International Journal of Nursing Studies 154 (2024) 104735

Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/locate/ns

The impact of frailty on short-term prognosis in discharged adult stroke patients: A multicenter prospective cohort study

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ARTICLE INFO

Article history:
Received 15 August 2023
Received in revised form 2 January 2024
Accepted 24 February 2024

Keywords:
Adverse event
Cognitive impairment
Disability
Frailty
Prognosis
Readmission
Follow-up studies
Stroke patients

ABSTRACT

Background: Frailty is commonly observed in stroke patients and it is associated with adverse outcomes. However, there remains a gap in longitudinal studies investigating the causal relationship between baseline frailty and short-term prognosis in discharged adult stroke patients.
Objective: To examine the causal impact of frailty on non-elective readmission and major adverse cardiac and cerebral events, and investigate its associations with cognitive impairment and post-stroke disability.
Design: A multicenter prospective cohort study.
Setting: Two tertiary hospitals in Central and Northwest China.
Participants: 667 adult stroke patients in stroke units were included from January 2022 to June 2022.
Methods: Baseline frailty was assessed by the Frailty Scale. Custom-designed questions were utilized to assess non-elective readmission and major adverse cardiac and cerebral events as primary outcomes. Cognitive impairment, assessed using the Mini-Mental State Examination Scale (MMSE), and post-stroke disability, measured with the Modified Rankin Scale (mRS), were considered secondary outcomes at a 3-month follow-up. The impact of baseline frailty on non-elective readmission and major adverse cardiac and cerebral events was examined using bivariate and multiple Cox regression analyses. Furthermore, associations between baseline frailty and cognitive impairment, or post-stroke disability, were investigated through generalized linear models.
Results: A total of 5 participants died, 12 had major adverse cardiac and cerebral events, and 57 had non-selective readmission among 667 adult stroke patients. Frailty was an independent risk factor for non-selective readmission (hazard ratio [HR]: 2.71, 95 % confidence interval [CI]: 1.59, 4.62) and major adverse cardiac and cerebral events (HR: 3.77, 95 % CI: 1.07, 13.22) for stroke patients. Baseline frailty was correlated with cognitive impairment (regression coefficient [β]: −2.68, 95 % CI: −3.78, −1.58) adjusting for socio-demographic and clinical factors and follow-up interval. However, the relationship between frailty and cognitive impairment did not reach statistical significance when further adjusting for baseline MMSE (β: −0.39, 95 % CI: −1.43, 0.64). Moreover, baseline frailty was associated with post-stroke disability (β: 0.36, 95 % CI: 0.08, 0.65) adjusting for socio-demographic and clinical variables, follow-up interval, and baseline mRS.
Conclusions: The finding highlights the importance of assessing baseline frailty in discharged adult stroke patients, as it is significantly associated with non-elective readmission, major adverse cardiac and cerebral events, and post-stroke disability at 3 months. These results highlight the crucial role of screening and evaluating frailty status in improving short-term prognosis for adult stroke patients. Interventions should be developed to address baseline frailty and mitigate the short-term prognosis of stroke.
Tweetable abstract: Baseline frailty predicts non-elective readmission, major adverse cardiac and cerebral events, and post-stroke disability in adult stroke patients. @haiyanhexyyy

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https://doi.org/10.1016/j.ijnurstu.2024.104735
0020-7489/

What is already known

- Frailty is commonly observed in stroke patients, and pre-existing frailty is associated with adverse outcomes, including non-elective readmission, major adverse cardiac and cerebral events, cognitive impairment, and disability.
- Insufficient attention has been given to exploring the causal impact of frailty on the short-term prognosis of discharged adult stroke patients.
- More evidence from comprehensive clinical studies, covering a wider age range, especially younger individuals, is required to address this knowledge gap.

What this paper adds

- This is the first prospective multicenter cohort study to investigate the relationship between frailty and short-term prognosis among discharged adult stroke patients including non-elective readmission, major adverse cardiac and cerebral events, cognitive impairment, and post-stroke disability.
- Frailty status independently predicted non-elective readmission and major adverse cardiac and cerebral events at a 3-month follow-up in adult stroke patients discharged from hospitals.
- Baseline frailty was significantly linked to post-stroke disability at a 3-month follow-up among discharged adult stroke patients, while the correlation with cognitive impairment lost statistical significance after adjusting for baseline cognitive function.

1. Introduction

Stroke remains a leading cause of mortality and disability, imposing substantial economic costs on health and social care worldwide (Thayabaranathan et al., 2022; Collaborators, 2021). Age-specific stroke prevalence and incidence rates have seen substantial growth among individuals under 70 years old (Collaborators, 2021). Notably, 16 % of strokes occur in ages 15–49, with over 62 % in those under 70 (Feigin et al., 2022). From 2008 to 2019, hospitalization rates for ischemic stroke surged among adults aged 25–64 from 76.3 to 108.1 per 100,000, a significant absolute change of 31.7 (Henry et al., 2023). The 30-day readmission rates ranged from 1.4 % to 27.6 % (Deng et al., 2021), and the 1-year stroke recurrence rates varied from 5.7 % to 51.3 % for ischemic stroke patients (Kolmos et al., 2021). Following discharge, younger and older adult patients hospitalized for stroke also often face challenges including cognitive impairment (Mahadevan et al., 2021) and functional disabilities (Collaborators, 2021).

Frailty is characterized by a decline in physiological reserve and increased vulnerability to adverse health outcomes (Veronese et al., 2021). It is associated with aging but remains independent of age (Spiers et al., 2021). Frailty was prevalent in 27 % of younger patients admitted to acute care, and it was associated with extended hospital stays (Gordon et al., 2023). Frailty was also prevalent in 22 % to 35 % of stroke patients, affecting approximately one-fourth of adult stroke patients (Palmer et al., 2019; Burton et al., 2022; Bao et al., 2023). Frailty has been linked to increased mortality and a higher likelihood of adverse health outcomes, such as 30-day readmissions and extended hospitalization (Sapp et al., 2023). It is emerging as an important clinical risk factor for stroke (Evans et al., 2022). Burton et al. (2022) highlighted frailty was associated with adverse outcomes in acute stroke, including prolonged mortality, length of stays in hospital, and disability. In a separate systematic review, Bao et al. (2023) confirmed that frailty was a significant predictor of poor functional outcomes and mortality in acute ischemic stroke patients undergoing endovascular treatment. Furthermore, frailty was associated with a higher risk of readmission within 90 days among stroke patients aged over 18 years (Kilkenny et al., 2021) and major adverse cardiac and cerebral events in middle-aged and older adults undergoing non-cardiac surgery (Siddiqui et al., 2023). Moreover, frailty was associated with poorer cognitive function in adults aged over 55 years (Vahedi et al., 2022) and 1-year severe disability among elderly patients with acute cerebral infarction (Yang et al., 2022).

Frailty is consistently associated with adverse outcomes in stroke patients. However, the relationship between frailty and short-term prognosis in younger adults following discharge from the hospital remains largely unknown. While retrospective research has associated frailty derived from administrative data with 90-day readmissions after stroke/transient ischemic attack, there is a critical requirement for prospective longitudinal research (Kilkenny et al., 2021). High-quality, cohort studies are also lacking to examine the link between baseline frailty and major adverse cardiac and cerebral events among discharged adult stroke patients (J. Wang et al., 2021; Siddiqui et al., 2023; Damluji et al., 2021). Moreover, the majority of cross-sectional studies failed to establish the causal relationship between baseline frailty and cognitive impairment at 90 days post-discharge in younger stroke adults (Vahedi et al., 2022). Although previous findings demonstrated a strong correlation between frailty and 90-day post-stroke disability among elderly patients (Yang et al., 2022; Pilotto et al., 2022), limited evidence focused on younger and middle-aged adults. Additionally, current research primarily focuses on the relationship between frailty and health outcomes in individuals aged 65 and above, highlighting the need for more comprehensive studies to generate evidence across diverse age groups, particularly in younger adults (Sapp et al., 2023).

This study examined the impact of baseline frailty on non-elective readmission and major adverse cardiac and cerebral events, hypothesizing that higher baseline frailty was positively correlated with these adverse outcomes within 90-day discharge among adult stroke patients. Additionally, the study explored the association between baseline frailty and cognitive impairment as well as post-stroke disability in discharged stroke patients, offering supplementary insights into short-term prognosis.

2. Methods

2.1. Design, setting, and participants

We established a multicenter prospective cohort study recruiting participants from stroke units in two tertiary hospitals. Due to follow-up limitations in prior research, we adopted a cohort study design to longitudinally investigate the causal relationship between frailty and the short-term prognosis of discharged adult stroke patients within 90 days.

The two tertiary hospitals were selected because they were remote assisted, representing a national high level of teaching hospitals in Central China and Northwest China. One hospital has 3500 beds and serves about 3.4 million patients annually in Changsha City. Another hospital owned 1200 beds serving 2 million patients annually in Urumqi City.

Participants comprised adults aged over 18 years, admitted to the stroke units of two tertiary hospitals for the first time, and diagnosed with stroke by neurology specialists. Hospitalizations for ischemic stroke, intracerebral hemorrhage stroke, and subarachnoid hemorrhage stroke were identified using the International Classification of Diseases, 10th Revision (Wang et al., 2022).

Exclusion criteria encompassed individuals in the terminal stage of hospice care with a life expectancy of fewer than 6 months (Roth and Canedo, 2019). Those unable to conduct questionnaire surveys and follow-ups due to aphasia assessed by physicians were excluded (RELEASE Collaborators, 2021). Participants without baseline data of frailty, cognitive function, or disability were also excluded.

According to the previous study, the prevalence of non-frailty and frailty among stroke patients at the 3-month follow-up was 78 % and 22 %, respectively (Kilkenny et al., 2021). Assuming a sampling ratio of

3.5 and a non-inferiority margin of 0.44, we calculated that 596 samples were needed with 90 % power and 5 % significance (Chow et al., 2017). Considering 10 % to 15 % of the loss to follow-ups, 665 samples were required in this study.

2.2. Data collection

The cohort study enrolled adult patients diagnosed with stroke by physicians from January 2022 to June 2022. All hospitalized stroke patients were recruited and evaluated by specialist nurses at the baseline assessment when admitted to stroke units in 24 h. They were then followed up 3 months after discharge from stroke units. Follow-ups were conducted with a telephone call to evaluate prognosis including readmission, major adverse cardiac and cerebral events, cognitive function, and disability. Specialist nurses collected self-reported information on short-term prognosis using follow-up questionnaires on the telephone. Patients who changed their telephone numbers, could not be connected, or refused to follow up, were reported as a loss to follow-up. The data collection ended on 1st October 2022. Details on participant recruitment and selection are demonstrated in Supplementary material Fig. 1.

2.3. Measures

2.3.1. Socio-demographic and clinical factors

Socio-demographic and clinical factors were controlled for confounders including age, gender, education level, marital status, insurance type, Body Mass Index (BMI), nutritious risk, smoking status, alcohol status, stroke type, history of hospitalization, surgical history, history of hypertension, diabetes, hyperlipidemia, and coronary heart disease, comorbidities (≥3 types), poly-pharmacy (≥5 types), time intervals (days), post-stroke disability, and cognitive impairment at baseline (Lv et al., 2021; Deng et al., 2021; Vahedi et al., 2022; Huang et al., 2023). Specialist nurses administered questionnaires to collect socio-demographic and clinical data after admission.

2.3.2. Frailty

The Frailty Scale is employed as a practical and efficient tool for baseline frailty assessment (Si et al., 2021). The scale utilizes dichotomous responses for illness, weight loss, fatigue, resistance, and ambulation (Kim et al., 2021). This self-report physical assessment has been culturally adapted and validated in China (Dong et al., 2018). Scores on the total scale ranged from 0 to 5, with a designated cut-off point for frailty set at 2 (Dong et al., 2018). Scores of 0 to 2 indicated the non-frailty group, while scores from 3 to 5 indicated the frailty group. The Chinese version exhibited adequate internal consistency (Kuder–Richardson formula 20 = 0.485) and good test–retest reliability, with an Intraclass Correlation Coefficient (ICC) of 0.708 (Dong et al., 2018).

2.3.3. Non-elective readmission and major adverse cardiac and cerebral events

Non-elective readmission and major adverse cardiac and cerebral events were selected as primary outcomes due to their relevance to adverse outcomes in stroke patients (Yao et al., 2020). Non-elective readmission offered a comprehensive view of post-discharge complications, reflecting overall recovery status (Yao et al., 2020). Major adverse cardiac and cerebral events were critical for evaluating the broader impact on the cardiovascular and cerebral systems, often interconnected with stroke outcomes (Siddiqui et al., 2023). Non-elective hospital readmission encompassed any type of readmission, including emergency visits or urgent admissions requested by the general practitioner (Yao et al., 2020). Major adverse cardiac and cerebral events were defined as stroke recurrence, angina pectoris, myocardial infarctions, heart failure, and death based on the International Classification of Diseases 10th Revision (J. Wang et al., 2021). Non-elective readmission and major adverse cardiac and cerebral events were assessed through custom-designed questions. Participants were asked if they had experienced these events within 90 days after discharge, providing binary responses of "yes" or "no."

2.3.4. Cognitive impairment and post-stroke disability

We selected cognitive impairment and post-stroke disability as secondary outcomes to offer a comprehensive understanding of short-term prognosis, encompassing both physical and cognitive aspects. Cognitive function at baseline and follow-up was assessed using the Mini-Mental State Examination Scale (MMSE) (Li et al., 2016; Wong and Fong, 2009). The MMSE, with 30 items measuring five cognitive aspects (orientation, memory, attention and calculation, recall ability, and language ability assessment), underwent modifications and translations into various languages (Jia et al., 2021). The MMSE shows good internal consistency ($\alpha = 0.833$), and high test–retest reliability for the total score (ICC = 0.924, 95 % confidence interval (CI): 0.889–0.948). It also exhibits strong validity, confirmed by content validity experts for each item ($P < 0.001$) (Li et al., 2016). Cognitive function was identified using education-specific cutoff points of the total MMSE score, ranging from 0 to 30, with a lower score indicating a severe level of cognitive impairment (Li et al., 2016).

A phone-based MMSE provides a practical method for remote cognitive assessment at follow-up (Wong and Fong, 2009). To assess orientation, direct inquiries about the date and location were made. Memory and calculation were evaluated through verbal tasks like word recall and arithmetic problems. Recall was assessed by prompting the patient to remember verbal information. Language skills were gauged through conversation, naming objects, describing scenarios, and following verbal commands. Essential insights into comprehension were gained by providing verbal instructions and assessing the patient's ability to follow them. The phone-based MMSE may not cover all aspects of the traditional MMSE, but designing verbal tasks and using video technology with WeChat enhance cognitive assessment.

The post-stroke disability status at baseline and follow-up was measured by the Modified Rankin Scale (mRS). The mRS stands as the most widely utilized tool for assessing functional outcomes in stroke patients (Bruno et al., 2011). Categorizing functional disability into seven grades from 0 to 6, it defines varying levels of disability: 0 = no symptoms, 1 = no significant disability, 2 = slight disability, 3 = moderate disability, 4 = moderately severe disability, 5 = severe disability, and 6 = death (Liu et al., 2022b). The mRS score ranged from 0 to 6 with a cut-off of 2 (Liu et al., 2022b). Translated into Chinese by Yuan et al. (2020), the newly developed Chinese version demonstrates favorable clinometric properties, ensuring precise mRS scoring for Chinese stroke patients. The inter-rater reliability of the mRS demonstrated a high level of agreement, with paired raters reaching 87 % and a weighted kappa of 0.96. Spearman's correlation coefficient between mRS scores and the Barthel index was −0.86 in construct validity testing (Yuan et al., 2020). A higher score reflects increased post-stroke disability severity (Yuan et al., 2020).

2.4. Statistical analysis

The socio-demographic and clinical variables were listed as category variables. Baseline frailty, non-elective readmission, and major adverse cardiac and cerebral events were categorized as dichotomous variables. Continuous variables were directly assigned to calculation including MMSE and mRS at baseline and at follow-up and time intervals. Categorical data were presented as frequencies and proportions, while continuous data were summarized using mean and standard deviation (normally distributed) or medians and interquartile range (IQR) (skewed distributed). Demographic and clinical characteristics of participants with and without frailty were compared utilizing independent samples *t*-tests for normally distributed continuous variables, Mann–Whitney *U* tests for skewed continuous variables, and chi-square tests for categorical variables. The baseline characteristics of participants in the follow-up and lost groups will be compared.

We conducted bivariate and multivariate Cox regression analyses to assess the relationship between socio-demographic and clinical variables with non-elective readmission and major adverse cardiac and cerebral events. The multivariate analysis included all independent variables that exhibited clinical or statistical significance in the bivariate Cox regression analysis. Hazard ratios (HRs) and 95 % CIs were calculated to assess the impact of these factors on event risks.

The generalized linear model was utilized to examine the relationship between baseline frailty and MMSE or mRS at follow-ups, accounting for potential confounding factors relevant to the outcomes. We incorporated statistically significant and clinically significant variables from the univariate analysis into the generalized linear model to explore the associations between baseline frailty and cognitive function or disability (Polit, 2017; Y. Wang et al., 2021). Variables for inclusion were carefully chosen to ensure the accuracy of the models. For the follow-up MMSE or mRS scores, we utilized four models: model 1 (adjusting for socio-demographic factors), model 2 (adjusting for socio-demographic and clinical factors), model 3 (adjusting for socio-demographic and clinical factors as well as follow-up time intervals), and model 4 (adjusting for socio-demographic and clinical factors, and follow-up time intervals as well as baseline MMSE or mRS). The regression coefficient (β) and 95 % CIs were estimated. The Multiple Imputation method was employed to address the missing data. A two-sided *P*-value less than 0.05 indicated statistical significance. Statistical analysis was performed using SPSS version 28.0.

2.5. Ethical approval

The research received approval from the institutional review board of the ethics committee (202104171) and adhered to the principles of the Declaration of Helsinki. Strict measures were implemented to safeguard the privacy and confidentiality of participants' personal information. Participation in medical research was voluntary and based on informed consent. If participants refuse to participate in or withdraw from the study, it would not adversely affect the doctor–patient relationship. We prioritized special care for vulnerable groups, tailoring information to diverse audiences by addressing language barriers, literacy levels, and cognitive impairments. Cultural sensitivity was emphasized to respect the needs and values of various populations.

3. Results

Table 1 presents the sociodemographic and clinical characteristics of the frailty and non-frailty groups. Among 667 eligible participants, 144 (21.7 %) were under 50 years old, 382 (57.2 %) were aged 50–70, and 141 (21.1 %) were over 70. A total of 215 were frail (32.2 %), and 452 (67.8 %) were non-frail comprised of 264 pre-frail (39.6 %) and 188 robust (28.2 %). Frailty prevalence was 15.3 %, 54.9 %, and 29.8 % in younger (aged $<$50), middle-aged (aged 50–70), and older adults (aged $>$70), respectively. The frailty group exhibited a statistically significantly higher proportion of males, individuals aged 70 years or older, abnormal BMI, nutritional risk, non-ischemic stroke, and history of hospitalization, surgical operation, hypertension, diabetes, coronary heart disease, comorbidities, and poly-pharmacy than the non-frailty group. Additionally, the MMSE and mRS scores at baseline and follow-up exhibited a skewed distribution as indicated by normalcy testing. The frail group showed lower baseline MMSE scores and higher baseline mRS scores than the non-frail group. The median follow-up time was 91 days (IQR: 63, 121).

Outcome data are summarized in Table 1, indicating that 5 patients died, 12 experienced major adverse cardiac and cerebral events, and 57 had non-elective readmission during the follow-up period. Statistically significant differences were observed in terms of non-elective readmission ($P < 0.001$) and major adverse cardiac and cerebral events ($P = 0.011$) at follow-up between the frailty and non-frailty groups. There were also statistically significant differences in the MMSE ($P <$ 0.001) and mRS ($P < 0.001$) scores at follow-up between the two groups. The frailty group displayed higher levels of cognitive impairment (median: 25, IQR: 17, 29) compared to the non-frail group (median: 27, IQR: 23, 30) and greater disability (median: 2, IQR: 1, 4) compared to the non-frail group (median: 1, IQR: 0, 2) during the follow-up period. The baseline characteristics of participants who were followed up and those who were lost to follow-up are compared in Supplementary material Table 1. Participants lost to follow-up (43.5 %) exhibited a higher prevalence of frail status than those who remained in the study (30.9 %). Details of participation and reasons for non-participation at each stage are demonstrated in Supplementary material Fig. 1.

Fig. 1 demonstrates the bivariate Cox regression model of non-elective readmission and major adverse cardiac and cerebral events. Baseline frailty, insurance type, nutritional risk, stroke type, baseline MMSE, and baseline mRS were statistically significant factors of non-elective readmission. Additionally, baseline frailty, gender, nutritional risks, stroke type, surgical history, baseline MMSE, and baseline mRS showed statistical significance in the bivariate Cox regression model of major adverse cardiac and cerebral events.

Table 2 indicates that frailty status was an independent risk factor for non-elective readmission (HR: 2.71, 95 % CI: 1.59, 4.62) and major adverse cardiac and cerebral events (HR: 3.77, 95 % CI: 1.07, 13.22) for discharged stroke patients in multivariate Cox regression analysis.

Fig. 2 presents a correlation between baseline frailty and cognitive impairment and post-stroke disability at follow-ups in generalized linear models. Supplementary material Figs. 2 and 3 demonstrate the results of four different models investigating the association between baseline frailty and cognitive impairment, along with post-stroke disability at follow-ups after adjusting for important confounders. Baseline frailty was correlated with cognitive impairment (β: −2.68, 95 % CI: −3.78, −1.58) adjusting for socio-demographic and clinical variables and time intervals. However, there was no statistical significance in the relationship between baseline frailty and follow-up MMSE when further adjusting for baseline MMSE (β: −0.39, 95 % CI: −1.43, 0.64). Additionally, baseline frailty showed a statistically significant correlation with post-stroke disability at follow-up (β: 0.36, 95 % CI: 0.08, 0.65) adjusting for socio-demographic and clinical variables, time intervals, and baseline mRS. A higher frail score was indicative of a more severe level of disability.

4. Discussion

The present study aimed to investigate the impact of frailty on the short-term prognosis of adult stroke patients discharged from hospitals. The findings revealed a high prevalence of frailty among these patients. Baseline frailty was identified as a crucial predictor for the short-term prognosis of discharged stroke patients. It emerged as an independent risk factor for non-elective readmission and major adverse cardiac and cerebral events. Moreover, it was associated with post-stroke disability in discharged adult stroke patients.

4.1. Impact of frailty on readmission and major adverse cardiac and cerebral events

The result indicated that frailty was found to predict non-elective readmission in discharged stroke patients. The frailty group had a higher risk of non-elective readmission than the non-frailty group among adult stroke patients, surpassing findings from similar studies in different populations (Kilkenny et al., 2021; Yao et al., 2020). Kilkenny et al. (2021) reported an association between frailty from administrated data and readmissions within 90 days among stroke patients aged over 18. Similarly, Yao et al. (2020) predicted non-elective readmission over 6 months in elderly patients with cardiovascular diseases. The results can be attributed to three main factors. Firstly, approximately two-thirds of the stroke population exhibited frailty or pre-frailty status,

Table 1
Patient characteristics between the frail and non-frail groups (n = 667).

	Total (n = 667) n (%)	Frailty (n = 215) n (%)	Non-frailty (n = 452) n (%)	*P* value
Gender				
Male	433 (64.9)	128 (59.5)	305 (67.5)	**0.045**
Female	234 (35.1)	87 (40.5)	147 (32.5)	
Age				
≤50	144 (21.7)	33 (15.3)	111 (24.6)	**<0.001**
51–60	197 (29.5)	62 (28.8)	135 (29.9)	
61–70	185 (27.7)	56 (26.1)	129 (28.5)	
≥71	141 (21.1)	64 (29.8)	77 (17.0)	
Education level				
Junior school or below	394 (59.1)	136 (63.3)	258 (57.1)	0.13
High school or above	273 (40.9)	79 (36.7)	194 (42.9)	
Marital status				
Single	76 (11.4)	32 (14.9)	44 (9.7)	0.07
Married	591 (88.6)	183 (85.1)	408 (90.3)	
Insurance type				
Urban employees	201 (30.1)	71 (33.0)	130 (28.8)	0.55
Urban residents	142 (21.3)	44 (20.5)	98 (21.7)	
Rural cooperative	124 (18.6)	42 (19.5)	82 (18.1)	
Other	200 (30.0)	58 (27.0)	142 (31.4)	
BMI (kg/m^2)				
<18.5	24 (3.6)	14 (6.5)	10 (2.2)	**0.002**
18.5–24	468 (70.2)	135 (62.8)	333 (73.7)	
>24	175 (26.2)	66 (30.7)	109 (24.1)	
Nutrition risk				
Normal	516 (77.4)	138 (64.2)	378 (83.6)	**<0.001**
Abnormal	151 (22.6)	77 (35.8)	74 (16.4)	
Smoking status				
Current smoker	264 (39.6)	76 (35.3)	188 (41.6)	0.12
Non-current smoker	403 (60.4)	139 (64.7)	264 (58.4)	
Alcohol status				
Drinker	475 (71.2)	161 (74.9)	314 (69.5)	0.15
Non-drinker	192 (28.8)	54 (25.1)	138 (30.5)	
Stroke type				
Ischemic	452 (67.8)	125 (58.1)	327 (72.3)	**<0.001**
Others	215 (32.2)	90 (41.9)	125 (27.7)	
History of hospitalization				
Yes	415 (62.2)	150 (69.8)	265 (58.6)	**0.006**
No	252 (37.8)	65 (30.2)	187 (41.4)	
Surgical history				
Yes	240 (36.0)	96 (44.7)	144 (31.9)	**0.001**
No	427 (64.0)	119 (55.3)	308 (68.1)	
Hypertension				
Yes	471 (70.6)	168 (78.1)	303 (67.0)	**0.003**
No	196 (29.4)	47 (21.9)	149 (33.0)	
Diabetes				
Yes	205 (30.7)	78 (36.3)	127 (28.1)	**0.032**
No	462 (69.3)	137 (63.7)	325 (71.9)	
Hyperlipidemia				
Yes	125 (18.7)	41 (19.1)	84 (18.6)	0.88
No	542 (81.3)	174 (80.9)	368 (81.4)	
Coronary heart disease				
Yes	93 (13.9)	39 (18.1)	54 (11.9)	**0.031**
No	574 (86.1)	176 (81.9)	398 (88.1)	
Comorbidities				
Yes	290 (43.5)	112 (52.1)	178 (39.4)	**0.002**
No	377 (56.5)	103 (47.9)	274 (60.6)	
Polypharmacy				
Yes	200 (30.0)	82 (38.1)	118 (26.1)	**0.002**
No	467 (70.0)	133 (61.9)	334 (73.9)	
Baseline MMSE [median (IQR)]	26 (20,30)	20.5 (12,27)	28 (23,30)	**<0.001**
Baseline mRS [median (IQR)]	3 (2,5)	5 (4,5)	2 (2,3)	**<0.001**
Outcomes				
Readmission				
Yes	57 (9.5)	34 (18.4)	23 (5.6)	**<0.001**
No	541 (90.5)	151 (81.6)	390 (94.4)	
Major adverse cardiac and cerebral events				
Yes	12 (2.0)	8 (4.3)	4 (1.0)	**0.011**
No	585 (98.0)	176 (95.7)	409 (99.0)	
Follow-up MMSE [median (IQR)]	27 (22,30)	25 (17,29)	27 (23,30)	**<0.001**
Follow-up mRS [median (IQR)]	1 (1,3)	2 (1,4)	1 (0,2)	**<0.001**

Note, BMI, Body Mass Index. MMSE, Mental State Examination Scale. mRS, Modified Rankin Scale. Bold indicates statistically significant p-values.

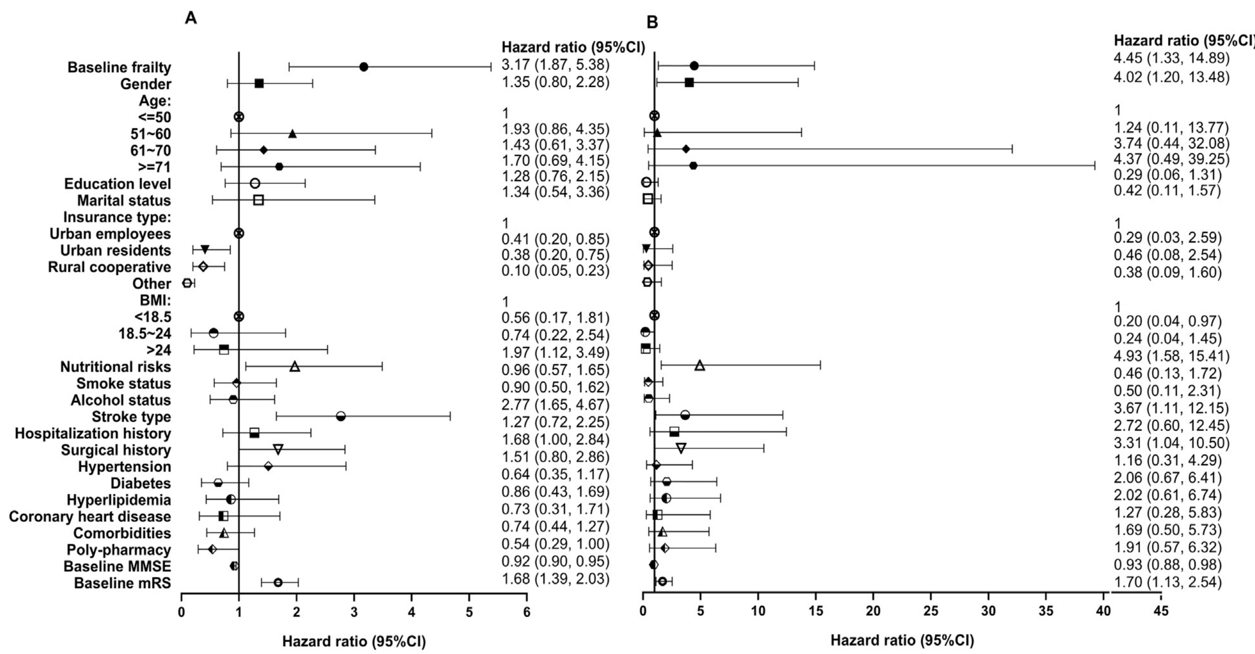

Fig. 1. Bivariate Cox regression analysis of (A) readmission and (B) major adverse cardiac and cerebral events.

a condition associated with increased vulnerability to both physical disability and cognitive decline (Vahedi et al., 2022). Secondly, the majority of frail individuals were often characterized by a great likelihood of comorbidities and polypharmacy, consequently increasing the likelihood of hospitalization (Guidet et al., 2020; Smart et al., 2017). Thirdly, frailty was characterized by a decline in physiological regulatory systems, leading to dynamic imbalance and impaired resilience, which resulted in an increased vulnerability to stressors (Evans et al., 2022). In the context of stressful events, such as stroke recurrence, the functional ability of frail individuals deteriorates rapidly, heightening the risk of acute disease severity and hospitalization (Yang et al., 2022). Hence, evaluating and screening baseline frailty is crucial to reversing or delaying frailty progression and reducing readmission risks in adult stroke patients. This leads to improved overall health outcomes and alleviates the burden on healthcare resources.

Frailty was also found to be a significant predictor of major adverse cardiac and cerebral disease events in adult stroke patients. This finding aligns with previous studies reporting that an elevated degree of frailty was associated with increased odds of major adverse cardiac and cerebral events in elderly patients after endovascular aortic aneurysm repair (J. Wang et al., 2021) or in old individuals without coronary heart disease (Damluji et al., 2021) or in adults aged over 45 years hospitalized for non-cardiac surgery (Siddiqui et al., 2023). There are two potential reasons as elaborated in the following. First, frail patients in this study exhibited a high prevalence of cardiovascular disease including hypertension, diabetes, and coronary heart disease, aligning with the findings from a cross-sectional survey that reported a robust association between frailty and cardiovascular disease in middle-aged and elderly adults (Liu et al., 2022a). Frailty independently contributed to all stages of the trajectory of cardiovascular disease progression, and a heightened frailty status was associated with an increased risk of both cardiovascular disease progression and mortality (Ma et al., 2023). Hence, the frailty group exhibited elevated odds of stroke recurrence (Zhao et al., 2023), heart failure (Talha et al., 2023), and mortality (Hirsch, 2020), thus increasing the development of major adverse cardiac and cerebral events. Second, the frail group exhibited a heightened prevalence of nutrition risk, identified as a predictor of major adverse cardiac and cerebral events among stroke patients in this study. Malnourished older adults are susceptible to physical impairment, diminished cognitive function, and frailty (Kim et al., 2021). The interaction between frailty and nutritional risk may contribute to an increased risk of major adverse cardiac and cerebral events (Miura et al., 2021; Jayanama et al., 2018). Therefore, it is imperative to treat cardiac and cerebral diseases and improve nutritional status to reduce the incidence of major adverse cardiac and cerebral events among discharged stroke patients.

Table 2
Multivariate Cox regression analysis of readmission and major adverse cardiac and cerebral events (n = 667).

	HR (95.0 % CI)	*P* value
Readmission		
Baseline frailty	2.71 (1.59, 4.62)	**<0.001**
Insurance type		
Urban employees	Ref	**<0.001**
Urban residents	0.40 (0.19, 0.83)	0.014
Rural cooperative	0.40 (0.21, 0.79)	0.009
Other	0.11 (0.05, 0.25)	<0.001
Stroke type	2.31 (1.36, 3.93)	**0.002**
Major adverse cardiac and cerebral events		
Baseline frailty	3.77 (1.07, 13.22)	**0.038**
Gender	4.02 (1.16, 13.92)	**0.028**
Nutritional risks	4.33 (1.34, 13.96)	**0.014**

Note. HR, hazard ratio. CI, confidence interval. Bold indicates statistically significant p-values.

4.2. Association between frailty and cognitive impairment or disability

Despite accounting for socio-demographic, clinical factors, and follow-up intervals, the initially observed relationship between baseline frailty and cognitive impairment at 3 months became statistically insignificant when further adjusted for baseline MMSE. The finding was slightly different from a systematic review, which concluded that frail individuals had significantly lower MMSE scores compared to robust and pre-frail individuals, highlighting the strong association between physical frailty and cognitive impairment (Vahedi et al., 2022). It should be noted that the studies in the systematic review specifically concentrated on individuals aged over 55 years. A study across seven Chinese cities confirmed a higher risk of cognitive impairment in frail patients, highlighting a significant association between frailty and cognitive function (Ma et al., 2019). However, the cross-sectional study focused mainly on community-dwelling older adults and lacked an in-depth

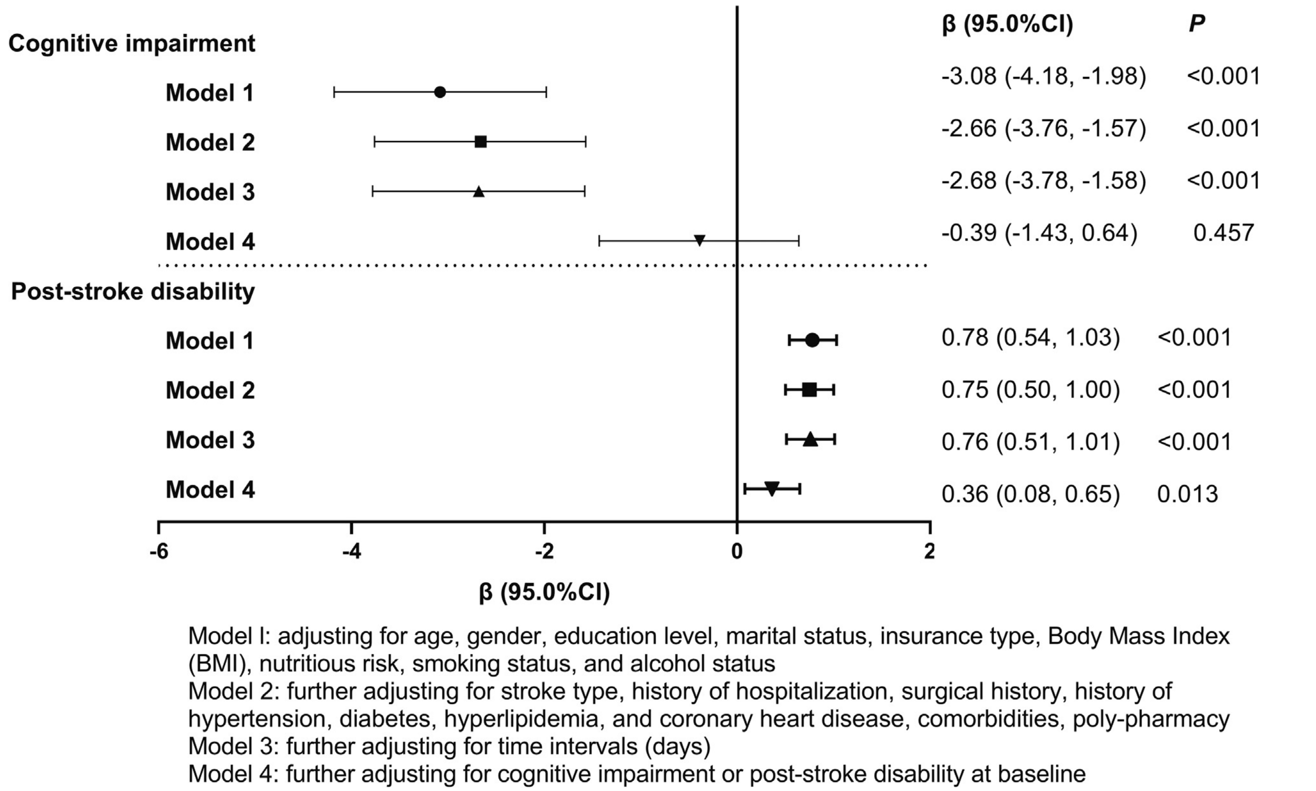

Fig. 2. Correlation between baseline frailty and (A) cognitive impairment and (B) post-stroke disability.

exploration of the causal relationship between frailty and cognitive impairment (Ma et al., 2019). Further prospective cohort studies to monitor the trajectories of cognitive function are essential to explore the influence of baseline frailty on short-term or long-term prognosis among discharged stroke patients. Empirical research encompassing a diverse age range within the population is warranted to offer clear and robust explanations for our research findings. This could enhance our understanding of the intricate relationship between frailty and cognitive impairment in adult stroke patients.

Baseline frailty was identified as an independent risk factor for 90-day post-stroke disability among adult patients, in line with the existing literature which aims to evaluate the performance of the frailty criteria for predicting disability after acute ischemic stroke (Miranda et al., 2022). It was also consistent with previous studies that investigated the association between frailty status and functional outcomes at 90 days among elderly patients following mechanical thrombectomy (Joyce et al., 2022), submitted to endovascular stroke treatment (Pinho et al., 2021), and experiencing endovascular treated large vessel occlusion stroke (Schnieder et al., 2021). It was reported that factors associated with cerebral frailty may influence post-stroke disability, implying a potential role of frailty in shaping post-stroke functional outcomes (Bu et al., 2021). This relationship underscored the strong association between frailty and functional recovery, with a significant reduction in functional improvement noted in cases of pre-stroke frailty deterioration (Yang et al., 2022; Kanai et al., 2020). Frailty is also associated with an increased likelihood of limitations in activities of daily living (Miranda et al., 2022). Moreover, a detrimental cycle is observed and described, as pre-stroke frailty is significantly correlated with stroke severity (Noguchi et al., 2021), and post-stroke neurologic impairment exacerbates the progression toward frailty (Evans et al., 2022). Therefore, it was essential to consider other confounding factors including functional outcomes and stroke severity in future research. This would provide valuable insights into the comprehensive understanding of frailty and facilitate the development of targeted interventions to mitigate its detrimental effects.

4.3. Strengths and limitations

This study represents the first prospective cohort investigation employing a multicenter dataset to analyze the temporal impact of frailty on the 90-day prognosis of adult stroke patients discharged from hospitals, including non-elective readmission, major adverse cardiac and cerebral events, cognitive impairment, and post-stroke disability. Rigorous adjustments for a comprehensive list of confounders were undertaken to ensure the robustness of the findings. This study still has the following limitations. First, the evaluation of a cognitive function at 90 days post-discharge was conducted via phone-based MMSE. While reading and writing were infeasible, the test accuracy made them suitable as initial cognitive screens where face-to-face assessment was not possible (Elliott et al., 2020). Second, self-reported data on readmission and major adverse cardiac and cerebral events may be susceptible to inaccuracy, as older adults tend to underreport hospital visits or cerebral and cardiac adverse events. This tendency introduces the possibility of recall bias, impacting the precision of the study results (Hou et al., 2021). Third, sample attrition in the cohort study, resulting from loss to follow-up and mortality over time, has constrained the sample size and may influence the magnitudes of the results (Fustinoni et al., 2022). It is acknowledged that these participants were likely to be frail; consequently, the findings may be underestimated. Finally, the study results, being derived from adult stroke patients in two tertiary public hospitals, may limit generalizability to discharged stroke patients in other levels of hospitals.

4.4. Impact on practice and research

The study has key implications for practice and research. First, the identification of pre-stroke frailty as a pivotal factor influencing the short-term prognosis of stroke patients within 90-day discharge emphasizes the critical importance of timely frailty evaluation and screening during hospitalization. Second, it is imperative to initiate nurse-led intervention programs for frailty as patients move from hospital to home. This proactive approach can significantly contribute to improving functional outcomes, concurrently reducing non-elective readmission rates and major adverse cerebral and cardiac events. Third, there is a need for high-quality longitudinal studies to explore the long-term or short-term impact of frailty on cognitive function among adult stroke patients using objective measurements, especially among younger stroke adults. In addition, more prospective cohort studies are warranted to control factors including functional outcomes and stroke severity to examine the association between frailty and post-stroke disability in younger and middle-aged adult patients in different medical contexts.

5. Conclusions

In conclusion, our study revealed significant associations between baseline frailty and non-elective readmission, major adverse cardiac and cerebral events, and post-stroke disability among adult stroke patients at 3 months. These findings emphasize the importance of evaluating and screening frailty status, as it can play a crucial role in improving short-term prognosis for adult stroke patients. Nurses need to be cognizant of the short-term implications of baseline frailty to effectively provide transitional care for discharged adult stroke patients during the hospital-to-home transition.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijnurstu.2024.104735.

Funding

This work was supported by the Hunan Provincial Science and Technology Plan Project (Grant No. 2021SK53801) and the Project Program of the National Clinical Research Center for Geriatric Disorders (Xiangya Hospital, Grant No. 2020LNJJ19).

CRediT authorship contribution statement

Haiyan He: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Minhui Liu:** Writing – review & editing, Validation. **Yueping Zheng:** Validation, Investigation. **Yuqin Nie:** Validation, Resources, Investigation. **Lily Dongxia Xiao:** Writing – review & editing. **Yinglan Li:** Supervision, Resources. **Siyuan Tang:** Visualization, Supervision, Conceptualization.

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors would like to thank all the healthcare professionals and discharged stroke patients from the two tertiary hospitals. Our sincere appreciation is given to all participating stroke units.

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