Research article

Association between functional dependence and cardiovascular disease among middle-aged and older adults: Findings from the China health and retirement longitudinal study

Yaxi Yang [a,1], Chaonian Li [b,1], Ye Hong [b], Jinqi Sun [b], Guoping Chen [b,c,**], Kangkang Ji [a,b,d,*]

[a] College of Life Science and Technology, Huazhong Agricultural University, Wuhan, Hubei, 430070, China
[b] Department of Clinical Medical Research, Binhai County People's Hospital, Clinical Medical College of Yangzhou University, Yancheng, Jiangsu, 224500, China
[c] Institute of Translational Medicine, Yangzhou University, Yangzhou, Jiangsu, 225002, China
[d] College of Biomedicine and Health, Huazhong Agricultural University, Wuhan, Hubei, 430070, China

ARTICLE INFO

ABSTRACT

Background: The effect of different functional dependency types on cardiovascular disease (CVD) is largely unknown. Here, we aimed to investigate the association between functional dependence and CVD among middle-aged and older adults by conducting a cross-sectional and longitudinal study.

Methods: The study sample comprised 16,459 individuals of ≥40 years (including 10,438 without CVD) who had participated in the 2011 China Health and Retirement Longitudinal Study (CHARLS). Functional dependence was categorized based on the "interval-of-need" method, while CVD was defined as physician-diagnosed heart disease or stroke. Cox proportional hazard regression was employed to assess the effects of functional dependence on CVD. Moreover, patients were grouped according to the functional status changes, and the impact of these changes on CVD was observed. Heterogeneity, subgroup, and interaction analyses were used to evaluate the consistency of the study findings. Finally, a mediation analysis was performed to estimate the potential mediation effects on the relationship between functional dependence and CVD risk.

Results: CVD prevalence in the overall study population was 13.73 % (2260/16,459), while its prevalence among individuals with functional independence, low dependency, medium dependency, and high dependency was 9.60 % (1085/11,302), 14.25 % (119/835), 17.72 % (115/649), and 25.01 % (941/3763), respectively. Additionally, medium (odds ratio: 1.33, 95 % confidence interval: 1.06–1.68) and high functional dependency (1.55, 95 % CI: 1.38–1.75) were associated with CVD. A total of 2987 (28.62 %) participants with CVD were identified during the 9-year follow-up, with 4.85 % (145/2987) of the CVD cases being attributed to functional dependence. The individuals with medium (HR: 1.20, 95 % CI: 1.01–1.44) and high functional dependency (1.25, 95 % CI: 1.14–1.37) were more likely to develop CVD than their peers with functional independence. Furthermore, persistent functional dependence (HR: 1.72, 95 % CI:

* Corresponding author. Kangkang Ji Huazhong Agricultural University, China.
** Corresponding author. Department of Clinical Medical Research, Binhai County People's Hospital, Clinical Medical College of Yangzhou University, Yancheng, Jiangsu, 224500, China.
E-mail addresses: cgp20212021@163.com (G. Chen), kyrie@mail.ustc.edu.cn (K. Ji).
[1] Yaxi Yang and Chaonian Li contributed equally to this work.

1.52–1.94) and transition from functional independence to dependence (1.79, 95 % CI: 1.61–1.98) were associated with a higher CVD risk than continuous functional independence. Hypertension and diabetes may partially mediate CVD caused by functional dependence.

Conclusion: Functional dependence is associated with high CVD risk. Therefore, appropriate healthcare attention must be directed towards functionally dependent populations to protect their cardiovascular health.

1. Introduction

The continuing demographic shift towards an older population across almost every country worldwide has led to the emergence of functional dependence as a popular indicator of quality of life and health status [1]. Functional dependence is defined as a substantial impairment of an individual's ability to effectively perform physical activities and routine tasks, including mobility and household chores. This impairment is commonly experienced by middle-aged and older adults, posing a prominent concern to global public health [2,3]. The prevalence of functional dependence among individuals aged ≥60 years is estimated at 14.3 % in China, whereas this prevalence has reached 20 % in European countries [4]. Previous studies have also reported on the adverse effects of functional dependence, such as long-term care and hospitalization [5,6], suicidal ideation [7], depressive symptoms [8,9], cognitive dysfunction [10], comorbidity burden [11], and chronic diseases [12], as well as the heavy burden that these effects can place on families and society. Conversely, functional independence provides benefits beyond improving the quality of life, encompassing an enhanced health status and decreased medical stress.

Cardiovascular disease (CVD) is the leading cause of death worldwide [13,14]. In 2022, the age-standardized mortality rate of CVD ranged from 73.6 per 100,000 individuals in the high-income Asia-Pacific nations to 432.3 per 100,000 in Eastern Europe [15]. Although the clinical symptoms of CVD typically manifest later in life, the natural history of this disease begins decades earlier [16]. A growing number of recent studies have implied an association between functional dependence and CVD; however, their exact relationship requires further elucidation [12,17–19]. Moreover, functional status changes have been observed at least 2 years prior to CVD hospitalization events, but a causal association remains to be established [20]. Additionally, most previous studies were either cross-sectional designs focusing on a single population and without a detailed categorization of functional dependence or prospective investigations considering only functional status type at baseline and not the functional status changes during follow-up. To date, scarce cross-sectional and longitudinal studies have examined the association between various types of functional dependencies and CVD. Furthermore, only a few studies have unveiled potential mediators between functional dependence and CVD. Nevertheless, CVD burden due to functional dependence has still not been quantified from a population-attributable perspective. Considering these existing research gaps, we hypothesized that functional dependence would lead to increased CVD risk and that transitioning from functional dependence to independence might diminish this risk.

In the current study, we conducted cross-sectional and longitudinal analyses to explore the association between the distinct types of functional dependencies and CVD in the middle-aged and older populations in China using nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS). Our investigation focused on the effect of changes in the functional dependency status on CVD outcomes during follow-up. We also performed subgroup and interaction analyses to determine the groups more likely to experience functional dependence in the context of CVD. Lastly, we conducted mediation analyses to identify the potential mechanisms and estimated the attributable burden of CVD due to functional dependence. We hope our study findings will provide a solid basis for developing strategies to improve functional dependence and reduce the CVD burden.

2. Methods

2.1. Study population

CHARLS is a nationally representative longitudinal survey conducted in China using a multi-stage stratified probability-proportionate-to-size sampling method [21]. Briefly, the survey population is primarily aged ≥45 years, along with some participants of <45 years to facilitate long-term follow-up. All participants were administered a standardized questionnaire to collect data, including socio-demographic characteristics, lifestyle factors, and health-related information [22]. The national baseline survey was conducted in 2011, with four follow-ups conducted in 2013, 2015, 2018, and 2020. The CHARLS surveyed participants belonging to 10,257 households from 150 counties/districts and 450 rural/urban communities across the country. All participants enrolled voluntarily and provided informed consent before participating in the study. Ethical approval for the CHARLS survey was obtained from the Ethical Review Committee at Peking University in June 2008 (IRB00001052-11015). This investigation conforms to the principles outlined in the Declaration of Helsinki. CHARLS follows the reporting guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [23].

In this study, 2011 was considered the baseline year, and the follow-up period consisted of the subsequent 9 years. The inclusion criteria for the study participants were as follows: 1) baseline age of ≥40 years; 2) availability of data on functional dependency status (including basic activities of daily living [BADL] and instrumental activities of daily living [IADL]); and 3) availability of CVD data. Participants were excluded if they met any of the following exclusion criteria: 1) missing data on functional dependency status and CVD in 2011; 2) age <40 years; 3) missing demographic information characteristics such as age, sex, and education level; and 4)

missing data on other important covariates. The final sample sizes in this study were 16,459 participants for the cross-sectional investigation and 10,438 for the longitudinal assessment. The detailed selection process of the study participants is shown in Fig. 1.

2.2. Assessment of functional dependency status

In this study, functional dependence was defined as a participant's inability to independently perform BADL and IADL. BADL involve daily physical tasks, including eating, dressing, getting in/out of bed, using the toilet, bathing, and walking [24], while IADL entail more complex activities necessary for living independently, such as preparing hot meals, taking medications, managing money, shopping, and cleaning the house [25]. The total scores of the BADL and IADL items were determined by the participant responses to the question, "Do you have difficulty with any of these items?" Each item could be responded to with the following four options: (1) "No, I do not have any difficulty," (2) "I have difficulty but can still do it," (3) "Yes, I have difficulty and need help," and (4) "I cannot do it." The first option was scored as 0 points, while the remaining three were scored as 1 point, amounting to total scores of 6 and 5 points for BADL and IADL, respectively. Functional dependency was categorized based on the "interval-of-need" method developed by Isaacs and Neville [26]. This measure divides the functional dependency types according to the various care need categories in England [27], specifically classified as "high dependency" (requiring around-the-clock care), "medium dependency" (necessitating care several times per day), "low dependency" (needing care less than once a day), or "independent" (not requiring care) (Table S1).

2.3. Assessment of CVD events

CVD was defined as a diagnosis of heart disease or stroke following previously published studies [28–30]. CVD events were assessed via the question: "Have you ever been diagnosed with a heart disease (heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems) or stroke?" Participants who responded affirmatively to a heart disease or stroke diagnosis were considered to have CVD.

2.4. Covariates and mediators

The notable health-related risk factors for CVD included hypertension [31], dyslipidemia [32], diabetes [33], chronic kidney diseases [34], chronic liver disease [35], and psychiatric problems [36]. Socio-demographic variables comprised age (continuous variable), sex (male or female), residence (rural or urban), education level (i.e., "<MS" [elementary school or below], "MS" [middle school], or "HS or HS+" [high school and above]), and marital status (married or other [never married, separated, divorced, or widowed]). Health-related factors consisted of smoking status (no or yes), alcohol consumption status (no or yes), self-assessed health
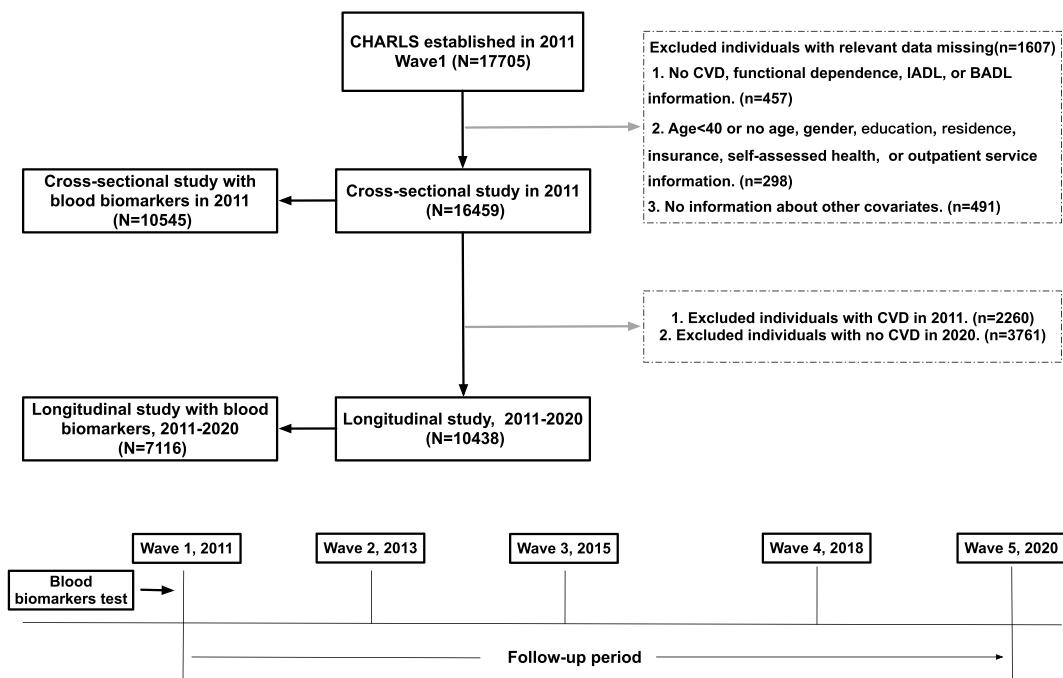
Figcc 1. Flow diagram of the participant selection process in the study.
Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; CVD, cardiovascular disease; BADL, basic activities of daily living; IADL, instrumental activities of daily living.

(extremely poor, poor, fair, good, or extremely good), insurance (no or yes), hospital visits (whether hospitalized in the past year, [no or yes]), and outpatient service (whether utilized outpatient services in the last year, [no or yes]). In the cross-sectional analysis, a subgroup of 10,545 participants underwent measurement of numerous blood biomarkers, including white blood cells, mean corpuscular volume, platelets, blood urea nitrogen, glucose, creatinine, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, C-reactive protein, glycated hemoglobin, uric acid, and hemoglobin.

2.5. Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile range), whereas categorical variables are expressed as numerical values (percentages). Baseline characteristics in the cross-sectional and longitudinal analyses were compared according to the functional dependence categories using the chi-square test, analysis of variance, and Tukey's test, as appropriate. In the cross-sectional analysis, the odds ratios (ORs) and corresponding 95 % confidence intervals (CIs) were calculated to assess the associations of functional dependence with CVD and its components using logistic regression, and these relationships were validated using the four waves of data collected in 2013, 2015, 2018, and 2020. In the longitudinal analysis, CVD incidence per 1000 person-years during the follow-up period from 2011 to 2020 was calculated after grouping according to age, sex, and place of residence. Furthermore, the follow-up time was recorded, and a Cox proportional hazards model was applied to estimate the association between baseline functional status and CVD incidence, with the results described as hazard ratios (HRs) and 95 % CIs. Moreover, given that the functional dependency status of the participants may have changed during the follow-up period, we performed a more comprehensive classification of the functional dependency status. Consequently, functional dependency status was categorized into persistent functional independence, functional dependence converted to functional independence, functional independence transitioned to functional dependence, and persistent functional dependence, and these categories underwent further analysis with a Cox proportional hazards model.

Next, we performed subgroup and interaction analyses by employing the baseline characteristics as moderators and evaluated the potential differences in the impact of functional dependence on CVD across different subgroups. Further, mediation analyses were conducted utilizing the "mediation" R package, which employed a quasi-Bayesian Monte Carlo simulation method with 1000 iterations. In this analysis, the average direct effect represented the effect of baseline functional dependence on CVD, excluding mediating

Table 1
Baseline characteristics of all participants according to functional dependency status.

Characteristic	Independent (N = 11,302)	Low dependency (N = 835)	Medium dependency (N = 649)	High dependency (N = 3673)	P
Age, (mean $\pm$ SD, years)	57.2 $\pm$ 9.0	60.0 $\pm$ 9.5[c]	61.2 $\pm$ 10.4[c]	64.7 $\pm$ 10.8[c]	**<0.001**
Male, n (%)	5870 (51.9)	338 (40.5)[c]	311 (47.9)[a]	1431 (39.0)[c]	**<0.001**
Rural (vs urban)	9894 (87.5)	784 (93.9)[c]	591 (91.1)[b]	3406 (92.7)[c]	**<0.001**
Education level, n (%)					**<0.001**
Elementary school or below	6731 (59.6)	694 (83.1)[c]	476 (73.3)[c]	3032 (82.5)[c]	
Middle school	2744 (24.3)	101 (12.1)[c]	121 (18.6)[c]	450 (12.3)[c]	
High school and above	1827 (16.2)	40 (4.8)[c]	52 (8.0)[c]	191 (5.2)[c]	
Married (vs others)	10,250 (90.7)	714 (85.5)[c]	531 (81.8)[c]	2898 (78.9)[c]	**<0.001**
Smoking, n (%)	4671 (41.3)	313 (37.5)[a]	258 (39.8)	1303 (35.5)[c]	**<0.001**
Drinking, n (%)	4918 (43.5)	330 (39.5)[a]	278 (42.8)	1271 (34.6)[c]	**<0.001**
Self-assessed health, n (%)					**<0.001**
Very poor	182 (1.6)	41 (4.9)[c]	58 (8.9)[c]	512 (13.9)[c]	
Poor	1707 (15.1)	208 (24.9)[b]	205 (31.6)[c]	1625 (44.2)[c]	
Fair	6008 (53.2)	442 (52.9)[c]	296 (45.6)[c]	1273 (34.7)[c]	
Good	2466 (21.8)	110 (13.2)[c]	74 (11.4)[c]	209 (5.7)[c]	
Very good	939 (8.3)	34 (4.1)[c]	16 (2.5)[c]	54 (1.5)[c]	
Insurance, (Yes, n, %)	10,358 (93.7)	789 (94.5)	591 (91.1)[b]	3414 (92.9)	**0.02**
Hospital, (Yes, n, %)	754 (6.7)	75 (9.0)[a]	87 (13.4)[c]	656 (17.9)[c]	**<0.001**
Outpatient service, (Yes, n, %)	1720 (15.2)	166 (19.9)[c]	157 (24.2)[c]	990 (27.0)[c]	**<0.001**
Hypertension, (Yes, n, %)	2347 (20.8)	214 (25.6)[b]	172 (26.5)[b]	1289 (35.1)[c]	**<0.001**
Dyslipidemia, (Yes, n, %)	942 (8.3)	83 (9.9)	70 (10.8)[a]	432 (11.8)[c]	**<0.001**
Diabetes, (Yes, n, %)	514 (4.5)	52 (6.2)[a]	50 (7.7)[c]	332 (9.0)[c]	**<0.001**
Chronic liver disease, (Yes, n, %)	349 (3.1)	45 (5.4)[c]	33 (5.1)[b]	208 (5.7)[c]	**<0.001**
Chronic kidney disease, (Yes, n, %)	580 (5.1)	55 (6.6)	52 (8.0)[b]	359 (9.8)[c]	**<0.001**
Psychiatric problems, (Yes, n, %)	71 (0.6)	24 (2.9)[c]	33 (5.1)[c]	103 (2.8)[c]	**<0.001**
BADL, median (IQR)	0 (0)	0 (0)[c]	0 (0)[c]	1.0 (2.0)[c]	**<0.001**
IADL, median (IQR)	0 (0)	1.0 (0)[c]	2.0 (1.0)[c]	1.0 (3.0)[c]	**<0.001**

Note: BADL, basic activities of daily living; IADL, instrumental activities of daily living.

[a] P < 0.05.

[b] P < 0.01.

[c] P < 0.001.

effects. Moreover, the average causal mediation effect (ACME) depicted the effect of baseline functional dependence on CVD via the mediators. The mediation proportion was calculated by dividing ACME by total effect, with the results illustrated in directed acyclic graphs. Subsequently, attributable cases (AT) and population-attributable fractions (PAFs) were used to quantify the burden of CVD arising from functional dependence in the middle-aged and older populations. CVD incidence due to functional dependence was estimated using the following formula: $AT = p_0 \times (HR - 1) \times Nr$, where AT is the number of CVD cases caused by functional dependence, p_0 is the incidence of CVD in individuals with functional independence, HR is the hazard ratio for the association between functional dependence and CVD, and Nr is the high-risk population. The PAF was derived using the following formula: $PAF = AT/Nt \times 100\%$, in which PAF is the population-attributable fraction, AT is the number of CVD cases associated with functional dependence, and Nt is the total number of CVD cases [37].

Finally, three prediction models were constructed for the cross-sectional and longitudinal analyses. Model 1 was adjusted for age and gender, while model 2 was adjusted for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, and insurance. In model 3, all adjustments in model 2 were made, along with further adjustments for hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, chronic liver disease, chronic kidney disease, and psychiatric problems. Additionally, we further adjusted for biomarkers in the subgroups that participated in the blood marker assay (10,545 and 7107 individuals in the cross-sectional and longitudinal analyses, respectively). All statistical analyses were performed using SPSS 26.0, Stata 17, and R version 4.2.1., with a two-tailed *P*-value of <0.05 denoting statistical significance.

3. Results

3.1. Descriptive statistics of all participants in the cross-sectional and longitudinal analyses

A total of 16,459 participants were included in the cross-sectional analysis (Table 1). The baseline characteristics of all participants according to the type of functional dependency are presented in Table 1. The mean age (±SD) of the participants based on their functional dependency status was as follows: independent, 57.2 ± 9.0 years; low dependency, 60.0 ± 9.5 years; medium dependency, 61.2 ± 10.4 years; and high dependency, 64.7 ± 10.8 years. At baseline, 31.3 % of the participants exhibited functional dependence, with 5.1 %, 3.9 %, and 22.3 % having low, medium, and high dependency, respectively. Furthermore, the degree of functional dependence was found to be positively associated with age. In terms of gender distribution, the functional dependency group had a greater proportion of females (59.5 % [low dependency], 52.1 % [medium dependency], and 61 % [high dependency] vs. 48.1 % [independent]), particularly those with high functional dependence (61 % vs. 48.1 %). Individuals with functional dependence were also more likely to be unmarried (14.5 % [low dependency], 18.2 % [medium dependency], and 21.1 % [high dependency] vs. 8.8 % [independent]) and live in rural areas (93.9 % [low dependency], 91.1 % [medium dependency], and 92.7 % [high dependency] vs.
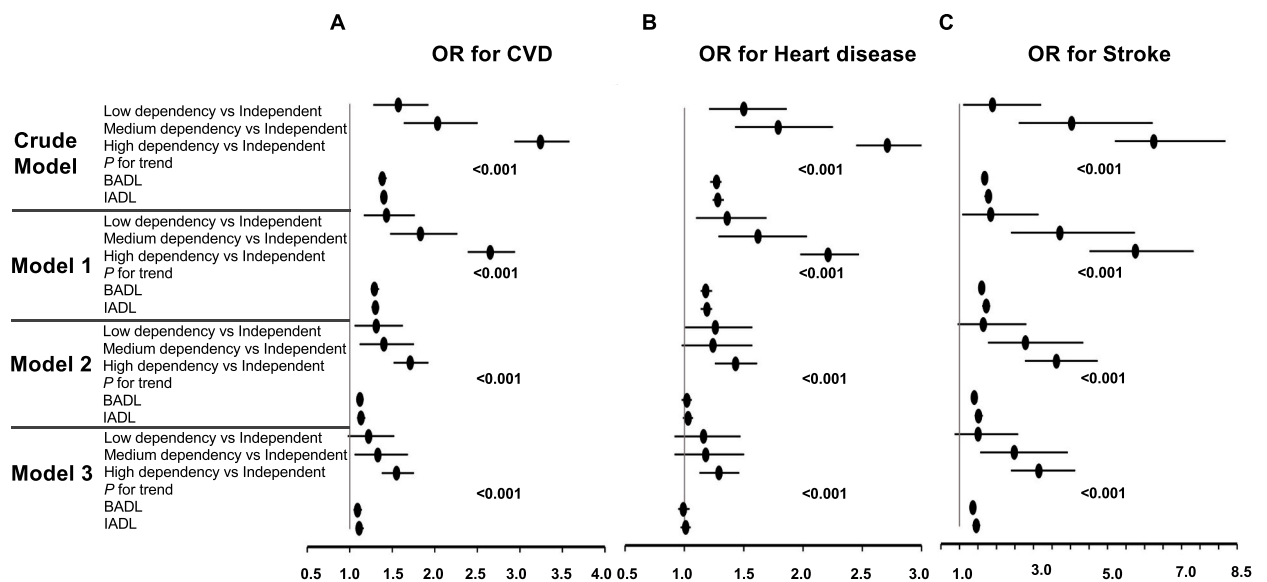

Fig. 2. ORs and 95 % CIs for CVD and its components in the cross-sectional analysis by functional dependence, BADL, and IADL.
Forest plots depict the ORs and 95 % CIs for A) CVD, B) heart disease, and C) stroke.
Model 1 is adjusted for age and gender.
Model 2 is adjusted for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, and insurance.
Model 3 is adjusted as model 2, along with further adjustments for hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, liver disease, kidney disease, and psychiatric problems.
ORs, odd ratios; CIs, confidence internals; CVD, cardiovascular disease.

87.5 % [independent]) than their functionally independent peers. In the case of chronic diseases, a higher proportion of participants with functional dependence had hypertension, dyslipidemia, diabetes, chronic liver disease, and chronic kidney disease compared to their peers with functional independence, with this difference becoming more extensive with the increasing degree of functional dependence. Moreover, the prevalence of psychiatric problems was higher among the population with functional dependence than those who were independent (2.9 % [low dependency], 5.1 % [medium dependency], and 2.8 % [high dependency] vs. 0.6 % [independent]), especially among those with medium dependency (5.1 % vs. 0.6 %). Table S2 presents the baseline characteristics of the 10,438 participants in the longitudinal analysis who were not diagnosed with CVD. Similarly, Baseline information and blood biomarker levels in cross-sectional and longitudinal studies are provided in Tables S3 and S4, respectively.

3.2. Functional dependence and cardiovascular disease in the cross-sectional analysis

In the cross-sectional analysis, CVD prevalence in the total population and among individuals with functional independence, low dependency, medium dependency, and high dependency were 13.73 % (2260/16,459), 9.60 % (1085/11,302), 14.25 % (119/835), 17.72 % (115/649), and 25.01 % (941/3763), respectively (Table 1). After adjustment for socio-demographic characteristics and health-related factors, medium dependency (OR: 1.33, 95 % CI: 1.06–1.68), high dependency (1.55, 95 % CI: 1.38–1.75), BADL (1.09, 95 % CI: 1.05–1.14), and IADL (1.11, 95 % CI: 1.07–1.16) were all significantly associated with CVD (Fig. 2, Table S5). After further adjustment for blood biomarkers in a subpopulation of 10,545 participants, the relationship between functional dependence and CVD did not change significantly (Table S6). A heterogeneity analysis was further performed to investigate the association between functional dependence and CVD components. The analysis revealed that functional dependence was linked to heart disease only in participants with high dependency (1.29, 95 % CI: 1.13–1.46). In contrast, the association of functional dependence with stroke was consistent with that observed in overall CVD, demonstrating differences only in the higher coefficient ratios (medium dependency: 2.48, 95 % CI: 1.57–3.92, high dependency: 3.14, 95 % CI: 2.40–4.12, BADL: 1.36, 95 % CI: 1.28–1.45, and IADL: 1.45, 95 % CI: 1.36–1.55; Fig. 2 and Table S5). In the heterogeneity analysis after adjusting for the blood biomarkers, functional dependence was significantly associated with stroke (medium dependency: 3.32, 95 % CI: 1.98–5.57, high dependency: 2.92, 95 % CI: 2.10–4.06, BADL: 1.37, 95 % CI: 1.27, 1.48, and IADL: 1.48, 95 % CI: 1.35–1.61), whereas no such association was detected in heart disease (Table S6). Lastly, the reliability of these findings was verified by conducting similar analyses for the four waves of data acquired in 2013, 2015, 2018, and 2020. The results were found to be nearly identical to the findings obtained in the cross-sectional analysis of the 2011 data (Fig. S1, Tables S7–S10).

3.3. Longitudinal association between baseline functional dependence and incident cardiovascular disease during follow-up from 2011 to 2020

During the 9-year follow-up from 2011 to 2020, CVD events were reported in 2987 (28.62 %) participants (Table 2). The incidence rate of CVD per 1000 person-years across different participant populations was examined via subgroup analyses by age, sex, residence, and functional dependency status. The results showed that CVD incidence rate in women was 4–6 percentage points higher than that in men (40–59 years: 30.56 vs. 26.35; 60+ years: 52.38 vs. 46.45), with this disparity being more pronounced for heart disease occurrence (40–59 years: 25.15 vs. 18.75; 60+ years: 42.80 vs. 34.95) (Table 2). Additionally, the CVD incidence rate was higher in urban than in rural areas in both sexes, although the men and women in rural areas exhibited a larger difference in prevalence than their peers in urban areas (Table S11). In terms of different functional dependency statuses, the CVD incidence rate per 1000 person-years in individuals with functional independence, low dependency, medium dependency, and high dependency was 31.24, 35.78, 46.33, and 55.85 cases, respectively, indicating that worsening functional status was associated with higher CVD occurrence rate (Table 3). After adjusting for all covariates in the model, individuals with medium (HR: 1.20, 95 % CI: 1.01–1.44) and high dependency (1.25, 95 % CI: 1.14–1.37) were more likely to develop CVD than their peers with functional independence. Furthermore, higher values of BADL (1.07, 95 % CI: 1.03–1.12) and IADL (1.09, 95 % CI: 1.05–1.13) were associated with higher CVD risk (Table 3). Further adjustment for the blood biomarkers also indicated an association between high functional dependency (1.22, 95 % CI: 1.09–1.36) and CVD. Correspondingly, higher BADL (1.06, 95 % CI: 1.01–1.12) and IADL (1.09, 95 % CI: 1.04–1.14) scores were associated with greater CVD risk (Table S12), even after adjusting for the blood biomarkers (Table S12).

In the case of CVD components, individuals with medium (1.23, 95 % CI: 1.02–1.50) and high dependency (1.19, 95 % CI: 1.07–1.32) were found to be at a higher risk of heart disease, whereas those with high dependency (1.46, 95 % CI: 1.27–1.68) had an

Table 2

CVD incidence rates per 1000 person-years in all participants grouped by gender and age, 2011–2020.

Gender	Age (years)	CVD		Heart disease		Stroke	
		Cases, No.	Rate	Cases, No.	Rate	Cases, No.	Rate
Male	40–59	676	26.35	491	18.75	289	10.23
	60+	659	46.45	506	34.95	287	17.06
Female	40–59	894	30.56	749	25.15	301	8.72
	60+	758	52.38	635	42.80	320	17.59
Overall		2987	35.75	2381	27.92	1197	12.24

Note: CVD, cardiovascular disease.

Table 3
CVD incidence according to baseline functional dependency status, 2011–2020.

Outcome	Cases, No.	Incidence Rate, per 1000 Person-Years	HR (95 % CI)		
			[a] Model 1	[b] Model 2	[c] Model 3
CVD					
Independent	1988	31.24	Reference	Reference	Reference
Low dependency	155	35.78	1.04(0.89,1.23)	1.02(0.87,1.21)	0.99(0.84,1.17)
Medium dependency	134	46.33	1.34(1.12,1.59)[e]	1.22(1.02,1.46)[d]	1.20(1.01,1.44)[d]
High dependency	710	55.85	1.51(1.38,1.65)[f]	1.27(1.16,1.40)[f]	1.25(1.14,1.37)[f]
BADL (0–6)	2987	35.75	1.15(1.10,1.19)[f]	1.08(1.03,1.12)[f]	1.07(1.03,1.12)[e]
IADL (0–5)			1.16(1.12,1.20)[f]	1.10(1.06,1.14)[f]	1.09(1.05,1.13)[f]
Heart disease					
Independent	1575	24.39	Reference	Reference	Reference
Low dependency	132	29.48	1.09(0.91,1.30)	1.07(0.90,1.28)	1.03(0.86,1.24)
Medium dependency	113	37.68	1.38(1.14,1.68)[e]	1.27(1.05,1.54)[d]	1.23(1.02,1.50)[d]
High dependency	561	42.34	1.44(1.30,1.59)[f]	1.23(1.10,1.37)[f]	1.19(1.07,1.32)[e]
BADL (0–6)	2381	27.92	1.11(1.06,1.16)[f]	1.04(1.00,1.09)	1.03(0.99,1.08)
IADL (0–5)			1.12(1.08,1.17)[f]	1.07(1.02,1.11)[e]	1.05(1.01,1.10)[d]
Stroke					
Independent	714	9.85	Reference	Reference	Reference
Low dependency	68	13.14	1.24(0.97,1.59)	1.16(0.90,1.49)	1.12(0.87,1.45)
Medium dependency	57	15.94	1.47(1.12,1.92)[e]	1.28(0.97,1.68)	1.27(0.96,1.66)
High dependency	358	21.66	1.91(1.67,2.18)[f]	1.53(1.33,1.76)[f]	1.46(1.27,1.68)[f]
BADL (0–6)	1197	12.24	1.28(1.22,1.34)[f]	1.19(1.13,1.25)[f]	1.18(1.13,1.25)[f]
IADL (0–5)			1.27(1.21,1.34)[f]	1.19(1.13,1.26)[f]	1.18(1.12,1.26)[f]

Note.

HRs, hazard ratios; CVD, cardiovascular disease.

[a] Model 1 is adjusted for age and gender.

[b] Model 2 is adjusted for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, and insurance.

[c] Model 3 is adjusted as model 2, with additional adjustments for hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, chronic liver disease, chronic kidney disease, and psychiatric problems.

[d] $P < 0.05$.

[e] $P < 0.01$.

[f] $P < 0.001$.

elevated stroke risk. Moreover, IADL score (1.05, 95 % CI: 1.01–1.10) was linked to heart disease, while BADL (1.18, 95 % CI: 1.13–1.25) and IADL (1.18, 95 % CI: 1.12–1.26) values were associated with stroke (Table 3). After further adjusting for the blood biomarkers, individuals with medium (1.27, 95 % CI: 1.00–1.61) and high dependency (1.17, 95 % CI: 1.03–1.32) had a greater chance of developing heart disease than their independent peers. Similarly, individuals with high dependency (1.34, 95 % CI: 1.14–1.59) exhibited a higher stroke risk than their independent peers after adjustment for the blood biomarkers (Table S12). Furthermore, we assessed the link between BADL and IADL scores and the risk of CVD components. As presented in Table S12, higher BADL (1.17, 95 % CI: 1.09–1.24) and IADL (1.20, 95 % CI: 1.12–1.27) values were associated with an increased risk of stroke but not heart disease.

3.4. Longitudinal association between functional status changes and cardiovascular disease incidence during follow-up from 2011 to 2020

Considering that functional status may change over time, the effect of functional status transition on CVD was explored (Table 4, Table S13). According to the baseline and follow-up data, the trajectories of functional status transition could be categorized into the following four types: persistent functional independence (group 1), functional dependence to independence (group 2), functional independence to dependence (group 3), and persistent functional dependence (group 4). In the fully adjusted model, groups 2 (OR: 1.17, 95 % CI: 1.02–1.34), 3 (OR: 1.75, 95 % CI: 1.58–1.94), and 4 (OR: 1.66, 95 % CI: 1.47–1.88) had a greater likelihood of experiencing CVD than those who reported persistent functional independence (group 1). In particular, CVD risk was the highest among participants transitioning from functional independence to dependence, even more than that in those with persistent functional dependence (1.75, 95 % CI: 1.58, 1.94 vs. 1.66, 95 % CI: 1.47, 1.88). In contrast, excluding the participants in the persistent functional independence group, those who transitioned from functional dependence to independence had the lowest CVD risk compared to those in the other two groups (1.17, 95 % CI: 1.02, 1.34 vs. 1.75, 95 % CI: 1.58, 1.94 and 1.66, 95 % CI: 1.47, 1.88; Table 4). After further adjustment for the blood biomarkers, the results were demonstrated to be generally consistent with the main analysis findings (Table S13). Additionally, a heterogeneity analysis was conducted to investigate the effect of functional status changes on the CVD components (Table 4, Table S13). The analysis for heart disease showed that the findings were in line with the primary analysis. However, the heterogeneity results for stroke revealed that participants in the persistent functional dependence group had a higher risk of developing CVD than their peers in the functional independence to dependence group (2.45, 95 % CI: 2.02, 2.96 vs. 2.38, 95 % CI: 2.01, 2.82; Table 4). After further adjustment for the blood biomarkers, the results remained consistent with the primary analysis (Table S13).

Table 4
Incidence of CVD and its components according to the four groups of functional dependency changes, 2011–2020.

Outcome	Cases, No.	Incidence Rate, per 1000 Person-Years	HR (95 % Cl)		
			[a] Model 1	[b] Model 2	[c] Model 3
CVD					
Group 1	1055	21.98	Reference	Reference	Reference
Group 2	286	30.18	1.29(1.13,1.48)[f]	1.18(1.03,1.35)[d]	1.17(1.02,1.34)[d]
Group 3	620	43.32	1.87(1.69,2.07)[f]	1.79(1.61,1.98)[f]	1.75(1.58,1.94)[f]
Group 4	460	48.38	1.97(1.76,2.21)[f]	1.72(1.52,1.94)[f]	1.66(1.47,1.88)[f]
Heart disease					
Group 1	863	17.66	Reference	Reference	Reference
Group 2	239	24.36	1.27(1.10,1.47)[e]	1.17(1.01,1.35)[d]	1.15(0.99,1.33)
Group 3	475	32.15	1.69(1.51,1.89)[f]	1.62(1.44,1.82)[f]	1.58(1.41,1.77)[f]
Group 4	382	37.31	1.83(1.62,2.08)[f]	1.60(1.39,1.83)[f]	1.52(1.32,1.74)[f]
Stroke					
Group 1	317	5.83	Reference	Reference	Reference
Group 2	108	9.12	1.53(1.22,1.90)[f]	1.37(1.09,1.71)[e]	1.32(1.06,1.66)[d]
Group 3	268	15.34	2.59(2.20,3.06)[f]	2.46(2.08,2.91)[f]	2.38(2.01,2.82)[f]
Group 4	243	18.86	3.08(2.59,3.68)[f]	2.59(2.15,3.13)[f]	2.45(2.02,2.96)[f]

Group 1: "Functionally independent" (2011) to "Functionally independent" (2020).
Group 2: "Low, medium, or high functional dependency" (2011) to "Functionally independent" (2020).
Group 3: "Functionally independent" (2011) to "Low, medium, or high functional dependency" (2020).
Group 1: "Low, medium, or high functional dependency" (2011) to "Low, medium, or functional high dependency" (2020).
HRs, hazard ratios; CVD, cardiovascular disease.
Note.
[a] Model 1 is adjusted for age and gender.
[b] Model 2 is adjusted for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, and insurance.
[c] Model 3 is adjusted as model 2, followed by adjustments for hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, chronic liver disease, chronic kidney disease, and psychiatric problems.
[d] $P < 0.05$.
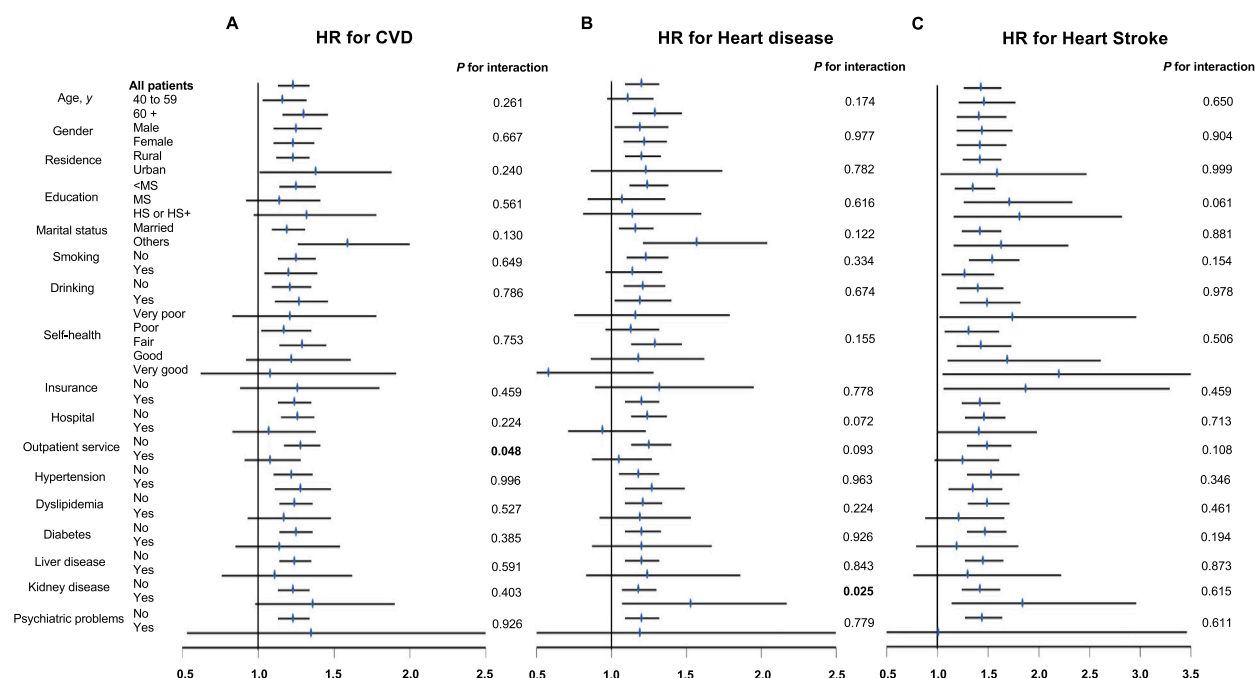[e] $P < 0.01$.
[f] $P < 0.001$.

Fig. 3. Subgroup and interaction analyses for CVD and its components in the longitudinal analysis from 2011 to 2020.
Forest plots depict the HRs and 95 % CIs for A) CVD, B) heart disease, and C) stroke after adjustments for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, insurance, hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, liver disease, kidney disease, and psychiatric problems. HRs, hazard ratios; CIs, confidence intervals; CVD, cardiovascular disease.

3.5. Subgroup and interaction analyses

Subgroup analysis in the cross-sectional investigation of the study revealed that the association between functional dependence and CVD was similar across various subgroups (Fig. S2, Table S14). Furthermore, the relationship between functional dependence and CVD may be modified by several factors, including age, self-assessed health, insurance, outpatient service, and psychological problems (*P* for interaction: <0.001, 0.012, 0.038, 0.041, and 0.048, respectively). However, the CVD components did not show consistent findings. For example, age, self-assessed health, and hospital visits exhibited potential effects on the relationship between functional dependence and the end event of heart disease (*P* for interaction: <0.001, 0.015, and 0.012, respectively), whereas outpatient service, diabetes, and chronic liver disease were the influencing factors in the end event of stroke (*P* for interaction: <0.001, 0.026, and 0.018, respectively) (Fig. S2, Table S14). Subgroup analysis in the longitudinal investigation also demonstrated no apparent differences in the association between functional dependence and CVD across various subgroups (Fig. 3, Table S15). Furthermore, only outpatient service (*P* for interaction = 0.048) was found to influence the link between functional dependence and the end events of CVD, while chronic kidney disease was the influencing factor in the end event of heart disease (*P* for interaction = 0.025). Finally, no relevant factors were demonstrated to affect the association between functional dependence and the end event of stroke (Fig. 3, Table S15).

3.6. Mediation analyses

In the cross-sectional investigation, mediation analysis indicated that hospital visits, hypertension, chronic liver disease, and chronic kidney disease might partially mediate the relationship between functional dependence and CVD, displaying mediation proportions of 7.21 %, 10.01 %, 1.30 %, and 1.55 %, respectively (Fig. S3). However, these mediation effects were not entirely
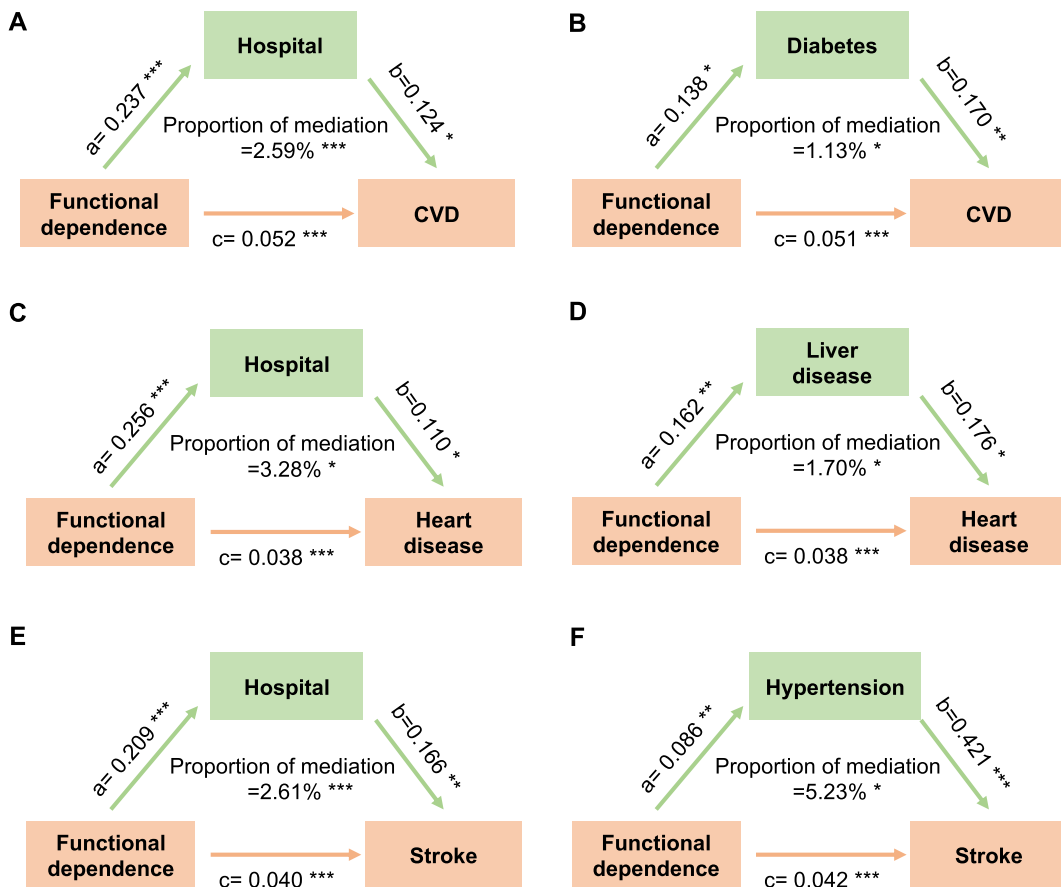

Fig. 4. Association between functional dependence, mediator variables, and CVD in the longitudinal analysis from 2011 to 2020.
(A, B) mediating variable display for CVD. (C, D) mediating variable display for heart disease. (E, F) mediating variable display for stroke. Fully adjusted logistic regression models are controlled for age, gender, residence, education level, marital status, smoking status, alcohol consumption status, self-assessed health, insurance, hospital visits, outpatient service, hypertension, dyslipidemia, diabetes, liver disease, kidney disease, and psychiatric problems. "a" represents the effects of the baseline functional dependence on the mediators. "b" depicts the effects of the mediators on CVD. "c" indicates the effects of the baseline functional dependence on CVD with the mediators. The average causal mediation effect (ACME) represents the effects of the baseline functional dependence on CVD through the mediators. The mediation proportion was derived by dividing ACME by total effect (TE). CVD, cardiovascular disease. *P < 0.05, **P < 0.01, ***P < 0.001.

consistent in the case of heart disease and stroke (Fig. S4). In the longitudinal study, mediation analysis demonstrated that hospital visits and diabetes might partly mediate the association between functional dependence and CVD (mediation proportions of 2.59 % and 1.13 %, Fig. 4). In terms of the CVD components, hospital visits partially contributed to the link between functional dependence and outcome events (mediation proportions of 3.28 % for heart disease and 2.61 % for stroke), while chronic liver disease mediated the effect of functional dependence on heart disease (mediation proportion of 1.70 %) and hypertension mediated the effect of functional dependence on stroke (mediation proportion of 5.23 %) (Fig. 4).

3.7. Population-attributable fraction

AT and PAF results indicated that the burden of CVD and its components could be attributed to functional dependence (Table 5). Among all middle-aged and older participants, 4.85 % of CVD, 4.67 % of heart disease, and 11.13 % of stroke cases were attributed to functional dependence, corresponding to 145, 111, and 133 end-event cases.

4. Discussion

In this study, we conducted cross-sectional and longitudinal analyses of middle-aged and older adults of >40 years using five data waves from the CHARLS survey (i.e., 2011 to 2020). Our results revealed that functional dependence was associated with CVD and that individuals with medium and high dependency had a relatively higher CVD risk. Furthermore, transitioning from functional dependence to independence was demonstrated to have a protective role in cardiovascular health. Hospital visits, hypertension, and diabetes may partially contribute to the relationship between functional dependence and CVD. Lastly, 4.85 %, 4.67 %, and 11.13 % of the end-stage cases of CVD, heart disease, and stroke, respectively, were attributed to functional dependence.

Several previous studies have reported on the association between functional status and CVD and its components (i.e., heart disease and stroke). For instance, Hu et al. demonstrated that functional limitations were significantly related to subsequent CVD incidence in middle-aged and older adults in China [18]. Sharma et al. also showed a high burden of functional limitations in older adults and a strong association of functional limitations with pre-existing chronic conditions, including CVD [38]. Another investigation by Li et al. highlighted that hypertension and ADL/IADL limitations increased CVD risk [39], while Peralta et al. observed that functional limitations had a modifying effect on the association of systolic and diastolic blood pressure with CVD events in the older population [40]. In line with these findings, a prospective study based on the UK Biobank data found that intrinsic capacity, including physical and mental function, was related to CVD mortality [41]. A different prospective study utilizing data from the Atherosclerosis Risk in Communities (ARIC) study cohort revealed that functional status declined from an average of 2 and 3 years before hospitalization in cases of myocardial infarction and stroke/heart failure, respectively [20]. All these prior research findings correspond to the primary finding in our study despite the marked differences in the cohort data and functional classification criteria employed across these studies. Additionally, our primary finding of the association between functional dependence and high CVD risk suggests that assessing the functional status of patients during community health screenings and routine clinical practice is crucial to protecting those with elevated CVD risk and implementing early protective measures.

Another notable result of this study was the identification of several interaction variables that potentially modified the association between functional dependence and CVD. In the cross-sectional analysis, age, self-assessed health, insurance, outpatient service, and psychological problems were found to influence the relationship between functional dependence and CVD, whereas outpatient service was the only interaction variable detected in the longitudinal analysis. To our knowledge, this study is the first large population-based cross-sectional and longitudinal investigation that examined the interaction variables affecting the association between functional dependence and CVD. The intricate impact of increasing age on the relationship between functional dependence and CVD may be ascribed to the fact that age is the most significant risk factor for CVD [42] and the most direct cause of functional dependence [2]. Self-rated health (SRH) is a commonly employed measure of an individual's health status and is related to functional dependence [43], with poorer SRH tending to be associated with greater CVD risk [44,45]. The social determinants of health, including health-related economic, insurance [46], and psychosocial factors, play a pivotal role in the development of CVD risk factors, as well as CVD morbidity and mortality [47]. Among these factors, psychological problems have a prominent effect on functional status [48] and CVD [49,50]. Due to the loss of labor capacity, the population with functional dependence often faces economic difficulties and psychological barriers, which further reduces their access to socio-medical services, such as insurance and outpatient service [51]. However, the effects of these factors on the association between functional dependence and CVD are highly complicated and warrant in-depth studies in the future.

Additionally, the mediating effects of several potential factors on the relationship between functional dependence and CVD were

Table 5
Estimated burden of CVD and its components attributable to the functional dependence of the participants.

	No. of cases	Attributed cases	Population attributable Fraction (PAF), %
CVD	2987	145	4.85
Heart disease	2381	111	4.67
Stroke	1197	133	11.13

Note: CVD, cardiovascular disease.

assessed for the first time in our cross-sectional and longitudinal analyses. Our findings indicated that hospital visits, hypertension, diabetes, chronic liver disease, and chronic kidney disease might partly contribute to the association between functional dependence and CVD events, aligning with certain observations reported in previous findings. For example, a study involving patients in England showed that myocardial infarction-related pre-hospital mortality was higher than myocardial infarction mortality after hospital admission, with most changes in the case-fatality rates occurring before rather than after admittance [52]. Therefore, hospital visits may exert a protective effect on CVD incidence. In the current scenario, older adults with functional dependence typically prefer medical treatment, contributing to lower CVD incidence. Among the CVD risk factors, hypertension has the strongest evidence for causation and a high prevalence of exposure [53]. Correspondingly, a recent study demonstrated that hypertension accompanied by BADL/IADL limitations increased the risk of CVD, stroke, and cardiac events [39]. However, no earlier study has reported a direct relationship between functional dependence and hypertension. In contrast, our study findings implied a link between functional dependence and hypertension, suggesting hypertension to be a potential mediator of this relationship. Another cross-sectional investigation demonstrated that diabetes was associated with subclinical functional limitations in older adults with no disabilities [54]. Diabetes has also been reported to be associated with higher CVD risk [55], providing substantial theoretical support for diabetes as a mediating factor in the effect of functional dependence on CVD. Several studies have also identified an association between chronic liver disease and elevated CVD risk [35,56]. Moreover, chronic liver disease has been linked to functional dependence [57], with a study showing that patients with alcoholic chronic liver disease tend to have worse functional status at the time of liver transplant registration [58]. All these study findings emphasize that chronic liver disease may mediate the relationship between functional dependence and CVD; however, the exact mediation mechanism requires further exploration. Chronic kidney disease is a prevalent disorder in the general population and is associated with heightened CVD risk [59]. A prospective cohort study demonstrated that chronic kidney disease was independently associated with physical function limitation [60], suggesting chronic kidney disease as a plausible mediating effector between functional dependence and CVD. Although previous studies have laid the groundwork for the theoretical framework of future research, the underlying mechanisms by which these potential mediators influence the effects of functional dependence on CVD remain poorly understood.

Furthermore, our study revealed that 4%–12 % of the cases of CVD, heart disease, and stroke were attributable to functional dependence. This estimation of the effect of functional dependence on CVD using PAFs provides valuable insights into the public health context. To our knowledge, no studies have focused on CVD occurrence due to functional dependence, and our findings fill this research gap. Functional dependence may not only contribute directly to the CVD burden but also indirectly influence CVD via other factors not identified in the current study. For example, functional dependence has been previously associated with digital exclusion [2] and social isolation [61,62], often leading to elevated CVD risk [63,64]. Our study also showed that transitioning from functional dependence to independence might diminish CVD risk to some extent. Moreover, earlier studies have mainly focused on the association between baseline functional dependency status and CVD without considering the impact of functional status changes on CVD [18,20, 38,39,41]. Our study addresses this shortcoming as well; however, the classification of functional status changes may require further refinement.

Although the precise underpinnings of the effects of functional dependence on CVD are still unclear, current research suggests that functional dependence may result in CVD via multiple processes. For instance, aging-associated physiological changes are typically involved in functional dependence and CVD [65,66]. Aging is generally accompanied by damage to the heart and vascular structure and function, which can aggravate CVD risk [18]. Additionally, aging of the heart is characterized by fibrosis, misfolded proteins, and the accumulation of dysfunctional mitochondria [67]. The cardiovascular aging process is also strongly associated with common or rare gene variants that regulate sarcomere homeostasis, myocardial immunomodulation, and tissue responses to biophysical stresses [68]. Cardiac degeneration and aging may involve essential metabolic reprogramming processes, including autophagy, oxidative stress, epigenetic modifications, chronic inflammation [69], and the regulation of contractile phenotypes of cardiomyocytes [70]. Previous studies have observed a progressive decline in mitochondrial function in CVD, as evidenced by abnormalities in the respiratory chain and ATP synthesis, increased oxidative stress, and a loss of mitochondrial structural integrity [71,72]. Based on these existing findings, we hypothesize that functional dependence exerts its influence on CVD through one or more of these biological pathways. Nevertheless, comprehensive studies are necessitated in the future to bridge these mechanistic gaps. From a psychosocial perspective, disability in later life is linked to increased dependence and the loss of labor capacity of the affected individuals. These adverse changes can lead to functional dependence among older adults and accompanying decreased social participation [61,62], ultimately increasing CVD risk [47,73]. Therefore, starting with aging and/or CVD biomarkers may be the most effective approach for future research investigating these mechanisms. Interestingly, in recent years artificial intelligence techniques (e.g., machine learning algorithms) have been able to predict CVD in an ultra-correct manner [74–76]. In the future, by combining existing machine learning algorithms to deeply study the association between functional dependence and CVD, we may well realize the accurate prediction of CVD. Meanwhile, the development of large-scale, multicenter randomized controlled trials is also a future task for the field. Furthermore, whether medically intervened functionally dependent patients can directly influence the incidence of CVD is also an interesting area for future research.

Our study has several noteworthy strengths. First, this study employed a nationally representative sample and a longitudinal design with long-term follow-up, thereby allowing the findings from this large sample investigation to be widely generalized to the middle-aged and older population in China. Second, in contrast to most previous studies, the present study focused on the effects of different functional dependency types on CVD and the longitudinal associations of functional status changes during follow-up with CVD outcomes. The current and future increasing trend of the aging population will lead to functional status changes, and our study presents evidence underlining the need to protect the cardiovascular health of middle-aged and older adults with functional dependence. Third, this study determined the potential interacting and mediating factors in the association between functional dependence and CVD, thus

providing theoretical evidence for future mechanistic studies. Finally, our study comprised a combination of cross-sectional and longitudinal analyses that broadly validated the relationship between functional dependence and CVD. However, this study has a few limitations that should be considered. First, some study participants who were previously functionally independent may have shifted to functional dependence before the baseline survey, and the categorization of functional status changes may not have been sufficiently detailed, potentially resulting in biases in the effect values. Moreover, this was a cohort with long-term follow-up, and there were interchangeable patients between the different functional dependency groups, which can be a confounding factor associated with adverse outcomes. Although we examined functional status at both the starting point of follow-up (2011) and the end point of follow-up (2020) nodes, we cannot exclude that attenuation or exacerbation of functional dependence can happen in any of the years during follow-up. Second, given that our study utilized observational data, the presence of confounders may have biased the calculated association. Nevertheless, our analyses accounted for as many relevant factors as possible to reduce this bias. However, the influence of other potential confounders, such as socioeconomic status, lifestyle factors (e.g., diet, physical activity), other comorbidities, social isolation, and sarcopenia, cannot be disregarded and should be adapted for further refining the analysis in the future. Third, the CVD diagnoses in this study were based on self-reported physician diagnoses, consistent with the strategy applied in previous studies. Furthermore, participant medical records were not available in the CHARLS survey; therefore, the use of self-reported measures of chronic diseases, including CVD, may have also introduced some degree of bias. Furthermore, the lack of a detailed CVD classification in this study prevented an in-depth analysis of the association between functional dependence and specific heart diseases. Lastly, as a cohort study, the paper cannot establish causality between functional dependence and CVD. The observed association could be due to confounding factors or reverse causation. A randomized controlled trial is urgently needed to provide stronger evidence for a causal relationship between functional dependence and CVD.

In summary, this cross-sectional and longitudinal study revealed that functional dependence was associated with increased CVD risk, with escalating CVD incidence as the functional dependence worsened. Moreover, hospital visits, hypertension, chronic liver disease, and chronic kidney disease may partially mediate this association, suggesting that the CVD burden can be alleviated by risk factor modifications such as preventing chronic diseases and fostering a philosophy of equitable healthcare access. Our study findings also highlighted that transitioning from functional dependence to independence may protect cardiovascular health, stressing the significance of promoting medical assistance for the global population of middle-aged and older adults with functional dependence.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ethics Review Committee of Peking University. The patients/participants provided their written informed consent to participate in this study.

Consent for publication

All authors approved the final version of the manuscript.

Data availability statement

The datasets generated and/or analyzed during the current study are available in the [CHARLS] repository, [https://charls.charlsdata.com/].

Funding

CRediT authorship contribution statement

Yaxi Yang: Writing – original draft, Validation, Software, Project administration, Formal analysis, Data curation. **Chaonian Li:** Writing – original draft, Software, Resources, Project administration, Methodology, Data curation. **Ye Hong:** Project administration, Methodology. **Jinqi Sun:** Methodology, Formal analysis, Data curation. **Guoping Chen:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Formal analysis, Data curation. **Kangkang Ji:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation.

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.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37821.

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