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ORIGINAL RESEARCH

Impact of Combined Cognitive and Physical Impairments on Long-Term Prognosis in Elderly Cardiovascular Disease Patients: A Prospective Cohort Study

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Purpose: This study aimed to evaluate the association between physical and cognitive function and long-term outcomes in elderly cardiovascular disease (CVD) patients, using the Short Physical Performance Battery (SPPB) and the Mini-Mental State Examination (MMSE).

Patients and Methods: In this prospective cohort study, 524 patients aged ≥65 years hospitalized in the Department of Cardiology at Beijing Hospital from September 2018 to April 2019 were evaluated. Baseline demographic, clinical, laboratory, and functional data were collected, and physical and cognitive function were assessed using SPPB and MMSE scores. Patients were followed for all-cause mortality over a 5-year period. Kaplan-Meier survival analysis and Cox proportional hazards models were used to examine the mortality risk associated with impairments.

Results: Physical impairment was identified in 28.2% and cognitive impairment in 12.4% of patients. The combination of both impairments was associated with a 5.47-fold increased mortality risk (HR: 5.47; 95% CI: 2.78–10.78; p<0.001). Each 1-point increase in SPPB and MMSE scores correlated with a 16.3% and 8.7% reduction in mortality risk, respectively. Cognitive function, particularly attention and calculation ability, has emerged as a significant predictor of survival.

Conclusion: Combined physical and cognitive impairments are prevalent in elderly CVD patients and strongly predict poor long-term prognosis. Routine assessment of cognitive function alongside physical performance can improve clinical decision-making, intervention strategies, and patient management, offering the potential to enhance outcomes in this high-risk population.

Keywords: cognitive impairment, physical impairment, cardiovascular disease, all-cause mortality, elderly inpatients

Introduction

Cardiovascular disease (CVD) refers to a group of disorders arising from structural or functional abnormalities in the heart and blood vessels, such as coronary artery disease, myocardial infarction, arrhythmias, and heart failure. As the leading cause of mortality and morbidity among noncommunicable diseases worldwide, the burden of CVD is increasing, particularly with the aging population. This trend has led to higher incidence and mortality rates, significantly impacting the health of older adults.[1–3] Elderly patients with CVD frequently suffer from physical functional impairments due to compromised cardiac pump function, chronic inflammation, and neurohumoral dysregulation, resulting in diminished quality of life and adverse clinical outcomes.[4] More recently, cognitive impairments associated with CVD, such as deficits in memory, executive function, and processing speed, have drawn increasing attention.[5] Although physical impairments in CVD patients have been widely studied, there is limited

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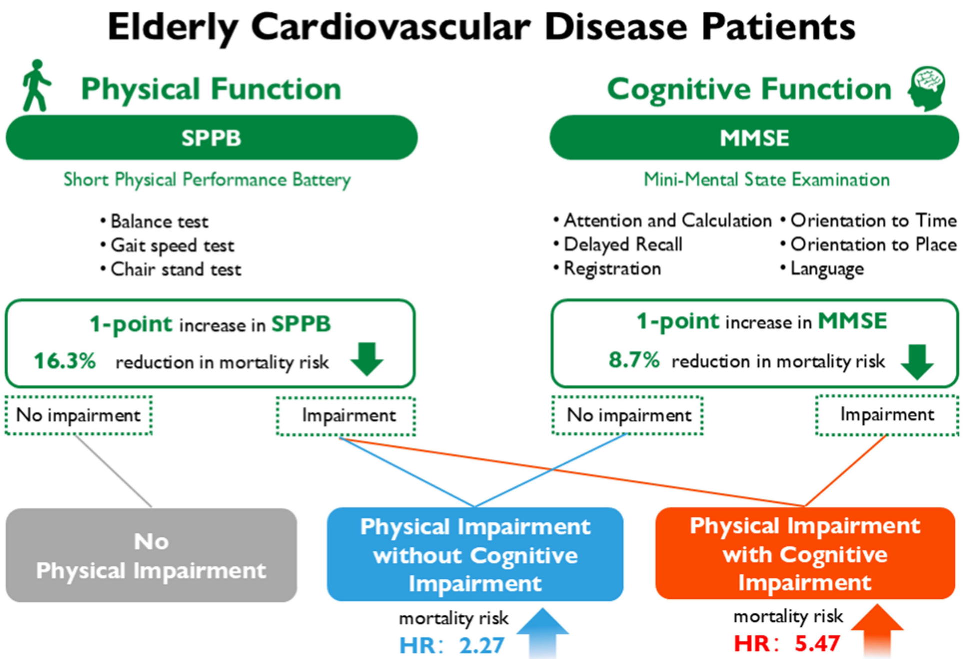
Graphical Abstract



research on the long-term impact of cognitive dysfunction in this population, particularly regarding how concurrent physical and cognitive impairments together influence long-term prognosis.

This study employs the Short Physical Performance Battery (SPPB) and the Mini-Mental State Examination (MMSE) to assess both physical and cognitive functions in elderly patients with CVD and track their long-term outcomes. The goal is to highlight the importance of evaluating both physical and cognitive impairments in this population and underscore the need for early, targeted interventions in high-risk individuals to improve long-term prognosis. By doing so, this study aims to guide clinical decision-making and enhance management strategies for elderly CVD patients.

Materials and Methods

Study Participants

We utilized data from a prospective observational cohort study on frailty conducted in China. The study recruited individuals who were consecutively admitted to three tertiary referral hospitals in Beijing between September 2018 and April 2019. Inclusion criteria were: (1) age 65 years or older; (2) hospitalized patients. Exclusion criteria were: (1) could not cooperate with the assessment procedure (such as severe dementia, deafness, unstable vital signs, etc); (2) refused to sign the informed consent; (3) patients with a life expectancy of 1 year or less (clinician-determined based on presence of a known terminal illness). For the current analysis, we enrolled 525 inpatients from the Department of Cardiology at Beijing Hospital, all diagnosed with cardiovascular disease. One patient was excluded from the MMSE assessment due to severe illness. Therefore, a total of 524 patients were included in this study, all of whom completed both the MMSE and SPPB assessments. The study was approved by the Ethics Committee of Beijing Hospital (Ethics Approval No. 2018BJYYEC-121-02) and registered in the Chinese Clinical Trial Registry (Registration No. ChiCTR1800017204). All participants provided written informed consent prior to enrollment, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Data collection, entry, and management were carried out using the electronic data capture system (REDCap), with oversight of the study progress and data quality provided by the Peking University Clinical Research Institute.[6]

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General Clinical Data and Data Management

All patients underwent fasting venous blood sampling within three days of enrollment. The following baseline data were collected from the study participants: (1) demographic characteristics: age, sex, years of education, smoking and alcohol consumption habits, and body mass index (BMI); (2) chronic disease history: history of hypertension, coronary artery disease, atrial fibrillation or atrial flutter (AF/AFL), stroke or transient ischemic attack (TIA), diabetes, dyslipidaemia, renal insufficiency, chronic lung disease, malignancy, and peripheral artery disease; and (3) laboratory data: serum levels of potassium, sodium, hemoglobin, albumin, blood glucose, glycated hemoglobin, total cholesterol, triglycerides, low-density lipoprotein (LDL), N-terminal pro-brain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hs-CRP), and D-dimer. For details on methods and devices, see supplementary materials. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula. Left ventricular ejection fraction (LVEF) was measured with the Vivid E9 ultrasound system (GE Vingmed Ultrasound, Horten, Norway), employing the biplane Simpson method in both the apical four-chamber and two-chamber views.

Assessment of Cognitive and Physical Function

The MMSE is widely used to assess overall cognitive decline because of its high sensitivity. It evaluates multiple cognitive domains, including orientation to time and place, memory, attention and calculation, recall, and language skills. The MMSE consists of 30 questions, with each correctly answered question earning 1 point. Lower scores indicate worse cognitive function. The scores are adjusted for education level: illiterate individuals scoring ≤17, those with a primary school education score ≤20, and individuals with junior high school education or higher scoring ≤24 are classified as having cognitive impairment.[7]

The SPPB is used to assess physical function and consists of three tests: (1) balance test: This test includes a side-by-side stand, a semi-tandem stand, and a tandem stand (heel-to-toe). The time at which a patient can maintain each position is recorded, with longer times resulting in higher scores. (2) gait speed test: This test measures the time taken to walk 4 meters at a usual pace; shorter times indicate better performance and higher scores. (3) chair stand test: This test assesses the time required to complete five chair stands with arms crossed over the chest; shorter times result in higher scores. Each test is scored out of 4 points, for a total possible score of 12 points, with higher scores indicating better physical function. Scores of ≤6 are considered indicative of physical function impairment.[8] All assessments were performed by skilled nurses and completed within three days of patient enrollment.

Follow-Up and Outcomes

Patients enrolled in the study were followed up at 3, 6, and 12 months after discharge, and annually thereafter, through outpatient visits or telephone interviews. During each follow-up, data on all-cause mortality and the exact time of death between follow-ups were collected. The primary outcome was all-cause mortality, with patients who died within 5 years considered to have a poor long-term prognosis. All-cause mortality was defined as death from any cause.

The start time was defined as the date when the patient signed the informed consent form, and the end time was defined as the date of death for those who experienced the event of interest. For patients who did not experience the endpoint event, the end time was the date of study termination, and for those lost to follow-up, the latest follow-up date was used. Survival time (in days) was calculated as the difference between the start and end times.

Statistical Methods

Multiple imputation for continuous variables was performed using predictive mean matching (PMM), and for categorical variables, logistic regression models were applied. Patients were classified into three groups on the basis of MMSE and SPPB scores: no physical function impairment, physical function impairment without cognitive impairment, and both cognitive and physical function impairment. The Kolmogorov–Smirnov (K-S) test was used to assess the normality of continuous variables. Continuous variables with a normal distribution were expressed as mean ± standard deviation (SD) and compared between groups using analysis of variance (ANOVA). Non-normally distributed continuous variables were expressed as medians and interquartile ranges, M (Q1, Q3), with group comparisons conducted using the Kruskal–Wallis *H*-test. Categorical variables were presented as frequencies and percentages, with group comparisons made using the Chi-square test. Kaplan-Meier survival curves were plotted for each group, and survival differences were analyzed using the Log rank test. The associations between cognitive impairment, physical function impairment, and all-cause mortality were assessed using the Cox proportional hazards regression model. Univariate Cox regression analysis was conducted on all potential influencing factors, followed by multivariate Cox regression analysis for variables that reached statistical significance in the univariate analysis (p<0.05). The models were structured as follows: (1) Model 1: Adjusted for age and sex only; (2) Model 2: Significant variables from univariate analysis were further optimized using stepwise forward and backward regression to identify the best combination of predictive variables; and (3) Model 3: Grouping of cognitive and physical function impairment replaced MMSE and SPPB scores, along with significant variables from Model 2, in the multivariate Cox regression analysis. The results were presented as hazard ratios (HRs) with 95% confidence intervals (CIs). Schoenfeld residual test was applied to check the proportional hazard (PH) assumptions. We used restricted cubic spline (RCS) models to examine the associations of MMSE or SPPB scores with mortality risk, adjusting for key covariates. HRs with 95% CIs were plotted to illustrate risk variations. Statistical tests were two-sided, with *P* values <0.05 considered statistically significant. Data analysis and visualization were performed using R version 4.4.1.

Results

Baseline Characteristics

A total of 524 patients age ≥65 years, hospitalized in the cardiology department, were included in this study. The average age was 75.18 ± 6.51 years, with 271 (51.7%) male patients, and 9.4% of the cohort were current smokers. Common comorbidities included hypertension in 383 (73.1%) patients, coronary artery disease in 359 (68.5%), diabetes in 187 (35.7%), AF/AFL in 118 (22.5%), stroke/TIA in 90 (17.2%), heart failure in 87 (16.6%) and chronic kidney disease in 36 (6.9%). The overall SPPB score was 8 (6, 10), with physical impairment observed in 148 (28.2%) patients. The MMSE score was 28 (26, 29), and cognitive impairment was identified in 65 (12.4%) patients.

Our study found that the majority of patients (n=354, 67.6%) had neither cognitive nor physical impairments, while a minority (n=22, 4.2%) had cognitive impairment without physical impairment. These patients were categorized into the "no physical impairment" group (n=376, 71.8%). Additionally, 43 patients (8.2%) had both cognitive and physical impairments, and 105 patients (20.0%) had physical impairment without cognitive impairment. Among those with physical impairment, 29.1% also exhibited cognitive impairment. In contrast, only 5.9% of those without physical impairment exhibited cognitive impairment. Notably, among patients with cognitive impairment, the majority (66.2%) also had physical impairment.

Patients in the group with both cognitive and physical impairments were significantly older, with an average age of 82.32 ± 5.02 years, compared with 73.68 ± 5.84 years in the group without either impairment. The years of education in the combined impairment group were significantly lower (8.16 ± 4.84 years) than in the other two groups. This group also had higher rates of heart failure, renal insufficiency, stroke/TIA, and peripheral artery disease, along with elevated levels of NT-proBNP, D-dimer, hs-CRP, fasting glucose, and hemoglobin A1c (HbA1c). Conversely, the levels of eGFR, albumin, hemoglobin, serum sodium, and LVEF were significantly lower in these patients. There were no significant differences among the three groups regarding the prevalence of AF/AFL, hypertension, coronary artery disease, diabetes, dyslipidemia, malignancy, or chronic lung disease, or in laboratory findings such as serum potassium and lipid profiles. Additional baseline characteristics are provided in Table 1.

Table 1 Baseline Information

	All Patients (n=524)	No Physical Impairment (n=376)	Physical Impairment without Cognitive Impairment (n=105)	Physical Impairment with Cognitive Impairment (n=43)	*P* value
Age, years	75.18 ± 6.51	73.68 ± 5.84	77.62 ± 6.65	82.32 ± 5.02	<0.001
Male	271 (51.7%)	198 (52.7%)	53 (50.5%)	20 (46.5%)	0.72
Widowed	85 (16.2%)	56 (14.9%)	15 (14.3%)	14 (32.6%)	0.01
Years of education, years	11.18 ± 4.18	11.59 ± 4.00	10.97 ± 3.99	8.16 ± 4.84	<0.001

(*Continued*)

Table 1 (Continued).

	All Patients (n=524)	No Physical Impairment (n=376)	Physical Impairment without Cognitive Impairment (n=105)	Physical Impairment with Cognitive Impairment (n=43)	*P* value
BMI, kg/m^2	25.23 ± 3.36	25.35 ± 3.29	25.48 ± 3.33	23.58 ± 3.59	0.003
Smoking	49 (9.4%)	40 (10.6%)	7 (6.7%)	2 (4.7%)	0.25
Alcohol consumption	33 (6.3%)	25 (6.6%)	7 (6.7%)	1 (2.3%)	0.53
Heart failure	87 (16.6%)	43 (11.4%)	24 (22.9%)	20 (46.5%)	<0.001
Coronary artery disease	359 (68.5%)	263 (69.9%)	72 (68.6%)	24 (55.8%)	0.17
Hypertension	383 (73.1%)	269 (71.5%)	80 (76.2%)	34 (79.1%)	0.42
AF/AFL	118 (22.5%)	76 (20.2%)	28 (26.7%)	14 (32.6%)	0.10
Stroke/TIA	90 (17.2%)	45 (12.0%)	27 (25.7%)	18 (41.9%)	<0.001
CKD	36 (6.9%)	19 (5.1%)	9 (8.6%)	8 (18.6%)	0.003
Peripheral arterial disease	92 (17.6%)	63 (16.8%)	15 (14.3%)	14 (32.6%)	0.02
Diabetes	187 (35.7%)	127 (33.8%)	38 (36.2%)	22 (51.2%)	0.08
Dyslipidemia	335 (63.9%)	244 (64.9%)	66 (62.9%)	25 (58.1%)	0.66
Malignancy	42 (8.0%)	24 (6.4%)	13 (12.4%)	5 (11.6%)	0.09
Hemoglobin, g/L	128.82 ± 15.72	130.82 ± 14.72	125.02 ± 16.50	120.63 ± 17.71	<0.001
K, mmol/L	4.09 ± 0.38	4.07 ± 0.36	4.15 ± 0.41	4.14 ± 0.43	0.12
Na, mmol/L	140.90 ± 2.88	141.17 ± 2.44	140.50 ± 3.19	139.55 ± 4.63	<0.001
eGFR, mL/min/1.73 m^2	71.93 ± 23.90	74.63 ± 21.99	71.20 ± 25.80	50.07 ± 23.72	<0.001
Albumin, g/L	39.79 ± 2.99	40.14 ± 2.81	39.27 ± 2.90	38.02 ± 3.80	<0.001
Triglycerides, mmol/L	1.30 ± 0.76	1.31 ± 0.77	1.27 ± 0.78	1.22 ± 0.55	0.663
Total cholesterol, mmol/L	3.75 ± 0.91	3.77 ± 0.88	3.78 ± 1.05	3.49 ± 0.71	0.137
LDL, mmol/L	2.21 ± 0.73	2.22 ± 0.69	2.24 ± 0.88	2.05 ± 0.61	0.312
Blood glucose, mmol/L	5.98 ± 1.86	5.83 ± 1.63	6.14 ± 1.84	6.91 ± 3.10	<0.001
HbA1c, %	6.61 ± 1.06	6.54 ± 1.01	6.71 ± 1.08	7.02 ± 1.32	0.01
D-dimer, ng/mL	206.86 ± 357.47	170.63 ± 254.28	222.63 ± 270.43	485.16 ± 850.72	<0.001
hs-CRP, mg/dl	3.64 ± 11.21	2.87 ± 7.81	3.85 ± 16.22	9.94 ± 17.59	<0.001
LVEF, %	60.81 ± 8.36	61.38 ± 7.73	61.04 ± 7.98	55.35 ± 11.87	<0.001
NT-proBNP, pg/mL	171.40 (76.06, 532.95)	150.55 (67.62, 337.43)	245.90 (81.67, 756.10)	1133.00 (322.55, 1849.00)	<0.001
SPPB	8 (6, 10)	9 (8, 11)	5 (3, 6)	2 (0, 4)	<0.001
MMSE	28 (26, 29)	28 (27, 29)	28 (27, 29)	18 (14.5, 22.5)	<0.001

Notes: Baseline patient and hospital characteristics of elderly CVD patients by cognitive and physical impairment groups.
Abbreviations: BMI, body mass index; AF/AFL, atrial fibrillation or atrial flutter; TIA, transient ischemic attack; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; hs-CRP, high-sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; SPPB, Short Physical Performance Battery; MMSE, Mini-Mental State Examination; CVD, cardiovascular disease.

Prognostic Analysis of Elderly Cardiovascular Disease Inpatients

A total of 491 patients completed the 5-year follow-up, with a total loss rate of 6.3%. The overall survival time for the patients ranged from 21 to 1976 days, with a median survival time of 1871 (1816, 1920) days. During the follow-up period, 13.7% (72 patients) experienced all-cause mortality. Patients without physical impairment had survival times ranging from 21 to 1976 days, with a median survival time of 1871 (1816, 1920) days. Those with physical impairment but no cognitive impairment had a survival time of 116 to 1976 days, with a median survival time of 1833 (1144, 1939) days. Patients with both physical and cognitive impairments had a survival time of 28 to 1946 days, with a median survival time of 1041 (436, 1498) days. There were significant differences in survival curves among the three groups, with patients with both cognitive and physical impairments showing a higher and earlier incidence of all-cause mortality (Log rank test, p<0.001) (Figure 1).

Univariate Cox regression analysis showed that both SPPB and MMSE scores were significantly associated with all-cause mortality (p<0.001), along with other predictors such as age, BMI, creatinine, serum sodium, and hs-CRP. (1) Model 1: After adjusting for age and sex, each additional year of age increased the risk of death by 17.7% (HR: 1.18, 95% CI: 1.13–1.22, p<0.001). Sex had no significant effect on all-cause mortality. (2) Model 2: In the multivariate Cox regression, incorporating significant variables from the univariate analysis through stepwise forward and backward selection, two models were derived—one with MMSE scores and the other with SPPB scores—along with age, BMI, creatinine, serum sodium, and hs-CRP. Each 1-point increase in the SPPB score was associated with a 16.3% reduction in mortality risk (HR: 0.84, 95% CI: 0.78–0.91, p<0.001), while each 1-point increase in MMSE score was associated with an 8.7% reduction in mortality risk (HR: 0.91, 95% CI: 0.86–0.96, p<0.001). (3) Model 3: In the analysis, patients were grouped by the presence of cognitive and/or physical impairments, and stepwise regression was used to establish a model incorporating cognitive-physical function groupings, age, BMI, creatinine, serum sodium, and hs-CRP. Compared with the group without physical impairment, the group with physical impairment but no cognitive impairment had a 2.27-fold increased risk of mortality (HR: 2.27, 95% CI: 1.20–4.29, p=0.012). The group with both physical and cognitive impairments had a 5.47-fold increased mortality risk (HR: 5.47, 95% CI: 2.78–10.78, p<0.001), with significant differences observed across all three groups. Restricted cubic spline analysis revealed an inverse relationship between SPPB and MMSE scores and mortality risk. Higher SPPB and MMSE scores, indicating improved cognitive and physical function, were associated with a reduced hazard ratio for mortality (Figure 2).

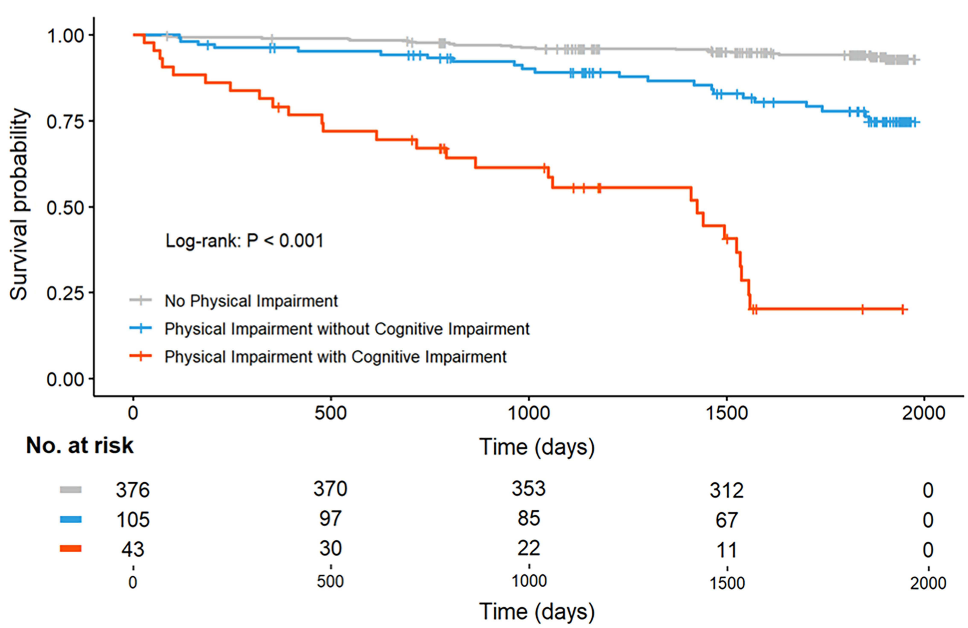

Figure 1 Kaplan-Meier survival curves stratified by physical and cognitive impairment status.

Notes: Kaplan-Meier survival curves illustrating the impact of physical and cognitive impairment status on survival. Individuals with both physical and cognitive impairments have the lowest survival, while those with no impairments show the highest survival. Statistical significance was observed among groups (Log rank test, p < 0.001).

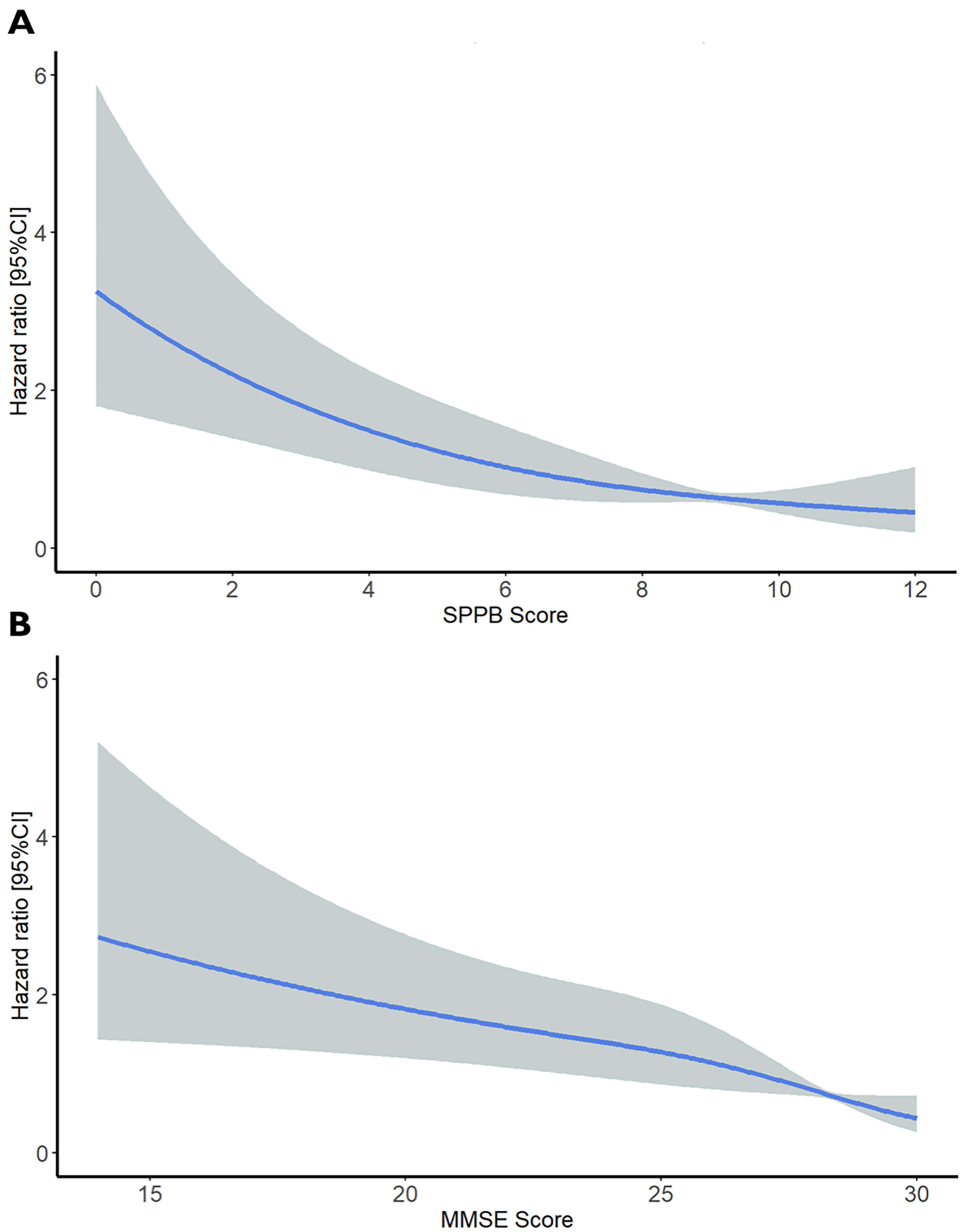

Figure 2 Restricted cubic spline analysis of SPPB scores or MMSE scores and hazard ratio for mortality.
Notes: (**A**) illustrates the association between SPPB (Short Physical Performance Battery) scores and hazard ratio for mortality. (**B**) shows the association between MMSE (Mini-Mental State Examination) scores and hazard ratio for mortality. As SPPB or MMSE scores increase, the mortality risk progressively decreases.

ROC analysis was conducted to evaluate the discriminative ability of the SPPB score and the combined score (MMSE + SPPB) in predicting study endpoints among all participants. Incorporating MMSE into the SPPB model resulted in a significant improvement in area under the curve (AUC) from 0.78 to 0.81, emphasizing the advantage of integrating cognitive and physical performance measures. At the optimal cut-off point of 33.5 for the combined score, the sensitivity and specificity were 76.4% and 77.2%, respectively. Notably, these findings highlight the potential utility of the combined score in improving the prediction of 5-year all-cause mortality (Figure S1).

In MMSE subdomains, deceased patients scored significantly lower in orientation to time, orientation to place, attention and calculation, delayed recall, and language abilities compared to survivors, except for registration, where no significant difference was found ($p>0.05$). Multivariate Cox regression analysis revealed that impaired attention and calculation ability was significantly associated with mortality ($p<0.001$) (Figure 3).

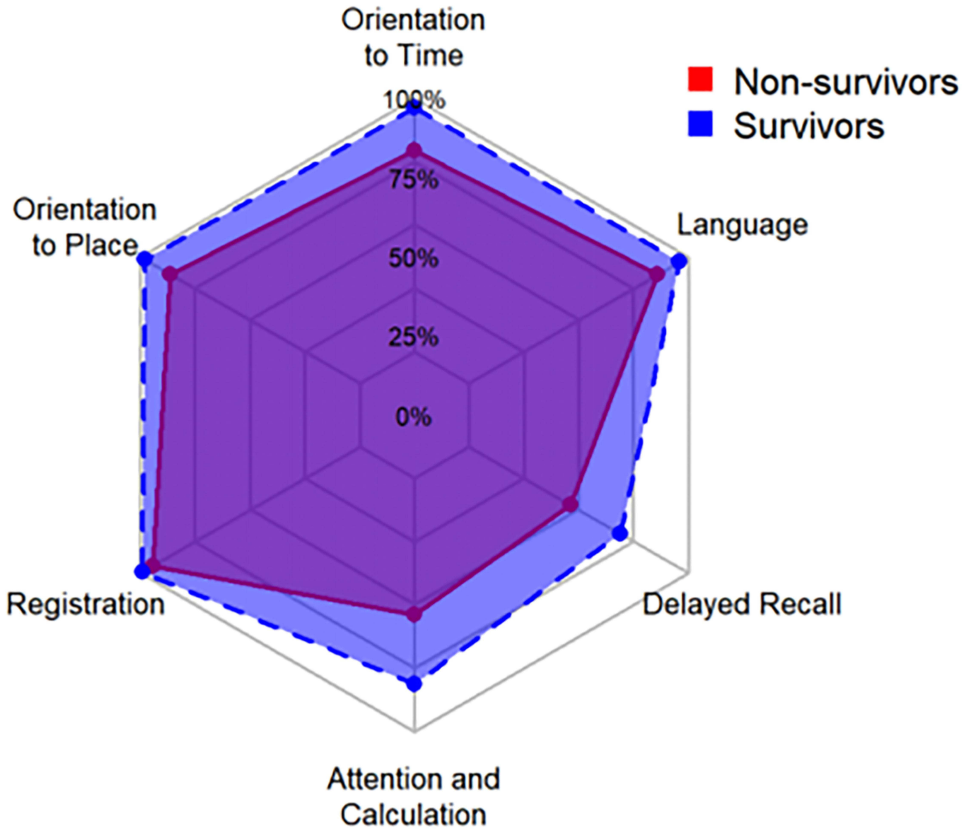

Figure 3 Cognitive domain scores in non-survivors vs survivors.
Notes: This radar chart compares cognitive subdomain scores—Orientation to Time, Orientation to Place, Registration, Attention and Calculation, Delayed Recall, and Language—between non-survivors and survivors, based on MMSE (Mini-Mental State Examination) assessment.

Discussion

CVD are among the most prevalent chronic conditions in elderly individuals and remain one of the leading causes of death worldwide. Physical dysfunction is common in patients with CVD and is often linked to poor prognosis. In 2024, the American Heart Association (AHA) issued a statement discussing the increased risk of cognitive impairment and dementia associated with heart failure, AF, and coronary artery disease. The findings highlighted the connection between these cardiovascular conditions and brain health, emphasizing their potential impact on cognitive function and the increased risk of dementia.[5] However, cognitive function is frequently overlooked in clinical practice, and the long-term impact of coexisting physical and cognitive impairments on the prognosis of CVD patients remains unclear. In this study, we used both the SPPB and the MMSE to assess physical and cognitive functions, respectively, and followed the patients to evaluate their long-term outcomes. Our findings emphasize the importance of assessing both physical and cognitive impairments in elderly patients with CVD, offering valuable insights for the clinical management and treatment of this population.

Physical function refers to the body's ability to perform daily activities and movements, encompassing strength, endurance, balance, flexibility, and coordination. In patients with CVD, factors such as cardiac dysfunction, inflammatory responses, neurohumoral dysregulation, and increased vascular resistance lead to inadequate muscle perfusion, resulting in reduced exercise tolerance and physical dysfunction. The cumulative effect of CVD risk factors further exacerbates these physical impairments.[9–11] In this study, the SPPB, as recommended by the Asian Working Group for Sarcopenia, was used to assess physical function in elderly CVD inpatients. The median SPPB score was 8 (6, 10), with 28.2% of patients exhibiting varying degrees of physical dysfunction. These findings are consistent with the studies conducted by Hashimoto et al and Kitai et al, respectively, highlighting the high prevalence of physical impairments among elderly CVD patients.[12,13]

Cognition refers to the ability of the brain to process external information and transform it into internal psychological functions for acquiring and applying knowledge. This encompasses various aspects, such as memory, language, executive function, attention and calculation, and comprehension. CVD can disrupt cerebral perfusion, leading to brain atrophy and cognitive decline. Additionally, factors such as thromboembolism, oxidative stress, inflammatory responses, and neurohumoral mechanisms are pivotal in the onset and progression of cognitive impairment.[14] In this study, cognitive function was assessed using the widely used MMSE, which is known for its simplicity and high patient compliance, making it ideal for clinical application. Our results revealed that 12.4% of hospitalized elderly CVD patients experienced cognitive impairment, with a median MMSE score of 28 (26, 29), which aligns with the findings reported in the study by Hashimoto et al.[12] Our study found that the risk of cognitive impairment varied across different types of CVD, with prevalence rates ranging from 10% to 20%. Multiple meta-analyses have demonstrated that heart failure increases the risk of cognitive decline by 60%, AF by 36%, and coronary artery disease by 45%.[15,16] Variations in cognitive impairment rates among CVD likely reflect distinct pathophysiological mechanisms, highlighting the complex relationship between cardiovascular and cognitive health and underscoring the need for targeted, disease-specific interventions.[5]

Our study revealed that 8.2% of patients experienced both physical and cognitive impairments, underscoring a strong association between these two conditions. On one hand, the current study demonstrates that physical activity enhances cerebral blood flow, improves cerebrovascular endothelium, and reduces inflammatory processes, among other benefits.[17] Physical impairments increase the risk of metabolic diseases, which in turn heighten the likelihood of developing cognitive impairments.[18] On the other hand, cognitive impairments can lead to neuronal changes in the central nervous system, altering neurotransmitter levels and activity. These brain changes may reduce motor unit recruitment and hinder muscle activation, potentially connecting cognitive decline with sarcopenia.[19] Therefore, these mechanisms may explain the close relationship between cognitive impairments and physical impairments.

Our study demonstrates that the prevalence of physical impairment (28.2%) is higher than that of cognitive impairment (12.4%) among elderly hospitalized CVD patients. A previous study found that a decline in physical function precedes the decline in cognitive function in older adults.[20] Thus, physical impairment is more prevalent than cognitive impairment in elderly inpatients. Furthermore, our study found that only 5.8% of patients with good physical function exhibited cognitive impairment, whereas 29.1% of those with physical impairment also had cognitive decline. This highlights the importance of assessing cognitive function in patients with physical dysfunction to identify those at greater clinical risk. Our study also showed that the majority (66.2%) of patients with cognitive impairment also had physical impairment. Since the SPPB assessment includes tasks that rely on cognitive function, cognitive decline can directly affect a patient's ability to follow instructions, thereby influencing physical performance. Therefore, the proportion of physical impairments is high among patients with cognitive impairments.

This study found that only 22 patients (4.2%) had cognitive impairment without physical impairment. This low proportion may be related to the generally small number of patients with isolated cognitive impairment in the cardiology department. Based on these findings, we classified the patients into three groups: those without physical impairments, those with physical impairments but without cognitive impairments, and those with both cognitive and physical impairments. A comparison between these groups revealed that older age and fewer years of education were associated with a higher likelihood of exhibiting both cognitive and physical impairments, consistent with the findings reported in the study by Yao et al.[21] This highlights the importance of prioritizing the evaluation of both cognitive and physical function in older and less-educated patients. Additionally, patients with heart failure and renal insufficiency showed a higher incidence of combined cognitive and physical impairments, emphasizing the need for more comprehensive assessments of both functions in these populations.

Our study found that NT-proBNP level was significantly higher in the group with both cognitive impairments and physical impairments compared to the other two groups. Elevated NT-proBNP levels indicate impaired cardiac function. Patients with compromised cardiac function often exhibit reduced physical capabilities and are also more prone to cognitive dysfunction. A study from Japan suggested that elevated serum NT-proBNP levels were associated with gray matter atrophy in brain regions critical for cognitive function.[22] Additionally, the group with both cognitive and physical impairments exhibits higher hs-CRP levels, which reflect systemic inflammation. On one hand, systemic inflammation can damage muscle structure and function, ultimately reducing muscle mass, strength, and physical performance.[23] On the other hand, it may disrupt the blood-brain barrier, leading to excessive activation of microglia and astrocytes, which ultimately contributes to cognitive impairment.[24] The group with combined impairments also exhibited lower levels of albumin, hemoglobin, and sodium, along with elevated levels of blood glucose, HbA1c, and D-dimer. These findings suggest that nutritional interventions should be prioritized, blood glucose levels should be closely monitored, and prevention of lower extremity thrombosis should be emphasized.

This study demonstrates that both physical and cognitive impairments are linked to poor long-term prognosis in elderly CVD patients. For each 1-point increase in the SPPB or MMSE score, the risk of death was significantly reduced. Previous studies have evaluated cognitive and physical function separately, finding that impairments in either domain are associated with a poor prognosis, which is consistent with the findings of our study.[25–30] The reduction in mortality risk was most prominent at lower MMSE and SPPB scores, with the curve leveling off at higher scores. This suggests a diminishing effect of cognitive and physical function on mortality risk as scores increase. These findings indicate a non-linear protective effect of cognitive and physical abilities on survival, potentially offering greater survival benefits for individuals with lower baseline scores.

A subgroup analysis revealed that, compared with the group without physical impairments, the mortality risk in the group with physical impairments but no cognitive impairments was 2.27 times higher. The group with both cognitive and physical impairments had a mortality risk 5.47 times higher, with significant differences observed among the three groups. In contrast, the study by Fujita et al found that SPPB was significantly associated with increased 1-year mortality in patients with cognitive impairments, but no such association was observed in those with normal cognitive function.[31] The study by Ament et al found that among patients with physical impairments, those with cognitive impairments did not show a significant increase in the risk of rehospitalization one year later.[32] These discrepancies may be attributed to the relatively short follow-up periods in those studies. Our study, which included a 5-year follow-up, revealed that physical and cognitive impairments significantly affect long-term prognosis. Patients with physical impairments have worse outcomes, whereas those with both cognitive and physical impairments experienced even poorer long-term prognoses.

Early identification of physical impairments and timely interventions, such as exercise training and rehabilitation programs, can delay or even reverse their progression, thereby improving patients' quality of life and long-term prognosis.[33–37] However, once cognitive impairments develop in CVD patients, medication adherence and compliance with rehabilitation therapy are significantly compromised, leading to higher rates of hospitalization and mortality.[38] Currently, cognitive function is not routinely screened in cardiology departments, underscoring the need to assess cognitive function in patients with physical impairments to identify those with combined cognitive and physical impairments. Simultaneous cognitive and physical training can further enhance overall quality of life and clinical outcomes in these patients.[39–41]

Within MMSE assessments, attention and calculation are complex cognitive functions closely linked to frontal lobe activity and involve coordination across multiple brain regions. These elements are among the most challenging MMSE components and often serve as early indicators of cognitive decline.[42–44] This study revealed a significant association between impairments in attention and calculation and increased mortality risk. Similarly, previous studies have highlighted the correlation between deficits in these cognitive domains and elevated mortality among older adults.[42,45,46] Clinically, incorporating the attention and calculation components of the MMSE as part of preliminary screening could aid in the early identification of high-risk patients. Those with lower scores may benefit from closer monitoring and more tailored rehabilitation interventions.

Limitations

Our study investigates the combined impact of cognitive and physical impairments on long-term mortality in elderly patients with CVD, highlighting the importance of integrated assessments in improving patient outcomes. However, this study had some limitations. First, it is a single-center study with a relatively small sample size, so future research should include larger, more diverse populations to yield more reliable results. Second, for feasibility, this study, like other cognitive assessment studies, excluded patients with severe dementia who were unable to cooperate with the assessments, which may have introduced some bias into the results. Additionally, whether separate interventions targeting physical and cognitive impairments in patients with both conditions can provide clinical benefits warrants further investigation.

Conclusions

This study revealed a high prevalence of both physical and cognitive impairments among elderly hospitalized CVD patients, with those having combined impairments showing significantly worse long-term outcomes. Notably, in the assessment of cognitive function, attention and calculation ability was found to be significantly associated with long-term prognosis. Therefore, in elderly CVD patients with physical impairments, it is crucial to prioritize cognitive function screening and implement targeted, personalized interventions to enhance cognitive abilities such as attention and calculation. This approach may help improve the quality of life and long-term outcomes of these patients.

Abbreviations

CVD, cardiovascular disease; SPPB, Short Physical Performance Battery; MMSE, Mini-Mental State Examination; BMI, body mass index; AF, atrial fibrillation; AFL, atrial flutter; TIA, transient ischemic attack; LDL, low-density lipoprotein; NT-proBNP, N-terminal pro-brain natriuretic peptide; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; LVEF, Left ventricular ejection fraction; PMM, predictive mean matching; K-S, Kolmogorov–Smirnov; SD, standard deviation; ANOVA, analysis of variance; HRs, hazard ratios; CIs, confidence intervals; PH, proportional hazard; RCS, restricted cubic spline; HbA1c, hemoglobin A1c; AUC, area under the curve; AHA, American Heart Association.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The trial was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and the research protocol was approved by the Ethics Committee of Beijing Hospital (ID number: 2018BJYYEC-121-02). Written informed consent was obtained from the patients or their legal representatives.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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