Two-Dimensional and Three-Dimensional Transthoracic Echocardiography as Predictive and Prognostic Indicators of All-Cause Mortality in Heart Failure with Reduced Ejection Fraction in Patients with Ischemic Heart Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: This study aimed to compare the predictive role of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) on in-hospital all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Material/Methods: Patients (N-224) with HFrEF due to IHD who had a left ventricular ejection fraction (LVEF) <40% on admission when measured by 2D-TTE and 3D-TTE were studied and divided into survival and mortality groups. Baseline demographic and clinical characteristics were compared.

Results: Compared with the survival group (n=142), patients who died during hospitalization (n=82) were more commonly older (67.3 *vs.* 62.6 years), female (48.8% *vs.* 38.7%), with diabetes mellitus (51.2% *vs.* 32.4%), chronic kidney disease (48.8% *vs.* 32.4%), intravenous inotropes (85.4% *vs.* 76.1%), and intravenous vasodilators (70.7% *vs.* 61.3%). Regression model analysis for all-cause mortality identified significant associations with age, diabetes mellitus, myocardial infarction (MI), intravenous inotropes, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and LVEF following 2D-TTE. Age, diabetes mellitus, prior MI, the use of intravenous inotropes, NT-proBNP, LVEF, and left ventricular end-diastolic volume (LVEDV) index following 3D-TTE were significantly associated with all-cause mortality. Modeling of 2D-TTE parameters showed that the concordance statistic (C-index) increased significantly after including the LVEF, from 0.72 to 0.77 and from 0.72 to 0.80, respectively. Modeling of 3D-TTE parameters showed that the C-index increased significantly after including the LVEDV index (from 0.80 to 0.76).

Conclusions: In patients with HFrEF due to IHD, 3D-TTE was a better predictor than 2D-TTE of in-hospital all-cause mortality.

MeSH Keywords: Mortality • Heart Failure • Echocardiography, Doppler

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Background

Worldwide, congestive heart failure (CHF) remains a leading cause of morbidity and mortality [1–4]. Several diagnostic and prognostic markers are used in patients with CHF, including serum N-terminal pro-B-type natriuretic peptide (NT-proBNP), which are used to guide clinical management [4–7].

Transthoracic echocardiography (TTE) is commonly used to evaluate cardiac function and cardiac structure in clinical practice [8]. The left ventricular ejection fraction (LVEF) can be measured by TTE and is an important parameter that reflects left ventricular systolic function [8]. Previously published studies have shown that increased left ventricular volume (LVV) is significantly associated with worse prognosis in patients with heart failure and reduced ejection fraction (HFrEF) [9–11]. Post previously published studies have investigated two-dimensional transthoracic echocardiography (2D-TTE) to evaluate LVEF and LVV, but these values may be underestimated, especially when the left ventricle does not conform to a normal geometric shape [8]. Recently, the use of three-dimensional transthoracic echocardiography (3D-TTE) to assess cardiac function and structure has gradually increased, which is largely attributed to its advantages in the imaging quality and accuracy for the estimation of LVEF and LVV estimation [12–14]. However, little is known about the differences between 2D-TTE and 3D-TTE predicting prognosis in patients with HFrEF, which may guide clinical therapy.

Therefore, this study aimed to compare the predictive role of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) on in-hospital all-cause mortality in patients with HFrEF due to ischemic heart disease (IHD).

Material and Methods

Patients studied

The protocol of this retrospective study was approved by the local Research Ethics Committee, which did not require informed patient consent. Patients were diagnosed with heart failure on hospital admission between January 2018 to July 2019. The study included patients with ischemic heart disease (IHD) who had a left ventricular ejection fraction (LVEF) <40% on admission when measured by two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE). The definition of heart failure due to IHD was based on a prior documented history of myocardial infarction (MI), or coronary heart disease, prior percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) surgery. The flowchart of the study design is shown in Figure 1.
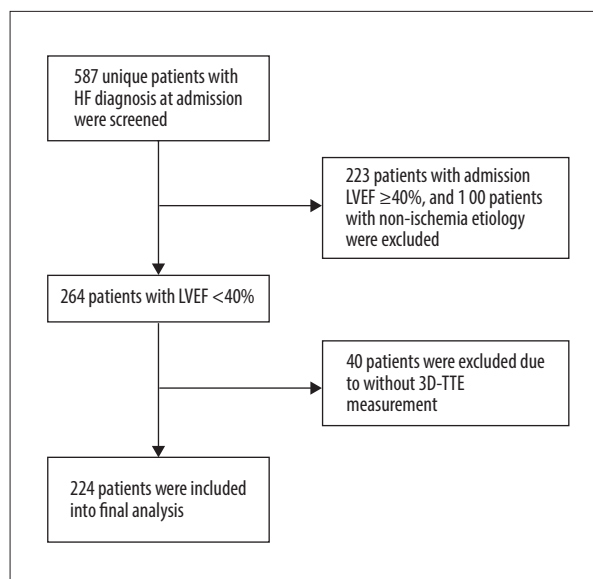

Figure 1. The flowchart of the study to compare the predictive role of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) on in-hospital all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Clinical and laboratory data

Baseline data were extracted from the patient electronic health records by two independent investigators. The clinical data at admission included the vital signs of systolic and diastolic blood pressure (SBP/DBP) and the heart rate (HR). Patient demographic data included age and gender. Risk factors included smoking status, obesity, hypertension, diabetes mellitus, and dyslipidemia. Comorbidities documented included ischemic stroke, chronic kidney disease (CKD), atrial fibrillation, and previous MI, PCI, and CABG. Specifically, obesity was defined as a body mass index (BMI) ≥30 kg/m². The laboratory results recorded on hospital admission included serum hemoglobin (Hb) levels, fasting blood glucose (FBG), total cholesterol (TC), high-sensitivity cardiac troponin I (hs-cTnI), and N-terminal pro-B-type natriuretic peptide (NT-proBNP). The creatinine level was used to calculate the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula [15], and CKD was defined as an eGFR <60 ml/min/1.73 m². Medications used on hospital admission and during hospitalization were also recorded.

The 2D-TTE and 3D-TTE examinations

Certified and experienced clinicians performed the 2D-TTE and 3D-TTE, and all measurements were conducted in accordance with the current guideline recommendations [8]. The 2D-TTE was performed with the patient placed in the left lateral decubitus

position, and the left ventricular volume (LVV) was obtained from the apical views. Data of the LV end-diastolic volume (LVEDV) were obtained from the frame after the mitral valve was closed, The LV end-systolic volume (LVESV) was obtained on the image with the smallest LV cavity. The left ventricular ejection fraction (LVEF) was calculated using the Sonos 7500 software for the ie33 system (Philips Medical Systems, Andover, MA, USA).

The 3D-TTE was performed with a similar patient procedure to the 2D-TTE. The volume data were shown in three different cross-sections, and images for the LVEDV and LVESV measured were identified by the same method as for 2D-TTE. Measurements were obtained with semi-automated LV border detection based on fiducial marks on the annulus and apex. Both 2D-TTE and 3D-TTE volumes were indexed to body surface area, as appropriate.

Assessment of the clinical endpoint of all-cause mortality

The clinical endpoint was defined as all-cause mortality during hospitalization. This endpoint and mortality were evaluated by an independent cardiologist who reviewed the clinical records.

Statistical analysis

Continuous variables were presented as the mean±standard deviation (SD), and categorical variables were presented as the number and percentage. Student's t-test was used to compare continuous variables and the chi-squared (χ^2) test was used to compare categorical variables. Univariate and multivariate regression analysis were used to evaluate the factors associated with the clinical endpoint. The factor with a P-value <0.1 in the univariate regression model was entered into the multivariate regression model. The LVEF and LVV measured by 2D-TTE and 3D-TTE were entered into the models separately. The significant factors identified in the multivariate regression model were used to generate the risk prediction model, and parameters derived from 2D-TTE and 3D-TTE were entered into these models separately. Models discrimination were compared by the concordance statistic (C-index). The odds ratio (OR) and the 95% confidence interval (CI) were calculated. All statistical tests were two-sided and were considered to be statistically significant with a P-value <0.05. Statistical analysis was performed using SPSS version 21.0 software (IBM Corp., Armonk, NY, USA).

Results

Comparison of the demographic and clinical characteristics of the patients in the survival group and the mortality group

The study included 224 patients with heart failure with reduced ejection fraction (HFrEF), or systolic heart failure, due to

ischemic heart disease (IHD) who had a left ventricular ejection fraction (LVEF) <40% on admission when measured by two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE). Patients were classified as the survival group (n=142) and the mortality group (n=82). Between-group differences were evaluated. As shown in Table 1, compared with patients in the survival group, patients in the mortality group were older (67.3±15.5 *vs.* 62.6±14.6 years) and more likely to be women (48.8% *vs.* 38.7%). Systolic blood pressure (121±16 *vs.* 109±12 mmHg) and heart rate (89±15 *vs.* 82±12 mmHg) on hospital admission were also significantly higher in the mortality group compared with patients in the mortality group. Patients in the mortality group were also more likely to have diabetes mellitus (51.2% *vs.* 32.4%), chronic kidney disease (48.8% *vs.* 32.4%), and lower eGFR (61.9±10.5 *vs.* 68.6±12.7 ml/min/1.73 m^2). Serum levels of high-sensitivity cardiac troponin I (hs-cTnI) (45±16 *vs.* 32±12 ng/L) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) (1224±106 *vs.* 946±88 pg/mL) on hospital admission were also significantly higher in mortality versus survival patients. Also, compared with the patients in the survival group, patients in the mortality group had a higher functional class 9Class III/IV) in the New York Heart Association (NYHA) classification of heart failure (46.3% *vs.* 39.4%).

Comparison of the medications used on admission and during hospitalization of the patients in the survival group and the mortality group

As shown in Table 2, compared with patients in the survival group, patients in the mortality group were less likely to be treated with beta-blockers (54.9% *vs.* 66.9%) and more likely to receive digoxin therapy on hospital admission (43.9% *vs.* 30.3%). During hospitalization, all patients received intravenous furosemide, and the use of beta-blockers were reduced in both groups. The use of an intravenous inotrope (85.4% *vs.* 76.1%) and an intravenous vasodilator (70.7% *vs.* 61.3%) was significantly increased in the mortality group compared with the survival group.

Comparisons of 2D-TTE and 3D-TTE parameters

Table 3 shows that from 2D-TTE, there were only differences in the left ventricular end-diastolic volume (LVEDV) and the LVEDV index between patients in the survival group and patients in the mortality group. Measurements by 3D-TTE showed significant differences in LVEF (32±7% *vs.* 29±8%), LVEDV (91.7±20.8 *vs.* 96.5±22.4 ml), and the LVEDV index (45.8±10.4 *vs.* 49.1±12.6 ml/m^2), the LVESV (45.9±13.3 *vs.* 49.6±14.0 ml) and LVESV index (23.6±6.3 *vs.* 26.0±7.9 ml/m^2) were observed between patients in the survival group and patients in the mortality group.

Table 1. The demographic and clinical characteristics of the survival group and the mortality group of patients with heart failure with reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Variable	Survival group (n=142)	Mortality group (n=82)
Age (years)	62.6±14.6	67.3±15.5*
Female patient, n (%)	55 (38.7)	40 (48.8)*
Systolic blood pressure, (mmHg)	109±12	121±16*
Diastolic blood pressure, (mmHg)	74±10	72±8
Heart rate, (beat per minute)	82±12	89±15*
Current smoker, n (%)	62 (43.7)	38 (46.3)
Obese, n (%)	38 (26.8)	20 (24.4)
Hypertension, n (%)	102 (71.8)	60 (73.2)
Dyslipidemia, n (%)	74 (52.1)	44 (53.7)
Diabetes mellitus, n (%)	46 (32.4)	42 (51.2)*
Ischemic stroke, n (%)	31 (21.8)	20 (24.4)
Chronic kidney disease, n (%)	46 (32.4)	40 (48.8)*
Atrial fibrillation, n (%)	41 (28.9)	23 (28)
Myocardial infarction, n (%)	125 (88)	72 (87.8)
Previous PCI, n (%)	96 (67.6)	55 (67.1)
Previous CABG, n (%)	34 (23.9)	18 (22)
Hemoglobin (g/dL)	13.6±2.2	13.3±2.4
Total cholesterol (mmol/L)	5.1±1.0	5.0±1.1
Fasting blood glucose (mmol/L)	6.0±0.8	6.2±1.0
hs-cTnI (ng/L)	32±12	45±16*
NT-proBNP (pg/mL)	946±88	1224±106*
eGFR (ml/min/1.73 m^2)	68.6±12.7	61.9±10.5*
NYHA class I/II	86 (60.6)	44 (53.7)*
NYHA class III/IV	56 (39.4)	38 (46.3)*

PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; hs-cTnI – high-sensitivity cardiac troponin I (hs-cTnI); NT-proBNP – N-terminal pro-B-type natriuretic peptide; eGFR – estimated glomerular filtration rate; NYHA – New York Heart Association; * $P<0.05$ versus the survival group

Factors associated with all-cause mortality during hospitalization

Table 4 shows that in the univariate regression model that included the 2D-TTE parameters, increased age, female gender, increased systolic blood pressure (SBP), smoking, hypertension, diabetes mellitus, a history of myocardial infarction (MI) and coronary artery bypass graft (CABG) surgery, the use of intravenous inotropes, increased levels of high-sensitivity cardiac troponin I (hs-cTnI) and NT-proBNP, and increased LVEDV

index were associated with an increased risk of all-cause mortality. In contrast, an increased eGFR and LVEF were associated with a reduced risk of all-cause mortality. In the multivariate regression model, only age, diabetes mellitus, a previous MI, the use of intravenous inotropes, the levels of NT-proBNP, and the LVEF were significantly associated with all-cause mortality. The univariate regression model using the 3D-TTE parameters showed similar associations between factors and all-cause mortality. In the multivariate regression model, age, diabetes mellitus, prior MI, intravenous inotrope use, NT-proBNP, LVEF,

Table 2. Medications used on admission to hospital admission and during hospitalization in the survival group and the mortality group of patients with heart failure with reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Medications	Survival group (n=142)		Mortality group (n=82)	
On hospital admission:				
Antiplatelet, n (%)	130	(91.5)	76	(92.7)
Statins, n (%)	89	(62.7)	51	(62.2)
ACEi/ARB, n (%)	106	(74.6)	60	(73.2)
Spironolactone, n (%)	47	(33.1)	28	(34.1)
Beta-blocker, n (%)	95	(66.9)	45	(54.9)*
Oral hypoglycemic drugs, n (%)	32	(22.5)	20	(24.4)
Insulin, n (%)	18	(12.7)	17	(20.7)
Oral diuretic, n (%)	134	(94.4)	77	(93.9)
Calcium channel blocker, n (%)	20	(14.1)	13	(15.9)
Digoxin, n (%)	43	(30.3)	36	(43.9)*
Potassium supplement, n (%)	59	(41.5)	35	(42.7)
In-hospital:				
Antiplatelet, n (%)	130	(91.5)	76	(92.7)
Statins, n (%)	89	(62.7)	51	(62.2)
ACEi/ARB, n (%)	108	(76.1)	59	(72)
Spironolactone, n (%)	47	(33.1)	28	(34.1)
Beta-blocker, n (%)	52	(36.6)	28	(34.1)
Oral hypoglycemic drugs, n (%)	29	(20.4)	18	(22)
Insulin, n (%)	20	(14.1)	16	(19.5)
Oral diuretic, n (%)	68	(47.9)	38	(46.3)
Intravenous furosemide, n (%)	142	(100)	82	(100)
Calcium channel blocker, n (%)	10	(7)	6	(4.2)
Digoxin, n (%)	26	(18.3)	16	(19.5)
Potassium supplement, n (%)	97	(68.3)	58	(70.7)
Intravenous inotrope, n (%)	108	(76.1)	70	(85.4)*
Intravenous vasodilator, n (%)	87	(61.3)	58	(70.7)*

ACEi/ARB – angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; Intravenous inotrope, dopamine or dobutamine; Intravenous vasodilator, nitroprusside or nitroglycerine; * P<0.05 versus the survival group

and the LVEDV index remained significantly associated with all-cause mortality.

Comparisons between 2D-TTE and 3D-TTE parameters for the risk of in-hospital all-cause mortality

Significant factors identified in the multivariate regression model were used to generate the predictive models for the risk of in-hospital all-cause mortality. Table 5 shows the data from the models using the 2D-TTE parameters. The concordance statistic (C-index) was increased significantly after adding LVEF into model 1 (from 0.72 to 0.77). In the model with 3D-TTE parameters, the C-index increased significantly after including the LVEF (from 0.72 to 0.80) and the LVEDV index (from 0.80 to 0.76) into model 1.

Table 3. Comparisons of the two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) parameters in the survival group and the mortality group of patients with heart failure with reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Parameters	Survival group (n=142)	Mortality group (n=82)
2D-TTE		
LVEF (%)	34±5	32±7
LVEDV (ml)	85.4±18.5	89.7±20.5*
LVEDV index (ml/m²)	42.2±9.1	45.3±10.3*
LVESV (ml)	42.6±11.7	44.8±12.9
LVESV index (ml/m²)	21.2±5.8	22.4±6.1
3D-TTE		
LVEF (%)	32±7	29±8*
LVEDV (ml)	91.7±20.8	96.5±22.4*
LVEDV index (ml/m²)	45.8±10.4	49.1±12.6*
LVESV (ml)	45.9±13.3	49.6±14.0*
LVESV index (ml/m²)	23.6±6.3	26.0±7.9*

LVEF – left ventricular ejection fraction; LVEDV – left ventricular end diastolic volume; LVESV – left ventricular end systolic volume; * $P<0.05$ versus the survival group

Discussion

In this study, a comparison of the predictive role of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) on in-hospital all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD) showed two main findings. The left ventricular ejection fraction (LVEF), which was assessed by either 2D-TTE or 3D-TTE, was independently associated with in-hospital all-cause mortality in HFrEF patients with IHD, but only the left ventricular end-diastolic volume (LVEDV) index measured by 3D-TTE was independently associated with in-hospital all-cause mortality. Secondly, the LVEF measured by 3D-TTE was superior to 2D-TTE in predicting in-hospital all-cause mortality according to the change in the concordance statistic (C-index). Also, the LVEDV index measured by 3D-TTE improved the predictive model generated by traditional clinical risk factors. These findings of this preliminary study may have clinical implications for the prediction of in-hospital all-cause mortality and in guiding clinical therapy for patients with HFrEF.

According to the reports of epidemiologic studies, heart failure causes substantial morbidity and mortality around the world, including China [16–19]. The 5-year mortality rate is up to 50% after the onset of clinical symptoms [20–22]. A variety of clinical factors have been identified associated with worse outcomes in HFrEF patients. For example, combing cohorts from HF-ACTION trial and the ASIAN-HF registry, Cooper et al. reported that after adjusted for other covariates, diabetes mellitus was significantly associated with the composite 1-year overall mortality and hospitalization for heart failure, with a hazard ratio (HR) of 1.37 (95% CI, 1.19–1.57) [23]. Consistent to this report, our current study also showed that the presence of diabetes mellitus was associated with a 17–25% increased risk of in-hospital mortality. These findings suggest that well-controlled diabetes may improve the prognosis of patients with heart failure. Recent studies have shown that sodium-glucose cotransporter-2 (SGLT-2) inhibitor improved prognosis in diabetic patients with coexistent heart failure [24–27]. Also, N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a sensitive and specific biomarker for heart failure, and previous studies have shown that change in serum NT-proBNP level can be used to predict progress and prognosis of HFrEF patients [6,7,27]. In the present study, an increased serum NT-proBNP level on hospital admission was associated with a 21–28% increased risk of in-hospital mortality.

LVEF is another useful marker to predict the outcome in patients with HFrEF. Previous studies have shown that reduced LVEF was independently associated with increased mortality and re-hospitalization for heart failure [28–30]. However, most previously published studies have used 2D-TTE to assess LVEF. To our knowledge, few previous studies have evaluated the prognostic value of 3D-TTE for the patients with HFrEF. The present study was an extension of previous studies reported by our group [31–33]. Among the parameters from 2D-TTE, only LVEF was independently associated with in-hospital mortality, after adjusting for covariates. However, both the LVEF and the LVEDV index derived from 3D-TTE were independently associated with in-hospital mortality, suggesting that the parameters from 3D-TTE might provide more data on assessing mortality risk in patients with HFrEF. In the risk-predictive model, after adding parameters into clinical factors, only LVEF from 2D-TTE increased the concordance statistic (C-index) while both the LVEF and the LVEDV index from 3D-TTE significantly increased the C-index. These findings suggested that the LVEF and the LVEDV derived from 3D-TTE were superior to those derived from 2D-TTE to predict in-hospital mortality in patients with HFrEF.

The clinical implications of current findings were in HFrEF patients, 3D-TTE might be better than 2D-TTE in evaluating the severity and in-hospital prognosis of HFrEF patients, and physicians might use parameters from 3D-TTE to better guide the therapy. Future research directions should focus on whether

Table 4. Factors associated with all-cause mortality during hospitalizationusing two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE).

Factors	Univariate regression		Multivariate regression	
2D-TTE	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Age	1.28 (1.13–1.97)	0.004	1.14 (1.05–1.39)	0.031
Female *vs.* Male	1.09 (1.04–1.33)	0.026	1.02 (0.96–1.17)	0.182
Systolic blood pressure	1.13 (1.07–1.42)	0.011	1.05 (0.98–1.20)	0.075
Heart rate	1.03 (0.97–1.13)	0.184	NA	
Smoking status (yes *vs.* no)	1.16 (1.02–1.28)	0.033	1.06 (0.94–1.17)	0.069
Obesity (yes *vs.* no)	1.05 (0.98–1.07)	0.340	NA	
Hypertension (yes *vs.* no)	1.18 (1.09–1.39)	0.009	1.08 (0.99–1.25)	0.060
Diabetes mellitus (yes *vs.* no)	1.37 (1.19–1.67)	0.001	1.25 (1.10–1.44)	0.007
Dyslipidemia (yes *vs.* no)	1.01 (0.92–1.08)	0.255	NA	
Prior MI (yes *vs.* no)	1.20 (1.11–1.32)	0.018	1.09 (1.02–1.21)	0.043
Prior PCI (yes *vs.* no)	1.05 (0.97–1.18)	0.075	1.01 (0.92–1.08)	0.335
Prior CABG (yes *vs.* no)	1.09 (1.01–1.22)	0.017	1.02 (0.96–1.13)	0.086
eGFR	0.92 (0.85–0.97)	0.031	0.96 (0.90–1.02)	0.067
Intravenous inotrope (yes *vs.* no)	1.24 (1.12–1.50)	0.006	1.19 (1.08–1.37)	0.027
Intravenous vasodilator (yes *vs.* no)	1.08 (0.96–1.20)	0.093	1.04 (0.90–1.07)	0.155
hs-cTNI	1.16 (1.08–1.25)	0.004	1.09 (0.99–1.20)	0.052
NT-proBNP	1.39 (1.27–1.87)	<0.001	1.28 (1.18–1.45)	0.005
LVEF	0.92 (0.86–0.97)	0.029	0.94 (0.91–0.98)	0.043
LVEDV index	1.17 (1.08–1.28)	0.035	1.05 (0.99–1.18)	0.061
LVESV index	1.10 (0.99–1.16)	0.051	1.02 (0.95–1.10)	0.136
3D-TTE	**OR (95% CI)**	**P–value**	**OR (95% CI)**	**P–value**
Age	1.25 (1.11–1.82)	0.008	1.10 (1.03–1.31)	0.038
Female *vs.* Male	1.07 (1.01–1.26)	0.041	1.01 (0.92–1.10)	0.204
Systolic blood pressure	1.10 (1.02–1.28)	0.036	1.02 (0.93–1.11)	0.163
Heart rate	1.01 (0.95–1.09)	0.202	NA	
Smoking status (yes *vs.* no)	1.12 (1.00–1.20)	0.051	1.03 (0.90–1.07)	0.084
Obesity (yes *vs.* no)	1.02 (0.92–1.06)	0.450	NA	
Hypertension (yes *vs.* no)	1.15 (1.04–1.25)	0.017	1.04 (0.96–1.17)	0.069
Diabetes mellitus (yes *vs.* no)	1.30 (1.15–1.57)	0.006	1.17 (1.08–1.34)	0.025
Dyslipidemia (yes *vs.* no)	1.01 (0.94–1.06)	0.532	NA	
Prior MI (yes *vs.* no)	1.18 (1.10–1.30)	0.026	1.05 (1.00–1.18)	0.051
Prior PCI (yes *vs.* no)	1.02 (0.94–1.15)	0.090	1.00 (0.90–1.07)	0.208
Prior CABG (yes *vs.* no)	1.06 (1.01–1.16)	0.047	1.01 (0.93–1.08)	0.097

Table 4 continued. Factors associated with all-cause mortality during hospitalizationusing two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE).

Factors	Univariate regression			Multivariate regression		
eGFR	0.93	(0.86–0.98)	0.032	0.97	(0.91–1.05)	0.084
Intravenous inotrope (yes *vs.* no)	1.20	(1.10–1.43)	0.009	1.12	(1.04–1.27)	0.036
Intravenous vasodilator (yes *vs.* no)	1.05	(0.92–1.17)	0.098	1.01	(0.90–1.05)	0.236
hs-cTNI	1.14	(1.05–1.22)	0.006	1.07	(0.95–1.14)	0.073
NT-proBNP	1.32	(1.20–1.68)	<0.001	1.21	(1.11–1.35)	0.008
LVEF	0.88	(0.83–0.95)	0.021	0.92	(0.87–0.98)	0.039
LVEDV index	1.20	(1.12–1.30)	0.015	1.11	(1.03–1.21)	0.043
LVESV index	1.11	(0.98–1.22)	0.086	1.04	(0.92–1.08)	0.078

OR – odds ratio; CI – confidence interval; MI – myocardial infarction; PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; eGFR – estimated glomerular filtration rate; hs-cTNI – high-sensitivity cardiac troponin I; NT-proBNP – N-terminal pro-B-type natriuretic peptide; LVEF – left ventricular ejection faction; LVEDV – left ventricular end diastolic volume; LVESV – left ventricular end systolic volume.

Table 5. Comparisons of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) parameters for the prediction of in-hospital all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF) due to ischemic heart disease (IHD).

Model	Odds ratio (95% CI)	Concordance statistic (C-index) (95% CI)
2D-TTE		
Model 1	1.78 (1.49–2.34)	0.72 (0.68–0.76)
Model 2	1.82 (1.53–2.45)	0.77 (0.72–0.80)
Model 3	1.79 (1.50–2.36)	0.74 (0.69–0.77)
Model 4	1.77 (1.48–2.32)	0.71 (0.66–0.75)
3D-TTE		
Model 1	1.78 (1.49–2.34)	0.72 (0.68–0.76)
Model 2	1.87 (1.60–2.59)	0.80 (0.73–0.85)
Model 3	1.82 (1.54–2.44)	0.76 (0.71–0.80)
Model 4	1.78 (1.47–2.30)	0.73 (0.67–0.75)

CI – confidence interval; Model 1 – age, diabetes mellitus, prior MI, intravenous inotrope use, NT-proBNP. Model 2 – model 1 plus LVEF. Model 3 – model 1 plus LVEDV index. Model 4 – model plus LVESV index.

3D-TTE can improve predictive value in a larger and prospective cohort of HFrEF patients; and whether 3D-TTE guided therapy can improve clinical outcomes in patients with HFrEF.

This study had several limitations. This study was retrospective, and no causal relationship can be established from the findings. Second, only HFrEF patients with IHD were enrolled in the study, and whether these findings can be extrapolated to patients with heart failure and preserved ejection fraction (HFpEF) or HFrEF patients with a non-ischemic etiology remain unknown. Finally, only the in-hospital all-cause mortality was evaluated, and whether these models can be used to predict long-term mortality and re-hospitalization for heart failure require further study.

Conclusions

This study aimed to compare the predictive and prognostic role of two-dimensional transthoracic echocardiography (2D-TTE) and three-dimensional transthoracic echocardiography (3D-TTE) on in-hospital all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF), or systolic heart failure, due to ischemic heart disease (IHD). In patients with HFrEF due to IHD, 3D-TTE was a better predictor than 2D-TTE of in-hospital all-cause mortality. Further prospective and multicenter studies are needed to validate these preliminary findings.

Conflict of interest

None.

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