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Association between echocardiographic parameters of cardiac structure and function and mild cognitive impairment

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Abstract

Background Cardiovascular diseases (CVDs) marked with cardiac morphological or hemodynamical abnormalities are associated with mild cognitive impairment (MCI). The links between cardiac structure and function and MCI are not well understood. We aimed to explore the association between echocardiographic parameters of cardiac structure and function and MCI in CVD patients.

Methods We conducted an age-, gender-, and education level-matched case–control study in general CVD participants with a 1:3 ratio of MCI (Montreal Cognitive Assessment [MoCA] score < 26 and Mini-Mental State Examination [MMSE] score ≥ 24) and cognitively normal participants at a tertiary hospital in Beijing, China. The echocardiographic cardiac parameters and cognitive status were retrieved through the clinical electronic database from May 2021 to August 2023. Principal component analysis (PCA), negative binomial, and conditional multivariate regression were performed.

Results A total of 1136 CVD participants (mean age, 61.2 ± 8.3 years) were included in the study, comprising 289 (25.3%) MCI and 847 cognitively normal participants. Compared to cognitively normal participants, MCI participants had a higher prevalence of left ventricular (LV) diastolic dysfunction (54.0% vs. 40.3%; $P < 0.001$) and greater interventricular septal thickness (IVST) (1.04 ± 0.20 cm vs. 1.00 ± 0.17 cm; $P = 0.002$). LV diastolic dysfunction (Beta [SE], 0.234 [0.045]; $P < 0.001$) and IVST (Beta [SE], 0.034 [0.016]; $P = 0.036$) were negatively correlated with the MoCA score of global cognitive function. LV diastolic dysfunction (OR, 2.03; 95% CI, 1.48–2.79; $P < 0.001$) and IVST (OR, 1.14; 95% CI, 1.03–1.27; $P = 0.014$) were positively associated with MCI, independent of diagnosed CVDs and the conventional MCI risk factors.

Conclusions General CVD patients with abnormal echocardiographic LV diastolic dysfunction and IVST were associated with cognitive decline, suggesting further cognitive assessment for MCI.

Trial registration Retrospectively registered.

Keywords Echocardiography, Cardiac structure and function, Mild cognitive impairment

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Background

With the trends in population growth and fast-aging population worldwide, cognitive impairment has increasingly become a serious health concern and imposed a tremendous public health and socioeconomic burden [1, 2]. By 2050, it is projected that the cases of dementia worldwide will increase to more than 150 million, nearly 3 times the number in 2019 [1]. Among the various modifiable risk factors that impact cognitive functions, CVDs are the most challenging one [3]. One in 3 patients at cardiology clinics have some degree of cognitive impairment [4]. Clinical researches have consistently shown a strong co-occurring or interaction between the four types of general CVDs (i.e., hypertension, coronary heart disease [CHD], atrial fibrillation [AF], and chronic heart failure [CHF]) and declining neurological conditions linked to MCI and dementia [4, 5]. Recent studies indicated that cardiac dysfunctions, marked by low LV ejection fraction, high LV mass index, and concentric remodeling, were associated with lower cognitive function [6–10]. However, other researchers draw inconsistent results indicating that none of abnormalities of cardiac structure and function was significantly associated with cognitive impairment [11]. The relationship of heart-brain cognition, although incompletely understood, might facilitate the development of assessment biomarkers for neurovascular health [12, 13].

MCI, a condition with objective cognitive impairment but minor effect on daily activities, is a transitional stage from normal cognitive function to dementia and has pivotal clinical significance [14, 15]. Early detection and intervention for patients with MCI may help slow cognitive decline and reduce medical costs [16]. CVD guidelines highlight the importance of considering cognitive impairment as an essential comorbidity of cardiac diseases in disease management [17–19]. However, most cardiologists have not fully recognized MCI due to the subtle or hidden clinical symptoms and a lack of specialized knowledge in neuropsychology [20, 21]. It is increasingly clear that we need to explore whether cognitive decline in CVDs can be evaluated by some essential cardiovascular biomarkers (e.g., body fluid, imaging, genetics), which might have potential value for MCI assessment.

To address this unmet need, our group recently performed a matched case–control study to analyze the association between cardiac structure and function by echocardiography and MCI among general CVD participants at a tertiary hospital. We hypothesized that individuals with MCI would have higher prevalence of abnormalities in cardiac structure and function independent of diagnosed CVDs and the conventional MCI risk factors.

Methods

Study design and participants

This study was a matched case–control study for CVD participants at Beijing Anzhen Hospital, Capital Medical University, China, where more than 70% of CVD patients were from different provinces other than Beijing. The data collection spanned the period from May 2021 to August 2023. Patients were eligible if they were hospitalized because of CVD conditions, had a prior or concurrent diagnosis of hypertension, and/or CHD, and/or AF, and/or CHF, and underwent neuropsychological tests of MoCA and MMSE within a 14-day window. Patients with serious infection, congenital cardiac conditions, significant valve disease, terminal malignancy, or subsequent acute cardiac events within 30 days of the hospital were excluded from the study. The exclusion criteria also included age < 18 years, no record of echocardiography or cognitive function assessment, diagnosed dementia, and psychiatric illness.

Propensity score matching was done by a 1:3 ratio of pairing MCI participants with age-, gender- and education-matched controls of cognitively normal CVD participants. This study followed the Declaration of Helsinki and was approved by the Institutional Ethics Review Board at Beijing Anzhen Hospital (No.2022–17-1). Informed consent for this study was waived from all participants because it was retrospective and we do not involve sensitive personal information.

Measurements of echocardiographic parameters

Echocardiographic examinations were performed by trained cardiac sonographers using a GE Vivid E9 ultrasound machine with an M5S probe (2–4 MHz; GE Healthcare, Chicago, IL, USA) or a Philips IE33 ultrasound machine with an S5-1 probe (2.5–3.5 MHz; Philips Healthcare, Andover, MA, USA) at the Echocardiography Medical Center office of Beijing Anzhen Hospital.

All participants underwent standard transthoracic echocardiography within a 14-day window of hospitalization to assess cardiac structural and functional status because of the need for CVD management. The quantitative and qualitative diagnosis of cardiac structural and functional abnormalities were produced according to the echocardiographic guideline [22] and checked by an independent board-certified cardiac sonographer blinded to the clinical data. LV ejection fraction was calculated using the biplane Simpsons method in the apical four-chamber and two-chamber views. Early diastolic transmitral flow velocity (E), late atrial diastolic transmitral flow velocity (A), and early diastolic mitral annular velocity (e') were measured through pulsed-wave Doppler. According to the guideline, patients with normal LV ejection fraction (> 50%) are considered to have LV diastolic

dysfunction if they meet two or more of the following criteria: 1) average E/e' ratio > 14; 2) e' of interventricular septal < 7 cm/s or e' of lateral wall < 14 cm/s; 3) maximum tricuspid regurgitation velocity > 2.8 m/s; 4) left atrial volume index > 34 ml/m^2 [22]. For those few patients with reduced LV ejection fraction, LV diastolic dysfunction is defined based on the aforementioned criteria as well as the clinical experience of the echocardiographer. Other cardiac abnormalities included LV hypertrophy, enhanced IVST, valvular dysfunction, atrial enlargement, regional wall motion abnormality, and aortic sinus enlargement. LV mass index was calculated by the LV end-diastolic dimension, IVST, LV posterior wall thickness, and body surface area (using Stevenson formula). Relative wall thickness (RWT) was calculated from LV posterior wall thickness and LV end-diastolic dimension.

Assessment of cognitive ability

We only conducted a cognitive assessment after hospital admission for CVDs and only for subjects who met the cognitive complaints (i.e., self-reported problems with memory or other aspects of cognition) [23, 24]. Two validated tools, namely MoCA [25, 26] and MMSE [26], were performed by trained neuropsychological assessors for screening MCI. MoCA is a cognitive screening tool that has been extensively verified for detecting MCI with high sensitivity and specificity [25–28]. The total score of MoCA is 30 points, with a score of 26 points marking the cutoff between MCI and normal cognition. For those with ≤ 12 years of formal education, 1 point is added to the final score. MMSE is a 30-point questionnaire widely used for detecting dementia, while it has lower sensitivity in detecting MCI compared to MoCA [27, 28]. The MMSE is used to screen out individuals with dementia, with a score of < 24 points being considered indicative of dementia rather than MCI.

All participants completed Chinese version of the MOCA and the MMSE under the guidance of trained professional investigators in the present study. MCI was defined by a MoCA score of < 26 points and an MMSE score of ≥ 24 points [29]. Normal cognition was defined by a MoCA score of ≥ 26 points and an MMSE score of ≥ 24 points. All participants included in the study had an MMSE score of ≥ 24 points, as an MMSE score < 24 points are generally indicative of dementia.

Covariates measurement

Potential confounders were identified by reviewing the literature and consulting clinical experts [5, 30, 31]. All covariates from standard demographic and clinical data of each participant, including age, sex, education level, smoking status, hypertension, AF, CHD, CHF, stroke, chronic kidney disease, diabetes mellitus, and hyperlipidemia, were ascertained from self-reported medical history or physicians' diagnosis in the clinical electronic database based on the International Classification of Diseases (ICD)−10 codes [32]—I10, I48.9, I20.9, I25.1, I50.9, I63, N18.9, E14, and E78.5. Participants' height and weight were measured to compute body mass index (BMI). After a 15-min rest, blood pressure (BP) was measured twice at a 2-min interval and was ascertained by the mean of them. Laboratory parameters included fasting plasma glucose (FPG), estimated glomerular filtration rate (eGFR), total cholesterol, and low- density lipoprotein cholesterol (LDL-C).

Missing data

The missing data for all variables was < 5%, excluding echocardiographic parameters of A peak and E/A (10.5%). Most participants (90.8%) with missing data of A peak and E/A ratio were those suffering from AF, for whom it was not possible to measure the A peak and E/A ratio because of left atrial systolic dysfunction.

Sample size calculation

This study used a 1:3 case–control design. We assumed the control group had a probability of 0.5 for each cardiac structural and functional abnormality (50/50 chance) and an odds ratio (OR) of 1.5 to have the same abnormality in the case versus control groups. Therefore, a sample size pair of 272 cases and 816 controls (after Fleiss correction for continuity) will have an 80% power to detect the difference (OR = 1.5) between the case and control with a 2-sided significant level of 5%.

Statistical analyses

All data were analyzed using R software (http://www.R-project.org.; Version 4.3.2). The Kolmogorov–Smirnov Test was used to verify normal distribution of numerical data. Continuous variables were described as mean ± standard deviation (normal distribution) or median and interquartile range (skewed distribution). The two-sample t-test or Mann–Whitney U-test was used for group comparisons of continuous variables, depending on the normality of distribution. Categorical variables were presented as the number of cases and percentages and were compared using the chi-square test. *P*-value < 0.05 was defined as statistically significant.

PCA was used to explore the correlation of cardiac structure and function with MoCA score and MCI. All variables have been normalized before PCA.

MoCA score is a count data. Therefore, variables that influenced the MoCA score were analyzed using either the Poisson or negative binomial regression dependent on the magnitude of dispersion strength (Supplementary Fig. 1 and Supplementary Tables 1–2).

Conditional univariate and multivariate logistic regression models were conducted to evaluate the association between MCI and echocardiographic parameters of cardiac structure and function. The echocardiographic parameters with p-value < 0.100 (i.e., at least marginally significant) in the univariate regression and the covariates described above were incorporated into the fully adjusted conditional multivariate logistic regression model. In further analysis, nonlinear transformations of continuous variables were conducted to explore potential nonlinear correlations.

Results

Study population characteristics

In this study, 1136 participants with CVDs were enrolled. The mean and standard deviation (SD) age of participants were 61.2 ± 8.3 years. Most (77.20%) of them were males. Among them, 289 participants were identified with MCI and 837 participants had normal cognitive function.

Demographic, clinical, cardiac, and cognitive characteristics are shown in Table 1. MCI group had higher systolic BP (132.3 ± 16.4 mmHg vs. 129.9 ± 15.8 mmHg, $P=0.026$), higher diastolic BP (79.1 ± 11.2 mmHg vs. 77.6 ± 11.3 mmHg, $P=0.044$) and higher rates of smoking status (50.2% vs. 43.1%, $P=0.037$), AF (31.5% vs. 19.8%, $P<0.001$), and CHF (9.3% vs. 4.5%, $P=0.002$).

The cardiac structural and functional parameters are significantly different between the two groups. LV diastolic dysfunction (54.0% vs. 40.3%, $P<0.001$) and biatrial enlargement (15.9% vs. 9.8%, $P=0.005$) were more common in the MCI group. IVST (1.04 ± 0.20 cm vs. 1.00 ± 0.17 cm, $P=0.002$) was greater in the MCI group.

Correlation between global cognitive function and cardiac structural/functional measurements

As shown in Fig. 1, PCA indicated that the total MoCA score was negatively correlated with LV diastolic dysfunction, aortic regurgitation (AR), LV mass index, aortic sinus diameter, IVST, and LV hypertrophy. LV diastolic dysfunction, LV hypertrophy, IVST, aortic sinus diameter, LV mass index, and AR were positively correlated with MCI.

Table 2 shows the correlation between the total MoCA score and cardiac structure and function in the negative binomial regression model. After adjusting for confounders, LV diastolic dysfunction (Beta [standard error, SE], 0.234 [0.045]; $P<0.001$) and higher IVST (Beta [SE], 0.034 [0.016]; $P=0.036$) demonstrated a negative correlation with the global cognitive score of MoCA.

Association between MCI and cardiac structure/function

In the conditional univariate logistic regression analysis (Table 3), biatrial enlargement (OR, 1.76; 95% CI, 1.18–2.62; $P=0.005$), IVST (OR, 1.14; 95% CI, 1.06–1.24; $P<0.001$), LV diastolic dysfunction (OR, 1.74; 95% CI, 1.33–2.28; $P<0.001$) were positively associated with MCI.

In the fully-adjusted conditional multivariate logistic regression model (Table 3), LV diastolic dysfunction (OR, 2.03; 95% CI, 1.48–2.79, $P<0.001$) and IVST (OR, 1.14; 95% CI, 1.03–1.27; $P=0.014$) were independently associated with MCI, after adjusting for the diagnosis CVDs and other conventional MCI risk factors. The association between MCI and biatrial enlargement lost significance in adjusted model. Upon further analysis, nonlinear transformations of continuous variables in univariate and multivariate logistic regression models did not produce significant effects on outcomes (Supplementary Tables 3–6).

Discussion

In this matched case–control study for general CVDs, we observed the association between MCI and abnormal cardiac structure and function as measured by echocardiography. PCA and negative binomial regression revealed that LV diastolic dysfunction and greater IVST were correlated with the co-occurring MCI and lower MoCA score. After adjusting for diagnosed CVDs and other MCI-relevant covariates, the incidence of LV diastolic dysfunction and greater IVST were strongly correlated with lower MoCA scores and associated with the co-occurring MCI in general CVD participants. Our finding implied that more attention should be paid to neurocognitive decline in general CVD patients with abnormal echocardiographic cardiac structure and function.

Cardiac structural and functional damages are the intermediate stages or consequences of CVD development and exacerbation [33]. Echocardiography is a first-line tool for assessing cardiac structure and function and plays a significant role in diagnosing and managing CVDs [17–19]. Our findings extended some previous studies that indicated the association between mitigating cognitive decline and cardiac structural and functional abnormalities measured by echocardiography [7–10]. The Rotterdam study of 3,291 elder participants, without clinical CVDs and stroke, found that LV diastolic dysfunction was associated with dementia [34]. With the CARDIA Study data, Rouch et al. indicated that midlife LV diastolic function and its 25-year change from early to middle adulthood were linked to lower cognitive function [3]. In a secondary analysis of Atherosclerosis Risk in Communities Study, Faulkner et al. found that worse LV diastolic function was associated with poorer performance in language, memory, and attention, although the links were weak [35]. However, none of the above three studies emphasized CVD patients the same as our target population, who were proven more likely to develop cognitive

Table 1 Baseline characteristics of different cognitive function group in patients with CVDs

Clinical variables	Normal ($n=847$)	MCI ($n=289$)	*p*-value
Demographic features			
Age, mean ± SD, years	61.2 ± 8.3	61.1 ± 8.3	0.951
Sex, male, n (%)	654 (77.2)	223 (77.2)	0.986
Education, n (%)			0.991
< 6 years	20 (2.4)	7 (2.4)	
7–12 years	496 (58.6)	168 (58.1)	
> 12 years	331 (39.1)	114 (39.4)	
BMI, mean ± SD, kg/m^2	26.1 ± 3.4	26.3 ± 3.3	0.280
Smoking, n (%)	365 (43.1)	145 (50.2)	0.037
Medical History			
Diabetes mellitus, n (%)	262 (30.9)	96 (33.2)	0.470
Hyperlipidemia, n (%)	621 (73.3)	206 (71.3)	0.502
Hypertension, n (%)	537 (63.4)	197 (68.2)	0.144
Atrial fibrillation, n (%)	168 (19.8)	91 (31.5)	< 0.001
Coronary artery disease, n (%)	583 (68.8)	181 (62.6)	0.052
Chronic heart failure, n (%)	38 (4.5)	27 (9.3)	0.002
Stroke, n (%)	61 (7.2)	25 (8.7)	0.422
Chronic kidney disease, n (%)	22 (2.6)	11 (3.8)	0.291
Clinical measures			
Systolic BP, mean ± SD, mmHg	129.9 ± 15.8	132.3 ± 16.4	0.026
Diastolic BP, mean ± SD, mmHg	77.6 ± 11.3	79.1 ± 11.2	0.044
FPG, mean ± SD, mg/dl	115.6 ± 40.8	118.6 ± 45.5	0.299
Total cholesterol, mean ± SD, mg/dl	159.6 ± 41.1	164.0 ± 42.3	0.128
Triglycerides, mean ± SD, mg/dl	150.0 ± 86.9	149.6 ± 118.5	0.960
HDL-C, mean ± SD, mg/dl	43.2 ± 11.2	43.4 ± 11.5	0.735
LDL-C, mean ± SD, mg/dl	88.5 ± 33.8	90.1 ± 32.8	0.471
eGFR, mean ± SD, mL/min/1.73m^2	87.1 ± 16.3	87.4 ± 16.0	0.791
Echocardiography measures			
Global cardiac status, n (%)			0.095
Normal	51 (6.0)	10 (3.5)	
Other cardiac abnormality	786 (92.8)	277 (95.8)	0.068
LV diastolic dysfunction	341 (40.3)	156 (54.0)	< 0.001
Cardiac structure			
LA diameter, mean ± SD, cm	3.79 ± 0.50	3.85 ± 0.55	0.093
LA enlargement, n (%)	416 (49.1)	148 (51.2)	0.538
Biatrial enlargement, n (%)	83 (9.8)	46 (15.9)	0.005
IVST, mean ± SD, cm	1.00 ± 0.17	1.04 ± 0.20	0.002
Relative wall thickness, mean ± SD	0.39 ± 0.06	0.40 ± 0.07	0.263
LV mass index, mean ± SD, g/m^2	88.30 ± 21.87	90.88 ± 22.99	0.089
LV hypertrophy, n (%)	44 (5.2)	18 (6.2)	0.504
Aortic sinus diameter, mean ± SD, cm	3.41 ± 0.39	3.40 ± 0.37	0.940
Aortic regurgitation, n (%)	236 (27.9)	88 (30.4)	0.400
Cardiac systolic function			
LV ejection fraction, median (IQR), %	64 (60–66)	62 (60–66)	0.025*
Cardiac diastolic function			
E, mean ± SD, m/s	0.74 ± 0.24	0.77 ± 0.26	0.095
A, mean ± SD, m/s	0.86 ± 0.20	0.85 ± 0.20	0.538
E/A, mean ± SD	0.87 ± 0.33	0.91 ± 0.43	0.140
Global Cognitive Function			
MoCA, median (IQR)	28 (27–28.5)	23 (22–25)	< 0.001*
MMSE, median (IQR)	30 (29–30)	28 (27–29)	< 0.001*

Data are mean ± standard deviation, median (interquartile range), or number of cases (%). *P*-values reflect the results of t-test, Mann-Whitney U-test, or χ^2
BMI body mass index, *BP* blood pressure, *FPG* fasting plasma glucose, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *eGFR* estimated glomerular filtration rate, *LV* left ventricular, *LA* left atrial, *IVST* interventricular septal thickness, *E* early diastolic transmitral flow velocity, *A* late atrial diastolic transmitral flow velocity, *MoCA* Montreal Cognitive Assessment, *MMSE* Mini-Mental State Examination
**P*-value of Mann-Whitney U-test due to skewed distribution

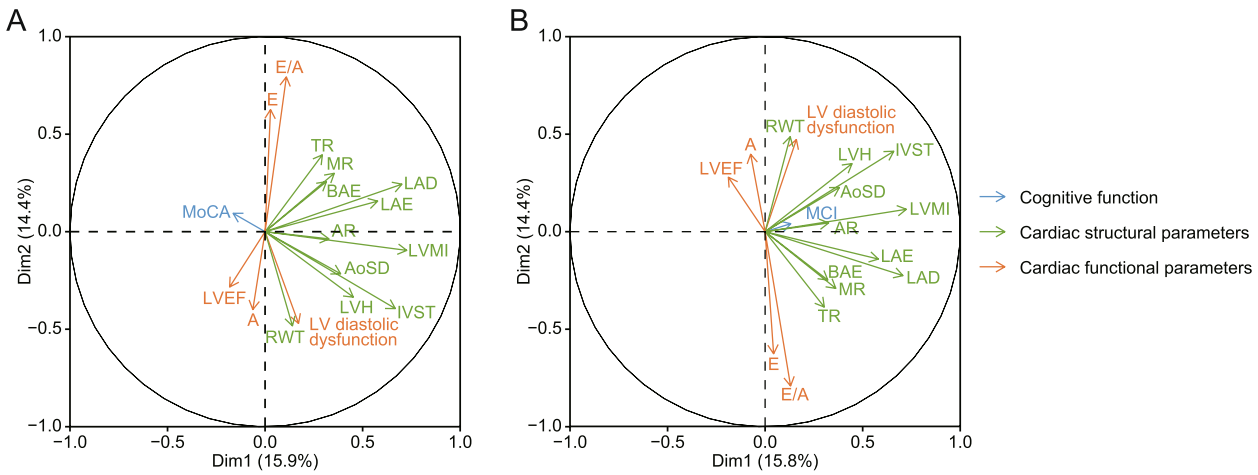

Fig. 1 Variables correlation circle of principal component analysis of the association between (**A**) the MoCA score and cardiac structure and function and (**B**) MCI and cardiac structure and function. All variables have been normalized. MCI, mild cognitive impairment; MR, mitral regurgitation; TR, tricuspid regurgitation; AR, aortic regurgitation; AoSD, aortic sinus diameter; LAD, left atrial diameter; LAE, left atrial enlargement; BAE, biatrial enlargement; IVST, interventricular septum thickness; RWT, relative wall thickness; LV, left ventricular; LVMI, left ventricular mass index; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction; E, early diastolic transmitral flow velocity; A, late atrial diastolic transmitral flow velocity

Table 2 Negative binomial regression for the correlation of echocardiographic cardiac parameters with global cognitive score of MoCA

Cardiac variables	30—global cognitive score			
	Beta (SE)	*p*-value	adj. Beta (SE)*	adj. *p*-value*
LV diastolic dysfunction	0.244 (0.045)	< 0.001	0.234 (0.045)	< 0.001
LA enlargement	−0.055 (0.045)	0.221	−0.052 (0.046)	0.264
Biatrial enlargement	0.090 (0.094)	0.341	0.066 (0.095)	0.489
IVST, per 1 mm	0.028 (0.016)	0.079	0.034 (0.016)	0.036
LV mass index, per 10 g/m^2	0.007 (0.013)	0.567	0.005 (0.014)	0.688
LV hypertrophy	−0.011 (0.100)	0.911	−0.080 (0.101)	0.426
Aortic sinus diameter, per 1 mm	−0.001 (0.006)	0.806	−0.001 (0.006)	0.839
Aortic regurgitation	0.032 (0.048)	0.506	0.020 (0.049)	0.682
LV ejection fraction, per 1%	−0.004 (0.003)	0.208	−0.002 (0.003)	0.512
E/A, per 0.1 unit	0.009 (0.006)	0.153	0.005 (0.006)	0.408

* Negative binomial regression was adjusted for age, sex, education, hypertension, atrial fibrillation, coronary artery disease, chronic heart failure, stroke, chronic kidney disease, diabetes mellitus, hyperlipidemia, smoking, systolic blood pressure, diastolic blood pressure, estimated glomerular filtration rate, fasting plasma glucose, total cholesterol, low-density lipoprotein cholesterol, and body mass index

SE standard error, *LV* left ventricular, *LA* left atrial, *IVST* interventricular septal thickness, *E/A* ratio of the early diastolic transmitral flow velocity and late atrial diastolic transmitral flow velocity

impairment. Sacre et al. conducted a study among participants from the Nurse-led Intervention for Less Chronic Heart Failure Study and reported a significantly positive association between LV diastolic dysfunction and MCI among CHF patients, supporting our results [8]. However, Sacre et al. used data from only CHF patients and did not conduct multivariable logistic regression with all echocardiographic variables included.

Inconsistent with our results, Eggermont et al. found that LV diastolic dysfunction was unrelated to memory and executive function among elder CVD participants [11]. Our study had more participants ($n=1136$) than this study ($n=117$ in Eggermont et al.). In addition, we utilized the MoCA to evaluate overall cognitive function and controlled for potential confounders that could influence cognitive function, which might facilitate obtaining more reliable conclusions.

CVDs may lead to cognitive impairment through a series of potential mechanisms, including decreases in cardiac output and cerebral perfusion, ischemic brain

Table 3 Association of echocardiographic measures of cardiac structure and function with MCI in conditional logistic regression models

Cardiac variables	Univariate model			Multivariate model[a]		
	n	OR (95% CI)	*p*-value	n	OR (95% CI)	*p*-value
Cardiac structure						
LA diameter, per 1 mm	1136	1.02 (0.99–1.05)	0.074	1091	0.99 (0.95–1.02)	0.431
LA enlargement	1136	1.09 (0.83–1.43)	0.540			
Biatrial enlargement	1136	1.76 (1.18–2.62)	0.005	1091	1.58 (0.95–2.62)	0.077
IVST, per 1 mm	1128	1.14 (1.06–1.24)	< 0.001	1091	1.14 (1.03–1.27)	0.014
Relative wall thickness, per 0.1 unit	1128	1.13 (0.92–1.39)	0.252			
LV mass index, per 10 g/m^2	1115	1.06 (0.99–1.12)	0.077	1091	0.97 (0.88–1.07)	0.555
LV hypertrophy	1136	1.25 (0.70–2.23)	0.444			
Aortic sinus diameter, per 1 mm	1136	1.00 (0.96–1.04)	0.955			
Aortic sinus enlargement	1136	1.12 (0.77–1.62)	0.571			
Aortic regurgitation	1136	1.13 (0.84–1.51)	0.437			
Cardiac systolic function						
LV ejection fraction, per 1%	1132	0.99 (0.98–1.01)	0.506			
Cardiac diastolic function						
LV diastolic dysfunction	1136	1.74 (1.33–2.28)	< 0.001	1091	2.03 (1.48–2.79)	< 0.001
E, per 0.1 m/s	1134	1.04 (0.99–1.10)	0.108			
A, per 0.1 m/s	909	0.99 (0.91–1.06)	0.722			
E/A, per 0.1 unit	909	1.03 (0.98–1.07)	0.224			

[a] The conditional multivariate logistic regression model was adjusted for hypertension, atrial fibrillation, coronary artery disease, chronic heart failure, stroke, chronic kidney disease, diabetes mellitus, hyperlipidemia, smoking, systolic blood pressure, diastolic blood pressure, estimated glomerular filtration rate, fasting plasma glucose, total cholesterol, low-density lipoprotein cholesterol, and body mass index

OR odds ratio, *CI* confidence interval, *LA* left atrial, *IVST* interventricular septal thickness, *LV* left ventricular, *E* early diastolic transmitral flow velocity, *A* late atrial diastolic transmitral flow velocity

injury (e.g., thromboembolism, transient ischemic attack), inflammation, and so on [4]. A study that used data from the Rotterdam Study reported worse LV diastolic function was associated with higher risks of stroke and silent cerebral infarction (SCI), which suggested that LV diastolic dysfunction may be associated with cerebral vessel disease and, therefore, contributed to MCI [34, 36]. Various studies have confirmed that stroke and SCI were important risk factors for cognitive impairment [26, 37, 38]. However, after adjusting for stroke as a covariate, a strong association between LV diastolic dysfunction and MCI remained, which suggested the existence of other underlying mechanisms. LV diastolic dysfunction is associated with reduced cardiac output, which may cause cerebral hypoperfusion and subsequently lead to cerebral structural and functional abnormalities. Cerebral hypoperfusion may attenuate the clearance of amyloid-beta and facilitate the phosphorylation and aggregation of tau [39], a significant pathological feature of dementia [40]. Although it is not feasible to screen all CVD patients for cognitive impairment, those with abnormal cardiac structure and function, such as LV diastolic dysfunction, might be considered to assess their cognitive function, which ensures some CVD patients at high risks of cognitive impairment be screened and managed appropriately, and timely to delay the progression of cognitive decline. While we may not be able to predict neurological impairment based solely on cardiac changes, however, adding cardiac parameters may improve our understanding of neurological impairment development in CVD patients.

Our data also showed that greater IVST was positively associated with MCI. Consistent with our results, an earlier initial study, which enrolled 22 participants with Alzheimer's disease (AD) and 23 age-matched control individuals, suggested that IVST was significantly greater in the AD group [41]. Furthermore, there is an association between IVST/LV mass index and surrogate outcomes of global cognitive function or specific cognitive domains [9, 42]. Apart from these, few studies have explored the association between IVST and MCI. Given our matched case–control study design, large-scale cohort studies are needed in the future.

In this study, we collected detailed clinical measures and included more echocardiographic parameters from more than 1000 participants, which allowed us to study the echocardiographic parameters linked to MCI more comprehensively. Since age, gender, and education level

are important factors affecting cognitive function, we used the propensity score matching to pair the MCI participants with the cognitively normal CVD participants based on age, gender, and education level to mitigate these influences. In addition, given many echocardiographic variables were continuous variables with strong collinearity, we found that PCA, a dimension reduction method, helped explore important variables correlated with MCI in our study. Furthermore, the MoCA score is a count data, so Poisson or negative binomial models are appropriate methods to determine the effect of echocardiographic measures of cardiac structure and function on MCI. Nonlinearity is probably another crucial point, but it has been far less explored in previous studies. We considered that pure linear correlation might not be robust for all variables and, therefore, applied nonlinear transformations on several numerical variables. Although it did not produce significant effects on outcomes in our study, considering its clinical importance, future studies should also consider exploring the nonlinear correlations to reach a more accurate conclusion.

Study limitations

Several limitations, including inherent defects in case-control study design, should be acknowledged and guided for future research. First, MCI was identified based on MoCA and MMSE rather than comprehensive neuropsychological evaluation. Therefore, the results may be interpreted with caution. Second, given some missing data, some individuals were excluded from different steps of statistical analysis, which might lead to selection-biased results. Third, as a single-center study, the generalizability of the results might be affected. Fortunately, most of our participants were from different provinces rather than Beijing. Therefore, the effect may be less significant. Nonetheless, cohort designs across broader geographical regions and populations are needed to validate the relationship and associated degree between echocardiographic variables and MCI. Last, although we have made efforts to recognize and control for confounders by reviewing extensive literature, some unknown and residual confounders may still exist.

Conclusions

The current study indicated the association between cognitive impairment and abnormal cardiac structure and function as measured by echocardiography. It revealed LV diastolic dysfunction and IVST were positively associated with MCI in general CVD patients, suggesting further attention to cognitive assessment in this population.

Supplementary Information

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Supplementary Material 1.

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Not applicable.

Authors' contributions
K.Z. designed the study and supervised the project. X.L. conducted the data analysis and interpretation. S.H. and X.L. performed the literature review and wrote the initial draft of the manuscript. M.Z. and C.X. prepared the figures and tables. S.X. and J.D. contributed to the methodology and provided critical revisions to the manuscript. C.M. offered valuable insights and guided the research direction. All authors reviewed and approved the final manuscript. K.Y. is the corresponding author and provided oversight for the overall project.

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Data availability
The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate
This study followed the Declaration of Helsinki and was approved by the Institutional Ethics Review Board at Beijing Anzhen Hospital (No.2022–17-1). Informed consent for this study was waived from all participants because it was retrospective and we do not involve sensitive personal information.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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