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Inferior vena cava diameter in patients with chronic heart failure and chronic kidney disease: a retrospective study

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Abstract

Background Chronic kidney disease (CKD) carries the highest population attributable risk for mortality among all comorbidities in chronic heart failure (CHF). No studies about the association between inferior vena cava (IVC) diameter and all-cause mortality in patients with the comorbidity of CKD and CHF has been published.

Methods In this retrospective cohort study, a total of 1327 patients with CHF and CKD were included. All patients underwent standardized echocardiography examination and data on demographic characteristics, medical history, and laboratory tests were recorded. Information on all-cause mortality was collected by telephone interview and medical records review. We used Cox regression to evaluate the risk of all-cause mortality among groups, and used mediation analysis to examine the mediation role of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) and serum albumin in the association between IVC and all-cause mortality.

Results During a median follow-up of 3.46 years (IQR: 1.55–5.15 years), 757 (57.05%) cases of all-cause mortality were observed. Compared with patients with IVC diameter < 21 mm, those with IVC diameter > 21 mm were associated with higher risk of all-cause mortality (HR (95%CI):1.31(1.07–1.61), log rank: $P = 0.01$) and cardiovascular mortality (HR (95%CI): 1.55(1.19–2.04), log rank: $P = 0.001$). When assessing IVC as a continuous variable, each 1% increase in IVC was associated with 4% increased risk of all-cause mortality (HR: 1.04, 95%CI 1.02–1.06, $P < 0.001$). This association were mediated by log NT-proBNP (mediated effect: 37.8% (95%CI 22.0–73.0%), $P < 0.001$) and serum albumin (mediated effect: 14.1% (95%CI 6.2–28.0%), $P < 0.001$). In subgroup analyses, there was no significant interaction in different subgroups of cardiac and renal function for the association between IVC and all-cause mortality.

Conclusions Elevated IVC diameter was associated with worse prognosis in patients with CHF and CKD, and the associations were mediated by log NT-proBNP and serum albumin.

Key points

1. Population with CKD and CHF experienced unfavorable prognosis with high mortality.
2. IVC diameter was associated with all-cause mortality in different subgroups of CHF or CKD, routine monitor of IVC diameter might contribute to the management of patients with CHF and CKD.

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3. The association between IVC diameter and all-cause mortality was mediated by log NT-proBNP and serum albumin.

Keywords IVC diameter, CHF, CKD, Mortality

Introduction

Due to shared risk factors including older age, hypertension, and diabetes mellitus, as well as common pathological mechanisms, chronic heart failure (CHF) and chronic kidney disease (CKD) usually coexist as comorbidity [1]. CKD has consistently been identified as one of the most prevalent comorbidities for CHF, 55%~60% patients with CHF occurred with CKD [2–4]. Meanwhile, about a quarter of CKD patients have CHF. Via mechanisms involving sodium and water retention, inflammation, and toxins accumulation, CKD patients are prone to have myocardial damage and, which forms a vicious circle of perpetual decrease in heart and kidney function [4–6]. In addition, diuretic resistance also deteriorates the outcomes [2, 7]. Due to all above reasons, CKD carries the highest population attributable risk for mortality among all comorbidities in CHF [4–6].

Inferior vena cava (IVC) diameter is an accurate and reproducible echocardiographic parameter reflecting central venous pressure [1]. And central venous pressure was demonstrated as an independent predictor for renal function deterioration and all-cause mortality in patients with cardiovascular disease [8, 9]. However, studies evaluating the predicting value of IVC in patients with CHF and CKD remain sparse. We aim to detect the association between IVC diameter and all-cause mortality and cardiovascular mortality in patients with CHF and CKD.

Methods

Study design

This retrospective study was approved by the ethics committee of Chinese PLA General Hospital (Number: S2018-269-02). Patients with CHF and CKD hospitalized in Chinese PLA General Hospital between January 2011 and July 2019 were consecutively included in the current study. CHF was defined according to the criteria of 2021 European Society of Cardiology Guidelines comprising heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF) [10]. Different subgroups of CHF were distinguished by ejection fraction (EF): EF < = 40% for HFrEF; EF 41–49% for HFmrEF; and EF ≥ 50% for HFpEF [4, 11–13]. Estimated glomerular filtration rate (eGFR) was calculated based on serum creatine according to the 2021 CKD–EPI (Chronic Kidney Disease Epidemiology Collaboration) creatine equation. Patients with eGFR less than 60 mL/min/1.73 m [2] was defined as CKD [14]. CKD was subclassified in to CKD stage 3 (eGFR 30–60 mL/min/1.73 m^2), CKD stage 4 (eGFR 15–30 mL/min/1.73 m^2), and CKD stage 5 (eGFR < = 15 mL/min/1.73 m^2) [15]. The exclusion criteria included: (1) younger than 18 years; (2) pregnancy; (3) Missing data of required echocardiography parameters, serum creatine or N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) value.

Data collection

Clinical characters including demographic information, laboratory test, comorbidities, and treatment during hospitalization and after discharge were derived from the hospital information system. Demographic information involving age, gender, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) was acquired directly and Body Mass Index (BMI) was calculated as weight (kg) /height^2 (m^2). The first laboratory examination result within 2 weeks before and 2 weeks after the date of in-hospital was considered as the baseline characteristics. Laboratory examination contained NT-proBNP, hemoglobin, white blood cells, total protein, serum albumin, Fasting blood glucose (FBG), random blood glucose, glycosylated hemoglobin, serum creatine, uric acid, and urinary albumin. Log transformed values for NT-proBNP were used to reduce skew. Comorbidities including myocardial infarction (MI), hypertension, diabetes (DM), and anemia were diagnosed according to the medical records, laboratory examination and medication records. FBG ≥ 7 mmol/l, or random blood glucose ≥ 11 mmol/l, or glycosylated hemoglobin ≥ 6.5%, or treatment of diabetes was diagnosed as DM [16]. Anemia was defined as hemoglobin < 120 g/L in women, or < 130 g/L in men, or usage of iron [17]. Hypertension was defined as SBP ≥ 140 mmHg, or DBP ≥ 90 mm Hg, or usage of antihypertension drugs [18]. Treatment information included history of percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), heart valve replacement, heart pacemaker implantation, and defibrillator, as well as medication of statin, angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), beta blocker, loop diuretic and potassium-sparing diuretic, and warfarin used during hospitalization or after discharge.

Echocardiographic parameters were recorded and analyzed. Twenty-four parameters including IVC (inferior vena cava) diameter, left ventricular end-diastolic diameter (LVDd) left ventricular end-systolic diameter (LVSd), IVS (interventricular septum), posterior wall thickness (PWT), end-diastolic volume (EDV) and end-systolic volume (ESV), anteroposterior diameter of left atrium (LA-AP), superior-infra dimensions of left atrium (LA-SI), transverse diameter of left atrium (LA-T), right atrium (RA) diameter, right ventricular (RV) diameter, aortic valve annulus, sinuses of Valsalva, sinotubular junction, proximal ascending aorta, pericardial effusion, segmental abnormal wall motion, mitral regurgitation, tricuspid regurgitation, aortic regurgitation, pulmonary regurgitation, mitral stenosis, and aortic stenosis were derived from the hospital electronic medical record database directly. And five parameters were calculated in accordance with the recommendations of the American Society of Echocardiography (ASE) [19, 20]. Relative wall thickness (RWT) was calculated by the formula: [(2 × diastolic posterior wall thickness)/diastolic LV internal diameter]. EF was calculated using the biplane Simpson's method from left ventricular EDV and ESV. Fractional shortening (FS) was calculated using LVDd and LVDs. The left ventricular mass (LVM) was calculated from LV linear dimensions and indexed to height (LVMi) [19].

In the subcostal view on B mode of ultrasound, the diameter of the IVC was measured perpendicular to the IVC long axis at 1.0 to 2.0 cm from the junction with the right atrium, with the patient in the supine position at end-expiration phase [21]. Patients were divided into two groups by normal IVC diameter (< = 21 mm) and abnormal IVC diameter (> 21 mm) according to consensus by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [21].

Outcomes

Clinical outcomes were obtained by telephonic interview and reviewing subsequent medical records. The primary outcome was all-cause mortality. The secondary outcome was cardiovascular mortality.

Statistical analysis

Baseline characteristics were summarized and compared between normal IVC diameter and abnormal IVC diameter groups. Continued values with normal distribution were presented as means and standard deviations and compared using *t* test. Continued values with abnormal distribution were presented as medium and interquartile ranges (IQR) and compared using Wilcoxon rank sum test. Category values were presented as percentages and compared with x^2 test. Multiple imputation was performed for missing data. Kaplan–Meier (KM) curves for outcomes were created in each group and compared using log-rank test. We also evaluated IVC diameter as a continuous variable in the association with outcomes. Univariate and multivariate Cox proportional hazards regression analysis were performed to estimate Hazard ratios (HRs) and 95% confidence interval (95% CI). All variables with p value < 0.05 in the univariate analysis were included as covariates in the multivariate analysis. The nonlinear relationship between IVC diameter and outcomes was assessed by restricted cubic spline (RCS). Mediation analysis quantified the mediation effect of log NT-proBNP and serum albumin in the association between IVC diameter and outcomes. Stratified analysis was used to evaluate the association between IVC diameter and outcomes in different subgroups of age, gender, EF and eGFR. Two-sided P value < 0.05 were considered statistically significant. All statistical analysis was conducted R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

Result

Patient characteristics

Of the 1759 patients with CHF and CKD with available echocardiograms, 154 patients were excluded, because lacking indexes and 278 patients were censored, as shown in Fig. 1. Eventually, 1327 patients were included in this study. Of them, 1167 (87.9%) patients had normal IVC diameter and 160 (12.1%) had abnormal IVC. In this cohort with CHF and CKD, the median (IQR) of IVC diameter was 16 mm (14–19 mm).

Baseline characteristics are shown in Table 1. The median age of these 1327 patients were 72.30 years and 63.2% of them are male. Patients with abnormal IVC were older, male, and more likely to have higher

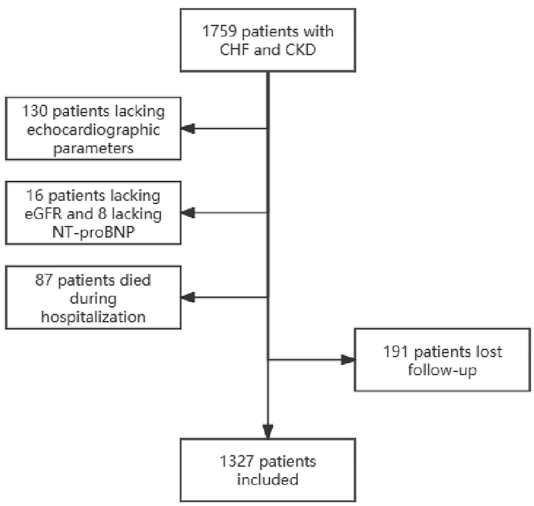

Fig. 1 Flow chart of the enrollment of participants in this study

Table 1 Baseline characteristics of 1327 patients with CHF and CKD

Baseline characteristics	Overall ($n=1327$)	Normal IVC ($n=1167$)	Abnormal IVC ($n=160$)	*p* value
Demography				
Age	72.30 (61.89, 80.73)	72.67 (62.45, 81.21)	67.36 (58.60, 77.25)	< 0.001
Male	839 (63.2)	731 (62.6)	108 (67.5)	0.001
SBP	135.00 (120.00, 151.00)	136.00 (120.00, 152.00)	130.00 (115.00, 149.00)	0.281
DBP	73.00 (64.50, 83.00)	73.00 (65.00, 84.00)	74.00 (63.00, 83.00)	0.001
HR	79.00 (70.00, 92.00)	79.00 (70.00, 92.00)	80.00 (69.00, 91.00)	0.563
BMI	24.67 (22.16, 27.06)	24.63 (22.10, 27.05)	24.80 (22.64, 27.70)	0.176
Laboratory tests				
NT-proBNP	5416.00 (2,049.50, 14,595.00)	4897.00 (1,899.00, 14,175.50)	8220.00 (3,895.00, 20,160.50)	< 0.001
Hemoglobin	119.00 (100.00, 136.00)	120.00 (101.00, 136.00)	116.00 (95.00, 136.50)	0.154
White blood cells	6.85 (5.53, 8.61)	6.90 (5.62, 8.61)	6.41 (4.85, 8.61)	0.02
Total protein	68.30 (64.12, 72.88)	68.30 (64.20, 72.97)	68.05 (62.18, 72.58)	0.177
Serum albumin	38.20 (34.85, 41.10)	38.30 (35.00, 41.20)	37.65 (33.60, 40.18)	0.026
FBG	5.56 (4.82, 7.21)	5.59 (4.85, 7.32)	5.36 (4.63, 6.58)	0.015
Serum creatine	143.30 (118.60, 214.15)	141.10 (117.65, 213.50)	156.95 (124.47, 228.20)	0.034
eGFR	41.48 (24.64, 52.46)	41.84 (24.64, 52.71)	39.47 (24.81, 50.61)	0.184
Uric acid	455.75 (378.05, 560.28)	445.15 (369.33, 543.78)	565.90 (475.82, 650.45)	< 0.001
Urinary albumin	20.00 (0.00, 75.00)	20.00 (0.00, 100.00)	20.00 (0.00, 70.00)	0.453
Comorbidities				
MI	566 (42.7)	532 (45.6)	34 (21.2)	< 0.001
Hypertension	1064 (80.2)	955 (81.8)	109 (68.1)	< 0.001
DM	710 (53.5)	639 (54.8)	71 (44.4)	0.017
Anemia	801 (60.4)	702 (60.2)	99 (61.9)	0.741
Treatment				
PCI	313 (23.6)	299 (25.6)	14 (8.8)	< 0.001
CABG	62 (4.7)	57 (4.9)	5 (3.1)	0.43
Heart valve replacement	28 (2.1)	14 (1.2)	14 (8.8)	< 0.001
Heart pacemaker implantation	93 (7.0)	75 (6.4)	18 (11.2)	0.038
Defibrillator	9 (0.7)	5 (0.4)	4 (2.5)	0.013
Statin	1017(76.6)	930 (79.7)	87 (54.4)	< 0.001
ACEI	438 (33.0)	377 (32.3)	61 (38.1)	0.168
ARB	429 (32.3)	381 (32.6)	48 (30.0)	0.561
Beta blocker	1129 (85.1)	1004 (86.0)	125 (78.1)	0.012
Loop diuretic	1167 (87.9)	1012 (86.7)	155 (96.9)	< 0.001
Potassium-sparing diuretic	961 (72.4)	829 (71.0)	132 (82.5)	0.003
Warfarin	166 (12.5)	123 (10.5)	43 (26.9)	< 0.001

Nonabnormal continuous values were showed as median (IQR) and categorical values were showed as number (%). *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *BMI* Body mass index, *eGFR* estimated glomerular filtration rate, *FBG* fasting blood glucose, *MI* myocardial infarction, *DM* diabetes, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass graft, *ACEI* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker; Statin 1, *ACEI 1*, ARB 1, beta blocker 1, loop diuretic 1 and potassium-sparing diuretic 1, warfarin 1 refers medication used during hospitalization, and Statin 2, ACEI 2, ARB 2, beta blocker 2, loop diuretic 2 and potassium-sparing diuretic 2, warfarin 2 refers medication used after discharge

diastolic blood pressure, higher NT-proBNP, lower hemoglobin, lower serum albumin, lower FBG, higher serum creatine and higher uric acid. They were with lower rate of MI, hypertension, DM and history of PCI, statin, beta blocker. They had higher prevalence of heart valve replacement, heart pacemaker implantation, defibrillator, and use of loop diuretic, potassium-sparing diuretic, and warfarin.

As shown in Table 2, patients with abnormal IVC had lower LVDd, LVSd, PWT, RWT, EF, FS, LVM, and higher EDV, ESV, LA-AP, LA-SI, LA-T, RA, RV, LVMi. They were more likely to have pericardial effusion, segmental abnormal wall motion, tricuspid regurgitation, aortic regurgitation, and pulmonary regurgitation.

This cohort included 508 (38.3%) patients with HFrEF, 290 (21.9%) with HFmrEF, and 529 (39.9%) with HFpEF.

Table 2 Echocardiographic parameters for participants

Echocardiographic parameters	Overall ($n=1327$)	Normal IVC ($n=1167$)	Abnormal IVC ($n=160$)	*p* value
LVDd	52.00 (46.00, 58.00)	52.00 (47.00, 58.00)	48.00 (42.00, 56.00)	< 0.001
LVSd	38.00 (33.00, 46.50)	39.00 (33.00, 47.00)	35.50 (30.00, 43.00)	< 0.001
IVS	11.00 (10.00, 12.00)	11.00 (10.00, 12.00)	11.00 (10.00, 12.00)	0.32
PWT	11.00 (10.00, 11.00)	11.00 (10.00, 11.00)	10.00 (9.00, 11.00)	0.048
RWT	0.41 (0.35, 0.47)	0.42 (0.36, 0.47)	0.39 (0.32, 0.46)	0.01
EDV	124.00 (96.00, 164.50)	123.00 (96.00, 159.00)	143.50 (107.75, 215.25)	< 0.001
ESV	62.00 (44.00, 100.50)	62.00 (43.00, 97.00)	81.00 (48.50, 135.50)	< 0.001
EF	46.00 (35.50, 55.00)	46.00 (36.00, 55.00)	44.00 (30.00, 54.00)	0.013
FS	24.00 (18.00, 29.00)	25.00 (18.00, 29.00)	23.00 (15.75, 29.00)	0.015
LA-AP	42.00 (38.00, 46.00)	41.00 (38.00, 45.00)	46.00 (42.00, 51.00)	< 0.001
LA-SI	59.00 (55.00, 65.00)	59.00 (54.00, 64.00)	66.00 (60.00, 72.00)	< 0.001
LA-T	43.00 (39.00, 47.00)	43.00 (39.00, 47.00)	47.00 (43.00, 51.25)	< 0.001
RA	38.00 (34.00, 43.00)	37.00 (33.00, 41.00)	47.00 (42.00, 53.00)	< 0.001
RV	36.00 (33.00, 40.00)	35.00 (32.00, 39.00)	44.00 (38.00, 50.00)	< 0.001
Aortic valve annulus	20.00 (19.00, 22.00)	20.00 (19.00, 22.00)	20.00 (19.00, 22.00)	0.241
Sinuses of Valsalva	32.00 (29.00, 34.00)	32.00 (29.00, 34.00)	32.00 (29.00, 35.00)	0.096
Sinotubular junction	27.00 (24.00, 29.00)	27.00 (24.00, 29.00)	27.00 (25.00, 30.00)	0.095
Proximal ascending aorta	32.00 (29.00, 35.00)	32.00 (29.00, 34.00)	32.00 (29.00, 36.00)	0.204
Pericardial effusion	120 (9.0)	89 (7.6)	31 (19.4)	< 0.001
Segmental abnormal wall motion	476 (35.9)	451 (38.6)	25 (15.6)	< 0.001
Mitral regurgitation	1033 (77.8)	901 (77.2)	132 (82.5)	0.158
Tricuspid regurgitation	1027 (77.4)	879 (75.3)	148 (92.5)	< 0.001
Aortic regurgitation	708 (53.4)	601 (51.5)	107 (66.9)	< 0.001
Pulmonary regurgitation	697 (52.5)	573 (49.1)	124 (77.5)	< 0.001
Mitral stenosis	29 (2.2)	29 (2.5)	0 (0.0)	0.084
Aortic stenosis	52 (3.9)	48 (4.1)	4 (2.5)	0.442
LVM	218.10 (176.04, 269.18)	220.14 (181.40, 271.56)	193.70 (147.00, 249.31)	< 0.001
LVMi	1.30 (1.09, 1.60)	1.29 (1.09, 1.57)	1.43 (1.09, 1.84)	0.004

Nonabnormal continuous values were showed as median (IQR) and categorical values were showed as number (%). LVDd, Left ventricular end-diastolic diameter; LVSd, left ventricular end-systolic diameter; IVS, interventricular septum; PWT, posterior wall thickness; EDV, end-diastolic volume; ESV, end-systolic volume; LA-AP, anteroposterior diameter of left atrium; LA-SI, superior-infra dimensions of left atrium; LA-T, transverse diameter of left atrium; RA, right atrium; RV, right ventricular; diameter; IVC diameter, inferior vena cava diameter; LA volume, left atrium volume; LVM, left ventricular mass; LVMi, left ventricular mass index; RWT, Relative wall thickness; EF, Ejection fraction; Fractional shortening, FS

898 (67.7%) of this cohort were at CKD stage 3, 258 (19.4%) at CKD stage 4, and 171 (12.9%) at CKD stage 5.

Outcomes

During a median follow-up of 3.46 years (IQR: 1.55 ~ 5.15 years), 757 (57.0%) cases of all-cause mortality and 381 (28.7%) cases of cardiovascular mortality were observed (Table 3).

The KM curves demonstrate that patients with abnormal IVC had higher risk of all-cause mortality [log rank: $p=0.01$, HR (95% CI) 1.31(1.07–1.61)] and cardiovascular mortality [log rank: $p=0.001$, HR (95%CI) 1.55(1.19–2.04)] than those with normal IVC (Fig. 2). Clinical variables associated with all-cause mortality in univariate analysis are shown in Fig. 3. After adjusted for confounding factors, abnormal IVC

Table 3 Outcomes according to IVC groups

	Total Population	Normal IVC	Abnormal IVC	*P* value
Follow-up (years)	3.46 (1.55, 5.15)	3.53 (1.61, 5.16)	3.05 (1.20, 5.02)	0.119
All-cause mortality	757 (57.0)	648 (55.5)	109 (68.1)	0.003
Cardiovascular mortality	381(28.7)	318(27.2)	63(39.4)	0.002

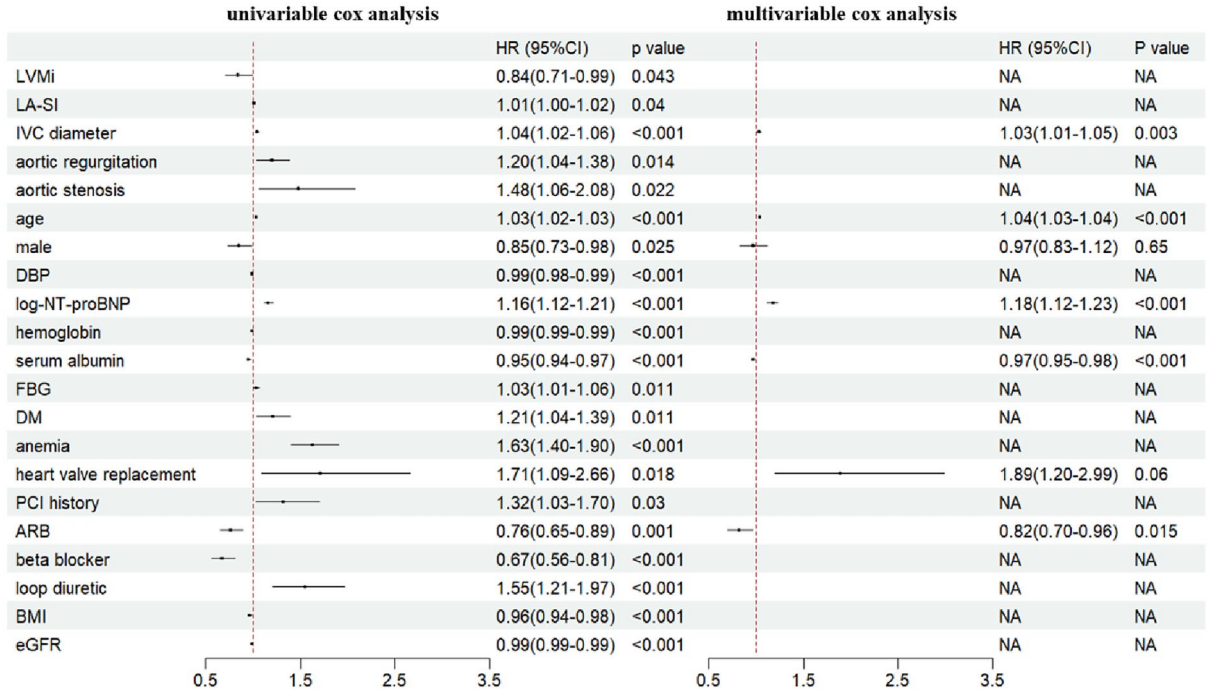

Fig. 2 Univariate and multivariate COX analyses for all-cause mortality of clinical and echocardiographic variables

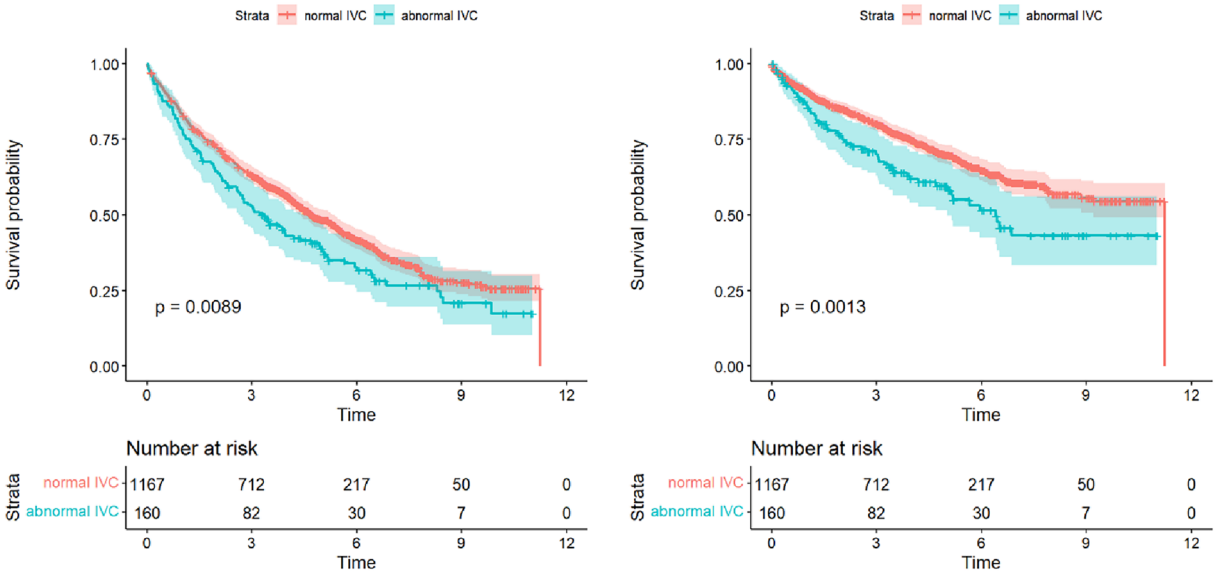

Fig. 3 K-M curves for all-cause mortality (left) and cardiovascular mortality (right) in patients with normal IVC and abnormal IVC

was associated with 1.24-fold increased risk of all-cause mortality (HR: 1.24, 95%CI 1.01–1.54, $p < 0.001$) than those with normal IVC (Table 4). There was no statistical significance for cardiovascular mortality between abnormal and normal IVC in multivariate COX analysis ($p = 0.17$) (Table 4). When evaluated as a continuous variable, each 1% increase in IVC diameter was associated with 4% increased risk for all-cause mortality (HR: 1.04, 95%CI 1.02–1.06, $p < 0.001$) (Table 4). There was no statistically significant association between cardiovascular mortality and IVC

Table 4 Univariate and multivariate cox analyses for IVC diameter

	Dichotomous HR (95% CI) for abnormal IVC	*P* value	Continuous HR (95% CI) per 1% increase in IVC	*P* value
All-cause mortality				
Unadjusted	1.31 (1.07–1.61)	0.009	1.04 (1.02–1.06)	< 0.001
Age and gender adjusted	1.47 (1.20–1.81)	< 0.001	1.05 (1.03–1.07)	< 0.001
All adjusted	1.24 (1.01–1.54)	< 0.001	1.03 (1.01–1.05)	0.003
Cardiovascular mortality				
Unadjusted	1.55 (1.19–2.04)	0.001	1.05 (1.03–1.08)	< 0.001
Age and gender adjusted	1.71 (1.30–2.25)	< 0.001	1.06 (1.04–1.09)	< 0.001
All adjusted	1.22 (0.92–1.62)	0.168	1.02 (0.99–1.05)	0.123

All-cause mortality adjusted for age, gender, log NT-proBNP, serum albumin, heart valve replacement and ARB

Cardiovascular mortality adjusted for age, gender, EF, AVSs, log NT-proBNP, serum albumin, uric acid and heart valve replacement

($p = 0.12$). The restricted cubic spline displayed the linear relation between IVC and all-cause mortality and cardiovascular mortality (Fig. 4).

Mediation analysis revealed that the proportion mediated by log NT-proBNP for the association between IVC and all-cause mortality was 37.8% (95%CI 22.0–73.0%, $P < 0.001$). The proportion mediated by serum albumin for the association between IVC and all-cause mortality was 14.1% (95%CI 6.2–28.0%, $P < 0.001$). In subgroup analyses, there was no significant interaction effect between IVC diameter and age, gender, CHF, and CKD categories in the association with all-cause mortality (P interaction > 0.05) (Fig. 5).

Discussion

Our results demonstrated that abnormal IVC was associated with increased risk of all-cause mortality in patients with CHF and CKD. The association was mediated by log NT-proBNP and serum albumin.

IVC was an independent predictor for all-cause mortality in patients with the comorbidity of cardiac and renal dysfunction. This result was consistent with previous studies. Sampath-Kumar et al. found that dilated IVC diameter (> 2.07 cm) is predictive of rehospitalization with 1 year in patients with acute decompensated heart failure [22]. In cohorts of CHF, IVC was also demonstrated associated with a composite endpoint of cardiovascular death or HF hospitalization and all-cause mortality [8, 9]. In summary, prior studies mainly

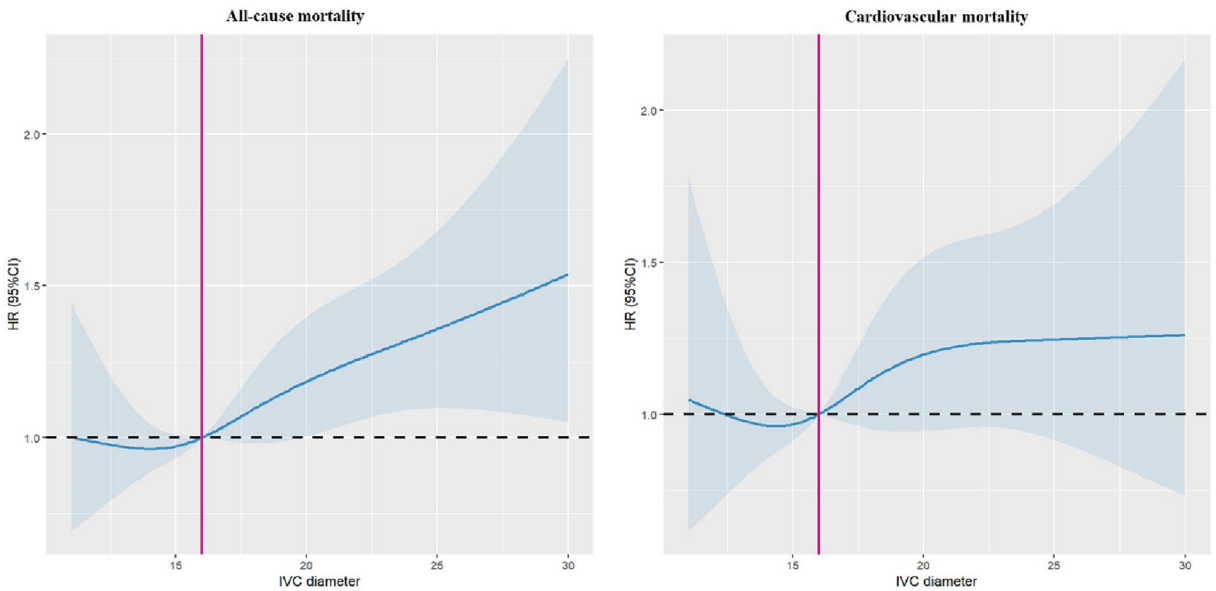

Fig. 4 Restricted cubic spline of all-cause mortality (left) and cardiovascular mortality (right) in patients with normal IVC and abnormal IVC

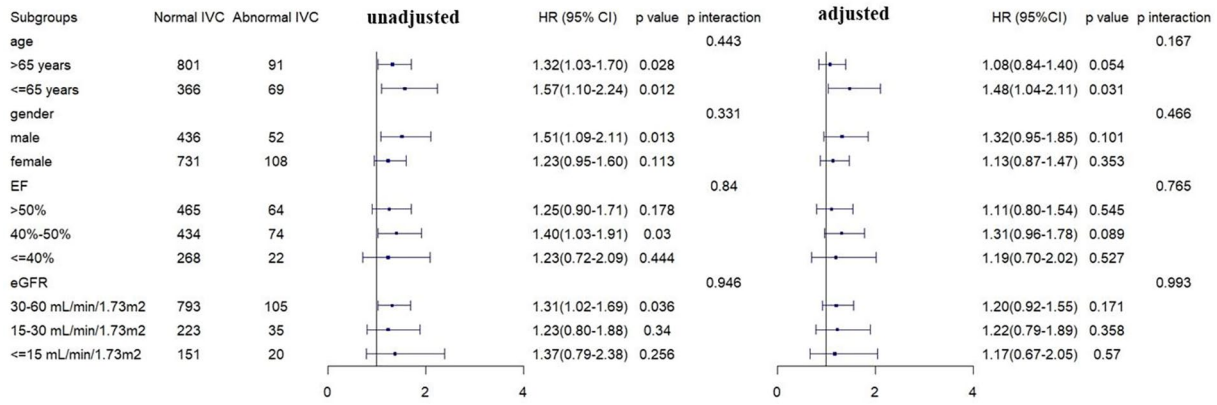

Fig. 5 Subgroup analyses of IVC for all-cause mortality, and adjusted by age, gender, log NT-proBNP, serum albumin, heart valve replacement history, and ARB

demonstrated association between IVC and adverse outcomes in patients with acute or chronic HF. However, cohorts with the comorbidity of CHF and CKD remains limited. Our study demonstrated that IVC was independently associated with all-cause mortality in a cohort with CHF and CKD with a long follow-up.

Our result demonstrated that population with CKD and CHF experienced unfavorable prognosis, 57.0% cases of all-cause mortality were recorded during the 3.46 year follow-up. Besides the poor prognosis of CKD and CHF themselves, respectively, high mortality was also attributed to the bidirectional causal relationship between CKD and CHF. Hemodynamic alteration and (neuro) hormonal activation are potential pathophysiological mechanisms which promote salt and water retention in the progression of cardio-renal and reno-cardiac interactions [23]. Thus, the central venous pressure increased and manifested as the abnormally increased IVC diameter. Moreover, persistent salt and water retention results in renal and cardiac fibrosis remodeling and function deterioration [3, 23, 24]. And the accelerated renal and cardiac function deterioration leads to the high all-cause mortality. As an important index reflecting central venous pressure in patients with CHF or those with CKD, IVC is not only an evident marker on imaging for the process vicious circle of CHF and CKD, but also a strong prognostic factor for the all-cause mortality [25, 26].

Our study demonstrated that 37.8% of the association between IVC and all-cause mortality was explained by log NT-proBNP and 14.1% was explained by serum albumin. The mediation effect implied that, in patients with CHF and CKD, the central venous pressure affected the poor outcomes via damage to cardiac and renal function. This is consistent with previous theories, that venous congestion leads to renal and cardiac remodeling and worsens their function, eventually contributes to poor outcomes. Data in previous studies also supported these results [27–29]. Elevated IVC diameter mirrors raised cardiac filling pressure affecting cardiac function, which remains as a major determinant of prognosis in patients with HF [30–32]. In a cohort with EF < 40% and repeated hospitalizations for HF, IVC > 21 mm was associated worsening renal function and the composite endpoints of death and HF re-hospitalization [31]. NT-proBNP is an index to reflex the heart function and serum albumin is an index for renal function. The mediation effect of NT-proBNP serum albumin in the association of IVC diameter and all-cause mortality proved that the usage of IVC diameter to monitor status of patients with CHF and CKD is reasonable and reliable.

Patients with the comorbidity of CHF and CKD go through a complex process, both the classification of cardiac and renal dysfunction should be taken into consideration. In addition, there is an interaction between them. We aim to detect a strong index to reflect the status of patients, so that it could predict the outcomes. To test the generalization of IVC diameter, patients at different categories of CHF (HFrEF, HFmrEF, and HFpEF) and different stages of CKD (CKD stage 3, CKD stage 4, and CKD stage 5) were analyzed in this study. In different subgroups of CHF or CKD, the association between IVC diameter and all-cause mortality remains similar. Which indicated that, despite of the status of cardiac or renal function, IVC diameter remains as an essential predictive factor for all-cause mortality in patients with the comorbidity of CHF and CKD.

The limitation of this study is that the study was a retrospective study. IVC was not the only index to reflect the central venous pressure, but the most convenient one. More echocardiographic parameters need to be analyzed. However, these parameters were missing, such as tricuspid regurgitation and E/e'. Prospective studies with large

sample were called for to detect more essential predictors for mortality in patients coexisting with CHF and CKD.

Conclusion

IVC diameter was associated with all-cause mortality in different subgroups of CHF or CKD, and the association was mediated by log NT-proBNP and serum albumin. Therefore, routine monitor of IVC diameter might contribute to the management of patients with CHF and CKD. And more echocardiographic parameters related with congestion need to be analyzed in this cohort.

Author contributions

All authors have made substantial contributions. JL performed study, statistical analysis and wrote manuscript. CW participated in study data collection and revised the manuscript. JQ and CR participated in data organization. HD and QL contributed discussion. KH provided funding support, designed study and reviewed manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the ethics committee of Chinese PLA General Hospital (Number: S2018-269-02).

Competing Interests

The authors declare no competing interests.

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