Research Square

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Age-stratified impact of the modified 5-item frailty index on postoperative pneumonia after aneurysmal subarachnoid hemorrhage

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Abstract

Objective

Postoperative pneumonia (POP) is a frequent and serious complication after aneurysmal subarachnoid hemorrhage (aSAH). Frailty has emerged as an important predictor of adverse surgical outcomes, yet its age-specific impact on POP after aSAH remains unclear. This study aimed to investigate the association between preoperative frailty assessed by the modified 5-item frailty index (mFI-5) and POP after aSAH, with particular attention to age-related effect modification.

Methods

We retrospectively reviewed consecutive adult patients with aSAH who underwent aneurysm repair (microsurgical clipping or endovascular coiling) at a tertiary center between January 2019 and July 2022. Frailty was defined as an mFI-5 score ≥ 2. POP occurring within 30 days after aneurysm repair was diagnosed using modified Centers for Disease Control and Prevention criteria. Multivariable logistic regression was performed in the overall cohort and in age-stratified subgroups (< 65 vs. ≥65 years), adjusting for demographic factors, neurological severity, comorbidities, and laboratory parameters.

Results

Among 539 included patients, 134 (24.9%) developed POP. In the overall multivariable analysis, older age, lower Glasgow Coma Scale score, higher C-reactive protein levels, and chronic obstructive pulmonary disease were independently associated with POP, whereas frailty was not. In age-stratified analyses, frailty was independently associated with an increased risk of POP in patients aged < 65 years (odds ratio [OR] 3.04, 95% confidence interval [CI] = 1.11–8.58; p = 0.031), but not in those aged ≥ 65 years (OR 0.85, 95% CI = 0.07–5.32; p = 0.88).

Conclusions

The association between preoperative frailty assessed by mFI-5 and postoperative pneumonia after aSAH is age dependent. Frailty was associated with a significantly increased risk of POP among younger patients, whereas its predictive value appears attenuated in older individuals. Incorporating frailty assessment into perioperative risk stratification may help identify vulnerable younger aSAH patients who could benefit from intensified pneumonia-prevention strategies.

1. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a life-threatening hemorrhagic stroke associated with substantial mortality and long-term disability despite advances in aneurysm occlusion and neurocritical care.

Postoperative pneumonia (POP) is among the most frequent medical complications after aSAH. Prior studies report that approximately 15–30% of surgically treated aSAH patients develop POP and that POP is associated with prolonged mechanical ventilation, longer hospital stay, and worse clinical outcomes(1–3). Reported clinical

predictors include advanced age, poor admission neurological status, cardiopulmonary comorbidities, and elevated inflammatory markers(1, 3).

Frailty is a multidimensional construct reflecting decreased physiological reserve and increased vulnerability to stressors. The modified frailty index (mFI) operationalizes frailty using routinely collected comorbidity and functional status variables and has been widely applied for perioperative risk stratification(4, 5). Higher mFI burden is associated with increased postoperative complications, mortality, prolonged length of stay, and readmission across multiple surgical populations, including neurosurgical procedures(4–6). In neurosurgery, frailty has been associated with adverse outcomes after cranial and spinal operations(5–9). However, evidence regarding frailty and postoperative infectious complications in aSAH is limited. A large national database study using the 11-item mFI suggested that frailty is independently associated with poor outcomes after aSAH(10), but the role of the simplified 5-item mFI (mFI-5) in predicting POP has not been clarified(11).

Therefore, we conducted a retrospective cohort study to examine the association between preoperative frailty (mFI-5) and POP after aSAH and to test whether the prognostic impact of frailty differs by age.

2. Methods

2.1 Study design and population

We retrospectively reviewed consecutive adult patients with aSAH treated at the First Affiliated Hospital of Wenzhou Medical University from January 1, 2020 to July 31, 2022. aSAH was diagnosed by head computed tomography (CT) demonstrating subarachnoid hemorrhage and confirmed aneurysmal etiology by computed tomography angiography (CTA) or digital subtraction angiography (DSA)(12)

2.2 Ethical approval

The study followed the STROBE recommendations and was approved by the Institutional Review Board (IRB) of the First Affiliated Hospital of Wenzhou Medical University (BR/NGGI-2412031). Informed consent was waived due to the retrospective design of the study and the absence of personal identifiers, in accordance with the principles of the Declaration of Helsinki(13).

2.3 Inclusion and exclusion criteria

Inclusion criteria were: (1) age ≥18 years; (2) diagnosis of aSAH confirmed by DSA angiography; (3) aneurysm secured by microsurgical clipping or endovascular coiling during the index hospitalization; and (4) availability of preoperative data sufficient to calculate mFI and main covariates. Exclusion criteria were: (1) Age<18 (N=3); (2) Presence of intracranial vascular malformations or moyamoya disease (N=24); (3) Patients with preoperative unexpected events that could affect the outcome: preoperative cardiac arrest (N=1), severe head trauma (N=2); (4) Intraoperative or postoperative rebleeding (N=13); (5) Missing critical information (N=4); (6) Positive SARS-CoV-2 PCR result (N=0). After applying the exclusion criteria, 539 patients were included in the final analysis (Figure 1).

2.4 Data collection and variables

All patients received standard aSAH management according to contemporary institutional protocols, including early aneurysm occlusion, blood pressure control, nimodipine administration, and surveillance for hydrocephalus and delayed cerebral ischemia. Treatment choice (clipping vs coiling) was determined by a multidisciplinary team

based on aneurysm anatomy and patient characteristics. Ventilatory support, extubation strategies, chest physiotherapy, and venous thromboembolism prophylaxis followed standard ICU practice.

From electronic records we extracted demographic data (age, sex, smoking status), comorbidities (hypertension, diabetes, congestive heart failure [CHF], COPD), and baseline functional status. Admission neurological status was assessed using Glasgow Coma Scale (GCS)(14), Hunt–Hess grade(15), and World Federation of Neurosurgical Societies (WFNS) grade(16).

Laboratory variables within 24 hours of admission included serum albumin, blood glucose, complete blood count, and C-reactive protein (CRP). Treatment modality (endovascular coiling or microsurgical clipping) and length of hospital stay (LOS) were recorded.

Frailty was assessed using the modified 5-item frailty index (mFI-5)(17). The mFI-5 includes five deficits (hypertension, diabetes, CHF, COPD, and functional dependence); each deficit was scored as 1 point and summed (range 0–5). For primary analyses, patients were categorized as non-frail (mFI-5 <2) or frail (mFI-5 ≥2), consistent with prior neurosurgical applications and the distribution in our cohort.

POP was defined as a lower respiratory tract infection occurring within 30 days after aneurysm repair, diagnosed according to modified Centers for Disease Control and Prevention (CDC) criteria(18). Patients with pre-existing pneumonia at admission were excluded.

2.5 Outcomes

The primary outcome was occurrence of POP within 30 days after aneurysm repair.

Statistical analysis

Continuous variables are reported as median (interquartile range [IQR]) and compared using the Mann–Whitney U test. Categorical variables are reported as number (percentage) and compared using the χ^2 test or Fisher's exact test, as appropriate. Multivariable logistic regression was performed to identify independent predictors of POP in the overall cohort. Prespecified covariates included age, GCS, albumin, glucose, CRP, CHF, COPD, mFI-5 frailty category, Hunt–Hess grade, and WFNS grade. To explore effect modification by age, we repeated multivariable analyses stratified by age (<65 vs ≥65 years), consistent with the subgroup models presented in Table 3. Kaplan–Meier curves were plotted to show 30-day No-POP probability according to mFI category (<2 vs ≥2) in each age group, with log-rank tests for group comparisons. All statistical analyses were performed using R version 3.6.3 and python version 3.7.

3. Results

3.1 Baseline characteristics

A total of 539 patients met inclusion criteria, of whom 134 (24.9%) developed POP within 30 days after aneurysm repair. Baseline characteristics stratified by POP status are summarized in Table 1. Patients who developed POP were older (median 65 vs 54 years, p<0.001), had longer hospital length of stay (median 16 vs 13 days, p=0.002), and had higher rates of CHF and COPD (both p<0.001). POP was also more frequent among patients with higher clinical severity (Hunt–Hess grades 4–5: 26.9% vs 8.2%; WFNS grades 4–5: 33.6% vs 13.1%; both p<0.001) and higher admission CRP (median 7.8 vs 4.7 mg/L, p<0.001).

Table 1. Characteristics of the study population.

Patient Characteristics	Total (n=539)	No POP (n=405)	POP (n=134)	p
Age ,median[IQR]	56.00[48.00,66.00]	54.00[47.00,65.00]	65.00[54.00,72.00]	**<0.001**
Gender (female), n(%)	354(65.68)	263(64.94)	91(67.91)	0.530
Smoking,n(%)	81(15.03)	59(13.69)	22(20.37)	0.082
LOS ,median[IQR]	14[11, 20]	13 [10, 19]	16[11, 24]	**0.002**
In-hospital complications				
Hypertension, n(%)	285(52.88)	205(50.62)	80(59.70)	0.068
Diabetes, n(%)	37(6.86)	23(5.68)	14(10.45)	0.058
CHF, n(%)	64(11.87)	33(8.15)	31(23.13)	**<0.001**
COPD, n(%)	32(5.94)	13(3.21)	19(14.18)	**<0.001**
Independent status, n(%)	10(1.86)	6(1.48)	4(2.99)	0.275
Treatment modality				
Endovascular coiling, n(%)	469(87.01)	358(88.40)	111(82.84)	0.097
Microsurgical clipping, n(%)	71(13.17)	47(11.60)	24(17.91)	0.061
Admission clinical grade				
GCS, median[IQR]	15[14,15]	15[15,15]	15[10,15]	**<0.001**
Hunt-Hess grades 4-5, n (%)	69(12.80)	33(8.15)	36(26.87)	**<0.001**
WFNS grade 4–5, n (%)	98(18.18)	53(13.09)	45(33.58)	**<0.001**
Laboratory values on admission				
Albumin (g/L),median[IQR]	39.10[36.50,41.50]	39.30[36.90,41.50]	38.30[35.80,41.00]	**0.048**
Glucose (mmlo /L) ,median[IQR]	6.40[5.30,7.60]	6.30[5.10,7.40]	6.60[5.90,8.20]	**<0.001**
Neutrophil counts (*10^9 /L),median[IQR]	9.24[6.63,12.09]	9.32[6.56,12.10]	8.91[6.68,11.80]	0.566

Patient Characteristics	Total (n=539)	No POP (n=405)	POP (n=134)	p
Lymphocyte count ($*10^9$ /L) ,median[IQR]	1.14[0.86,1.58]	1.17[0.86,1.58]	1.10[0.86,1.56]	0.487
Hemoglobin (g/L) ,median[IQR]	132.00[119.00,142.00]	133.00[120.00,143.00]	130.00[117.00,142.00]	0.152
Blood platelet count ($*10^9$ /L) ,median[IQR]	214.00[175.00,259.00]	214.00[176.00,257.00]	214.00[174.00,264.00]	0.886
CRP (mg/L),median[IQR]	5.00[1.90,10.50]	4.70[1.39,8.70]	7.80[3.70,20.00]	**<0.001**
mFI-5, n(%)				
<2	426(79.04)	343(84.69)	83(61.94)	**<0.001**
≥2	113(20.04)	57(15.31)	51(38.06)	

Table1. Characteristics of the study population

Abbreviation: LOS, Length of stay; POP, postoperative pneumonia; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; GCS, Glasgow Coma Scale; WFNS, World Federation of Neurosurgical Societies; mFI-5, 5-item modified frailty index.

3.2 Multivariable analysis in the overall cohort

In the overall multivariable logistic regression model (Table 2), older age, lower GCS score, higher CRP, and COPD were independently associated with POP. Frailty (mFI-5 ≥2) was not independently associated with POP in the overall cohort after adjustment for age, clinical severity, comorbidities, and laboratory variables.

Table 2. Multivariable logistic regression for POP in the overall cohort.

Predictor	Estimate	OR (95%CI)	p
Age	0.04	1.04(1.02 - 1.06)	**<0.001**
GCS	-1.08	0.83(0.74 - 0.96)	**0.021**
Albumin	-0.02	0.99(0.94 - 1.04)	0.56
Glucose	0.07	1.07(0.98 - 1.18)	0.14
CRP	0.07	1.07(1.05 - 1.10)	**<0.001**
CHF	0.69	2.00(0.81 - 5.07)	0.14
COPD	0.98	2.66(1.07 - 6.77)	**0.04**
mFI-5≥2	0.33	1.40(0.59 - 3.20)	0.44
Hunt-Hess grades 4-5	0.27	1.31(0.35 - 5.05)	0.69
WFNS grade 4–5	0.49	1.64(0.47 - 5.50)	0.43

3.3 Age-stratified multivariable analyses

Age-stratified multivariable logistic regression analyses were performed to assess whether the association between frailty and POP differed by age (<65 vs. ≥65 years) (Table 3). In patients aged <65 years, frailty (mFI-5 ≥2) was independently associated with an increased risk of POP (OR 3.04, 95% CI 1.11–8.58; p = 0.031). Lower GCS scores and higher CRP levels also remained significant predictors in this subgroup. In contrast, frailty was not independently associated with POP among patients aged ≥65 years (OR 0.85, 95% CI 0.07–5.32; p = 0.88), indicating an age-dependent association between frailty and POP.

Table 3. Age-stratified multivariable logistic regression models for POP.

	Subgroup, Age<65			Subgroup, Age≥65		
Predictor	**Estimate**	**OR (95%CI)**	**p**	**Estimate**	**OR (95%CI)**	**p**
Age	0.13	1.14(1.00 - 1.29)	**0.048**	0.069	1.12(1.09 - 1.14)	**0.042**
GCS	-0.82	0.72(0.49 - 0.89)	**0.004**	-0.95	0.85(0.59 - 0.99)	**0.034**
Albumin	0.02	1.02(0.94 - 1.10)	0.66	-0.05	0.95(0.88 - 1.03)	0.22
Glucose	0.46	1.59(0.57 - 4.31)	0.37	-0.08	0.93(0.76 - 1.10)	0.42
CRP	0.1	1.11(1.06 - 1.16)	**<0.001**	0.06	1.06(1.04 - 1.10)	**<0.001**
CHF	0.79	2.21(0.78 - 6.52)	0.14	0.82	2.26(0.17 - 31.22)	0.53
COPD	0.55	1.25(1.05-1.51)	**0.012**	-	-	-
mFI-5≥2	1.11	3.04(1.11 - 8.58)	**0.031**	-0.16	0.85(0.07 - 5.32)	0.88
WFNS	0.24	1.27(0.21 - 7.35)	0.79	0.61	1.84(0.22 - 12.39)	0.54
Hunt Hess	-0.84	0.43(0.06 - 3.00)	0.4	0.91	2.48(0.36 - 20.84)	0.37

3.4 Time-to-event analysis

Time-to-event analysis was used to visualize the temporal distribution of POP occurrence and to account for varying lengths of follow-up during hospitalization. Kaplan–Meier curves for 30-day pneumonia-free survival by frailty (mFI-5 ≥2) status are shown in Figure 2. Consistent with the logistic regression results, a greater separation of curves was visually observed in the <65-year subgroup (log-rank test, p< 0.05) than in the ≥65-year subgroup (log-rank test, p=0.57).

Kaplan-Meier curves compare the probability of remaining free from postoperative pneumonia (POP) within 30 days after aneurysm repair, stratified by age group (<65 years vs. ≥65 years) and frailty status (non-frail: mFI-5 <2; frail: mFI-5 ≥2). A. In patients aged <65 years, frail individuals showed a significantly lower pneumonia-free survival compared to non-frail patients (log-rank test, p< 0.05). B. In patients aged ≥65 years, the survival curves between frail and non-frail groups did not differ significantly (log-rank test, p=0.57). These findings highlight that the association between preoperative frailty and POP is significant primarily in younger patients.

Discussion

This retrospective study of 539 aSAH patients undergoing aneurysm repair found that POP occurred in 24.9% of patients within 30 days. Multivariable analysis identified older age, worse admission neurological status (lower GCS), higher systemic inflammation (elevated CRP), and the presence of COPD as independent predictors of POP. A key and novel finding is the age-dependent association of frailty, as defined by an mFI-5 score ≥2, with POP: frailty was an independent risk factor for POP in patients aged <65 years, but this association was not statistically significant in patients aged ≥65 years.

To our knowledge, this is the first study to demonstrate an age-dependent association between mFI-5–defined frailty and postoperative pneumonia after aSAH. These findings are consistent with prior work identifying age, neurological severity, and cardiopulmonary comorbidity as major determinants of pneumonia after aSAH. For example, Yuan et al. reported that POP occurred in roughly one-quarter to one-third of aSAH patients and was associated with in-hospital mortality and longer hospital stay, and identified age and poorer admission neurological status as key predictors(1). Similarly, a large database analysis focusing on hospital-acquired pneumonia after aSAH found that pneumonia was common and that affected patients had longer intensive care unit and hospital length of stay(2). In a surgical series of ruptured aneurysm clipping, postoperative pneumonia was also reported as a frequent complication associated with adverse outcomes(3). Age likely increases susceptibility to pneumonia through immunosenescence, reduced cough and swallowing reflexes, and higher burden of chronic disease. Poorer neurological status may promote aspiration, impaired airway protection, and prolonged mechanical ventilation, all of which predispose to lower respiratory tract infection. Elevated CRP likely reflects a heightened inflammatory response or early systemic stress that may identify patients at risk of subsequent pulmonary complications. COPD represents a direct pulmonary vulnerability and may exacerbate postoperative respiratory insufficiency, increasing the likelihood of infection.

A key contribution of this study is the age-stratified evaluation of frailty using the simplified mFI-5. Prior studies in aSAH have assessed frailty using more complex indices and primarily focused on global outcomes rather than specific postoperative infectious complications. Dicpinigaitis et al. used the 11-item mFI (mFI-11) in a national inpatient cohort and demonstrated that higher frailty status was independently associated with poorer outcomes and longer hospitalization after aSAH(10). This finding is further corroborated by the large-scale database study by Guo et al., which also identified frailty as a significant independent predictor of adverse discharge disposition (institutional care), need for procedural suppor, and postoperative complications in aSAH patients. Importantly,

and in alignment with the central finding of our present study, Guo et al. also reported that the impact of frailty on outcomes such as discharge to institutional care was more pronounced among patients younger than 65 years compared to their older counterparts(19, 20). Our study extends this insight by suggesting that in younger aSAH patients (<65 years), the cumulative deficit captured by the mFI-5 may be particularly sensitive in uncovering an underlying lack of physiological reserve, which significantly heightens susceptibility to postoperative complications like pneumonia. Conversely, in older patients (≥65 years), the dominant risks posed by advanced age itself and its attendant multimorbidity may overshadow the incremental predictive value of the mFI-5 for POP.

The mFI-5 offers distinct practical advantages over the 11-item MFI (MFI-11). Comprising only five easily ascertained items (hypertension, diabetes, congestive heart failure, COPD, and functional dependence), the mFI-5 is quicker to calculate and more feasible for routine use in busy clinical settings, especially during preoperative or emergency assessments(21, 22). This simplification enhances its utility without a substantial loss of predictive relevance. From a clinical perspective, the mFI-5 can be rapidly derived from routine history and may complement neurological grading scales in planning perioperative care. Particular attention should be given to patients aged <65 years who are classified as frail(23, 24). The identification of frailty, especially in younger patients, underscores the need for proactive, nurse-led preventive care. Evidence supports that structured nursing interventions significantly reduce pneumonia risk in vulnerable neurocritical patients. Key measures include rigorous adherence to ventilator-associated pneumonia (VAP) prevention bundles (elevating the head-of-bed, daily sedation breaks, and oral care with chlorhexidine)(25) and early, systematic swallowing assessments conducted by trained nurses to prevent aspiration(26). Integrating frailty screening into nursing admission assessments can trigger these targeted protocols, ensuring high-risk patients receive timely and intensified respiratory care.

This study has limitations. First, the retrospective single-center design introduces the potential for selection bias and residual confounding. Second, frailty was operationalized using comorbidity and dependence variables captured in medical records; such indices do not fully represent multidimensional frailty domains. Third, although we used modified CDC criteria to define POP, the lack of uniform microbiological confirmation could have led to some misclassification. Finally, external validation in independent cohorts is needed before routine implementation of age-stratified frailty-based prediction.

Conclusions

In patients with aneurysmal subarachnoid hemorrhage undergoing aneurysm repair, postoperative pneumonia occurred in approximately one-quarter of cases. Older age, lower admission GCS, higher CRP, and COPD were independent predictors. The association between preoperative frailty measured by mFI-5 and postoperative pneumonia was age-dependent and was evident in patients aged <65 years but not in those aged ≥65 years. Incorporating mFI-5 into perioperative risk assessment may help guide targeted pneumonia-prevention strategies for younger aSAH patients.

Declarations

Data Availability Statement

All data generated or analyzed during this study are provided within the article and its Supplementary Materials. Additional information can be obtained from the corresponding author upon reasonable request.

Ethics Statement

This retrospective study was performed in compliance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Biomedical Research Ethics Committee of Wenzhou Medical University (Approval No. BR/NGGI-2412031). Informed consent was waived because of the retrospective design and the use of de-identified data.

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Conflict of Interest

The authors report no commercial or financial relationships that could be perceived as potential conflicts of interest.

Consent for publication

Not Applicable.

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Figures

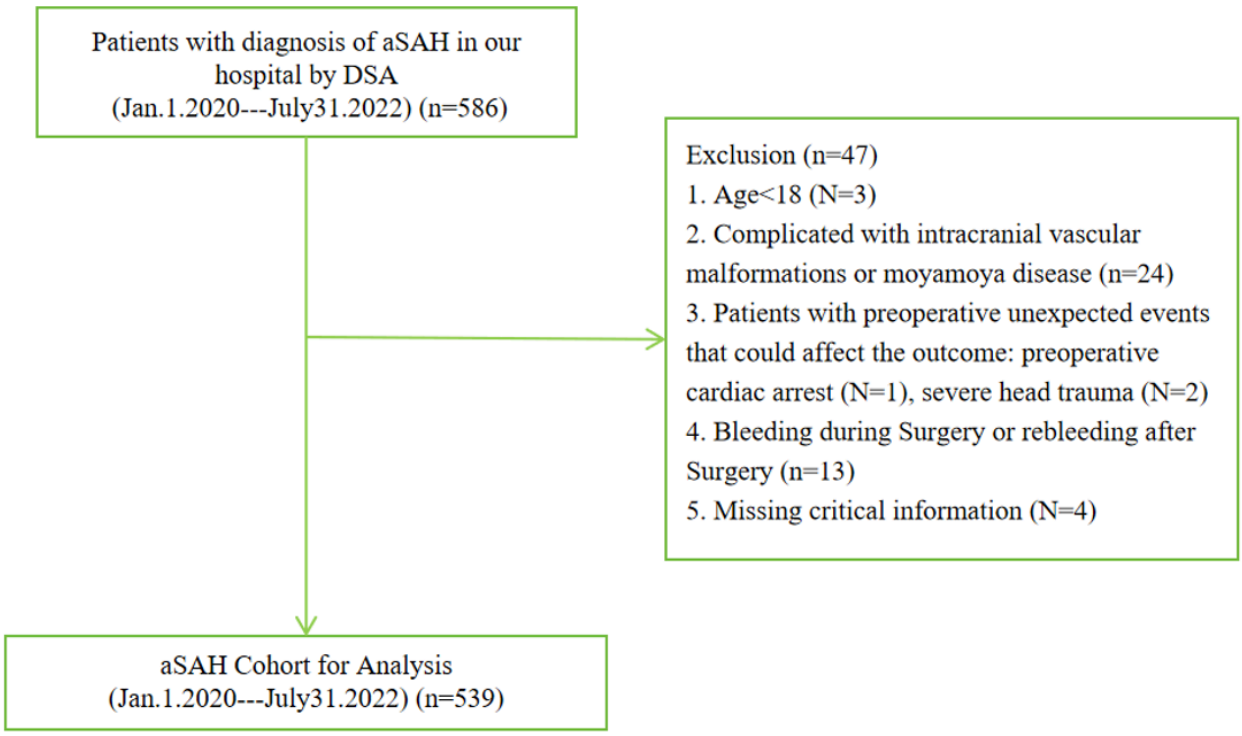


Figure 1 | Flowchart of Inclusion and exclusion

Figure 1

See image above for figure legend.

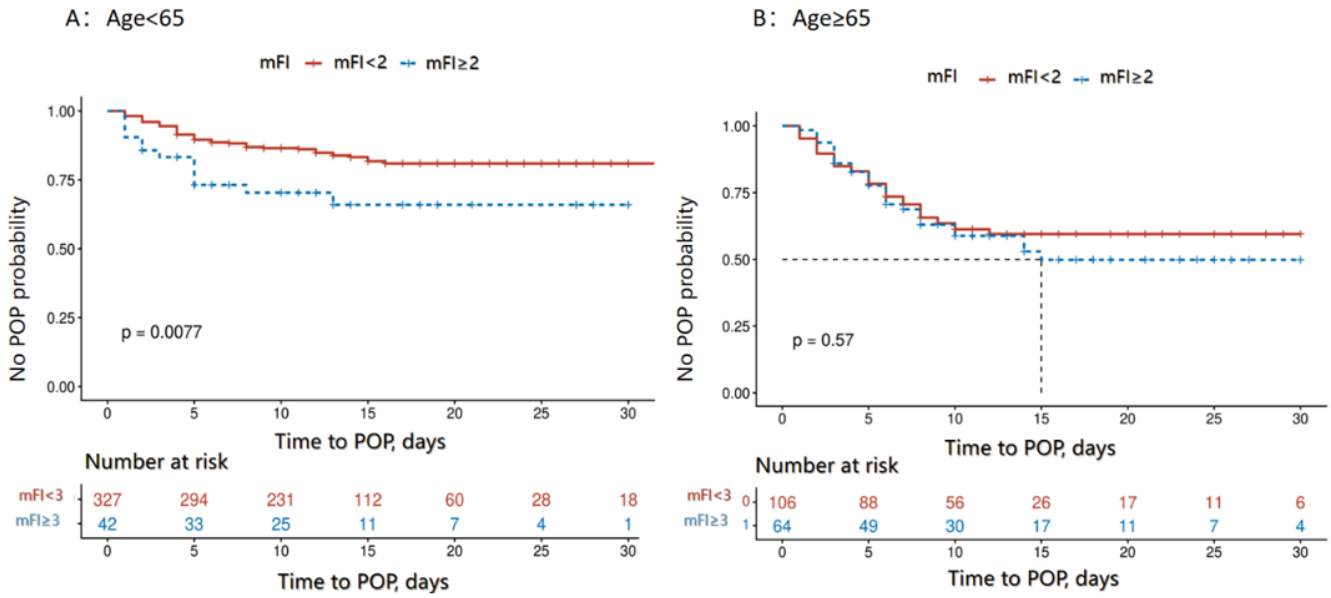


Figure 2

Age-stratified impact of frailty on postoperative pneumonia-free survival.