The 5-Factor Modified Frailty Index Predicts Complications and Worsening After Meningioma Surgery in Non-elderly Rather Than Elderly Patients: A Nationwide Registry Study

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Abstract

The simplified 5-factor modified frailty index (mFI-5) is a useful indicator of outcome for patients undergoing surgeries and considered as an important risk factor in elderly patients. However, its usefulness has not been validated based on age groups. We aimed to investigate the risk factors including the mFI-5 across age groups for complications and worse outcomes in meningioma surgery using data obtained from the nationwide database in Japan. We extracted data from the nationwide registry database in Japan between 2010 and 2015. Age (< 65, 65–74, and ≥ 75 years), sex, Barthel Index (BI), mFI-5 scores, and complications were evaluated. Multivariate logistic regression analyses identified risk factors across all age groups for worsening BI scores and complications after surgery. In 8,138 included cases, an mFI-5 score ≥ 2 items was a significant risk factor for worsening BI scores in patients aged < 65 years (odds ratio: 2.00; 95% confidence interval: 1.31-3.06), but not in patients aged 65-74 years and those aged ≥ 75 years. Similar results were noted for complications in patients aged < 65 years (2.40; 1.67–3.44), but not in patients aged 65-74 years and those aged ≥ 75 years. In conclusion, the mFI-5 scores can predict the risk of worsening outcome and complications in non-elderly patients aged < 65 years rather than in elderly patients aged ≥ 65 years. In meningioma surgeries, care must be taken when making decisions using the mFI-5 scores based on the patients' age.

Trial Registration

Name: Study on treatment method, age group, complications, and outcome of meningiomas and hemangioblastomas using DPC, URL: http://www.umin.ac.jp/ctr/index-j.htm

ID: UMIN000038486, No.: R000043856

Introduction

The recent increase in average life expectancy and frequency of diagnostic neuroimaging has resulted in a globally increased rate of incidental meningioma detection in the elderly [14]. Chronological age is considered one of the most effective surgical indications for elderly patients with meningioma worldwide; however, surgical decision-making strategies for elderly patients should be carefully reviewed considering the increased frailty and decline in health that are associated with advanced age.

To assess frailty, the 11-factor modified frailty index (mFI-11) was derived from the Canadian Study of Health and Aging Frailty Index [25] by matching 11 comorbidity and deficit variables from the American College of Surgeons' National Surgery Quality and Improvement Project, which are well-validated health measures that have been applied within general medical and surgical datasets [7, 23, 30, 33]. Recently, the simplified 5-factor modified frailty index (mFI-5) was introduced and validated within various fields of surgery, and it includes the following five factors: the prevalence of functional dependence, history of diabetes mellitus, history of chronic obstructive pulmonary disease, congestive heart failure, and hypertension [13, 26, 28, 31]. Frailty is observed more commonly among the elderly than non-elderly patients; therefore, the frailty index is generally considered an important risk factor in elderly patients.

However, it remains unknown whether the mFI-5 scores are associated with the same risk across each age group, and whether their predictive value is useful with regard to complications and outcomes of meningioma surgery across various age groups.

Therefore, the aim of this study was to investigate risk factors including the mFI-5 across various age groups for complications and worse outcomes in meningioma surgery, with data extracted from the nationwide database in Japan.

Methods

Protocol approval and patient consent

The present study was approved by the local Institutional Review Boards of Hiroshima University (no. E-631) and Tokyo University (no. 3501-[1]). Due to the anonymous nature of the data in this study, the requirement for informed consent was waived.

Data source and selection of patients

The Japanese Diagnosis Procedure Combination (DPC) is a registry-based national database that includes abstract discharge data and administrative claims on inpatients in Japan. It has been described thoroughly elsewhere [10, 11, 17]. Both the sensitivity and specificity of the procedure exceeded 90% [32].

We included patients aged 18–95 years who were admitted to the hospital with a primary diagnosis of intracranial meningioma between July 1, 2010, and March 31, 2015. Diagnoses of meningioma (ICD-10 codes; D32) and the intracranial tumor removal procedure (medical fee code; K169) were identified. In total, 10,530 patients with meningiomas were identified, and we excluded cases with unknown location of the meningioma, multiple meningiomas, and no detection of BI assessments and body mass index (BMI). Consequently, 8,138 patients with meningiomas were included in this study (Fig. 1).

The database incorporates the coded variables as per the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), and the Barthel Index (BI) at admission and at discharge were evaluated. We collected data on the patients' sex, age, BMI, medical history, internal oral medication on admission, location of the meningioma, BI score at admission and at discharge, and in-hospital complications. As part of the medical history, we included a review of diabetes mellitus (ICD-10 code: E14), hypertension (I10), cerebral infarction (I63), angina pectoris (I20), congestive heart failure (I50), and chronic obstructive pulmonary disease (J44). We reviewed the use of antiplatelet drugs (aspirin, ticlopidine hydrochloride, cilostazol, clopidogrel sulfate, clopidogrel–aspirin combination, and prasugrel hydrochloride), anticoagulation agents (warfarin, dabigatran etexilate, edoxaban tosilate hydrate, rivaroxaban, and apixaban), and statins (atorvastatin calcium hydrate, rosuvastatin calcium, and pitavastatin calcium hydrate). In addition, the patients for the presence of complications, including intracerebral hemorrhage (ICH; ICD-10 code: I61), subarachnoid hemorrhage (SAH; I60), cerebral infarction, congestive heart failure, and pneumonia (J18) was evaluated.

The BI was used to evaluate 10 activities of daily living (ADL) across two to four stages [2, 29]. The BI was classified into three categories: 0–55, 60–80, and 85–100 points according to ADL, with higher scores indicating a higher level of independent functioning. One of the five factors included in the mFI-5 was the functional status of requiring assistance with ADL. We defined this dependent functional status as a BI score < 85. The scores of the mFI-5 were classified into three categories, namely, 0, 1 item, and ≥ 2 items. A worsening BI score indicated patients who demonstrated a decreased BI score ≥ 5 points at discharge compared to that at admission, and in-hospital mortality indicated death from any cause. Any complications included any stroke, congestive heart failure, pneumonia, a decreased BI score, and in-hospital mortality.

The hospital data reviewed primarily assessed the case volume and type (academic or non-academic). Hospital case volume was defined as the number of patients with meningiomas treated surgically at an individual facility during the study period, and this was categorized into three groups according to terciles of case volume, with an approximately equal number of patients in each of the three groups. Hospital case volume was categorized from 1 to 3, ordered from the lowest to the highest value. The anatomical locations of the meningiomas were classified as convexity, falx, parasagittal, lateral (sphenoidal ridge, middle fossa), midline (tuberculum sellae, olfactory groove), posterior fossa (foramen magnum, petrous, petroclival, petrotentorial, tentorial), or deep (ventricle, anterior clinoid, posterior clinoid, cavernous, orbital, falcotentorial). Patients were categorized into three age groups, based on the classification of the World Health Organization and the Japan Geriatrics Society, as follows: < 65 years (non-elderly), 65–74 years (pre-elderly), and ≥ 75 years (elderly).[18] All patients according to their BMI were classified into the following groups: < 18.5 kg/m^2, 18.5–24.9 kg/m^2 (healthy weight), 25.0–29.9 kg/m^2, and ≥ 30.0 kg/m^2.

Statistical analyses

All statistical analyses were performed using Stata (version 15; StataCorp, College Station, TX, USA). Categorical variables were compared using a Chi-square or Fisher's exact test. To compare continuous variables, we performed a t-test or Mann–Whitney U test. Multivariate logistic regression analyses were performed on the overall cohort to analyze the risk factors for worsening BI scores between admission and discharge, in-hospital mortality, and any complications. The same analyses were performed separately across the three categories of age groups, except for in-hospital mortality where the numbers of participants in each subgroup were too low for statistical analysis. For multivariate logistic regression analyses, independent variables were selected based on the existing literature [4, 13, 19, 20, 26, 28, 31], and no variable selection method was applied; odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

Results

During the study period, 8,138 eligible patients were surgically treated. The mean (interquartile range) age was 63.0 (range: 53.0–71.0). Table 1 shows the baseline characteristics of patients with surgically treated meningioma based on age group. The mFI-5 score was significantly increased with age. Elderly

patients tended to undergo surgery in lower surgical volume and non-academic hospitals. The prevalence of ICH, SAH, cerebral infarction, congestive heart failure, and in-hospital mortality did not significantly increase with age. However, the prevalence of pneumonia, worsening BI scores, and any complications increased significantly with age.

Table 1
Baseline characteristics of patients surgically treated for meningioma based on age groups

Year age group (years)	Non-elderly; < 65	Pre-elderly; 65–74	Elderly; ≥ 75	
No.	4,378	2,421	1,339	*P*-value
Sex (male)	1305 (29.8%)	760 (31.4%)	479 (35.8%)	< 0.001*
Age, median (IQR)	54.0 (46.0, 60.0)	69.0 (67.0, 72.0)	78.0 (76.0, 81.0)	< 0.001*
BMI, median (IQR)	22.7 (20.4, 25.4)	23.0 (20.8, 25.3)	22.9 (20.8, 25.4)	0.082
BMI classification (kg/m2)				< 0.001*
< 18.5	351 (8.0%)	167 (6.9%)	116 (8.7%)	
18.5–24.9	2,821 (64.4%)	1,578 (65.2%)	851 (63.6%)	
25-29.9	942 (21.5%)	574 (23.7%)	321 (24.0%)	
30≤	264 (6.0%)	102 (4.2%)	51 (3.8%)	
Medical history				
Diabetes mellitus	387 (8.8%)	395 (16.3%)	218 (16.3%)	< 0.001*
Hypertension	736 (16.8%)	789 (32.6%)	494 (36.9%)	< 0.001*
Cerebral infarction	35 (0.8%)	48 (2.0%)	34 (2.5%)	< 0.001*
Angina pectoris	51 (1.2%)	69 (2.9%)	68 (5.1%)	< 0.001*
Congestive heart failure	20 (0.5%)	26 (1.1%)	36 (2.7%)	< 0.001*
Chronic obstructive pulmonary disease	1 (0.02%)	8 (0.3%)	4 (0.3%)	0.004*
The modified frailty index-5				< 0.001*
0 item	3112 (71.1%)	1202 (49.6%)	475 (35.5%)	

BI = Barthel Index; BMI = body mass index; ICH = intracerebral hemorrhage; IQR = interquartile range; No. = number; SAH = subarachnoid hemorrhage;

* $p < 0.05$

Year age group (years)	Non-elderly; < 65	Pre-elderly; 65–74	Elderly; ≥ 75	
1 item	1023 (23.4%)	910 (37.6%)	583 (43.5%)	
≥ 2 items	243 (5.6%)	309 (12.8%)	281 (21.0%)	
Internal oral medication on admission				
Antiplatelet	84 (1.9%)	139 (5.7%)	126 (9.4%)	< 0.001*
Anticoagulation	72 (1.6%)	105 (4.3%)	107 (8.0%)	< 0.001*
Statin	253 (5.8%)	279 (11.5%)	178 (13.3%)	< 0.001*
Barthel index on admission (points)				< 0.001*
0–55	264 (6.0%)	234 (9.7%)	314 (23.5%)	
60–80	119 (2.7%)	117 (4.8%)	113 (8.4%)	
85–100	3,995 (91.3%)	2,070 (85.5%)	912 (68.1%)	
Location				< 0.001*
Convexity	1,414 (32.3%)	809 (33.4%)	565 (42.2%)	
Falx	469 (10.7%)	291 (12.0%)	136 (10.2%)	
Parasagittal	741 (16.9%)	351 (14.5%)	141 (10.5%)	
Lateral	491 (11.2%)	277 (11.4%)	166 (12.4%)	
Midline	473 (10.8%)	274 (11.3%)	84 (6.3%)	
Posterior fossa	672 (15.3%)	381 (15.7%)	233 (17.4%)	
Deep	118 (2.7%)	38 (1.6%)	14 (1.0%)	
Hospital volume				< 0.001*
1	1,296 (29.6%)	866 (35.8%)	516 (38.5%)	
2	1,402 (32.0%)	765 (31.6%)	449 (33.5%)	

BI = Barthel Index; BMI = body mass index; ICH = intracerebral hemorrhage; IQR = interquartile range; No. = number; SAH = subarachnoid hemorrhage;

* $p < 0.05$

Year age group (years)	Non-elderly; < 65	Pre-elderly; 65–74	Elderly; ≥ 75	
3	1,680 (38.4%)	790 (32.6%)	374 (27.9%)	
Academic	1,838 (42.0%)	861 (35.6%)	422 (31.5%)	< 0.001*
Barthel index at discharge (points)				< 0.001*
0–55	141 (3.2%)	194 (8.1%)	278 (20.9%)	
60–80	137 (3.1%)	126 (5.2%)	161 (12.1%)	
85–100	4,079 (93.6%)	2,089 (86.7%)	888 (66.9%)	
Complication				
ICH	16 (0.4%)	14 (0.6%)	9 (0.7%)	0.260
SAH	3 (0.1%)	1 (< 1%)	0 (0.0%)	0.600
Cerebral infarction	85 (1.9%)	68 (2.8%)	30 (2.2%)	0.069
Congestive heart failure	15 (0.3%)	13 (0.5%)	8 (0.6%)	0.330
Pneumonia	81 (1.9%)	73 (3.0%)	56 (4.2%)	< 0.001*
Worsening BI scores	311 (7.1%)	305 (12.6%)	283 (21.1%)	< 0.001*
In-hospital mortality	22 (0.5%)	12 (0.5%)	12 (0.9%)	0.210
Any complications	454 (10.4%)	422 (17.4%)	341 (25.5%)	< 0.001*
BI = Barthel Index; BMI = body mass index; ICH = intracerebral hemorrhage; IQR = interquartile range; No. = number; SAH = subarachnoid hemorrhage;				
* $p < 0.05$				

Table 2 depicts the results of the multivariate logistic regression analyses for worsening BI scores, in-hospital mortality, and any complications in all the cases. For worsening BI scores, significant risk factors included being in the pre-elderly group (OR: 1.77; 95% CI: 1.49–2.11) and in the elderly group (3.21; 2.65–3.88), cerebral infarction (1.65; 1.03–2.65), an mFI-5 score ≥ 2 items (1.29; 1.03–1.62), anticoagulants on admission, and meningioma location (parasagittal, lateral, and deep). For in-hospital mortality, BMI < 18.5 kg/m^2 (3.30; 1.44–7.57), an mFI-5 score ≥ 2 items (5.37; 2.34–12.30), antiplatelet oral medications on admission, and tumor location (falx, parasagittal, midline, and posterior fossa) were significant risk factors, whereas hospital volume 3 (0.33; 0.14–0.82) was a significant inverse risk factor. For any complications, significant risk factors included being in the pre-elderly group (OR: 1.67; 95% CI: 1.44–1.93) and in the elderly group (2.55; 2.15–3.02), BMI < 18.5 (1.26; 1.00–1.58), an mFI-5 score ≥ 2 items

(1.54; 1.26–1.88), oral medications on the admission of antiplatelets and anticoagulants, and tumor location (falx, parasagittal, midline, posterior fossa, and deep). Figure 2 (a, b, and c) depicts, in the form of forest plots for risk factors adjusted for other variables, the results of the multivariate logistic regression analysis for worsening BI scores, in-hospital mortality, and any complications in the cases of all ages.

Table 2
Multivariate logistic regression analyses for worsening BI scores, in-hospital mortality, and any complications in the total cases

Objective variables (No.)	Worsening BI scores (8,138)		In-hospital mortality (7,428)		Any complications (8,138)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex male	1.04 (0.89–1.21)	0.655	1.41 (0.76–2.61)	0.273	1.07 (0.93–1.22)	0.356
Age group (years)						
Non-elderly; <65	Reference		Reference		Reference	
Pre-elderly; 65–74	1.77 (1.49–2.11)	< 0.001*	0.60 (0.28–1.29)	0.192	1.67 (1.44–1.93)	< 0.001*
Elderly; ≥75	3.21 (2.65–3.88)	< 0.001*	1.09 (0.50–2.38)	0.829	2.55 (2.15–3.02)	< 0.001*
BMI classification (kg/m2)						
< 18.5	1.15 (0.89–1.49)	0.285	3.30 (1.44–7.57)	0.005*	1.26 (1.00-1.58)	0.050*
18.5–24.9	Reference		Reference		Reference	
25-29.9	1.03 (0.86–1.22)	0.774	1.29 (0.62–2.69)	0.493	1.04 (0.90–1.22)	0.575
30≦	0.85 (0.60–1.21)	0.370	1.60 (0.53–4.85)	0.404	0.89 (0.66–1.20)	0.441
Medical history						
Cerebral infarction	1.65 (1.03–2.65)	0.035*	3.31 (0.94–11.68)	0.063	1.27 (0.82–1.98)	0.289
Angina pectoris	1.02 (0.67–1.54)	0.936	0.63 (0.08–4.97)	0.664	0.81 (0.55–1.19)	0.284
The modified frailty index-5						

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* $p < 0.05$

Objective variables (No.)	Worsening BI scores (8,138)		In-hospital mortality (7,428)		Any complications (8,138)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
0 item	Reference		Reference		Reference	
1 item	1.08 (0.92–1.28)	0.357	2.53 (1.22–5.22)	0.012*	1.14 (0.99–1.32)	0.074
≥ 2 items	1.29 (1.03–1.62)	0.026*	5.37 (2.34–12.30)	< 0.001*	1.54 (1.26–1.88)	< 0.001*
Internal oral medication on admission						
Antiplatelet	1.26 (0.93–1.71)	0.128	3.63 (1.49–8.85)	0.005*	2.00 (1.54–2.58)	< 0.001*
Anticoagulation	2.28 (1.71–3.03)	< 0.001*	1.66 (0.56–4.90)	0.357	2.56 (1.97–3.32)	< 0.001*
Statin	1.19 (0.94–1.49)	0.150	N/A		1.03 (0.83–1.27)	0.796
Location						
Convexity	Reference		Reference		Reference	
Falx	1.45 (1.13–1.84)	0.003*	4.84 (1.51–15.55)	0.008*	1.38 (1.12–1.71)	0.003*
Parasagittal	1.87 (1.51–2.32)	< 0.001*	5.17 (1.64–16.34)	0.005*	1.73 (1.43–2.09)	< 0.001*
Lateral	1.33 (1.05–1.70)	0.021*	0.64 (0.07–5.49)	0.681	1.02 (0.82–1.28)	0.839
Midline	1.17 (0.89–1.53)	0.263	9.27 (3.06–28.13)	< 0.001*	1.26 (1.00-1.58)	0.049*
Posterior fossa	1.22 (0.98–1.53)	0.076	6.96 (2.44–19.81)	< 0.001*	1.29 (1.06–1.56)	0.010*

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* $p < 0.05$

Objective variables (No.)	Worsening BI scores (8,138)		In-hospital mortality (7,428)		Any complications (8,138)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Deep	2.55 (1.64–3.94)	< 0.001*	9.97 (1.85–53.85)	0.008*	2.14 (1.43–3.20)	< 0.001*
Hospital volume						
1	Reference		Reference		Reference	
2	0.97 (0.81–1.16)	0.750	0.58 (0.29–1.17)	0.130	0.87 (0.74–1.02)	0.089
3	1.00 (0.82–1.22)	0.998	0.33 (0.14–0.82)	0.016*	0.92 (0.77–1.10)	0.361
Academic	1.05 (0.89–1.25)	0.542	1.03 (0.50–2.16)	0.927	1.15 (0.99–1.34)	0.064
BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;						
* $p < 0.05$						

Table 3 demonstrates the results of the multivariate logistic regression analyses for the worsening BI scores across all age groups. Age was a significant risk factor only in the pre-elderly and elderly groups. An mFI-5 score ≥ 2 items was considered as a significant risk only in the non-elderly group (OR: 2.00; 95% CI: 1.31–3.06), but not in the pre-elderly (1.25; 0.85–1.84) and elderly (0.97; 0.67–1.40) groups. The administration of oral anticoagulant medications on admission and several locations of meningiomas in the non-elderly and pre-elderly groups were also identified as significant risk factors. Figure 3 shows the results of the multivariate logistic regression analysis for the worsening BI scores across all age groups, depicted as forest plots for risk factors adjusted for other variables.

Table 3
Multivariate logistic regression analyses for worsening BI scores across all age groups

Objective variable	**Worsening BI scores**					
Year age group (No.)	Non-elderly; < 65 (4,378)		Pre-elderly; 65–74 (2,421)		Elderly; ≥ 75 (1,339)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex male	1.10 (0.85–1.42)	0.487	0.97 (0.74–1.28)	0.832	1.00 (0.76–1.33)	0.973
Age (year)	1.01 (0.99–1.02)	0.357	1.05 (1.01–1.10)	0.022*	1.07 (1.03–1.11)	< 0.001 *
BMI classification (kg/m2)						
< 18.5	1.00 (0.64–1.57)	0.992	1.21 (0.76–1.91)	0.427	1.25 (0.79–1.97)	0.350
18.5–24.9	Reference		Reference		Reference	
25-29.9	1.30 (0.98–1.72)	0.066	0.82 (0.60–1.11)	0.200	0.95 (0.69–1.30)	0.732
30≦	0.86 (0.51–1.44)	0.559	0.89 (0.49–1.64)	0.718	0.69 (0.31–1.51)	0.348
Medical history						
Cerebral infarction	1.53 (0.56–4.17)	0.404	1.83 (0.89–3.75)	0.099	1.33 (0.60–2.96)	0.479
Angina pectoris	0.68 (0.20–2.27)	0.532	0.76 (0.35–1.62)	0.476	1.39 (0.79–2.45)	0.253
The modified frailty index-5						
0 item	Reference		Reference		Reference	
1 item	1.06 (0.80–1.41)	0.668	1.20 (0.91–1.57)	0.192	0.90 (0.66–1.22)	0.500

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* p < 0.05

Objective variable	Worsening BI scores					
≥ 2 items	2.00 (1.31–3.06)	0.001*	1.25 (0.85–1.84)	0.252	0.97 (0.67–1.40)	0.863
Internal oral medication on admission						
Antiplatelet	1.86 (0.97–3.59)	0.064	1.34 (0.82–2.20)	0.247	1.07 (0.67–1.69)	0.784
Anticoagulation	2.95 (1.59–5.49)	0.001*	3.68 (2.38–5.69)	< 0.001*	1.34 (0.84–2.14)	0.224
Statin	0.98 (0.60–1.60)	0.932	1.27 (0.88–1.84)	0.195	1.18 (0.80–1.74)	0.406
Location						
Convexity	Reference		Reference		Reference	
Falx	2.21 (1.48–3.30)	< 0.001*	1.43 (0.94–2.16)	0.093	0.90 (0.55–1.46)	0.671
Parasagittal	2.55 (1.80–3.62)	< 0.001*	1.75 (1.20–2.55)	0.004*	1.29 (0.83–2.01)	0.257
Lateral	1.74 (1.14–2.65)	0.010*	1.48 (0.97–2.25)	0.068	0.97 (0.63–1.50)	0.900
Midline	1.37 (0.87–2.17)	0.172	1.30 (0.84-2.00)	0.236	0.87 (0.48–1.60)	0.656
Posterior fossa	1.34 (0.89–2.01)	0.162	1.18 (0.80–1.76)	0.408	1.25 (0.88–1.81)	0.230
Deep	3.13 (1.71–5.73)	< 0.001*	2.85 (1.28–6.34)	0.010*	1.51 (0.46–4.99)	0.496
Hospital volume						
1	Reference		Reference		Reference	

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* $p < 0.05$

Objective variable	Worsening BI scores					
2	0.99 (0.73–1.36)	0.974	0.98 (0.72–1.33)	0.881	1.01 (0.73–1.38)	0.975
3	1.14 (0.82–1.61)	0.436	0.86 (0.61–1.21)	0.372	1.06 (0.73–1.54)	0.748
Academic	1.05 (0.79–1.39)	0.740	1.29 (0.96–1.73)	0.086	0.81 (0.58–1.12)	0.207
BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;						
* $p < 0.05$						

Table 4 shows the results of the multivariate logistic regression analyses for any complications across all age groups. Age was a significant risk factor only in the pre-elderly and elderly groups. An mFI-5 score of ≥ 2 items was considered as a significant risk factor only in the non-elderly group (OR: 2.40; 95% CI: 1.67–3.44), but not in the pre-elderly (1.39; 1.00–1.94) and elderly (1.19; 0.85–1.69) groups. Oral administration of anticoagulant and antiplatelet medications on admission, several locations of meningioma in all groups, and admission in an academic hospital were significant risk factors in the pre-elderly group. Figure 4 shows the results of the multivariate logistic regression analysis for any complications in all age groups, depicted in the form of forest plots for risk factors adjusted for other variables.

Table 4
Multivariate logistic regression analyses for any complications across all age groups

Objective variable	**Any complications**					
Year age group (No.)	Non-elderly; < 65 (4,378)		Pre-elderly; 65–74 (2,421)		Elderly; ≥ 75 (1,339)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex male	1.07 (0.85–1.33)	0.572	1.08 (0.85–1.37)	0.509	1.04 (0.80–1.36)	0.757
Age (year)	1.00 (0.99–1.01)	0.861	1.04 (1.00-1.08)	0.034*	1.08 (1.04–1.12)	< 0.001 *
BMI classification (kg/m2)						
< 18.5	1.23 (0.86–1.75)	0.250	1.17 (0.77–1.77)	0.471	1.35 (0.87–2.08)	0.181
18.5–24.9	Reference		Reference		Reference	
25-29.9	1.21 (0.95–1.54)	0.121	0.88 (0.68–1.16)	0.382	1.01 (0.75–1.36)	0.957
30≦	0.83 (0.54–1.30)	0.419	0.97 (0.57–1.64)	0.909	0.87 (0.44–1.73)	0.701
Medical history						
Cerebral infarction	0.83 (0.31–2.27)	0.721	1.51 (0.78–2.93)	0.221	1.24 (0.58–2.65)	0.578
Angina pectoris	0.59 (0.20–1.73)	0.337	0.62 (0.31–1.23)	0.175	1.14 (0.66–1.98)	0.643
The modified frailty index-5						
0 item	Reference		Reference		Reference	
1 item	1.10 (0.87–1.40)	0.425	1.22 (0.97–1.55)	0.094	1.01 (0.76–1.35)	0.941

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* p < 0.05

Objective variable	Any complications					
≥ 2 items	2.40 (1.67–3.44)	< 0.001*	1.39 (1.00-1.94)	0.050	1.19 (0.85–1.69)	0.303
Internal oral medication on admission						
Antiplatelet	3.61 (2.14–6.08)	< 0.001*	2.01 (1.33–3.04)	0.001*	1.45 (0.95–2.20)	0.085
Anticoagulation	3.08 (1.78–5.33)	< 0.001*	3.31 (2.18–5.01)	< 0.001*	1.88 (1.23–2.87)	0.004*
Statin	0.68 (0.43–1.07)	0.098	1.18 (0.86–1.64)	0.309	1.09 (0.75–1.57)	0.647
Location						
Convexity	Reference		Reference		Reference	
Falx	1.74 (1.24–2.45)	0.001*	1.34 (0.94–1.92)	0.109	1.04 (0.67–1.62)	0.865
Parasagittal	2.07 (1.55–2.78)	< 0.001*	1.53 (1.10–2.13)	0.013*	1.37 (0.90–2.09)	0.144
Lateral	1.13 (0.77–1.65)	0.525	1.08 (0.74–1.59)	0.693	0.90 (0.60–1.38)	0.641
Midline	1.38 (0.96–1.99)	0.080	1.31 (0.91–1.89)	0.15	1.03 (0.60–1.80)	0.904
Posterior fossa	1.31 (0.95–1.83)	0.096	1.20 (0.86–1.67)	0.292	1.42 (1.00-2.01)	0.047*
Deep	2.22 (1.28–3.84)	0.004*	2.43 (1.16–5.11)	0.019*	1.72 (0.56–5.31)	0.348
Hospital volume						
1	Reference		Reference		Reference	

BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;

* $p < 0.05$

Objective variable	Any complications					
2	0.76 (0.58-1.00)	0.051	0.99 (0.76–1.30)	0.964	0.93 (0.69–1.26)	0.652
3	1.00 (0.76–1.33)	0.975	0.83 (0.61–1.12)	0.219	0.93 (0.65–1.32)	0.666
Academic	1.20 (0.95–1.53)	0.130	1.34 (1.04–1.74)	0.024*	0.83 (0.60–1.13)	0.229
BI = Barthel Index; BMI = body mass index; CI = confidence interval; OR = odds ratio;						
* $p < 0.05$						

Discussion

In this study, worsening BI and mFI-5 scores and the proportion of patients with medical history were significantly increased with age. An mFI-5 score ≥ 2 items was a significant risk factor for worsening BI scores, in-hospital mortality, and any complications after surgery. In the analysis of all age groups, an mFI-5 score ≥ 2 items was a significant risk factor for worsening BI scores and any complications after surgery only in the non-elderly group, but not in the pre-elderly and elderly groups.

The rate of mortality and complications after surgery

The rates of in-hospital mortality and any complications after surgery in our study were 0.5–0.9% and 10.4–25.5%, respectively. These rates were similar to those observed in previous studies; the rates of mortality and complications after surgery were reported as 0.5–1.5%, and 6.8–14.8% respectively [5, 8, 15, 27]. A recent systematic review reported that in elderly patients with meningiomas, the rate of one-year postoperative mortality and neurological complications after surgery ranged from 2.7–49.4% and from 0–16.7%, respectively [9].

mFI scores and age as predictors of surgical complications and worsening

In both sexes, there was a significant non-linear association between age and the FI scores.[22] Overall, the FI scores were much stronger predictors of mortality than age [22]. In this study, the mFI-5 scores increased with age, similar to findings from a previous report investigating the FI [12]. Aging is a heterogeneous process and chronologic age is not necessarily synonymous with an individual's health status. Even so, there is little evidence to determine whether there are differences in the frailty criteria in younger versus older adults. The relative risk of mortality in younger adults is associated more with frailty than age [21]. In the present study, the overall background of mFI-5 scores in the older groups were relatively higher; therefore, the mFI-5 may not be a significant predictor in advanced age groups. The mFI-

5 is a useful predictor of complications and worsening after surgery, specifically in non-elderly rather than elderly patients with meningiomas. While this may sound paradoxical at first, we believe that it may be true. In meningioma surgeries, care must be taken when making decisions using the mFI-5 scores based on the patients' age. Furthermore, we can recommend preoperative fitness recovery to improve frailty, especially in non-elderly patients, who have a greater potential to regain fitness than the elderly [21].

Advanced age as a risk factor of surgical complication and worsening BI score

We assessed the worsening BI scores between admission and discharge and found that the rate of worsening BI scores increased from 7.1–21.1% (mean = 11.0%) as age increased, which is comparable to the increase reported in previous studies (8.3–14.8%).[3, 5, 27] We found pneumonia and the worsening BI scores to be significantly correlated with advanced age in our study. The most common complications after surgery for meningioma were new focal neurological deficits and pneumonia [5, 27]. Notably, these two complications are currently considered common and inevitable in advanced aged patients with meningiomas [27].

However, we found no significant association between advanced age and in-hospital mortality. According to a recent systematic review of elderly patients with meningioma surgery, the rate of in-hospital mortality, worsening of the postoperative performance status, neurological deficits, and general complications ranged widely based on the reports and were not necessarily associated with advanced-age [9].

Other risk factors in meningioma surgery

The administration of antiplatelet and anticoagulation drugs was found to be a risk factor for worse outcomes in previous neurosurgical studies [1]. In our study, these medications were also risk factors for worsening BI scores, in-hospital mortality, and any complications after surgery regardless of the patients' age. Antithrombotic drugs have been administered for the prevention of recurrence in cardiac and cerebral vascular events, necessitating the correct use of these drugs in the elderly. Minimum necessary use of antithrombotic medication is required, especially in the elderly during the perioperative period since antithrombotic drugs are more frequently administered to the elderly.

Several risk factors for mortality in meningioma surgery in the elderly have been identified, such as location [20], preoperative Karnofsky performance status [6], the BI score [4], other grading systems [24] and advanced age [19]. Although parasagittal and deep locations of the meningioma were significant risk factors for the worsening BI scores and any complications in both non-elderly and pre-elderly groups, they were no longer risk factors in the elderly group (Tables 3 and 4, Figs. 3 and 4). This phenomenon may be due to differences in aggressive treatment based on the location, delicate treatment management in the elderly, and the selective indication of surgery in elderly patients with meningiomas.

In this study, the in-hospital mortality in high volume hospitals was a significant inverse risk factor, due to the ability of high volume hospitals to rescue patients from major perioperative complications [16]. Academic hospitals were found to be significant risk factors for postoperative complications in pre-

elderly patients. This may be likely because academic hospitals tend to receive the most serious and difficult cases.

Limitations

This study has some limitations. First, the DPC database does not include post-discharge data, meningioma size, pathological findings, and the extent of resection and perioperative radiation therapy. Therefore, we could not assess the long-term status of recurrence or BI scores after discharge. These variables are usually not recorded in other administrative in-hospital databases. Second, this was a registry-based study, not a randomized controlled study. Therefore, we could not completely exclude bias. However, we improved the integrity of this study by analyzing the location of meningiomas, as well as preoperative and postoperative BI scores. Third, some variables had wide CIs due to a limited number of cases. Fourth, our results may not be generalizable to other countries, which have different medical resources and systems, and they must be interpreted with caution considering that Japan has the highest proportion of elderly people worldwide.

Conclusions

Although advanced age could lead to postoperative functional decline and complications at discharge, the mFI-5 scores could predict the complication and worsening in the patients aged < 65 years, but not in the patients aged ≥ 65 years. Care must be taken when making decisions using the mFI-5 scores based on the patients' age.

Declarations

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Role of the Funding Source:

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of this report. The corresponding author has full access to all data in the study and has final responsibility for the decision to submit for publication.

Conflict of interest:

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

Data availability

The anonymized data for this study could be shared on the request of any qualified investigator to the corresponding author. Only the results of primary data from the DPC could be made available for reasonable requests in accordance with the review board.

Code availability

Stata software (version 15; StataCorp, College Station, TX, USA)

Contributors:

All authors made contributions to the intellectual content of this paper, contributed to data interpretation, approved the final manuscript, and agreed with submission to this journal. Fusao Ikawa: study design and concept; acquired funding; conducted research; collected, curated, managed, and analyzed data; quality control; statistical analysis; and drafted the manuscript. Nobuaki Michihata: collected, curated, and analyzed data; quality control; statistical analysis; and revised the manuscript. Soichi Oya, Toshikazu Hidaka, Shingo Matsuda, Iori Ozono, Kenji Ohata, Kiyoshi Saito, and Kazunari Yoshida: conceived and oversaw the study, as well as revised the manuscript. Kiyohide Fushimi, Hideo Yasunaga, Teiji Tominaga, and Kaoru Kurisu: conceived and oversaw the study, as well as assisted in collecting data.

Ethics approval

The present study was approved by the local Institutional Review Boards (no. E-631 and no. 3501-[1]). Due to the anonymous nature of the data in this study, the requirement for informed consent was waived.

Consent to participate

Not applicable

Consent for publication

Not applicable

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Figures

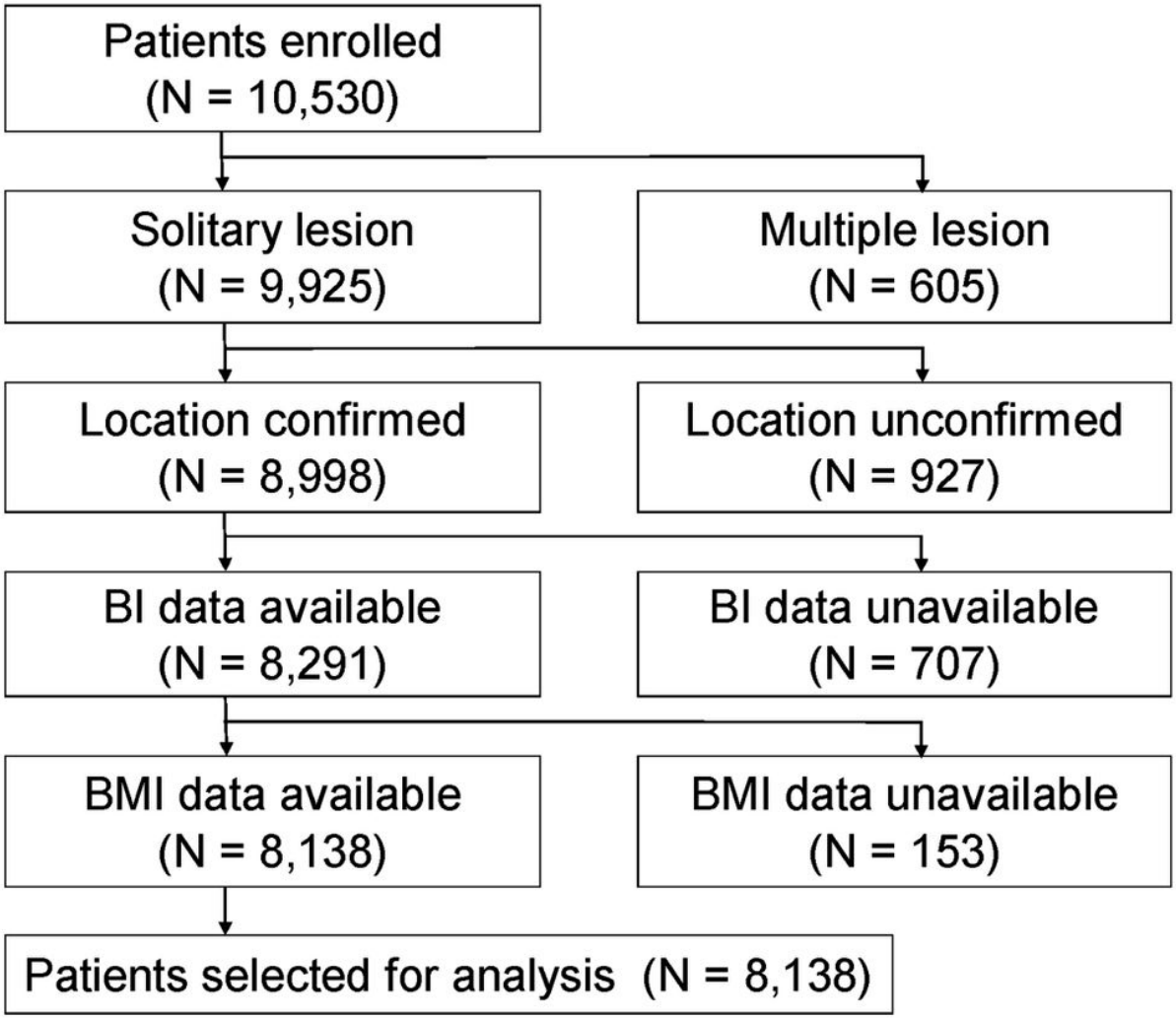

Figure 1

Selection of patients with surgically treated meningiomas Abbreviations: BI, Barthel Index; BMI, body mass index

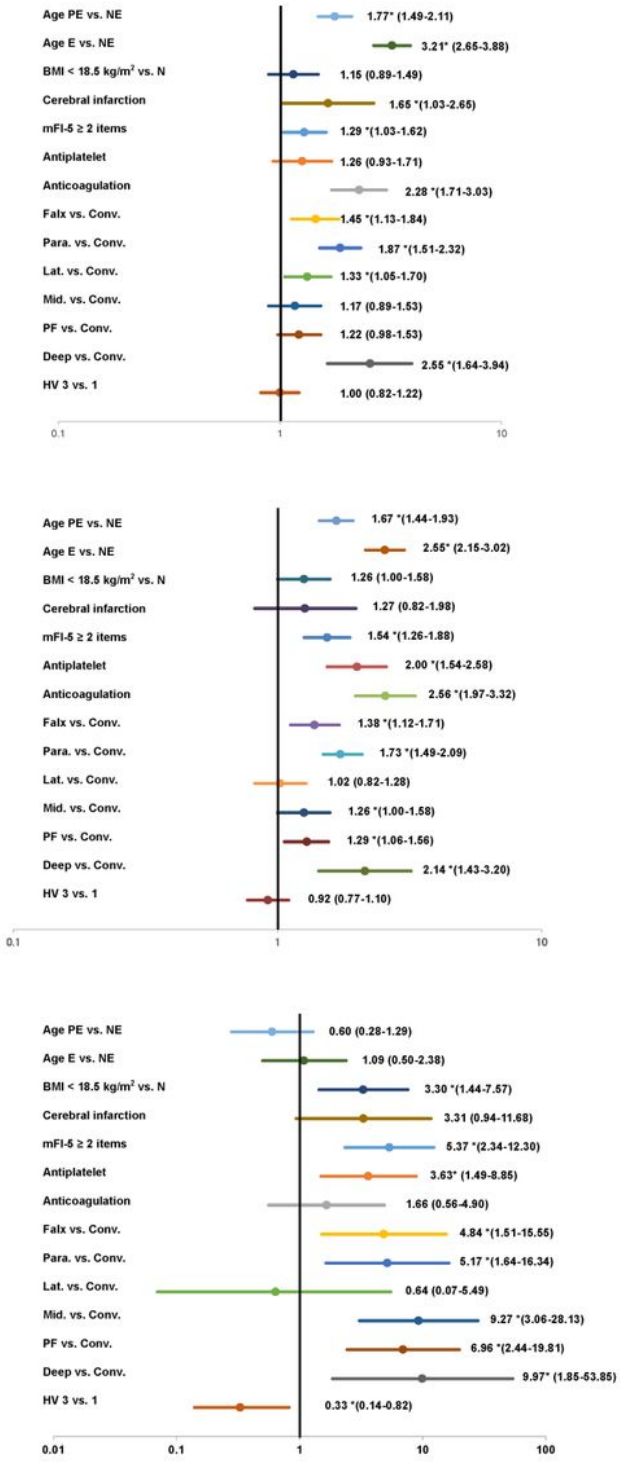

Figure 2

Forest plots for risk factors adjusted for other variables. (a) The worsening BI scores. (b) In-hospital mortality. (c) Any complications Abbreviations: BI, Barthel Index; BMI, body mass index; Conv, convexity; E, elderly; HV, hospital volume; Lat, lateral; Mid, midline; N, normal; Para, parasagittal; PE, pre-elderly; PF, posterior fossa. *p < 0.05

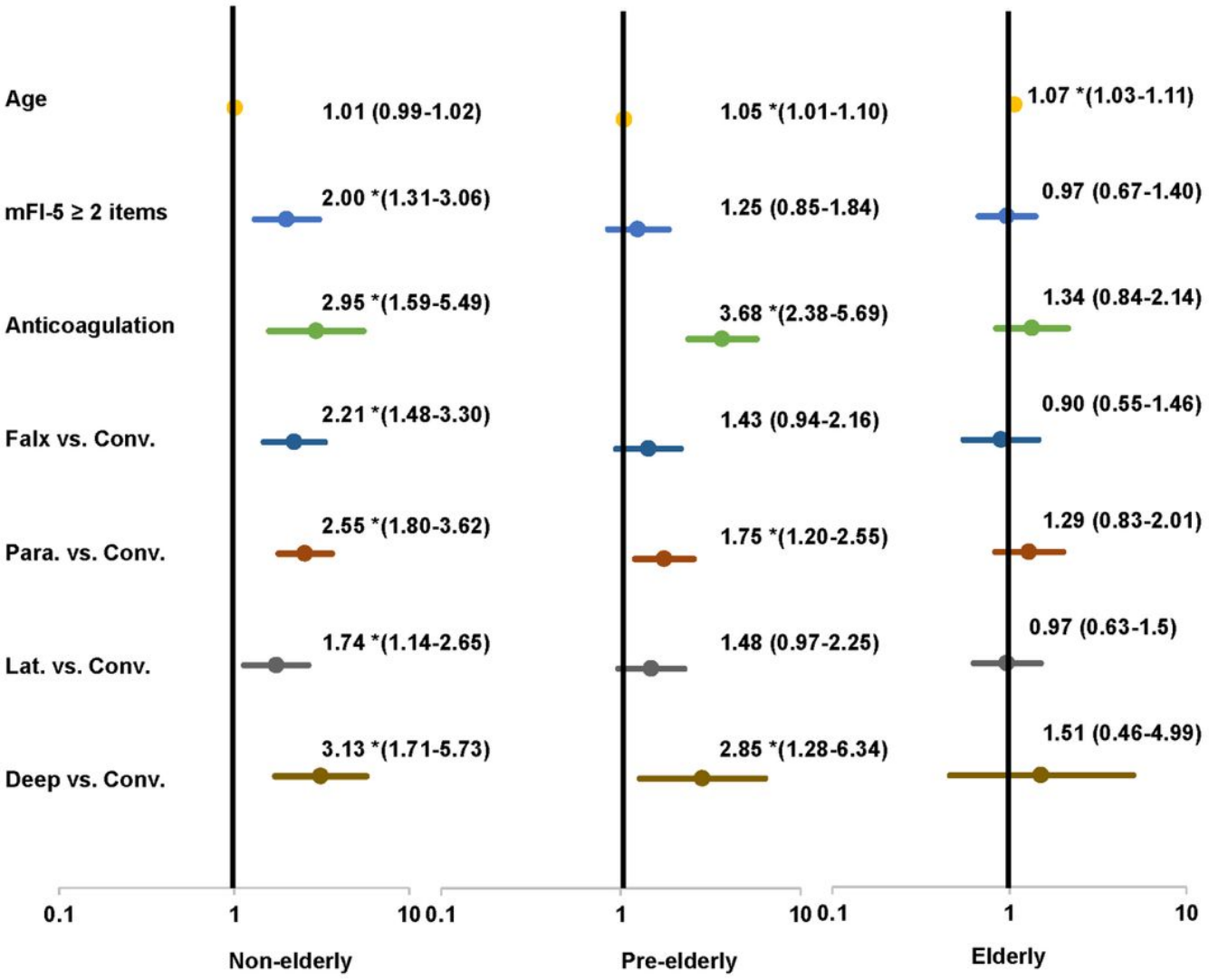

Figure 3

Forest plots of the risk factors adjusted for other variables for the worsening BI scores in the non-elderly, pre-elderly, and elderly Abbreviations: Conv, convexity; E, Lat, lateral; Para, parasagittal; PF, posterior fossa. *p < 0.05

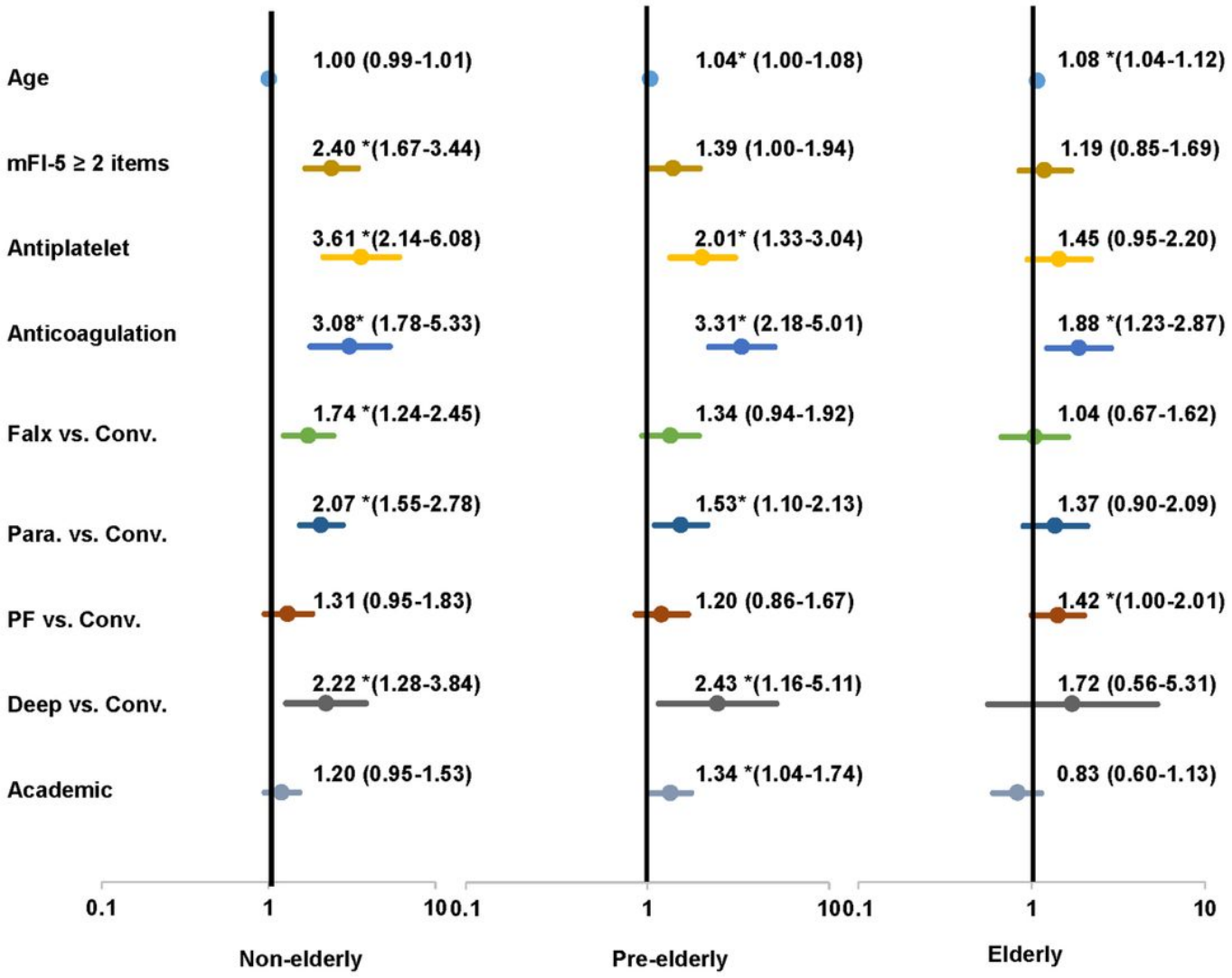

Figure 4

Forest plots of the risk factors adjusted for other variables for any complications in the non-elderly, pre-elderly, and elderly Abbreviations: Conv, convexity; Para, parasagittal; PF, posterior fossa. *p < 0.05