7.9	13.9	11.3	NA	2.67	6.25	3.5	5.3	NA
Median	NA	NA	NA	73.4	NA	43.5	52.1	NA	NA	56.8	1.85	50	48.3	4.8	88.2	10.9	NA	0	5.6	6.3	8	NA
25th to 75th percentile	NA	NA	NA	71 to 78	NA	39.6 to 47.75	42 to 53	NA	NA	46.65 to 70.1	0 to 13.8	29.7 to 61.1	30.3 to 59.9	0 to 9.3	75.3 to 94.4	6.8 to 21	NA	NA	0 to 12	0.7 to 7.1	4.8 to 9.4	NA

Asymp = asymptomatic; dia = diameter; Med = median; NA = not applicable; NR = not reported; TL/SB = tumor location: skull base.

* Definition of elderly age.

† Present study excluded from calculations.

TABLE 7. Comparison of our study results with the literature

Case No.	Variables	Our Study	Literature Review
1	Females	73.7%	44.95%
2	Median age in yrs	71	73.4
3	Skull base location	100%	52.15%
4	Tumor size ≥4 cm	42.1%	50.54%
5	Preop KPS score ≥80	82.5%	61.8%
6	ASA class <3	85.96%	53.58%
7	ASA class ≥3	14.03%	34.6%
8	WHO grade I	71.93%	86.6%
9	In-hospital mortality	1.8%	1.9%

in the elderly patients with skull base meningioma determined the outcome of the surgery. Treatment decisions in the elderly patient with skull base meningioma should be patient specific and are affected by patient-related factors (preoperative neurological status or KPS score, presence of comorbidities and/or ASA grade), tumor-related factors (location, size, location, calcification, perifocal edema), and surgery- or surgeon-related factors (timing, approach, and experience). This discrepancy in results warrants detailed evaluation of frailty factors as preoperative risk factors in elderly patients that may explain the differences in postoperative outcome.

The increased vulnerability to the stressors resulting from the poor general health and physiological reserve capacity of the elderly, which is also called frailty, might result in a difference in the outcome. Frailty, an indicator of functional and physiological vulnerability in the elderly, increases with age and exhibits a dose-response relationship with poor survival.[22] Frail patients are prone to increased risk of morbidity and death.[4,23,36] Very few studies have evaluated frailty as an independent risk factor for poor postoperative outcome in the elderly. The scoring systems used previously (i.e., the Clinical-Radiological Grading System [CRGS]; the Geriatric Scoring System [GSS]; and the sex, Karnofsky, American Society of Anesthesiology [ASA] score, location, and peritumoral edema [SKALE] system), although they provide valuable information for determining the treatment strategy in elderly patients with intracranial meningioma, do not incorporate frailty factors.[11,12,40]

Previous studies have already defined BMI[22] and serum albumin[3] as quantitative measures of physiological reserve capacity in the elderly, which is the hallmark of frailty. Sheehan et al. have reported a positive association of BMI (obesity) with frailty, which in turn is associated with death in the elderly.[41] Aghi et al. have reported a high risk of complications in obese male patients with meningioma following surgery; however, their study did not exclusively include elderly patients.[1] Lee et al. concluded that among older people who were of normal weight or were underweight, greater frailty was associated with poorer survival. Whereas overweight frail elderly patients tended to have no significant increase in mortality, those who were underweight and frail exhibited a significantly elevated rate of death.[22] Therefore, not only the highest BMI but also lower BMIs were a significant risk factor for frailty. In our patient series, there were only 2 obese patients with BMI > 30 kg/m^2. The English Longitudinal Study of Ageing[18] has reported frailty to be most common among those with a BMI < 20, and the Longitudinal Aging Study Amsterdam[34] has reported increased mortality in elderly patients with a BMI < 23. Because BMI is an indicator of the metabolic reserve, low or normal BMI may reflect low reserve capacity and unintentional weight loss, thus elevating the risk of adverse outcome, whereas a high BMI may provide metabolic reserve to withstand stressors.[8,15,37]

Our study results also support the consideration of low or normal BMI as a frailty factor and as an independent risk factor for adverse outcome and immediate KPS deterioration in elderly patients who undergo skull base meningioma surgery. Decreased physiological reserve capacity and slowed recovery associated with low or normal BMI might explain its association with adverse outcome. Several clinical and biochemical parameters have been reported for screening in patients at risk for in-hospital death.[3] Among the various biochemical markers, a serum albumin concentration of < 3 g/dl, a marker of aging, malnutrition, inflammation, and cachexia, has been reported to be highly sensitive parameter for predicting in-hospital mortality.[2,3] Our study results also show low serum albumin as a risk factor for adverse postoperative outcome in elderly patients with skull base meningioma. However, multivariate analysis did not show an association with poor outcome. Further prospective randomized controlled trials are warranted to identify an association of these factors with poor surgical outcome in elderly patients, and to minimize the adverse postoperative outcomes by addressing these readily modifiable frailty factors.

Limitations of the Study

Our study has some limitations. The small number of cases and lack of prospective studies limit the validity of the results. Other qualitative frailty factors such as muscle mass, low grip strength, low energy, slowed walking speed, low physical activity, unintentional weight loss, and preoperative cognitive function were not considered in the study. The retrospective design of our study did not allow for the analysis of the effect of modification of frailty factors. The follow-up period of the postoperative patients was limited. Our study was conducted in multiple institutions, which may have limited the uniformity in the operative skills and postoperative care, which in turn may have influenced the outcome.

Conclusions

Our study introduced BMI levels as frailty factors associated with adverse postoperative outcome and immediate KPS score deterioration following skull base meningioma surgery in elderly patients. Further randomized controlled trials are warranted to identify the association of these factors with poor surgical outcome in elderly patients and to minimize the adverse postoperative outcomes by modifying these frailty factors. Surgical treatment in elderly patients with skull base meningioma should be individualized and based on specific patient factors such as tumor characteristics and preoperative status in addition to

age, which should not be considered as the only barrier in achieving a good postoperative outcome.

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Disclosures

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

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Conception and design: Ikawa, Kolakshyapati. Acquisition of data: Ikawa, Kolakshyapati, Abiko, Mitsuhara, Kinoshita, Takeda. Analysis and interpretation of data: Ikawa, Kolakshyapati. Drafting the article: Kolakshyapati. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ikawa. Statistical analysis: Ikawa, Kolakshyapati. Administrative/technical/material support: Ikawa, Kurisu. Study supervision: Ikawa, Kurisu.

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