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The 5-Factor Modified Frailty Index as a More Useful Associated Factor Than Chronological Age After Unruptured Cerebral Aneurysm Surgery: A Nationwide Registry Study

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BACKGROUND: Although chronological age is associated with mortality and morbidity after surgery for unruptured cerebral aneurysms (UCAs), there is little evidence regarding an association between the simplified 5-factor modified frailty index (mFI-5) and postoperative outcomes based on age group.

OBJECTIVE: To investigate the association of the mFI-5 score with worse outcomes, mortality, and complications in patients after surgery for UCA by chronological age groups using a Japanese national database.

METHODS: This study included 32 902 patients with UCAs enrolled in a Japanese national database between 2011 and 2015. Age group (younger than 65 years, 65-74 years, and 75 years or older), sex, UCA location, treatment, medications, Barthel Index (BI), medical history, mFI-5 score, and in-hospital mortality and complications were evaluated. We identified risk factors for worsening BI score, in-hospital mortality, and overall postoperative complications in each age group.

RESULTS: In total, 14 465 patients were enrolled in this study. Multivariable analysis showed that elderly groups and patients with an mFI-5 score ≥2 items were associated with worsening BI scores (odds ratio 1.95; 95% CI 1.52-2.51) and in-hospital complications (odds ratio 1.79; CI 1.49-2.15), despite having no association with in-hospital mortality. Multivariable analysis by age groups showed that the mFI-5 score ≥2 items was associated with in-hospital complications in all age groups, unlike chronological age in patients younger than 74 years.

CONCLUSION: The mFI-5 score was a more useful associated factor of in-hospital complications than chronological age in patients younger than 74 years undergoing surgery for UCA.

KEY WORDS: Elderly patient, Functional outcome, Nationwide database, Unruptured cerebral aneurysm, 5-Factor modified frailty index

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Japan reportedly has the highest percentage of elderly people and the longest average life expectancy in the world.[1] Therefore, research about aging is appropriate in Japan. With increasing life expectancy, asymptomatic unruptured cerebral aneurysms (UCAs) have been detected in elderly persons worldwide through neuroimaging techniques such as brain magnetic resonance imaging. UCAs are 2.8 times more likely to rupture in Japanese individuals than in Europeans and Americans,[2] and older age is reportedly a risk factor for UCA rupture.[3] Therefore, in Japan, many elderly patients older than 65 years receive surgical treatment for UCAs. Owing to the wide variance between the decline in physical and cognitive functions associated with aging, there is dissociation between the chronological and biological ages. Although both the chronological and biological ages contribute to postoperative mortality and

ABBREVIATIONS: ACA, anterior cerebral artery; **ACoA,** anterior communicating artery; **BA,** basilar artery; **BI,** Barthel index; **MCA,** middle cerebral artery; **mFI-5,** 5-factor modified frailty index; **UCA,** unruptured cerebral aneurysm; **VA,** vertebral artery.

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in-hospital complications in patients with UCA, their usefulness when examined by age groups is not known.[4-6] The treatment risk in patients with UCAs is related to aging and the presence of comorbidities, indicating that careful follow-up is an alternative in older patients (older than 65 years) (class IIa; level of evidence B); however, the exact indications for surgery in elderly patients with UCAs are hitherto unclear.[7]

Currently, the 5-factor modified frailty index (mFI-5), which is more convenient than the 11-factor modified frailty index,[8-10] has been introduced in various areas of surgery and contains the following 5 factors: hypertension, diabetes mellitus history, functional dependence prevalence, congestive heart failure, and chronic obstructive pulmonary disease history.[11-14] Complementary to chronological age, these frailty indexes reflect biological age. Few reports have examined the usefulness of the mFI-5 score for its association with activities of daily living deterioration, in-hospital complications, and mortality in patients after UCA surgery.[15] It is unclear whether chronological or biological age could be a more appropriate indicator for UCA surgery outcomes based on age groups. Therefore, the purpose of this study was to investigate and compare the associations of the mFI-5 score and chronological age with worsening outcomes, in-hospital complications, and mortality after UCA surgery by age groups in Japan.

METHODS

Ethical Statements

We obtained approval from the Institutional Review Board of our university before study initiation. Because all data in this study were anonymous, informed consent from each of the eligible patients was substituted by the opt-out method.

Data Source

We conducted our study using the diagnosis procedure combination (DPC) database, a nationwide database in Japan,[16] which includes data on patient admission and discharge; other studies have explained this database in detail.[5,6,17] All data were coded according to the International Classification of Diseases and Related Health Problems, Tenth Revision. The validity of the DPC in-patient database is well established, and both sensitivity and specificity of the procedure records have been reported to be greater than 90%.[18] Details of the DPC database are presented in **Text 1** of **Supplemental Digital Content 1**, http://links.lww.com/NEU/D429.

Selection of Patients

In total, 32 902 patients treated for UCAs between January 2011 and March 2015 were enrolled in this study. The diagnosis of UCAs was identified as International Classification of Diseases and Related Health Problems, Tenth Revision, code I671. In this study, we included initially admitted patients and those 18 years or older who underwent a single treatment with surgical clipping or endovascular coiling (Figure). The treatment selection procedure is presented in **Text 2** of **Supplemental Digital Content 1**, http://links.lww.com/NEU/D429.

The data examined included patient age, sex, treatment method (clipping or coiling), comorbidities, medications at admission, aneurysm location, mFI-5 score, hospital volume, Barthel index (BI) score at admission and discharge, and in-hospital complications. Moreover, aneurysm location was examined and classified as follows: internal carotid artery, anterior communicating artery, middle cerebral artery, anterior cerebral artery, basilar artery (BA), vertebral artery (VA), and others. The specific comorbidities considered were diabetes mellitus, hypertension, dyslipidemia, stroke, angina pectoris, and congestive heart failure. Regarding medications taken at the time of hospitalization, antiplatelet agents, anticoagulants, and statins were recorded. Complications such as intracerebral hemorrhage, cerebral infarction, subarachnoid hemorrhage (SAH), congestive heart failure, and pneumonia were specifically examined.

The BI score was used to evaluate activities of daily livings (**Text 3** of **Supplemental Digital Content 1**, http://links.lww.com/NEU/D429). The patients were classified into 3 age groups based on the classifications of the World Health Organization and the Japanese Geriatrics Society: younger than 65 years (nonelderly), 65 to 74 years (pre-elderly), and 75 years or older (elderly).[19] Details of hospital information are presented in **Text 4** of **Supplemental Digital Content 1**, http://links.lww.com/NEU/D429. Finally, mFI-5 scores were classified into 3 categories: 0, 1 item, and ≥2 items. A worsening BI score was defined as a decrease in the BI score of 5 or more points at discharge compared with that at admission, and in-hospital mortality was defined as death from any cause. In-hospital complications due to surgery included stroke, congestive heart failure, pneumonia, worsening BI scores, and in-hospital mortality.

Statistical Analysis

Categorical variables were compared using the Fisher exact test or chi-square test. Continuous variables were compared using the *t* test or Mann-Whitney *U* test. Multivariable logistic regression analysis was used to reduce the potential sources of bias and examine risk factors for worsening BI scores, in-hospital mortality, and in-hospital complications from admission to discharge. The same analysis was performed separately for worsening BI scores from admission to discharge and for in-hospital complications in the 3 age groups. However, in-hospital mortality was excluded from the analysis because of the small number of in-hospital mortality patients. Only 0.26% of study data were missing because we previously deleted the missing data in the patient selection shown in Figure. In the logistic regression analysis, independent variables including sex, treatment, age, aneurysm location, mFI-5 score, internal oral medication on admission, and hospital volume were selected based on variables in the literature, and odds ratios (ORs) and 95% CIs were calculated.[11-14,20] Stata version 15 (StataCorp, College Station) was used to perform all the statistical analyses. A P value < .05 was considered to indicate statistical significance.

Data Availability

Only the results of the anonymized data for this study will be shared on request from any qualified investigator to the corresponding author.

RESULTS

Ultimately, 14 465 patients were included in this study (Figure), with a mean age of 64.0 (range: 56.0-71.0) years. Surgical clipping and endovascular coiling procedures were performed in 9082 and 5383 patients, respectively. Table 1 presents the baseline characteristics and outcomes of patients with UCAs

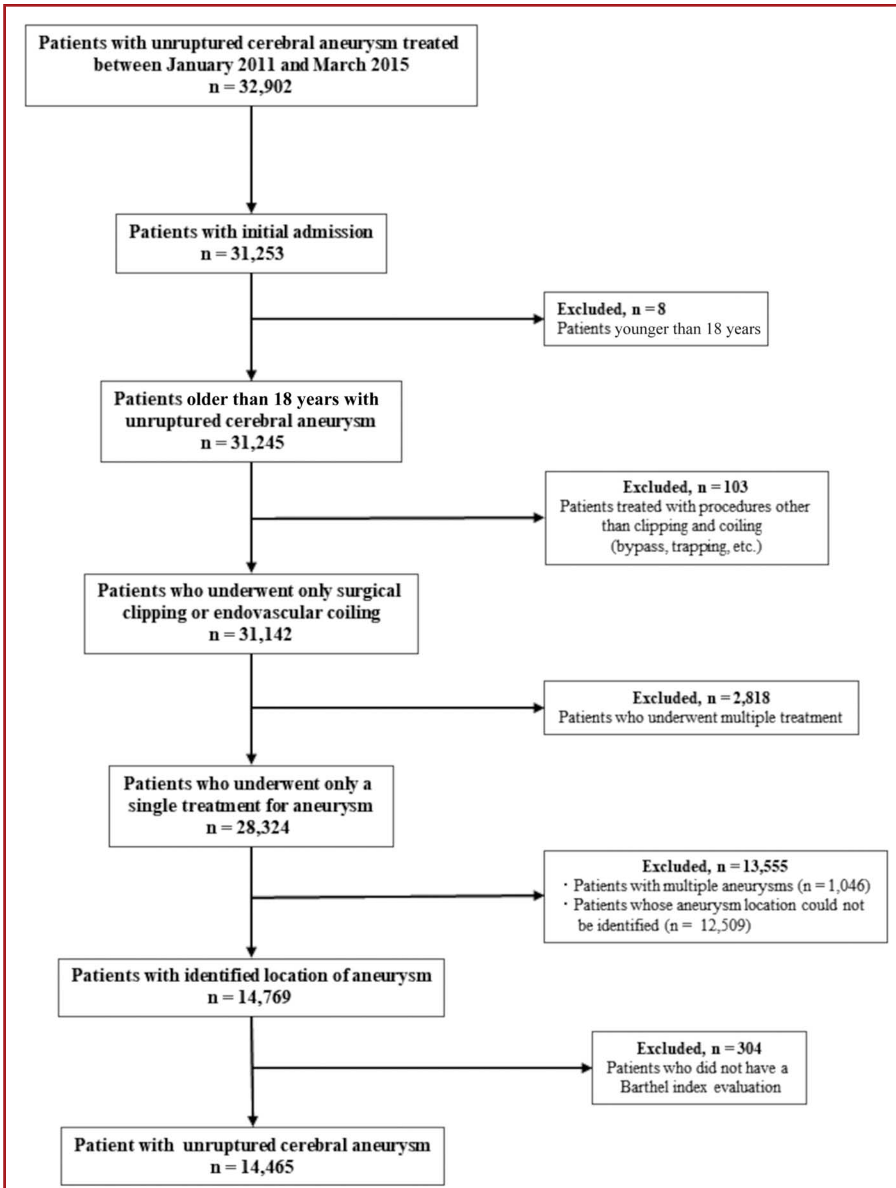

FIGURE. *Selection process for patients with unruptured cerebral aneurysms.*

treated with surgery by age group. The mFI-5 score increased significantly with age, as did a worsening BI score, and in-hospital mortality and complications. The incidences of postoperative complications such as intracerebral hemorrhage, SAH, congestive heart failure, and pneumonia did not increase significantly with age. Furthermore, 0.26% of all patients had missing values of BI scores at admission and discharge (Table 1); however, there were no missing data other than BI scores.

Table 2 presents the results of the multivariable logistic regression analysis of risk factors for worsening BI scores, in-hospital mortality, and in-hospital complications. The significant risk factors for worsening BI scores were the pre-elderly group (OR 1.84, 95% CI 1.52-2.25), elderly group (4.33, 3.47-5.39), mFI-5 score ≥2 items (1.95, 1.52-2.51), the use of anticoagulant and antiplatelet medications at admission, and aneurysm location (BA). However, endovascular coiling had a statistically inverse relationship as a risk factor compared with surgical clipping (0.41, 0.31-0.54). The elderly age group (3.26, 1.38-7.71), male sex (1.95, 1.00-3.78), and aneurysm location (BA and VA) were significant risk factors for in-hospital mortality. Concerning in-hospital complications, the significant risk factors were the pre-elderly group (1.21, 1.08-1.36), elderly group (1.76, 1.51-2.06),

TABLE 1. Baseline Characteristics of Patients With Surgically Treated UCAs, Based on Age Groups

No.	Total 14 465	Nonelderly, younger than 65 y 7380	Pre-elderly, 65-74 y 5364	Elderly, 75 y or older 1721	*P* value
Sex (male, %)	4380/14 465 (30.3%)	2578/7380 (34.9%)	1445/5364 (26.9%)	357/1721 (20.7%)	<.001[a]
Age (y), median (IQR)	64.0 (56.0, 71.0)	56.0 (49.0, 61.0)	69.0 (67.0, 72.0)	77.0/1721 (76.0, 80.0)	<.001[a]
Treatment					<.001[a]
Surgical clipping	9082/14 465 (62.8%)	4550/7380 (61.7%)	3598/5364 (67.1%)	934/1721 (54.3%)	
Endovascular coiling	5383/14 465 (37.2%)	2830/7380 (38.3%)	1766/5364 (32.9%)	787/1721 (45.7%)	
Location of the aneurysms					<.001[a]
ICA	5543/14 465 (38.3%)	3009/7380 (40.8%)	1776/5364 (33.1%)	758/1721 (44.0%)	
ACoA	2328/14 465 (16.1%)	1157/7380 (15.7%)	921/5364 (17.2%)	250/1721 (14.5%)	
MCA	4536/14 465 (31.4%)	2176/7380 (29.5%)	1885/5364 (35.1%)	475/1721 (27.6%)	
ACA	713/14 465 (4.9%)	321/7380 (4.3%)	308/5364 (5.7%)	84/1721 (4.9%)	
BA	812/14 465 (5.6%)	371/7380 (5.0%)	335/5364 (6.2%)	106/1721 (6.2%)	
VA	477/14 465 (3.3%)	310/7380 (4.2%)	126/5364 (2.3%)	41/1721 (2.4%)	
Other	56/14 465 (0.4%)	36/7380 (0.5%)	13/5364 (0.2%)	7/1721 (0.4%)	
Medical history					
Diabetes mellitus	1297/14 465 (9.0%)	504/7380 (6.8%)	601/5364 (11.2%)	192/1721 (11.2%)	<.001[a]
Hypertension	5987/14 465 (41.4%)	2680/7380 (36.3%)	2447/5364 (45.6%)	860/1721 (50.0%)	<.001[a]
Cerebral infarction	1500/14 465 (10.4%)	769/7380 (10.4%)	539/5364 (10.0%)	192/1721 (11.2%)	.411
Angina pectoris	527/14 465 (3.6%)	179/7380 (2.4%)	240/5364 (4.5%)	108/1721 (6.3%)	<.001[a]
Congestive heart failure	176/14 465 (1.2%)	57/7380 (0.8%)	79/5364 (1.5%)	40/1721 (2.3%)	<.001[a]
Myocardial infarction	11/14 465 (0.07%)	5/7380 (0.07%)	3/5364 (0.06%)	3/1721 (0.2%)	.282
Dyslipidemia	2644/14 465 (18.3%)	1119/7380 (15.2%)	1153/5364 (21.5%)	372/1721 (21.6%)	<.001[a]
mFI-5 score					<.001[a]
0 item	7457/14 465 (51.6%)	4292/7380 (58.2%)	2483/5364 (46.3%)	682/1721 (39.6%)	
1 item	5921/14 465 (40.9%)	2702/7380 (36.6%)	2408/5364 (44.9%)	811/1721 (47.1%)	
≥2 items	1087/14 465 (7.5%)	386/7380 (5.2%)	473/5364 (8.8%)	228/1721 (13.2%)	
Internal oral medication on admission					
Antiplatelet	5340/14 465 (36.9%)	2756/7380 (37.3%)	1847/5364 (34.4%)	737/1721 (42.8%)	<.001[a]
Anticoagulant	280/14 465 (1.9%)	79/7380 (1.1%)	133/5364 (2.5%)	68/1721 (4.0%)	<.001[a]
Statin	1377/14 465 (9.5%)	570/7380 (7.7%)	581/5364 (10.8%)	226/1721 (13.1%)	<.001[a]
Hospital volume					<.001[a]
1	4651/14 465 (32.2%)	2267/7380 (30.7%)	1815/5364 (33.8%)	569/1721 (33.1%)	
2	4767/14 465 (33.0%)	2439/7380 (33.0%)	1707/5364 (31.8%)	621/1721 (36.1%)	
3	5047/14 465 (34.9%)	2674/7380 (36.2%)	1842/5364 (34.3%)	531/1721 (30.9%)	
Barthel index at admission (points)					<.001[a]
0-95	929/14 443 (6.4%)	273/7367 (3.7%)	373/5356 (7.0%)	283/1720 (16.5%)	
100	13 514/14 443 (93.6%)	7094/7367 (96.3%)	4983/5356 (93.0%)	1437/1720 (83.5%)	
Barthel index at discharge (points)					<.001[a]
0-95	894/14 428 (6.2%)	263/7368 (3.6%)	357/5348 (6.7%)	274/1712 (16.0%)	
100	13 534/14 428 (93.8%)	7105/7368 (96.4%)	4991/5348 (93.3%)	1438/1712 (84.0%)	
Complications					
Intracerebral hemorrhage	36/14 465 (0.2%)	16/7380 (0.2%)	15/5364 (0.3%)	5/1721 (0.3%)	.730
Cerebral infarction	867/14 465 (6.0%)	424/7380 (5.7%)	329/5364 (6.1%)	114/1721 (6.6%)	.330
Subarachnoid hemorrhage	0/14 465 (0%)	0/7380 (0%)	0/5364 (0%)	3/1721 (0.2%)	
Congestive heart failure	67/14 465 (0.5%)	31/7380 (0.4%)	27/5364 (0.5%)	9/1721 (0.5%)	.730
Pneumonia	265/14 465 (1.8%)	127/7380 (1.7%)	97/5364 (1.8%)	41/1721 (2.4%)	.181
Worsening BI scores	631/14 465 (4.4%)	184/7380 (2.5%)	263/5364 (4.9%)	184/1721 (10.7%)	<.001[a]
In-hospital mortality	40/14 465 (0.3%)	13/7380 (0.2%)	17/5364 (0.3%)	10/1721 (0.6%)	.012[a]
In-hospital complications	1648/14 465 (11.4%)	709/7380 (9.6%)	638/5364 (11.9%)	301/1721 (17.5%)	<.001[a]

ACA, anterior cerebral artery; ACoA, anterior communicating artery; BA, basilar artery; BI, Barthel index; ICA, internal carotid artery; MCA, middle cerebral artery; mFI-5, 5-factor modified frailty index; UCAs, unruptured cerebral aneurysms; VA, vertebral artery.

[a]$P < .05$.

TABLE 2. Results of Multivariate Logistic Regression Analyses of Worsening BI Scores, In-Hospital Mortality, and In-Hospital Complications in All Cases

	Worsening BI scores (594/144 407[a])		In-hospital mortality (40/13 696[a])		In-hospital complications (1648/14 465[a])	
Objective variables (no.)	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Sex (male)	1.10 (0.92-1.33)	.270	1.95 (1.00-3.78)	.049[b]	1.06 (0.94-1.19)	.375
Treatment (endovascular coiling)	0.41 (0.31-0.54)	<.001[b]	2.21 (0.85-5.70)	.102	0.52 (0.44-0.62)	<.001[b]
Age group (y)						
Nonelderly, younger than 65	Reference		Reference		Reference	
Pre-elderly, 65-74	1.84 (1.52-2.25)	<.001[b]	1.88 (0.90-3.95)	.094	1.21 (1.08-1.36)	.001[b]
Elderly, 75 or older	4.33 (3.47-5.39)	<.001[b]	3.26 (1.38-7.71)	.007[b]	1.76 (1.51-2.06)	<.001[b]
Location of the aneurysms						
ICA	Reference		Reference		Reference	
ACoA	1.15 (0.89-1.48)	.263	1.80 (0.76-4.28)	.185	0.89 (0.75-1.05)	.155
MCA	0.91 (0.73-1.14)	.403	0.41 (0.12-1.36)	.145	0.74 (0.64-0.86)	<.001[b]
ACA	0.78 (0.51-1.19)	.252	N/A		0.66 (0.50-0.88)	.004[b]
BA	2.11 (1.54-2.90)	<.001[b]	3.42 (1.37-8.53)	.008[b]	1.43 (1.17-1.75)	<.001[b]
VA	1.54 (0.98-2.43)	.061	3.37 (1.05-10.83)	.041[b]	1.50 (1.17-1.75)	.002[b]
Other	3.76 (1.54-9.18)	.004[b]	N/A		1.86 (0.94-3.60)	.064
mFI-5 score						
0 item	Reference		Reference		Reference	
1 item	1.13 (0.95-1.36)	.164	1.64 (0.82-3.28)	.161	1.31 (1.17-1.47)	<.001[b]
≥2 items	1.95 (1.52-2.51)	<.001[b]	2.32 (0.86-6.26)	.095	1.79 (1.49-2.15)	<.001[b]
Internal oral medication on admission						
Antiplatelet	1.67 (1.31-2.12)	<.001[b]	0.55 (0.23-1.31)	.177	2.91 (2.47-3.40)	<.001[b]
Anticoagulant	2.01 (1.37-2.96)	<.001[b]	1.55 (0.36-6.72)	.557	1.84 (1.37-2.47)	<.001[b]
Statin	1.24 (0.98-1.58)	.072	0.64 (0.20-2.14)	.478	1.22 (1.04-1.44)	.013[b]
Hospital volume						
1	Reference		Reference		Reference	
2	0.89 (0.74-1.07)	.218	1.34 (0.67-2.69)	.410	0.88 (0.78-1.00)	.043[b]
3	0.59 (0.48-0.73)	<.001[b]	0.53 (0.21-1.31)	.170	0.71 (0.63-0.81)	<.001[b]

ACA, anterior cerebral artery; ACoA, anterior communicating artery; BA, basilar artery; BI, Barthel index; ICA, internal carotid artery; MCA, middle cerebral artery; mFI-5, 5-factor modified frailty index; OR, odds ratio; VA, vertebral artery.
[a]Complete cases without missing data.
[b]$P < .05$.

mFI-5 score of 1 item (1.31, 1.17-1.47), mFI-5 score ≥2 items (1.79, 1.49-2.15), anticoagulant and antiplatelet medication use, statin use, and aneurysm location (middle cerebral artery, BA, and VA). Conversely, endovascular coiling had a statistically inverse relationship as a risk factor compared with surgical clipping (0.52, 0.44-0.62).

Table 3 presents the results of multivariable logistic regression analysis of worsening BI scores in all age groups. Chronological age was a significant risk factor for worsening BI scores in all 3 age groups. An mFI-5 score ≥2 items was a statistically significant risk factor for worsening BI scores in all age groups (nonelderly [1.78, 1.05-3.02], pre-elderly [1.76, 1.20-2.60], and elderly [2.00, 1.28-3.14]). In all age groups, high-volume hospitals were inversely associated with worsening BI scores.

Table 4 presents the results of multivariable logistic regression analysis for in-hospital complications in the 3 age groups. Chronological age was a significant risk factor only in the elderly group, and there was no significant difference in the age group younger than 74 years. On the contrary, an mFI-5 score ≥2 items was a statistically significant risk factor of in-hospital complications in all 3 age groups (nonelderly [1.66, 1.20-2.28], pre-elderly [1.72, 1.30-2.29], and elderly [1.99, 1.36-2.93]). In addition, in the nonelderly and pre-elderly groups, an mFI-5 score of 1 item was associated with in-hospital complications. The use of oral anticoagulants, antiplatelet agents, or statins at the time of admission was a significant risk factor for in-hospital complications in all age groups. By contrast, treatment with endovascular coiling was inversely associated with the occurrence of in-hospital complications in all age groups. Furthermore, the high hospital volume was inversely associated with in-hospital complications. Although chronological age was not associated with the occurrence of in-hospital complications for patients younger than 74 years, an mFI-5 score ≥2 items was a statistically significant risk factor in all age groups.

Focusing on mFI-5 and chronological age, we found that an mFI-5 score ≥2 items was a significant risk factor for worsening BI

TABLE 3. Results of Multivariate Logistic Regression Analyses of Worsening BI Scores Across All Age Groups

Age group (no.)	Worsening BI scores					
	Nonelderly, younger than 65 y (172/7356[a])		Pre-elderly, 65-74 y (247/5340[a])		Elderly, 75 y or older (175/1711[a])	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Sex (male)	1.24 (0.90-1.69)	.187	1.26 (0.95-1.66)	.102	0.77 (0.51-1.17)	.222
Treatment (endovascular coiling)	0.53 (0.30-0.94)	.029[b]	0.25 (0.16-0.38)	<.001[b]	0.53 (0.33-0.85)	.008[b]
Age	1.02 (1.00-1.04)	.046[b]	1.40 (1.00-1.09)	.047[b]	1.11 (1.06-1.17)	<.001[b]
Location of the aneurysms						
ICA	Reference		Reference		Reference	
ACoA	1.35 (0.86-2.13)	.195	0.83 (0.56-1.23)	.349	1.69 (1.05-2.72)	.031[b]
MCA	1.01 (0.67-1.54)	.950	0.71 (0.51-0.99)	.044[b]	1.20 (0.78-1.85)	.395
ACA	0.91 (0.41-2.06)	.829	0.59 (0.31-1.13)	.111	0.93 (0.42-3.81)	.862
BA	2.36 (1.32-4.24)	.004[b]	2.22 (1.37-3.58)	.001[b]	1.91 (1.01-3.62)	.048[b]
VA	1.90 (0.96-3.76)	.065	1.52 (0.71-3.25)	.285	1.28 (0.43-3.81)	.660
Other	7.64 (2.55-22.87)	<.001[b]	1.85 (0.23-15.00)	.563	2.05 (0.23-18.63)	.524
mFI-5 score						
0 item	Reference		Reference		Reference	
1 item	1.15 (0.84-1.58)	.387	1.05 (0.79-1.38)	.747	1.13 (0.79-1.62)	.501
≥2 items	1.78 (1.05-3.02)	.032[b]	1.76 (1.20-2.60)	.004[b]	2.00 (1.28-3.14)	.002[b]
Internal oral medication on admission						
Antiplatelet	1.32 (0.78-2.23)	.302	2.14 (1.51-3.04)	<.001[b]	1.48 (0.98-2.25)	.064
Anticoagulant	1.94 (0.76-4.94)	.167	2.48 (1.44-4.27)	.001[b]	1.63 (0.84-3.16)	.151
Statin	1.42 (0.90-2.23)	.135	0.90 (0.60-1.33)	.594	1.73 (1.15-2.60)	.008[b]
Hospital volume						
1	Reference		Reference		Reference	
2	1.01 (0.72-1.41)	.961	0.88 (0.65-1.18)	.395	0.77 (0.54-1.11)	.162
3	0.54 (0.36-0.80)	.002[b]	0.62 (0.46-0.85)	.003[b]	0.62 (0.41-0.92)	.018[b]

ACA, anterior cerebral artery; ACoA, anterior communicating artery; BA, basilar artery; BI, Barthel index; ICA, internal carotid artery; MCA, middle cerebral artery; mFI-5, 5-factor modified frailty index; OR, odds ratio; VA, vertebral artery.
[a]Complete cases without missing data.
[b]$P < .05$.

scores and in-hospital complications in all age groups. However, chronological age was not associated with in-hospital complications in both the nonelderly and pre-elderly groups. Focusing on treatment, endovascular coiling was a significant inverse risk factor for worsening BI score and in-hospital complications compared with surgical clipping, regardless of age. **Supplemental Digital Content 2**, **Table**, http://links.lww.com/NEU/D430, presents the results of multivariable logistic regression analysis for in-hospital mortality in the nonelderly, pre-elderly, and elderly groups.

DISCUSSION

We demonstrated that chronological age was not associated with in-hospital complications in patients younger than 74 years undergoing treatment for UCA, whereas an mFI-5 score ≥2 items was associated with in-hospital complications in all age groups. This means that the mFI-5 score (biological age) may be an independent associated factor of post-UCA treatment outcomes, unlike chronological age. Our finding that frailty significantly affects the occurrence of complications after UCA treatment suggests that routine preoperative and prophylactic assessments of frailty should be considered for patients younger than 74 years before UCA treatment. Systematic screening for frailty would help identify patients at risk for complications after UCA treatment. Preoperative information on patient frailty status may help clinicians provide early treatment and rehabilitation interventions to mitigate the effects of postoperative complications.

With the increasing physical, mental, and social diversity of the elderly population, determining the optimal decision-making process for the treatment of elderly patients based on chronological age alone has become difficult.[21-23] The phenomenon of aging is not consistent for all individuals, and thus, it may be inappropriate to associate the physical and cognitive functions of individuals in a particular age group. Because of the great variability in the aging process at the individual level, some younger patients may have higher mFI-5 scores than elderly patients. In fact, in our study, frailty was more prevalent in the elderly, although it was also observed in some younger patients. Frailty has been defined as a multidimensional condition that independently

TABLE 4. Results of Multivariate Logistic Regression Analyses of In-Hospital Complications Across All Age Groups

Age group (no.)	In-hospital complications					
	Nonelderly, younger than 65 y (709/7380[a])		Pre-elderly, 65-74 y (638/5364[a])		Elderly, 75 y or older (301/1721[a])	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Sex (male)	1.12 (0.94-1.33)	.190	1.06 (0.87-1.29)	.545	0.85 (0.61-1.18)	.331
Treatment (endovascular coiling)	0.66 (0.49-0.88)	.005[b]	0.47 (0.36-0.62)	<.001[b]	0.37 (0.26-0.56)	<.001[b]
Age	1.00 (0.99-1.01)	.910	1.00 (0.97-1.03)	.924	1.08 (1.04-1.13)	<.001[b]
Location of the aneurysms						
ICA	Reference		Reference		Reference	
ACoA	0.92 (0.71-1.18)	.492	0.75 (0.58-0.98)	.033[b]	1.30 (0.87-1.93)	.196
MCA	0.77 (0.61-0.97)	.025[b]	0.66 (0.52-0.83)	<.001[b]	0.93 (0.65-1.33)	.701
ACA	0.78 (0.50-1.21)	.264	0.56 (0.36-1.93)	.011[b]	0.64 (0.32-1.28)	.205
BA	1.33 (0.97-1.83)	.075	1.42 (1.04-1.93)	.028[b]	1.88 (1.13-3.12)	.015[b]
VA	1.45 (1.04-2.02)	.028[b]	1.60 (1.01-2.52)	.045[b]	1.39 (0.61-3.18)	.432
Other	2.64 (1.21-5.74)	.014[b]	0.99 (0.21-4.59)	.986	0.96 (0.11-8.64)	.968
mFI-5 score						
0 item	Reference		Reference		Reference	
1 item	1.35 (1.14-1.60)	.001[b]	1.28 (1.07-1.54)	.008[b]	1.32 (0.98-1,77)	.068
≥2 items	1.66 (1.20-2.28)	.002[b]	1.72 (1.30-2.29)	<.001[b]	1.99 (1.36-2.93)	<.001[b]
Internal oral medication on admission						
Antiplatelet	2.52 (1.91-3.32)	<.001[b]	3.28 (2.57-4.18)	<.001[b]	2.81 (1.97-4.00)	<.001[b]
Anticoagulant	1.95 (1.10-3.45)	.022[b]	1.69 (1.08-2.63)	.021[b]	1.96 (1.12-3.41)	.018[b]
Statin	1.35 (1.04-1.74)	.024[b]	1.02 (0.79-1.32)	.852[b]	1.57 (1.12-2.22)	.010[b]
Hospital volume						
1	Reference		Reference		Reference	
2	0.87 (0.72-1.06)	.164	0.87 (0.71-1.07)	.190	0.89 (0.65-1.22)	.430
3	0.75 (0.62-0.91)	.004[b]	0.74 (0.60-0.91)	.004[b]	0.58 (0.42-0.82)	.002[b]

ACA, anterior cerebral artery; ACoA, anterior communicating artery; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; mFI-5, 5-factor modified frailty index; OR, odds ratio; VA, vertebral artery.
[a]Complete cases without missing data.
[b]$P < .05$.

affects a patient's functional prognosis. Therefore, when considering prognostic models, it is suggested that biological age (mFI-5 score), unlike chronological age, should be considered during the initial evaluation of patients undergoing UCA surgery.

In the field of neurosurgery, the mFI-5 score is reportedly associated with postoperative outcomes in patients with pituitary adenoma, meningioma, glioma, and UCAs.[13-15,24,25] Hitherto, no large-scale studies have been conducted on patients in separate age groups using nationwide UCA databases; only small-scale studies have been conducted.[15,26] Based on separate analyses for each age group (including elderly patients) using nationwide data, the mFI-5 score was found to be a potential associated factor of postoperative outcomes in patients with UCAs, regardless of age group. In this study, patients who underwent surgical clipping were more predisposed to developing worsening BI scores and in-hospital complications in all age groups than those who underwent coil embolization. In actual clinical practice, the mFI-5 score and treatment method should be considered in the decision making for patients undergoing surgery for UCA, irrespective of age.

Patient age is a poor prognostic factor in the treatment of UCA.[27,28] Owing to the global differences in population aging, the specific criteria for age vary by era and region. In the previous era, it was reported that age 50 years was the borderline for poor postoperative prognosis.[29,30] Japan has one of the fastest aging populations in the world, and because aging in the rest of the world will follow a similar pattern,[31] the results of this study may become a global standard.

Although worsening BI scores and in-hospital complications were associated with an mFI-5 score ≥2 items, in-hospital mortality was not associated with an mFI-5 score ≥2 items, probably because only 40 cases of in-hospital mortality were recorded, which were too small for statistical analysis. A hospital that handled a large number of surgical cases had significantly lower numbers of both in-hospital complications and worsening BI scores, probably because large hospitals with a high number of surgical cases are better equipped to prevent perioperative complications.[32]

Limitations

This study has several limitations. First, this study had a registry-based retrospective design, whereas a planned prospective cohort study or a randomized controlled trial would have offered a higher level of evidence. Furthermore, bias could not be eliminated completely. Second, the DPC database used in this study did not contain information pertaining to certain items. For example, we obtained data concerning aneurysm location but not aneurysm size, aneurysm morphology, SAH history, or family history, which, as shown in other national databases, may be unmeasurable confounders. Moreover, the clinicians who administered treatment to patients registered in this DPC database were working in different hospitals throughout Japan. Third, our data initially contain over half of the missing data; nevertheless, the final missing value is 0.26% for accurate analysis, which is small, and thus is not expected to significantly affect the overall results. Finally, our results should be interpreted with caution because they may not be generalizable to other countries with different health care resources and systems, given that the data in this study were obtained solely from the Japanese population, with the highest proportion of elderly people globally. However, our findings may present a standard for future research in other populations. In this study, we found a higher overall proportion of patients undergoing surgical clipping in Japan, with its unique characteristics.[33]

CONCLUSION

The mFI-5 score was a more useful associated factor for in-hospital complications than chronological age after UCA treatment in patients younger than 74 years. Considerations of both chronological age and the mFI-5 score may help better optimize therapeutic interventions for patients with UCA.

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Disclosures

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***Supplemental digital content** is available for this article at neurosurgery-online.com.*

Supplemental Digital Content 1. Text. Details of diagnosis procedure combination data, patient selection, Barthel index, and hospital information.
Supplemental Digital Content 2. Table. Results of multivariate logistic regression analyses for in-hospital mortality across all age groups.

COMMENTS

This paper demonstrates an association between the modified frailty index (mFI-5 score) and outcome and complications following treatment for un-ruptured intracranial aneurysms in the elderly. The results support the notion that chronological age alone is an inadequate predictor. The results are derived from a nationwide Japanese database and therefore represent a range of institutions and clinicians. Because the Japanese population is renowned for not only lifespan but also health span, it is unclear whether these results are generalizable to other populations. Unfortunately, the database lacks detailed information regarding aneurysm characteristics such as location and morphology, which precludes analysis of treatment specific variables. Also, the authors were forced to exclude 12 905 patients (nearly 25%) due to data integrity issues. Further prospective research may clarify the utility of this tool.

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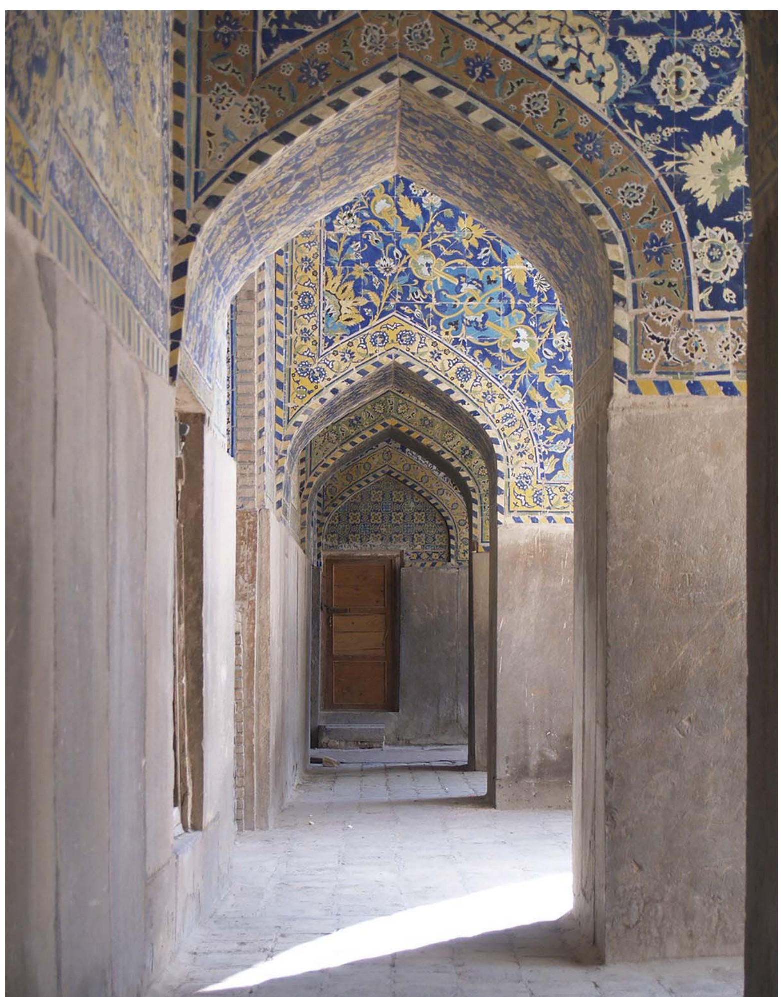

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