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Impact of laboratory-based frailty assessment on clinical outcomes following endovascular thrombectomy in elderly patients with acute ischemic stroke

[1]Hongli Liao, [2,3,4,5]Weiwei Gao, [2,3,4,5]Renjing Zhu, [2,3,4,5]Xingyu Chen

[1]Department of Internal Medicine, Guankou Town Central Health Center, Jimei District, Xiamen, Fujian, China; [2]The School of Clinical Medicine, Fujian Medical University, Fuzhou, Fujian, China; [3]Department of Neurology, Zhongshan Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; [4]Xiamen Clinical Research Center for Cerebrovascular Diseases, Xiamen, China; [5]Xiamen Quality Control Center for Stroke, Xiamen, China

Abstract

Objective: To investigate the prognostic value of frailty assessed by laboratory-based frailty index (FI-Lab) in elderly patients with acute ischemic stroke (AIS) undergoing endovascular thrombectomy (EVT). *Methods:* We conducted a single-center retrospective cohort study of elderly AIS patients who underwent EVT between January 2018 and April 2024. FI-Lab was constructed using a deficit accumulation model incorporating 44 laboratory parameters. Patients were categorized as robust (<0.20), pre-frail (0.20-0.35), or frail (≥0.35) based on established cutpoints. The primary endpoint was 90-day mortality; secondary endpoints included 90-day poor functional outcome and in-hospital mortality. We used multivariable logistic regression to examine associations between frailty and outcomes, restricted cubic spline analysis to assess dose-response relationships. *Results:* The study included 335 patients: 107 robust (31.9%), 170 pre-frail (50.7%), and 58 frail (17.3%). Ninety-day mortality increased with frailty severity: 12.1% (robust), 24.1% (pre-frail), and 34.5% (frail) (P=0.003). In fully adjusted models, pre-frail patients had 2.33-fold higher 90-day mortality risk compared with robust patients (95% CI: 1.07-5.37, P=0.038), while frail patients had 5.70-fold higher risk (95% CI: 2.22-15.46, P<0.001). Similarly, frail patients showed increased risks of poor functional outcome (adjusted odds ratio [OR]=4.05, 95% CI: 1.68-10.33, P=0.002) and in-hospital mortality (adjusted OR=6.34, 95% CI: 2.16-20.40, P=0.001). Each 0.1-unit increase in FI-Lab as a continuous variable was associated with 99%, 67%, and 105% higher risks of 90-day mortality, poor functional outcome, and in-hospital mortality, respectively (all P<0.05). Restricted cubic spline analysis confirmed significant linear dose-response relationships between FI-Lab and all adverse outcomes (all P-nonlinear >0.05). No significant interactions were observed across subgroups (all P for interaction >0.05).
Conclusion: Laboratory-based frailty assessment independently predicts adverse outcomes following EVT in elderly AIS patients. FI-Lab provides an objective, standardized tool for risk stratification and clinical decision-making in this population.

Keywords: Frailty, acute ischemic stroke, endovascular thrombectomy, laboratory assessment, prognosis

INTRODUCTION

Frailty is a geriatric syndrome characterized by declining physiological reserves across multiple systems and increased vulnerability to stressors.[1] Frail older adults face higher risks of adverse outcomes, including mortality, prolonged hospitalization, poor functional recovery, and increased healthcare utilization.[2] Stroke represents a particularly severe acute stressor that can overwhelm the diminished

Address correspondence to: Dr. Xingyu Chen, MD, The School of Clinical Medicine, Fujian Medical University, Fuzhou, Fujian, China. Email: Chenxingyu200504@126.com

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physiological reserves of frail individuals.[3] Recent meta-analyses show that frailty affects 23%-24.6% of patients with acute ischemic stroke (AIS).[4,5] Beyond its associations with stroke severity, mortality, and functional outcomes, frailty significantly influences recovery trajectories and increases rates of post-discharge institutionalization.[3-5] Although frailty assessment has proven valuable for stroke prognostication, current guidelines and clinical practice have not adequately incorporated frailty evaluation, creating an urgent need for standardized assessment protocols and frailty-based treatment strategies.[6,7]

Two primary theoretical frameworks underpin current frailty assessment tools: the phenotypic model and the deficit accumulation model.[8] The Fried frailty phenotype uses five criteria—weight loss, exhaustion, decreased grip strength, slow walking speed, and reduced physical activity—for categorical diagnosis. By contrast, the frailty index (FI) developed by Rockwood and Mitnitski quantifies frailty as a continuous variable by calculating the proportion of health deficits present in an individual. Unlike the binary classification of the phenotypic model, the FI captures gradations of frailty severity, enabling more nuanced clinical risk stratification.

The laboratory-based frailty index (FI-Lab) represents a novel approach constructed entirely from routine laboratory parameters.[9] This method offers several methodological advantages over traditional assessment tools: objective measurement unaffected by assessor bias, convenient implementation, high standardization, and suitability for multicenter research. Large cohort studies, including the Canadian Study of Health and Aging, have validated FI-Lab's ability to predict mortality in older populations, with subsequent research confirming its prognostic value for mortality, readmission, and healthcare resource utilization across diverse clinical settings.[9,10]

Endovascular thrombectomy (EVT) has become standard care for acute large vessel occlusion stroke, though treatment benefits vary considerably among patients. The severe neurological deficits and altered consciousness commonly seen in EVT candidates make traditional performance-based frailty assessments impractical in the acute setting. This population urgently needs objective, standardized frailty assessment tools to guide treatment decisions and prognostic discussions. However, FI-Lab has not been adequately validated in AIS patients undergoing EVT.

We therefore investigated associations between preoperative frailty status assessed by FI-Lab and 90-day mortality and functional outcomes in elderly AIS patients undergoing EVT. Our goal was to provide evidence for clinical decision-making, improve risk stratification, and establish a more precise method for evaluating baseline physiological reserves in elderly stroke patients.

METHODS

Study design and population

This single-center retrospective cohort study analyzed AIS patients aged ≥60 years who underwent EVT at a comprehensive stroke center between January 1, 2018, and April 30, 2024. Inclusion criteria were: (1) age ≥60 years; (2) AIS with large vessel occlusion confirmed by digital subtraction angiography, involving anterior circulation vessels (internal carotid artery, middle cerebral artery M1 or M2 segments) or posterior circulation vessels (vertebral artery V4 segment, basilar artery, posterior cerebral artery P1 segment). Exclusion criteria were: (1) baseline Alberta Stroke Program Early CT Score (ASPECTS) <6; (2) missing data for >30% of the 44 laboratory parameters required for FI-Lab construction; (3) loss to follow-up during the 90-day observation period. A total of 335 patients met inclusion criteria and formed the study cohort. Patient selection and exclusion processes are detailed in Figure 1. The institutional review board approved the study protocol and waived informed consent requirements given the retrospective design and complete anonymization of patient data. All procedures followed the Declaration of Helsinki and local regulations.

Flow diagram showing patient selection process for the study cohort. Of 520 patients with large vessel occlusion acute ischemic stroke (LVO-AIS) who underwent endovascular thrombectomy (EVT) between January 2018 and April 2024, 335 elderly patients (≥60 years) met inclusion criteria and formed the final study cohort. Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; EVT, endovascular thrombectomy; FI-Lab, laboratory-based frailty index; LVO-AIS, large vessel occlusion acute ischemic stroke.

Clinical data collection and assessment

Baseline characteristics included demographic

variables (age, sex), cerebrovascular risk factors (current smoking status, alcohol consumption, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, and history of stroke or transient ischemic attack), and clinical presentation parameters. Certified neurologists assessed admission National Institutes of Health Stroke Scale (NIHSS) scores. Stroke etiology was classified according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria as large-artery atherosclerosis, cardioembolism, or other subtypes (including other determined etiology, undetermined etiology, and multiple etiologies). Operators recorded procedural parameters in real time, including occlusion site, time metrics (onset-to-groin puncture time, onset-to-recanalization time), number of mechanical thrombectomy attempts, thrombectomy technique (stent retriever, direct aspiration, or combined approach), adjunctive interventions (balloon angioplasty or stent placement), and bridging intravenous thrombolysis status.

Laboratory parameters and frailty index construction

We collected laboratory parameters immediately upon admission and before EVT, totaling 44 parameters (Supplementary Table S1). FI-Lab was calculated using established methodology with binary scoring for each laboratory parameter[11-14]: values within normal reference ranges scored 0, while values outside normal ranges scored 1. The FI-Lab score was calculated as the ratio of abnormal laboratory parameters to total parameters assessed, ranging from 0 to 1. Based on cutpoints established in previous studies[15-17], patients were stratified into three groups: robust/non-frail (FI-Lab <0.20), pre-frail (FI-Lab 0.20-0.35), and frail (FI-Lab ≥0.35). FI-Lab values were standardized to 0.1-unit increments to enhance clinical interpretability.

Clinical outcome measures

The primary outcome was 90-day all-cause mortality. Secondary outcomes included 90-day poor functional outcome and in-hospital mortality. Good functional outcome was defined as mRS 0-2, and poor functional outcome as mRS 3-6. Follow-up data were collected and managed through the National Cerebrovascular Disease Database Platform. Certified personnel trained in mRS scoring conducted 90-day assessments via structured telephone interviews, with results recorded promptly in the system.

Statistical analysis

All analyses were performed using R software version 4.2.2. Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables are presented as mean ± standard deviation, non-normally distributed variables as median (Q1, Q3), and categorical variables as number (percentage). Group comparisons used appropriate statistical methods based on data type and distribution: one-way ANOVA for normally distributed continuous variables, Kruskal-Wallis test for non-normally distributed continuous variables, and χ^2 test or Fisher's exact test for categorical variables.

Before constructing multivariable logistic regression models, we assessed multicollinearity among candidate variables using Spearman correlation matrices, variance inflation factors (VIF), and tolerance values. Variables with $|r| > 0.7$, VIF ≥ 10, or tolerance ≤ 0.1 were excluded from analysis (Supplementary Figure 1; Supplementary Table S2). To examine FI-Lab associations with outcomes, we constructed three progressively adjusted multivariable logistic regression models: Model 1 (unadjusted); Model 2 (adjusted for demographics [age, sex] and cerebrovascular risk factors [current smoking, alcohol consumption, hypertension, diabetes, hyperlipidemia, atrial fibrillation, history of stroke or transient ischemic attack]); and Model 3 (fully adjusted, additionally including stroke severity [baseline NIHSS and ASPECT scores], stroke etiology, occlusion site, time parameters, EVT technical parameters [number of thrombectomy attempts, treatment strategy], adjunctive interventions [balloon angioplasty or stent placement], and bridging intravenous thrombolysis).

Restricted cubic spline (RCS) regression explored potential nonlinear dose-response relationships between FI-Lab and adverse outcomes, with 3-7 knots evaluated and optimal knot positions determined by Akaike information criterion (Supplementary Table S3). Subgroup analyses were performed by sex, age, and major cerebrovascular risk factors. Interactions between subgroups were assessed using multiplicative interaction terms in logistic regression models. All tests were two-sided, with $P<0.05$ considered statistically significant.

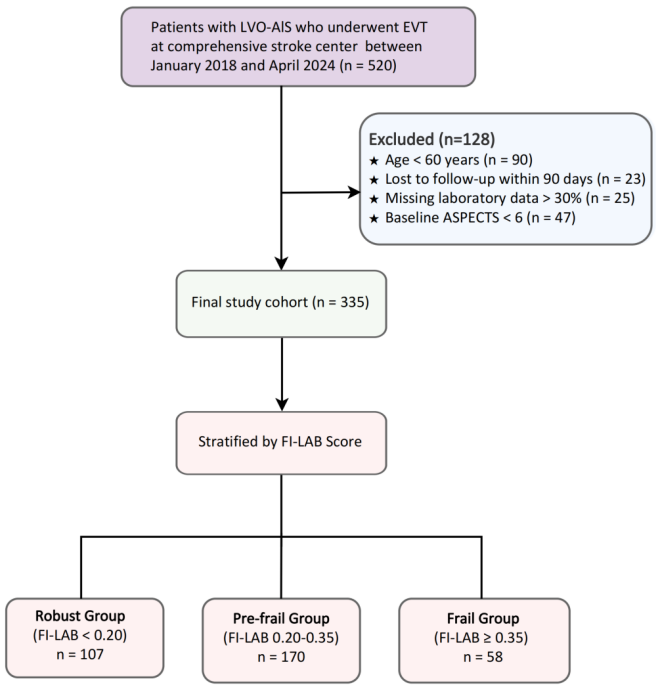

Figure 1. Patient flow chart and study population selection

RESULTS

Baseline characteristics

The study included 335 elderly AIS patients who underwent EVT, with a median age of 70 years and 67.2% male (Table 1). FI-Lab stratification identified 107 robust patients (31.9%), 170 pre-frail patients (50.7%), and 58 frail patients (17.3%). Demographic comparisons across frailty groups showed that frail patients had slightly higher median age and female representation than robust patients, though differences only approached statistical significance (p=0.071 and p=0.083, respectively). Among cerebrovascular risk factors, frail patients had significantly lower current smoking rates than robust patients (p=0.024). Additionally, frail patients had significantly lower baseline ASPECTS scores compared with robust patients (p=0.020).

Association between frailty status and 90-day mortality

Overall 90-day mortality was 22.1% (74 patients). Mortality rates increased significantly with frailty severity: 12.1% in robust, 24.1% in pre-frail, and 34.5% in frail patients (Figure 2A; p=0.003). Multivariable logistic regression confirmed the independent association between FI-Lab and 90-day mortality (Table 2). In the fully adjusted model (Model 3), frailty status maintained strong independent associations with 90-day mortality. Compared with robust patients, pre-frail patients had an adjusted odds ratio (OR) of 2.33 (95% CI: 1.07-5.37; p=0.038), while frail patients showed a 5.70-fold increased risk (95% CI: 2.22-15.46; p<0.001), demonstrating a clear dose-response relationship (p for trend <0.001). When analyzed as a continuous variable, each 0.1-unit increase in FI-Lab score was associated with a 99% increase in 90-day mortality risk (adjusted OR: 1.99; 95% CI: 1.43-2.82; p<0.001).

Association between frailty status and functional outcome

Functional outcome assessment revealed increasing median 90-day mRS scores across frailty groups (Figure 2D; p<0.001). Overall poor functional outcome occurred in 62.7% of patients: 50.5% in robust, 65.3% in pre-frail, and 77.6% in frail patients (Figure 2B; p=0.002). Multivariable analysis showed that frailty status independently predicted poor functional outcomes (Table 2). In the fully adjusted model, frail patients had a 4.05-fold increased risk of poor functional outcome compared with

Table 1: Baseline characteristics and clinical outcomes by laboratory-based frailty status in elderly patients with acute ischemic stroke undergoing endovascular thrombectomy

Characteristic	Overall (N = 335)	Robust (N = 107)	Pre-frail (N = 170)	Frail (N = 58)	P-value
Demographics					
Age, years	70 (63-78)	69 (62-76)	71 (64-79)	72 (64-81)	0.071
Male sex	225 (67.2)	77 (72.0)	116 (68.2)	32 (55.2)	0.083
Vascular Risk Factors					
Current smoker	120 (35.8)	48 (44.9)	58 (34.1)	14 (24.1)	0.024
Alcohol consumption	78 (23.3)	28 (26.2)	40 (23.5)	10 (17.2)	0.430
Hypertension	238 (71.0)	68 (63.6)	126 (74.1)	44 (75.9)	0.113
Diabetes mellitus	107 (31.9)	26 (24.3)	59 (34.7)	22 (37.9)	0.109
Hyperlipidemia	80 (23.9)	19 (17.8)	45 (26.5)	16 (27.6)	0.195
Atrial fibrillation	162 (48.4)	48 (44.9)	83 (48.8)	31 (53.4)	0.565
Previous stroke or TIA	52 (15.5)	15 (14.0)	29 (17.1)	8 (13.8)	0.732
Stroke Characteristics					
Baseline NIHSS score	15 (11-19)	14 (10-18)	15 (12-20)	16 (13-18)	0.065
Baseline ASPECT score	9 (8-10)	9 (8-10)	9 (8-10)	9 (8-10)	0.020
Stroke etiology					0.586
Large-artery atherosclerosis	167 (49.9)	54 (50.5)	86 (50.6)	27 (46.6)	
Cardioembolism	157 (46.9)	47 (43.9)	80 (47.1)	30 (51.7)	
Other subtypes	11 (3.3)	6 (5.6)	4 (2.4)	1 (1.7)	
Occlusion site					0.229
Internal carotid artery	46 (13.7)	15 (14.0)	22 (12.9)	9 (15.5)	
Middle cerebral artery M1	121 (36.1)	36 (33.6)	67 (39.4)	18 (31.0)	
Middle cerebral artery M2	44 (13.1)	15 (14.0)	15 (8.8)	14 (24.1)	
Tandem occlusion (ICA+MCA)	72 (21.5)	25 (23.4)	37 (21.8)	10 (17.2)	
Posterior Circulation	52 (15.5)	16 (15.0)	29 (17.1)	7 (12.1)	
Treatment Parameters					
Bridging IV thrombolysis	135 (40.3)	46 (43.0)	65 (38.2)	24 (41.4)	0.722
Onset to puncture time, min	360 (264-561)	360 (262-625)	369 (263-580)	350 (272-475)	0.712
Puncture to reperfusion, min	80 (50-119)	75 (40-120)	85 (57-120)	85 (53-100)	0.320
Number of thrombectomy attempts	2 (1-2)	2 (1-3)	2 (1-2)	2 (1-3)	0.621
Thrombectomy technique					0.576
Stent retriever	71 (21.2)	23 (21.5)	34 (20.0)	14 (24.1)	
Aspiration	26 (7.8)	5 (4.7)	17 (10.0)	4 (6.9)	
Combined approach	216 (64.5)	71 (66.4)	107 (62.9)	38 (65.5)	
Adjunctive interventions	84 (25.1)	30 (28.0)	46 (27.1)	8 (13.8)	0.091
Successful reperfusion[b]	246 (73.4)	80 (74.8)	122 (71.8)	44 (75.9)	0.773
Clinical outcomes, n (%)					
In-hospital mortality	52 (15.5)	8 (7.5)	29 (17.1)	15 (25.9)	0.006
90-day mortality	74 (22.1)	13 (12.1)	41 (24.1)	20 (34.5)	0.003
90-day mRS score	4 (2-5)	3 (1-5)	4 (2-5)	5 (3-6)	<0.001
Poor functional outcome[c]	210 (62.7)	54 (50.5)	111 (65.3)	45 (77.6)	0.002

Data are presented as median (interquartile range) for continuous variables and n (%) for categorical variables. Frailty status was determined using laboratory-based frailty index (FI-Lab): robust (FI-Lab <0.20), pre-frail (FI-Lab 0.20-0.35), and frail (FI-Lab ≥0.35). P-values were calculated using Kruskal-Wallis test for continuous variables and χ^2 test or Fisher's exact test for categorical variables. [a]Adjunctive interventions include balloon angioplasty or stent placement. [b]Successful reperfusion defined as modified Thrombolysis in Cerebral Infarction (mTICI) grade 2b-3. [c]Poor functional outcome defined as modified Rankin Scale (mRS) score 3-6 at 90 days. Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; FI-Lab, laboratory-based frailty index; ICA, internal carotid artery; IV, intravenous; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

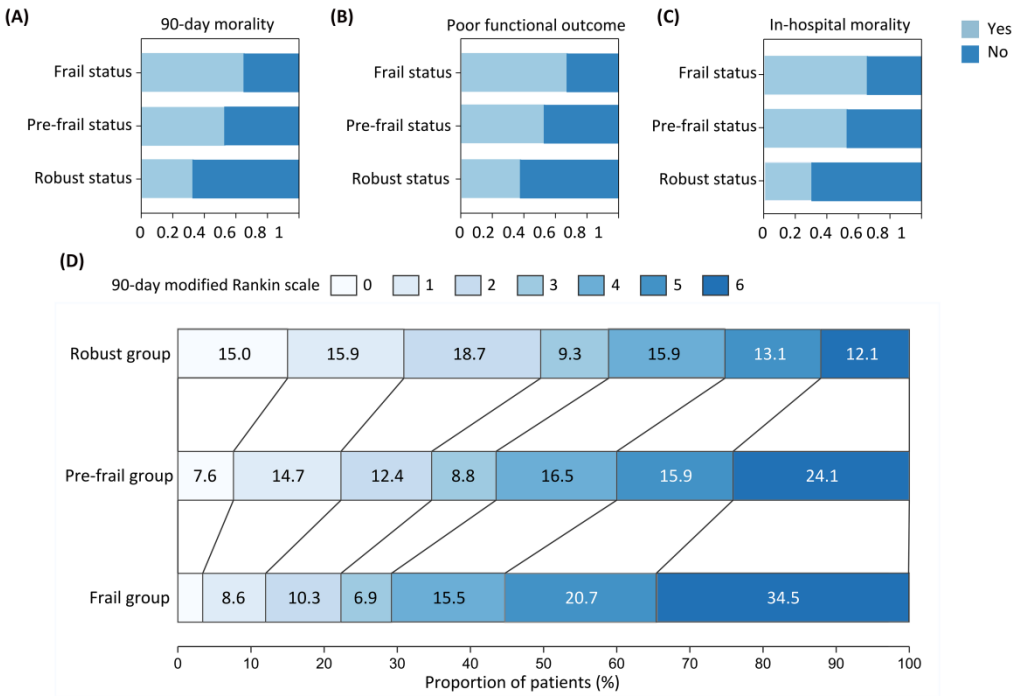

Figure 2. Clinical outcomes according to laboratory-based frailty status

robust patients (95% CI: 1.68-10.33; p=0.002), maintaining a significant dose-response relationship (p for trend =0.003). Continuous FI-Lab analysis showed that each 0.1-unit increase was associated with a 67% higher risk of poor functional outcome (adjusted OR: 1.67; 95% CI: 1.24-2.29; p=0.001).

Association between frailty status and in-hospital mortality

In-hospital mortality occurred in 52 patients (15.5%) and showed similar frailty-dependent patterns (Figure 2C): 7.5% in robust, 17.1% in pre-frail, and 25.9% in frail patients (p=0.006). After comprehensive adjustment for confounders, frail patients had a 6.34-fold higher risk of in-hospital mortality compared with robust patients (95% CI: 2.16-20.40; p=0.001), demonstrating a clear dose-response relationship (p for trend =0.001). Continuous FI-Lab analysis showed that each 0.1-unit increase was associated with a 105% higher risk of in-hospital mortality (adjusted OR: 2.05; 95% CI: 1.42-3.05; p=0.001).

Clinical outcomes stratified by frailty status in elderly patients with acute ischemic stroke undergoing endovascular thrombectomy. (A-C) Proportion of patients experiencing adverse outcomes across frailty groups: (A) 90-day mortality, (B) poor functional outcome at 90 days, and (C) in-hospital mortality. Light blue indicates presence of outcome; dark blue indicates absence of outcome. (D) Distribution of 90-day modified Rankin Scale (mRS) scores across frailty groups shown as stacked horizontal bar chart. Numbers within bars represent percentages of patients in each mRS category.

Restricted cubic spline analysis

To explore association patterns between FI-Lab and clinical outcomes, we performed RCS analysis to assess potential nonlinear relationships (Figure 3). Results consistently showed significant linear associations between FI-Lab and all three primary outcomes (90-day mortality, poor functional outcome, and in-hospital mortality). For 90-day mortality, overall association tests yielded p-values of <0.001, 0.002, and <0.001 in unadjusted, partially adjusted, and fully adjusted models, respectively, while nonlinearity tests showed p-values of 0.187, 0.273, and 0.523, none reaching statistical significance. Similarly, nonlinearity tests for 90-day poor functional outcome and in-hospital mortality all yielded p-values >0.05, indicating that FI-Lab demonstrated primarily linear dose-response relationships with adverse outcomes.

Table 2: Multivariable logistic regression analysis of laboratory-based frailty index and clinical outcomes following endovascular thrombectomy

Categories	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
90-day mortality						
FI-LAB [d]	1.64 (1.26-2.14)	<0.001	1.65 (1.25-2.19)	<0.001	1.99 (1.43-2.82)	<0.001
Frailty Status						
Robust	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Pre-frail	2.30 (1.19-4.68)	0.016	2.16 (1.09-4.47)	0.031	2.33 (1.07-5.37)	0.038
Frail	3.81 (1.74-8.59)	<0.001	3.48 (1.54-8.10)	0.003	5.7 (2.22-15.46)	<0.001
P for trend		<0.001		0.003		<0.001
Poor functional outcome						
FI-LAB [d]	1.62 (1.27-2.08)	<0.001	1.56 (1.21-2.03)	<0.001	1.67 (1.24-2.29)	0.001
Frailty Status						
Robust	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Pre-frail	1.85 (1.13-3.03)	0.015	1.66 (0.98-2.79)	0.057	1.54 (0.83-2.86)	0.172
Frail	3.40 (1.68-7.22)	<0.001	3.00 (1.43-6.59)	0.005	4.05 (1.68-10.33)	0.002
P for trend		<0.001		0.003		0.003
In-hospital mortality						
FI-LAB [d]	1.7 (1.27-2.29)	<0.001	1.7 (1.24-2.35)	0.001	2.05 (1.42-3.05)	<0.001
Frailty Status						
Robust	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Pre-frail	2.55 (1.17-6.18)	0.026	2.31 (1.03-5.72)	0.052	2.57 (1.03-7.10)	0.053
Frail	4.32 (1.74-11.44)	0.002	3.89 (1.51-10.66)	0.006	6.34 (2.16-20.40)	0.001
P for trend		0.002		0.005		0.001

Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Model 1: unadjusted associations. Model 2: adjusted for demographics (age, sex) and vascular risk factors (current smoking, alcohol consumption, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, previous stroke/TIA). Model 3: fully adjusted model including all Model 2 variables plus stroke severity (NIHSS and ASPECTS scores), stroke etiology, temporal parameters (onset-to-puncture and puncture-to-reperfusion times), procedural factors (number of thrombectomy attempts, treatment strategy, occlusion site), adjunctive interventions, and bridging intravenous thrombolysis. [d]FI-Lab analyzed as continuous variable per 0.1-unit increase. P for trend calculated using frailty status as ordinal variable.

Restricted cubic spline curves demonstrating linear associations between laboratory-based frailty index (FI-Lab) and clinical outcomes. (A-C) 90-day mortality, (D-F) poor functional outcome, and (G-I) in-hospital mortality across three models: Model 1 (unadjusted), Model 2 (adjusted for demographics and vascular risk factors), and Model 3 (fully adjusted). Histograms show FI-Lab distribution in the study population. Red lines represent spline curves with 95% confidence intervals (shaded areas). All relationships demonstrated significant linear associations (P-overall <0.05) without evidence of nonlinearity (P-nonlinear >0.05), supporting FI-Lab use as a continuous risk predictor.

Subgroup analysis

Forest plot analysis revealed significant predictive effects of FI-Lab for all three primary clinical outcomes, with good consistency across subgroups (Figure 4; Supplementary Figure 2; Supplementary Figure 3). Age-stratified analysis showed stronger predictive effects of FI-Lab for all three adverse outcomes in patients ≥70 years compared with those <70 years, though no significant interactions were observed between age groups and FI-Lab (p=0.332, 0.315, and 0.825, respectively). Sex-based subgroup analysis revealed stronger associations between FI-Lab and clinical outcomes in male patients, but interaction tests were not statistically significant

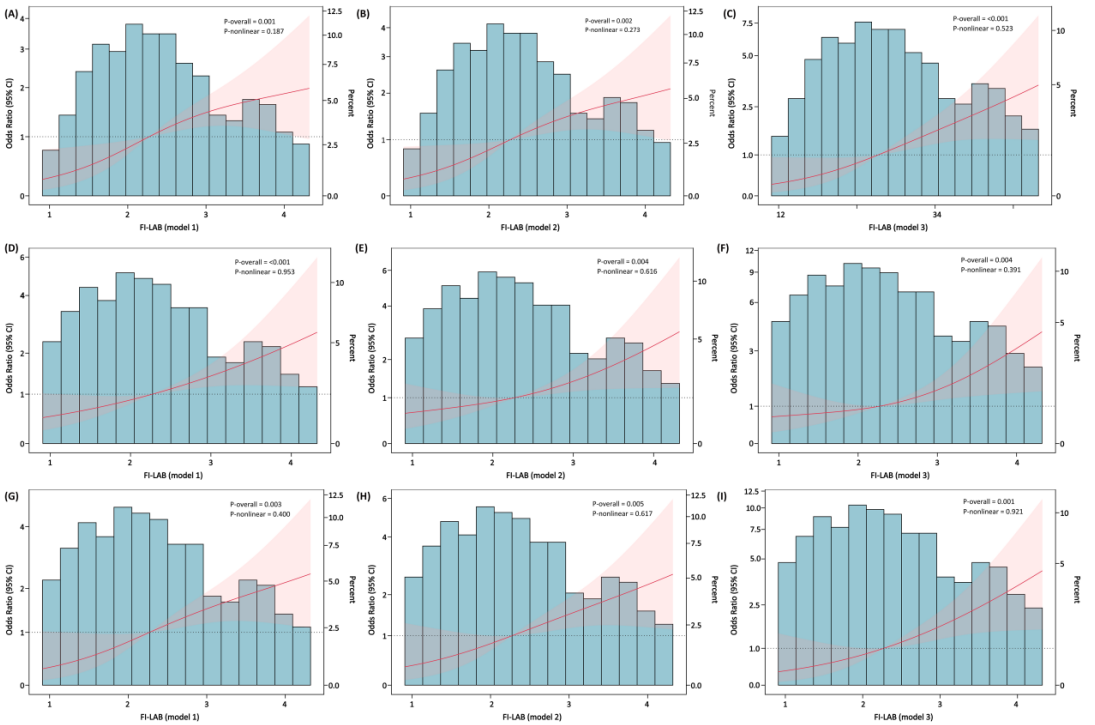

Figure 3. Dose-response relationships between laboratory-based frailty index and clinical outcomes using restricted cubic spline analysis

(p=0.746, 0.618, and 0.760, respectively). Among other covariate subgroups, FI-Lab showed relatively stronger predictive effects for adverse outcomes in non-smokers, non-drinkers, patients with hypertension, and those without hyperlipidemia, though no significant interactions were observed in any subgroup (all interaction p-values >0.05).

Results from adjusted multivariable logistic regression models including stroke severity (NIHSS and ASPECTS scores), stroke etiology, temporal parameters (onset-to-puncture and puncture-to-reperfusion times), procedural factors (number of thrombectomy attempts, treatment strategy, occlusion site), adjunctive interventions, and bridging intravenous thrombolysis. *Adjusted OR represents effect per 0.1-unit increase in FI-Lab score.

DISCUSSION

This study demonstrates that FI-Lab independently predicts adverse clinical outcomes following EVT in elderly AIS patients. Frail patients experienced 5.70-fold, 4.05-fold, and 6.34-fold higher risks of 90-day mortality, poor functional outcome, and in-hospital mortality, respectively, compared with robust patients. RCS analysis confirmed significant linear associations between FI-Lab and adverse outcomes, supporting its validity as a continuous risk assessment tool. These predictive effects remained consistent across subgroups defined by age, sex, and cerebrovascular risk factors, with no significant interactions observed. Our findings establish the clinical value of laboratory-based frailty assessment for prognostication in AIS patients undergoing EVT.

Consensus on frailty assessment tools for AIS patients remains elusive. Previous studies have examined various frailty measures in EVT populations with encouraging results. Clinical Frailty Scale (CFS) research has shown independent associations with mortality, with Evans et al. demonstrating 3% increased death risk per point increase in CFS scores at 28 days[18], while Tan et al. confirmed CFS as a significant predictor of 3-month poor functional outcome (adjusted OR=1.54).[19] Traditional frailty index studies have yielded similar findings, with Joyce *et al*. using 33-item deficit accumulation to show strong associations with

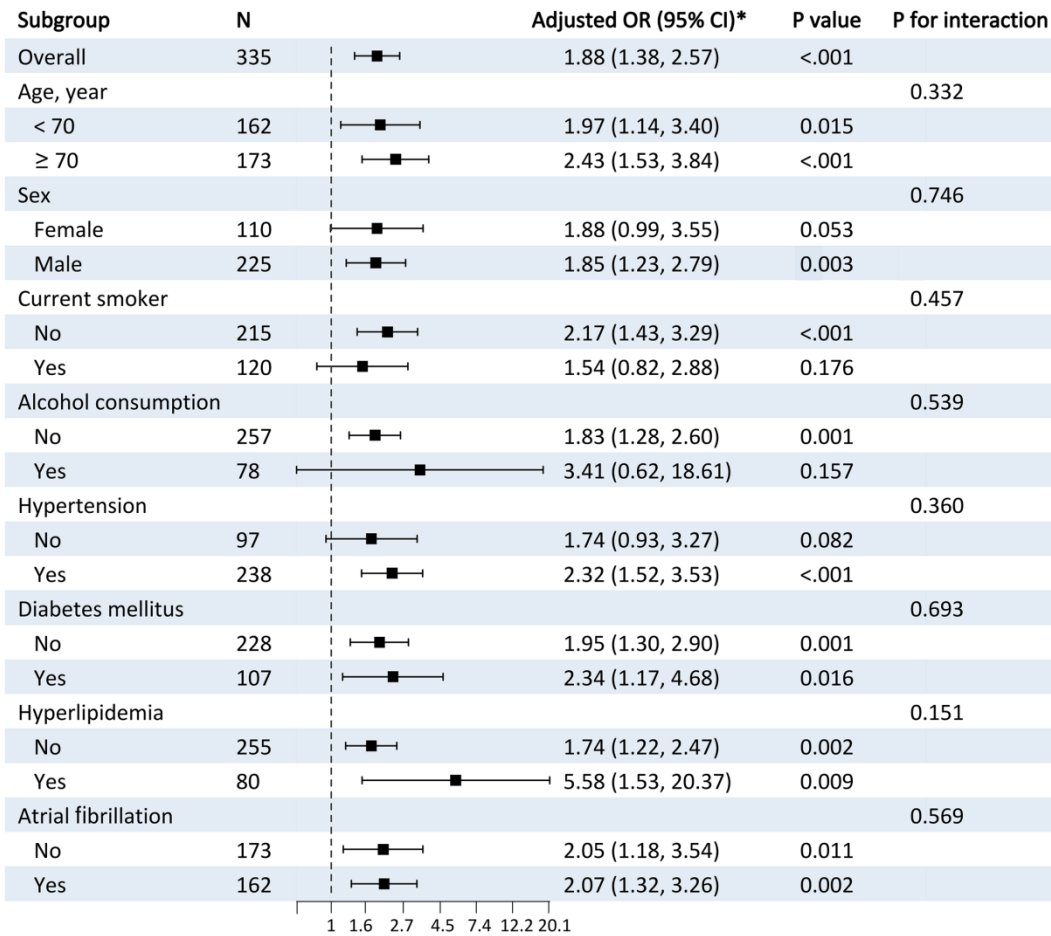

Figure 4. Subgroup analysis of laboratory-based frailty index association with 90-Day mortality

functional dependence (adjusted OR=3.04) and mortality (adjusted OR=3.12) in mechanical thrombectomy patients.[20] Huang *et al.* further validated these associations using a modified 5-item frailty index, demonstrating significantly reduced likelihood of functional independence (adjusted OR=0.37).[21] Hospital frailty risk scores have also shown promise, with high-risk AIS patients experiencing 52% lower probability of good 3-month outcomes after EVT.[22] Our study represents the first validation of FI-Lab in EVT-treated AIS patients. Unlike existing tools, FI-Lab relies entirely on objective laboratory parameters, eliminating assessor bias and proving particularly valuable for patients with acute consciousness impairment or cognitive dysfunction. This work provides novel evidence supporting laboratory-based frailty assessment in EVT populations and establishes FI-Lab's clinical applicability in this setting.

Several biological mechanisms may explain the associations between FI-Lab and adverse outcomes following EVT in large vessel occlusion AIS. Frailty fundamentally reflects accumulating functional deficits at subcellular, tissue, and organ levels, with underlying structural and functional damage ultimately leading to irreversible physiological decline.[23-25] Molecular evidence increasingly demonstrates that multiple blood biomarkers participate in frailty pathophysiology across hematologic, renal, metabolic, lipid, hepatic, and coagulation systems.[26] These findings provide theoretical support for FI-Lab construction, suggesting that laboratory abnormalities represent subclinical frailty states associated with microscopic pathological defects. Individual abnormal blood parameters have already demonstrated prognostic value in AIS, including white blood cell count, neutrophil count, lymphocyte count,

albumin levels, serum uric acid, creatinine, glucose, and electrolytes.[27-30] Our 44-parameter FI-Lab therefore captures functional status across multiple organ systems more comprehensively than single biomarkers, providing more accurate and stable physiological reserve assessment.

These findings have important clinical and translational implications. Our study provides the first real-world validation of FI-Lab's predictive performance and clinical applicability in large vessel occlusion AIS patients following EVT, offering a novel risk stratification tool for precision stroke medicine. FI-Lab can be integrated into existing electronic health record and clinical decision support systems for automated frailty assessment. The modifiable nature of frailty amplifies the clinical significance of our findings. Previous research has demonstrated that multimodal interventions—including structured exercise training, individualized nutritional support, cognitive training, and comprehensive geriatric management—can significantly improve frailty status.[31-33] Implementing targeted rehabilitation for high-risk frail patients and developing individualized, goal-directed multidimensional interventions for frail stroke survivors may effectively mitigate frailty's adverse impact on stroke outcomes and enhance overall EVT treatment benefits.[34]

Several limitations warrant consideration. First, as a single-center retrospective cohort study, our findings may be subject to selection and information bias. Notably, our cohort included only 335 elderly patients over a 6-year period, with merely 17.3% classified as frail. This relatively low proportion likely reflects treatment selection bias inherent in current clinical practice: physicians may be less inclined to offer EVT to patients perceived as frail due to concerns about procedural tolerance and anticipated poor prognosis, thereby systematically excluding the most vulnerable patients from thrombectomy consideration. Consequently, the frail patients in our cohort may represent a relatively "selected" subgroup with better baseline physiological reserves than the broader frail elderly stroke population, potentially underestimating the true magnitude of frailty's adverse impact on post-EVT outcomes. Second, although we used objective FI-Lab assessment, we lack direct comparisons with other validated frailty tools, limiting our ability to accurately assess FI-Lab's relative advantages and clinical value. Future research should address these limitations through several approaches. Large-scale multicenter prospective studies incorporating multiple frailty assessment tools are needed to establish more accurate, universally applicable frailty standards and clinical implementation guidelines. Simplified FI-Lab versions and automated calculation systems should be developed to enhance clinical feasibility. Intervention studies based on frailty stratification are required to validate whether individualized treatment strategies improve EVT outcomes. Such research will deepen understanding of frailty's role in stroke prognosis and provide stronger evidence for optimizing EVT treatment.

In conclusion, this study confirms that FI-Lab independently predicts adverse clinical outcomes in elderly AIS patients undergoing EVT. As an objective, standardized risk stratification tool, FI-Lab offers unique advantages through convenient assessment without subjective bias, making it particularly suitable for frailty evaluation in acute-phase patients with neurological impairment. Large-scale multicenter studies are needed to further validate FI-Lab's external validity and explore frailty-based individualized treatment strategies to ultimately improve clinical outcomes in elderly stroke patients.

DISCLOSURE

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Conflicts of interest: None

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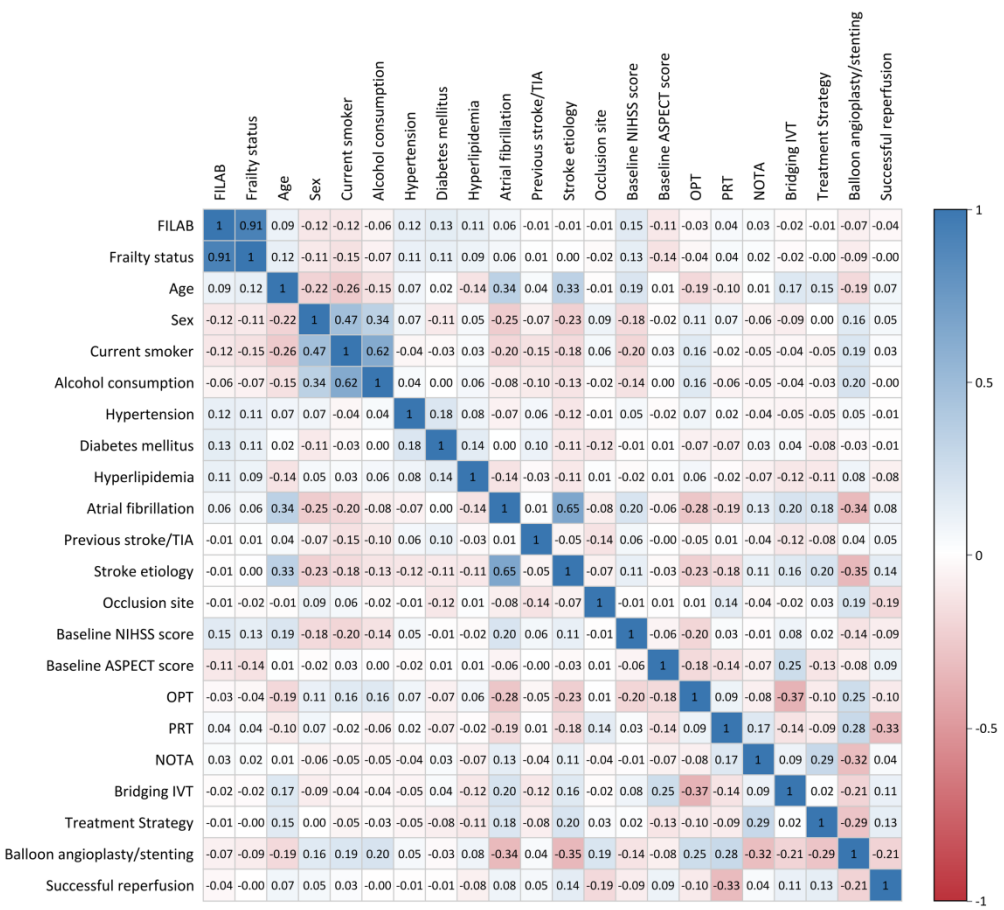
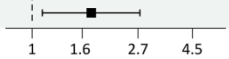


Supplementary Figure 1. Correlation Matrix of Study Variables

Spearman correlation coefficient matrix showing relationships between laboratory-based frailty index (FI-Lab), frailty status, and key clinical variables. Color intensity represents correlation strength: blue indicates positive correlations, red indicates negative correlations. Correlation analysis informed variable selection for multivariable modeling and multicollinearity assessment.

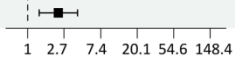
Subgroup	N	Adjusted OR (95% CI)*	P value	P for interaction
Overall	335	1.68 (1.26, 2.23)	<0.001	
Age, years				0.315
< 70	162	1.52 (1.05, 2.19)	0.027	
≥ 70	173	2.29 (1.31, 3.99)	0.004	
Sex				0.618
Female	110	1.47 (0.86, 2.53)	0.163	
Male	225	1.82 (1.24, 2.67)	0.002	
Current smoker				0.515
No	215	1.72 (1.16, 2.56)	0.007	
Yes	120	1.41 (0.84, 2.36)	0.196	
Alcohol consumption				0.978
No	257	1.67 (1.20, 2.32)	0.002	
Yes	78	2.15 (0.87, 5.31)	0.097	
Hypertension				0.302
No	97	1.36 (0.78, 2.39)	0.282	
Yes	238	1.82 (1.26, 2.64)	0.002	
Diabetes mellitus				0.375
No	228	1.60 (1.14, 2.25)	0.007	
Yes	107	2.80 (1.28, 6.15)	0.01	
Hyperlipidemia				0.859
No	255	1.82 (1.29, 2.56)	0.001	
Yes	80	2.07 (0.94, 4.56)	0.070	
Atrial fibrillation				0.833
No	173	1.66 (1.11, 2.49)	0.014	
Yes	162	1.74 (1.10, 2.75)	0.017	



Supplementary Figure 2. Subgroup Analysis of Laboratory-Based Frailty Index Association with Poor Functional Outcome

Results from adjusted multivariable logistic regression models including stroke severity (NIHSS and ASPECTS scores), stroke etiology, temporal parameters (onset-to-puncture and puncture-to-reperfusion times), procedural factors (number of thrombectomy attempts, treatment strategy, occlusion site), adjunctive interventions, and bridging intravenous thrombolysis. *Adjusted OR represents effect per 0.1-unit increase in FI-Lab score.

Subgroup	N	Adjusted OR (95% CI)*	P value	P for interaction
Overall	335	1.98 (1.39, 2.82)	<0.001	
Age, years				0.825
< 70	162	2.35 (1.19, 4.62)	0.013	
≥ 70	173	2.28 (1.40, 3.72)	0.001	
Sex				0.760
Female	110	2.74 (1.01, 7.47)	0.048	
Male	225	1.99 (1.27, 3.11)	0.002	
Current smoker				0.300
No	215	2.39 (1.50, 3.82)	<0.001	
Yes	120	1.68 (0.78, 3.65)	0.188	
Alcohol consumption				0.715
No	257	1.92 (1.29, 2.86)	0.001	
Yes	78	6.19 (0.55, 69.39)	0.14	
Hypertension				0.506
No	97	2.01 (0.83, 4.89)	0.122	
Yes	238	2.25 (1.46, 3.49)	<0.001	
Diabetes mellitus				0.525
No	228	1.97 (1.22, 3.20)	0.006	
Yes	107	2.86 (1.32, 6.17)	0.008	
Hyperlipidemia				0.081
No	255	1.63 (1.10, 2.42)	0.015	
Yes	80	14.13 (0.87, 228.67)	0.062	
Atrial fibrillation				0.736
No	173	2.18 (1.10, 4.34)	0.026	
Yes	162	2.32 (1.37, 3.92)	0.002	



Supplementary Figure 3. Subgroup Analysis of Laboratory-Based Frailty Index Association with In-Hospital Mortality

Results from adjusted multivariable logistic regression models including stroke severity (NIHSS and ASPECT scores), stroke etiology, temporal parameters (onset-to-puncture and puncture-to-reperfusion times), procedural factors (number of thrombectomy attempts, treatment strategy, occlusion site), adjunctive interventions, and bridging intravenous thrombolysis. *Adjusted OR represents effect per 0.1-unit increase in FI-Lab score.