Predicting Non-elective hospital readmission or Death using a Composite Assessment of Cognitive Impairment and Frailty in Elderly Inpatients With Cardiovascular Diseases

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Abstract

Background: No prior studies have assessed the role of cognitive impairment and physical frailty in elderly inpatients with cardiovascular disease (CVD). We aimed to assess the utility of a combination developed using the mini-mental state examination (MMSE) + clock drawing test (CDT) and the Fried phenotype for predicting non-elective hospital readmission or death within 6-month in elderly inpatients with CVD.

Methods : A single center prospective cohort was conducted between September 2018 and February 2019. Inpatients aged 65 years or older were recruited. All enrolled patients received a comprehensive geriatric assessment during hospitalization. The Kaplan-Meier curves were used to estimate the cumulative incidence of events. The multivariate Cox regression model was used to analyze the association between frailty and cognitive status and the non-elective hospital readmission or death.

Results : A total of 542 patients were included; and a total of 113 patients (20.9%) died or were readmitted at 6-month. Overall 20% screened positive for cognitive impairment, including 8% were cognitive impairment combined with physical frailty, which were more older, more common in women and non-married group, had a lower education and a higher risk of malnutrition. Frail participants with normal (hazard ratio [HR]:1.73, 95% confidence intervals [CI]:1.06-2.82, P=0.028) and impaired cognition (HR:2.50, 95% CI:1.27-4.91, P=0.008) had a higher risk of non-elective hospital readmission or death than robust patients, after adjustment for age, sex, education level, marital status, the presence of diabetes mellitus, heart failure, and previous stroke.

Conclusions : The presence of physical frailty and cognitive frailty were powerful predictors of non-elective hospital readmission or death in elderly inpatients with CVD, and taking cognitive impairment into account in the frailty model may allow better prediction of adverse outcomes of frailty in the short time. Trial registration: ChiCTR1800017204; date of registration: 07/18/2018.

Background

Cardiovascular disease (CVD) is the leading cause of death and disability[1]. Ischemic heart disease, heart failure (HF), and atrial fibrillation (AF) are the cardiovascular conditions with the higher rates of morbidity and mortality. Cardiovascular mortality in individuals 50 to 69 years of age was 436 deaths for every 100 000 people[2], and cardiovascular mortality is higher with age. China has the largest ageing population and is one of the fastest ageing countries in the world[3]. CVD and related complications are significant healthcare problems in the growing elderly population.

Metabolic factors are the predominant risk factors for CVD, behavioural risk factors, low education and low grip strength have stronger effects on CVD or mortality[4]. Sedentary behaviour and physical inactivity are major modifiable risk factors for CVD[5]. A significant association between frailty and a worse prognosis has been described in patients with CVD[6–9]. Age-associated cognitive decline and impairment have also been shown to be associated with an increased mortality[10–14]. However, most

reports only evaluated the relationship between physical frailty or cognitive impairment and CVD. In contrast, higher rates of cognitive impairment have been reported among older adults with increased levels of frailty, physical frailty and cognitive impairment often co-occur[15]. The definition of cognitive and physical frailty and its prediction for adverse outcome of elderly inpatients with CVD has apparently not been investigated.

Physical frailty represents a state of increased vulnerability to stressor events, weakness, risk of morbidity, disability, and mortality[16]. Cognitive frailty is a heterogeneous clinical manifestation characterized by the simultaneous presence of both physical frailty and cognitive impairment, in the absence of dementia and other neurodegenerative diseases[12].

Cognitive and physical components of frailty have pathophysiologic rationale as risk factors for CVD. There is a clinical need to identify more practical screens that can assist us to definite cognitive impairment and physical frailty, then to determine which patients with CVD are at high risk of adverse outcomes, early management of these high-risk patients can reduce readmission rates, healthcare spending, and improve quality of care[17]. Accordingly, the primary aim of the present study was to assess the utility of a combination developed using the MMSE + CDT and the Fried phenotype for predicting non-elective hospital readmission or death within 6-month in elderly inpatients with CVD. We also performed a sensitivity analysis substituting the Short Physical Performance Battery (SPPB), another more objective measure of simple physical condition for the Fried phenotype. Our secondary aim was to explore the clinical and laboratory characteristics of the MMSE + CDT-Fried phenotype composition in CVD in more detail to identifying which subcomponents were more commonly abnormal as compared to robust patients.

Methods

Participants

Inpatients aged 65 years or older who admitted to the department of Cardiology, from September 2018 to February 2019 were recruited. Among these patients, 746 eligible patients were enrolled, patients were excluded from the following reasons: patients could not cooperate with questionnaires and follow-up for various reasons (n = 17), patients did not agree to undergo the assessments (n = 175), patients quitted the test ahead of schedule (n = 12). A total of 204 subjects were excluded, and 542 subjects were enrolled into the final analyses. All patients enrolled in the study are followed subsequent to discharge. During the 6-month follow-up, the researchers followed up the patients mainly through outpatient visits and telephone calls. Of all patients, there was no patient lost to follow-up (Supplementary Data).

Definition of four groups

Physical frailty was defined according to the definition proposed by Fried and colleagues based on the 5 criteria of unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low

physical activity[16]. Participants were ranked as frail (3–5 criteria), prefrail (1 or 2 criteria), or robust (0 criteria).

The most widely used tool for evaluating of cognitive impairment will be the mini-mental state examination (MMSE)[18]. The total MMSE score ranges from 0 to 30 points, with higher scores reflecting better cognitive function. However, MMSE is language based and also considered to be influenced by the level of education. The clock drawing test (CDT) is one of the most used cognitive screening instruments for dementia[19] and it can be performed without being influenced by the patient's level of language or education and less affected by depression[20]. We used the Chinese version of the MMSE and CDT to define cognitive Impairment, the cut-off score is below 24 points of MMSE or $24 \leq MMSE \leq 26$ and incorrect CDT.

A four-level composite frailty scoring system was created via the combination of the MMSE + CDT-Fried phenotype. More than one article has a similar definition of the combination of cognition impairment and frailty[21], but this study is the first to formally use the MMSE + CDT as an assessment of cognition status. Robust Patients (RP): non-frail (Fried phenotype < 3) and non-cognitive impairment; Cognitive Impairment (CI): cognitive impairment and non-frail; Physical Frailty (PF): frail and non-cognitive impairment; and Cognitive Frailty (CF): physical frailty and cognitive impairment.

Outcome measures

The primary outcome for this study was the non-elective hospital readmission or death at 6-month, the former is considered any type of emergency readmission, such as emergency visits, or an urgent admission requested by the general practitioner[22]. The latter refers to death for any reason.

SPPB

Simple physical condition was measured by the SPPB, scored from 1 to 12 based on three tests: a set of balance tests, gait speed and repeated chair stands. The SPPB (cut-off value of 10) is an effective assessment tool for measuring lower extremity function for middle-aged and older CVD patients that is widely used in both clinical and research settings[23, 24].

MNA-SF

The MNA-SF is validated for diagnosis of malnutrition and prediction of clinical outcomes, includes six items and the total score is 14. Patients can be divided into three categories: 12–14 points indicated "well-nourished", 8–11 points indicated "at risk of malnutrition"' and 0–7 points indicated "malnourished"[25].

Statistical analyses

In this study, descriptive statistics were calculated for all variables. Continuous variables were expressed as mean ± standard deviation (SD) in a normal distribution, median and interquartile range (IQR) in a non-

normal distribution, categorical variables were expressed as numbers and percentages. ANOVA test for continuous variables and Chi square test for categorical variables when appropriate. The Kaplan-Meier curves with log-rank tests were used to estimate the cumulative incidence of events. The multivariate Cox regression model to estimate hazard ratios (HRs) with 95% confidence intervals (CI) was used to analyze the association between frailty status or other factors at baseline and the non-elective hospital readmission or death. The Cox regression was adjusted with age, sex, education level, marital status, the presence of heart failure (HF), diabetes mellitus (DM) and previous stroke. A p-value < 0.05 was considered statistically significant. All the data analysis was conducted using the IBM SPSS Statistics software (version 24; IBM Corporation).

Covariates

Several potential confounders and effect modifiers were measured and defined as follows: sociodemographic characteristics were age, sex, marital status (married or non-married -including single, divorced, separated and widowed), education level and body mass index (BMI). Lifestyle behaviours were smoking status (yes or no: including quitting smoking in the last 3-month), alcohol intake (yes or no: including quitting drinking in the last 3 months). Health status were medical history including hypertension, coronary atherosclerotic heart disease (CAD), AF, HF, DM and previous stroke. Laboratory indicators include serum free triiodothyronine (FT3), prealbumin (PA). All covariate information was obtained using a standardized and structured questionnaire in the baseline survey, venous blood samples were collected in the early morning from the fasting patients.

Results

Overall, The mean (SD) age was 75.17 (6.52) years old at baseline, and 48.5% of participants (263/542) were women with a mean BMI of 25.25 (3.37) kg/m^2. Of the total participants, 64% (348/542) were classified as RP, 12% (64/542) as CI, 16% (86/542) as PF and 8% (44/542) as CF. Those who were older, women, non-married, and of lower education tended to exhibit CF. Participants in the RP group were more likely to smoke and consume alcohol. The most frequent hospital admission diseases were hypertension (73.1%), CAD (59%), DM (34.8%), AF (22.2%), previous stroke (16.7%) and HF (12.2%). Participants in the CF group were more likely to have AF, HF and previous stroke, simultaneously, those participants had a higher risk of malnutrition or malnourished. Lower PA and FT3 were more common in participants with frailty, especially in CF group.

During the follow-up time, there were 113 events (4 deaths and 109 non-elective hospital readmissions). The clinical outcome of non-elective hospital readmission and death occurred with increased frequency in the four groups, 16% (57/348), 23% (15/64), 30% (26/86) and 34% (15/44) of patients with MMSE + CDT– Fried phenotype subcategories of RP, CI, PF and CF (Table 1).

Table 1

The baseline characteristics of the study sample and a 6-month outcomes.

	All (n = 542)	RP (n = 348)	CI (n = 64)	PF (n = 86)	CF (n = 44)	P value
Age (year)	75.17 ± 6.52	73.33 ± 5.73	78.87 ± 6.21*	76.62 ± 6.73*‡	81.65 ± 5.34*‡	<0.001
Women	263 (48.5%)	156 (44.8%)	35 (54.7%)	43 (50.0%)	29 (65.9%)	0.041
Married	446 (82.3%)	304 (87.4%)	43 (67.2%)*	70 (81.4%)	29 (65.9%)*	<0.001
Education (year)	11.13 ± 4.22	11.89 ± 3.65	8.55 ± 4.9*†	12.06 ± 3.54†‡	7.07 ± 4.78*‡	<0.001
BMI (kg/m^2)	25.25 ± 3.37	25.28 ± 3.31	25.41 ± 3.61	25.58 ± 3.43	24.07 ± 3.23	0.095
Smoke	173 (31.9%)	123 (35.3%)	17 (26.6%)	20 (23.3%)	13 (29.5%)	0.125
Alcohol intake	174 (32.1%)	130 (37.4%)	16 (25.0%)	20 (23.3%)	8 (18.2%)	0.005
Hypertension	395 (73.1%)	248 (71.5%)	50 (79.4%)	61 (70.9%)	36 (81.8%)	0.303
CAD	320 (59.0%)	197 (56.6%)	36 (56.0%)	48 (55.8%)	21 (44.7%)	0.749
AF	120 (22.2%)	61 (17.6%)	20 (31.7%)	23 (26.7%)	16 (36.5%)*	0.003
HF	66 (12.2%)	26 (7.5%)	13 (20.6%)*	17(19.8%)*	10 (22.7%)*	<0.001
DM	188 (34.8%)	106 (30.5%)	25 (39.7%)	40(46.5%)*	17 (38.6%)	0.031
Stroke	90 (16.7%)	45 (13.0%)	13 (20.6%)	17 (19.8%)	15 (34.1%)*	0.002
SPPB ≤10	362 (66.8%)	188 (54.0%)	55 (85.9%)*	78 (90.7%)*	41 (93.2%)*	<0.001

Notes: Values are showed as mean ± standard deviation or n (%). *p < 0.05 compared with RP; †p < 0.05 compared with CI; ‡p < 0.05 compared with PF.

Abbreviation: RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; BMI, body mass index; CAD, coronary atherosclerotic heart disease; AF, atrial fibrillation; HF, heart failure; DM, diabetes mellitus; SPPB, short physical performance battery; MNA-SF, mini nutritional assessment-short form; MMSE, mini-mental state examination; CDT, clock drawing test; PA, prealbumin; FT3, free triiodothyronine.

	All (n = 542)	RP (n = 348)	CI (n = 64)	PF (n = 86)	CF (n = 44)	P value
MNA-SF(≤12)	173 (31.9%)	86 (24.7%)	20 (31.2%)†	44 (51.2%)*†	23 (52.3%)*	≤0.001
MMSE	26.83 ± 3.92	28.32 ± 1.56	22.14 ± 4.43*†‡	28.06 ± 1.57)†‡	19.48 ± 5.64*†‡	≤0.001
CDT (Incorrect)	187 (24.6%)	77 (22.1%)	52 (82.5%)*†	22 (25.6%)†‡	36 (81.8%)*‡	≤0.001
PA (mg/dl)	24.30 ± 5.85	25.31 ± 5.84	23.64 ± 5.10‡	22.71 ± 5.08*	19.82 ± 5.60*†	≤0.001
FT3 (pg/ml)	3.11 ± 0.40	3.17 ± 0.39	3.06 ± 0.45	2.96 ± 0.36*	2.87 ± 0.36*	≤0.001
Readmission and death	113 (20.8%)	57 (16.0%)	15 (23.0%)	26 (30.0%)*	15 (34.0%)*	≤0.001

Notes: Values are showed as mean ± standard deviation or n (%). *p < 0.05 compared with RP; †p < 0.05 compared with CI; ‡p < 0.05 compared with PF.

Abbreviation: RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; BMI, body mass index; CAD, coronary atherosclerotic heart disease; AF, atrial fibrillation; HF, heart failure; DM, diabetes mellitus; SPPB, short physical performance battery; MNA-SF, mini nutritional assessment-short form; MMSE, mini-mental state examination; CDT, clock drawing test; PA, prealbumin; FT3, free triiodothyronine.

Worsening physical frailty and the presence of cognitive impairment were all associated with adverse events (Table 2). Frail participants with normal (HR:2.02, 95% CI:1.27–3.22, P = 0.002) and impaired cognition (HR:2.48, 95% CI:1.40–4.38, P = 0.003) had a higher risk of non-elective hospital readmission and death than RP (Fig. 1). After adjustment for age, sex, education level, marital status, the presence of DM, HF and previous stroke, PF and CF were independently significant predictors of non-elective hospital readmission or death (HR:1.73, 95% CI:1.06–2.82, P = 0.028; HR:2.50, 95% CI:1.27–4.91, P = 0.008) in elderly inpatients with CVD (Figs. 1 and 2) .

Table 2

Unadjusted and adjusted survival models for risk of 6-month non-elective hospital readmission or death.

Characteristic	Unadjusted		Adjusted	
	HR (95%CI)	P value	HR (95%CI)	P value
Frailty criteria				
RP	1 [Reference]	NA	1 [Reference]	NA
CI	1.29 (0.72–2.31	0.400	1.16 (0.61–2.20)	0.651
PF	2.02 (1.27–3.22)	0.002	1.73 (1.06–2.82)	0.028
CF	2.48 (1.40–4.38)	0.003	2.50 (1.27–4.91)	0.008
Age, year				
65–74	1 [Reference]	NA	1 [Reference]	NA
75–84	0.83 (0.43–1.59)	0.574	0.65 (0.31–1.37)	0.25
≥ 85	1.05 (0.54–2.01)	0.891	1.20 (0.79–1.81)	0.40
Sex, male	0.79 (0.54–1.14)	0.208	0.84 (0.56–1.26)	0.41
Non-married	1.6 (0.92–2.81)	0.099	1.84 (0.99–3.40)	0.052
Smoke	1.37 (0.94-2.00)	0.105	NA	NA
Alcohol intake	0.99 (0.66–1.47)	0.944	NA	NA
Hypertension	1.56 (0.98–2.49)	0.061	NA	NA
CAD	0.99 (0.68–1.46)	0.959	NA	NA
AF	1.39 (0.92–2.10)	0.118	NA	NA
HF	3.13 (2.06–4.76)	0.000	2.70 (1.69–4.30)	0.000
DM	1.51 (1.04–2.20)	0.031	1.30 (0.88–1.91)	0.188
Stroke	1.65 (1.06–2.56)	0.026	1.23 (0.78–1.95)	0.371
SPPB□10	2.53 (1.56–4.11)	0.000	2.33 (1.40–3.89)	0.001
MNA-SF				
MNA-SF (12–14)	1 [Reference]	NA	1 [Reference]	NA

Abbreviation: HR, hazard ratio; CI, confidence interval; RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; CAD, coronary atherosclerotic heart disease; AF, atrial fibrillation; HF, heart failure; DM, diabetes mellitus; SPPB, short physical performance battery; MNA-SF, mini nutritional assessment-short form; PA, prealbumin; FT3, free triiodothyronine.

Characteristic	Unadjusted		Adjusted	
MNA-SF (8–11)	1.33 (0.89–1.99)	0.161	1.14 (0.75–1.73)	0.534
MNA-SF (≤ 7)	2.28 (1.09–4.74)	0.028	2.26 (1.08–4.73)	0.030
PA (mg/dl)	1.27 (0.87–1.86)	0.217	NA	NA
FT3 (pg/ml)	1.77 (1.14–2.76)	0.011	1.59 (0.99–2.56)	0.06

Abbreviation: HR, hazard ratio; CI, confidence interval; RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; CAD, coronary atherosclerotic heart disease; AF, atrial fibrillation; HF, heart failure; DM, diabetes mellitus; SPPB, short physical performance battery; MNA-SF, mini nutritional assessment-short form; PA, prealbumin; FT3, free triiodothyronine.

Sensitivity analysis for the association between the MMSE + CDT-SPPB and non-elective hospital readmission or death at 6-month (Fig. 3). Participants with lower SPPB had a higher risk of advent events in both normal (HR:2.91, 95% CI: 1.63–5.19, P = 0.000) and impaired cognition (HR:2.29, 95%CI:1.37–3.83, P = 0.001). In the fully adjusted multivariable COX regression model, PF and CF were independently associated with non-elective hospital readmission or death respectively (HR:2.25, 95% CI:1.32–3.81, P = 0.001; HR:2.64, 95% CI:1.34–5.20, P = 0.000).

Discussion

Our study is one of the first to evaluate the impact of physical and cognitive status on the risk of subsequent events in elderly patients hospitalized for CVD. In common with previous studies, we found that elder patients with HF[26], DM[27], previous stroke[28], non-married[29], severe MNA-SF[30] and decreasing FT3[31] at baseline are more likely to have adverse events, but after being adjusted, only physical and cognitive frailty, HF and severe MNA-SF can be used as a predictor of short term prognosis. Patients with cognitive frailty experienced about 2.5 times more non-elective hospital readmission or death than robust patients. The significance of physical frailty assessed by Fried phenotype in predict of non-elective hospital readmission or death within 6-month in elderly patients with CVD increased significantly after the diagnosis of cognitive impairment was added. In our opinion, these findings support the routine use of MMSE + CDT-Fried phenotype for improving risk stratification in elder inpatients with CAD. Patients with cognitive frailty should need a closer follow-up to reduce their high readmission rate.

The detection of impaired physical performance and cognition in elder patients with CVD is essential for clinical management and therapeutic decision. Increasing age is an obvious risk factor for frailty[22], and patients admitted to hospital for CVD are more older. The most commonly used frailty assessment tools were the Frailty Index, the Clinical Frailty Scale, and the Fried phenotype[32], and there is a requirement for an assessment tool that can be used conveniently, rapidly, and securely in clinical practice for screening decreased physical performance, therefore, the Fried phenotype seems to be the best choice, which is a brief, interview and simple physical tests combined and easy to assessment instrument. There are recent

studies concluding that an indicator of frailty in routine care is related to readmission or mortality in patients[33, 34]. Vidan and colleagues included 450 patients aged 70 and older and found frailty to be an independent predictor of 12-month readmission[35]. In a longitudinal cohort Study examined the effect of frailty phenotype and cognitive impairment on mortality in community for a 5-year, frailty and cognitive impairment (MMSE < 21) were significant predictors of mortality[36]. The primary aim of the present study was to assess the utility of a combination developed using the MMSE + CDT and the Fried phenotype for predicting non-elective hospital readmission or death within 6-month in elderly inpatients with CVD. The results of the present study show a strong association between the presence of physical or cognitive frailty and the risk of follow-up, even after controlling for multiple variables (including age, sex, education level, marital status, the presence of DM, HF and previous stroke), which is identical with others results of study[37]. Sensitivity analysis for the association between the MMSE + CDT-SPPB confirmed these results, and it seems to have a higher predictive value for prognosis. Both the Fried phenotype assessment and SPPB test were performed safely even in patients with various chronic diseases. In the present study, there were no adverse events caused by the assessment and test.

Cognitive impairment is a risk factor for adverse events in patients with HF[13]. In older women free of prevalent CVD at baseline, lower baseline cognitive function or decline increased risk of incident CVD, CVD death, and all-cause mortality[10]. To the authors' knowledge, this study is the first to formally assess the MMSE + CDT as a predictor of clinically relevant outcomes in patients with CVD. But We found that cognitive impairment alone can not be a predictor of non-elective hospital readmission or death in elderly inpatients with CVD, only combined with physical frailty that would be a sensitive prognostic indicator.

In terms of laboratory indicators, a reduction in FT3 may be considered to be the consequence of multiple events, such as malnutrition as well as acute and chronic diseases[38]. Recent studies have suggested that reduced values of FT3 may be involved in the development of frailty and cognitive decline[38, 39], lower circulating FT3/ FT4 ratio represents a sensitive marker of frailty and may be an effective prognostic parameter of higher mortality in hospitalized older patients[31]. In this study, CF group showed the lowest mean level of FT3 compared to the other groups, thus, FT3 may be a useful laboratory parameter in clinical assessment, which can play an important role in identifying vulnerable elderly subjects, especially in the CF group.

Malnutrition and nutritional imbalance are thought to be strongly associated with development of frailty and cognitive impairment due to both the biological and the behavioural effects of diet[40]. The two main pathways to malnutrition in elderly patients are anorexia of aging, and disease-related energy needs after a stressful event[41]. The MNA-SF is validated for diagnosis of malnutrition and prediction of clinical outcomes. In our study, frailty with normal or impaired cognition are associated with poor nutritional status. We also found that malnourished status which was assessed by severe MNA-SF (≤ 7) is associated with an increased risk of non-elective hospital readmission or death in elderly inpatients with CVD.

Study limitations

There are some limitations to this study. We can point out that this is a cross-sectional study with a short term follow-up, and there were only 4 deaths, so the guidance of short-term prognosis focused on the non-elective hospital readmission, but a continued long follow-up study in this population is currently under way in our group, and a randomized controlled clinical trial about multidisciplinary and multifactorial intervention for frailty of elderly inpatients with CVD is also under way. Second, these data were collected from patients at one hospital, thus may not necessarily be directly transferable to patients from different locations, but it can provide more convenient follow-up for these patients. Third, the study only included hospitalized patients, thus, nothing can be inferred about elder people in the community-dwelling from this study. In addition, the small sample size is the main reason for we did not conduct a subgroup analysis of single disease. Fourth, the mean age of the patients in this study was 75 years. For such an old cohort, it is important to consider that a survival bias may be present when applying these finding. Finally, the MMSE or CDT is not a very sensitive means of detecting subtle impairments of cognitive function, and thus in the present study we may have underestimated the proportion of people with cognitive impairment.

Conclusions

The presence of physical frailty and cognitive frailty were powerful predictors of non-elective hospital readmission or death in elderly inpatients with CVD within 6-month, and taking cognitive impairment into account in the frailty model may allow better prediction of adverse outcomes of frailty in the short time. Understanding the cognitive impairment and frailty role in the process of ageing will help to identify elderly inpatients at risk of adverse outcomes. Learning how physical and cognitive status affect prognosis, and according to the specific processes and possible mechanisms, we can take new and appropriate interventions to reduce risk.

List Of Abbreviations

RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; SD, standard deviation; IQR, interquartile range; HR, hazard ratio; CI, confidence interval; BMI, body mass index; SPPB, short physical performance battery; MNA-SF, mini nutritional assessment-short form; MMSE, mini-mental state examination; CDT, clock drawing test; CAD, coronary atherosclerotic heart disease; AF, atrial fibrillation; HF, heart failure; DM, diabetes mellitus; PA, prealbumin; FT3, free triiodothyronine.

Declarations

Ethics approval and consent to participate

All participants will sign an informed consent according to the Declaration of Helsinki prior to data collection. This study is reviewed and approved by Ethics Committee of Beijing Hospital, China. (ID

number: 2018BJYYEC-121-02), the version date of the protocol approved by ethics is September 18, 2018, the version number is 1.0.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the REDCap electronic data capture tools, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the REDCap electronic data capture tools.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HW and JY contributed in the conception of the idea for the study. SY and PZ contributed in the development of the conceptualization, methodology, and writing - original draft. DYL and YW have made a substantial contribution to the analysis and interpretation of data. NS and YL were responsible for the revision of the manuscript. All the authors read the draft, made contributions and approved the final manuscript.

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Figures

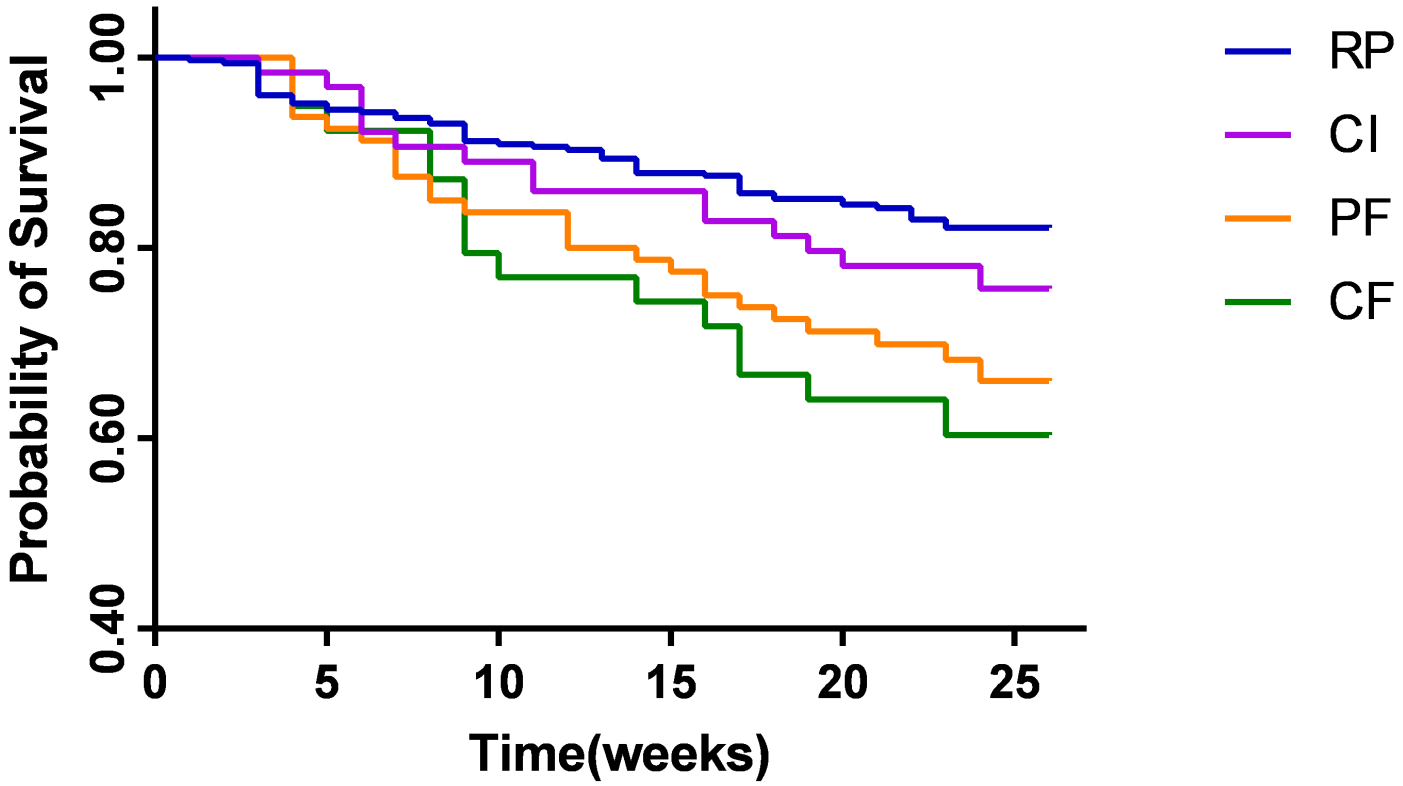

Figure 1

Kaplan-Meier survival curves by cognitive impairment and frailty status (n = 542). CF:HR=2.48(1.40-4.38), p:0.002 PF:HR=2.02(1.27-3.22), p:0.003 CI:HR=1.29(0.72-2.31), p:0.400 Patients were divided into groups with RP, CI, PF and CF via the combination of the MMSE + CDT and Fried phenotype (log-rank $\chi 2 = 15.78$; P <0 .001). Abbreviation: RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF,

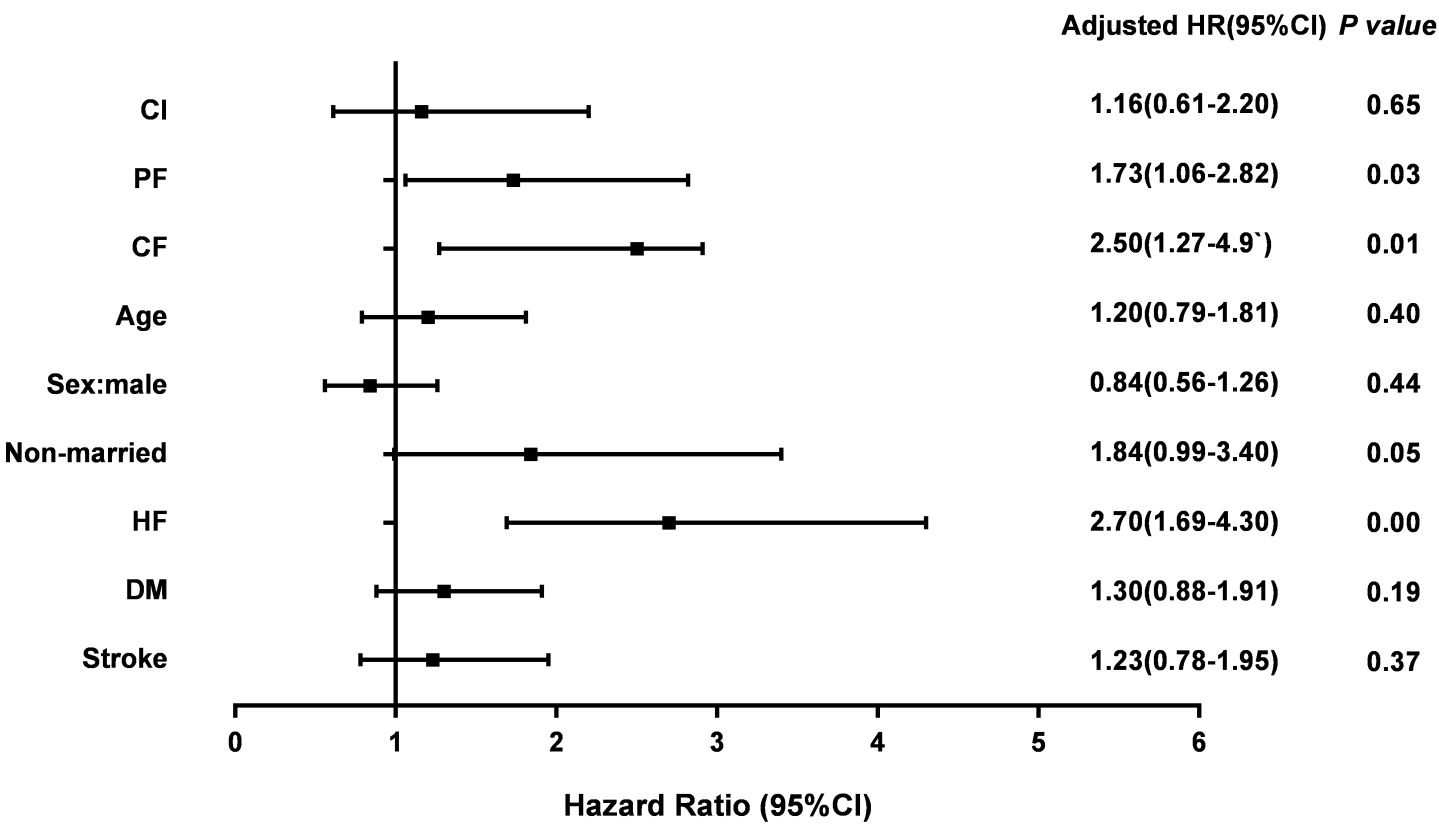

Figure 2

Relationship between non-elective hospital readmission and death outcomes and baseline (n=542): HR and 95% CI. Abbreviation: CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; HF, heart failure; DM, diabetes mellitus; HR, hazard ratio; CI, confifidence interval.

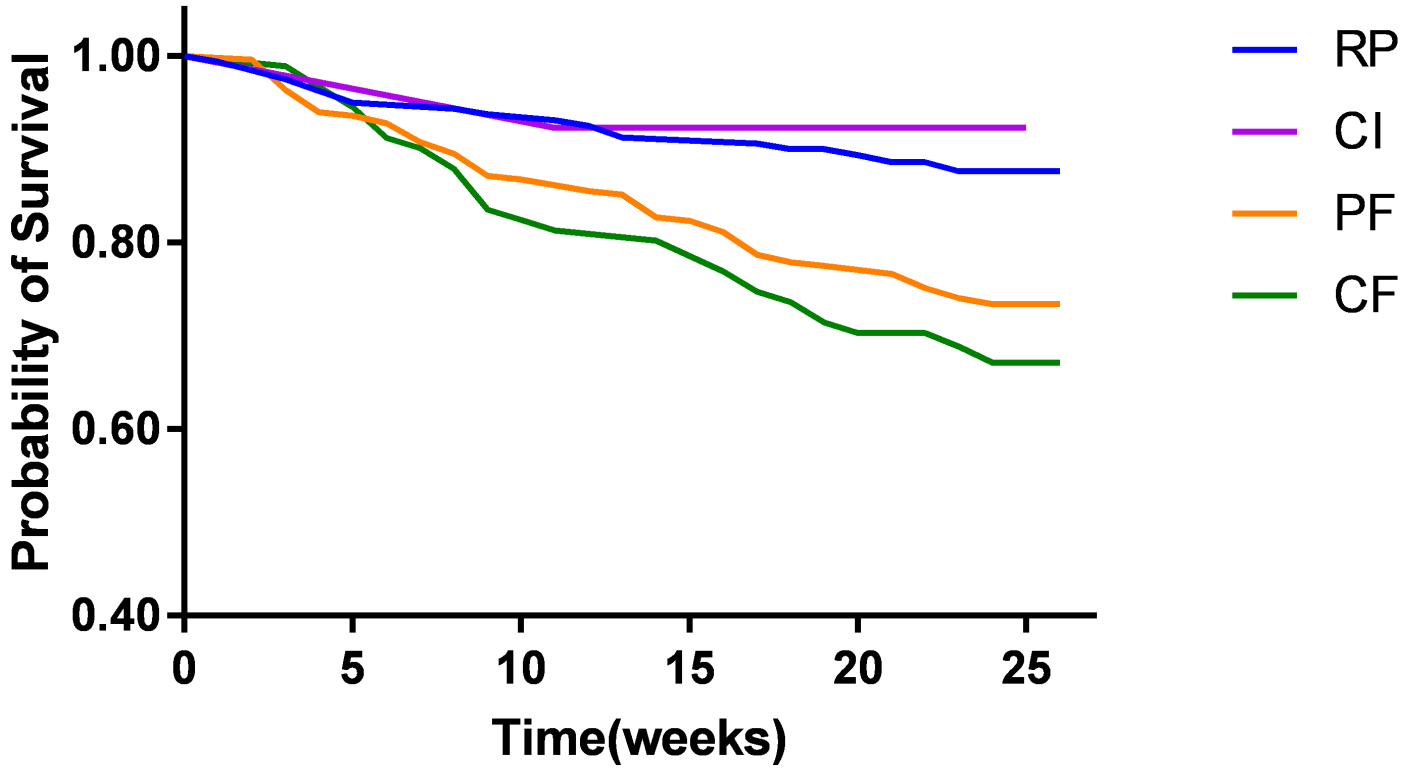

Figure 3

Kaplan-Meier survival curves by cognitive impairment and SPPB status (n = 542). CF:HR=2.91(1.63–5.19), p:0.000 PF:HR=2.29(1.37-3.83), p:0.001 CI:HR=0.62(0.08-4.60), p:0.640 Patients were divided into groups with RP, CI, PF and CF via the combination of the MMSE + CDT and SPPB (log-rank $\chi 2 = 17.04$; P <0 .001). Abbreviation: RP, Robust Patients; CI, Cognitive Impairment; PF, Physical Frailty; CF, Cognitive Frailty; SPPB, short physical performance battery; MMSE, mini-mental state examination; CDT, clock drawing test.

Supplementary Files

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