


# Left Ventricular Structure is Associated with Postoperative Death After Coronary Artery Bypass Grafting in Patients with Heart Failure with Reduced Ejection Fraction

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**Background:** The relationship between abnormal left ventricular (LV) structure and adverse outcomes has been confirmed in diverse patient groups in previous studies. However, it remains uncertain whether LV structure has predictive implications in heart failure with reduced ejection fraction (HFrEF) patients with coronary artery bypass grafting (CABG).

**Methods:** This study retrospectively enrolled patients who had HFrEF and underwent CABG between January 2013 and July 2019. According to LV hypertrophy (LVH) and LV enlargement (LVE) assessed by echocardiography, patients were classified into four LV structure types: (-)LVH/(-)LVE, (+)LVH/(-)LVE, (-)LVH/(+)LVE, and (+)LVH/(+)LVE.

**Results:** A total of 435 consecutive patients (mean age:  $59.4 \pm 9.6$  years; 14.9% female) were enrolled in the present study. Examined independently, either LVH ( $p < 0.001$ ) or LVE ( $p < 0.001$ ) was independently associated with postoperative mortality in multivariate analysis. When LVH and LVE were analyzed in combination, the risk of mortality after CABG was lowest in (-)LVH/(-)LVE and increased with (+)LVH/(-)LVE (odds ratio [OR]: 7.525; 95% confidence interval [CI]: 1.827–30.679,  $p = 0.004$ ), (-)LVH/(+)LVE (OR: 7.253; 95% CI: 1.950–27.185,  $p = 0.003$ ), and (+)LVH/(+)LVE (OR: 9.547; 95% CI: 2.726–34.805,  $p < 0.001$ ), independent of other risk factors. Adding LV structural types to the baseline model gained an incremental effect on the predictive value for postoperative mortality (AUC: baseline model, 0.838 vs baseline model + LV structural types, 0.901,  $p$  for comparison = 0.010; category-free net reclassification improvement (NRI): 0.764,  $p < 0.001$ ; integrated discrimination improvement (IDI): 0.061,  $p = 0.007$ ).

**Conclusion:** LVH and LVE were associated with an increased risk of postoperative mortality after CABG in patients with HFrEF. Categorizing LV structural patterns with LVH and LVE contributes to risk stratification and provides incremental predictive ability. Routine echocardiographic assessment of LVH and LVE is needed in clinical practice.

**Keywords:** left ventricular hypertrophy, left ventricular enlargement, postoperative death, coronary artery bypass grafting, heart failure with reduced ejection fraction

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## Introduction

Heart failure with reduced ejection fraction (HFrEF) is commonly defined as a reduction in LVEF to  $\leq 40\%$ , with symptoms and/or signs of heart failure.<sup>1,2</sup> The predominant cause of HFrEF is coronary artery disease (CAD), which accounts for approximately 60% of all causes of heart failure (HF).<sup>1</sup> Among patients with HFrEF and CAD suitable for

myocardial revascularization, coronary artery bypass grafting (CABG) is associated with a higher risk of morbidity and mortality than among other patients. Therefore, it is necessary to identify high-risk patients before surgery among patients with HFrEF undergoing CABG. Cardiac remodeling is currently recognized as a pivotal process of cardiovascular disease and is especially associated with the progression of HFrEF.<sup>2,3</sup> In HFrEF, cardiac remodeling progresses with changes in LV shape, accompanied by increasing LV dimensions, volume, or mass and the deterioration of systolic or diastolic functions at serial imaging evaluations.<sup>4</sup> It has long been confirmed that LV hypertrophy (LVH) determined by LV mass is associated with death and adverse cardiovascular disease (CVD) events in diverse patient groups, including essential hypertension, HF, CAD and CABG.<sup>5-9</sup> LV enlargement (LVE) assessed by the measurement of LV end-diastolic diameter has been recognized as a risk factor for adverse cardiovascular events in patients with reduced left ventricular ejection fraction (LVEF).<sup>10,11</sup> Furthermore, it was reported that assessment of LVE in combination with LVH contributes to risk stratification for future adverse cardiovascular outcomes in older adults<sup>12</sup> and preserved left ventricular ejection fraction (HFpEF).<sup>13</sup>

Given that LVH and LVE reflect adverse ventricular remodeling and are associated with adverse clinical outcomes, LVH combined with LVE may be a risk factor for death after CABG, especially in high-risk patients with HFrEF. The main aim of the study was to examine whether LV structure in terms of LVH or LVE is associated with postoperative death in patients with HFrEF undergoing CABG. In addition, we sought to determine whether a combination of LVH and LVE could contribute to risk stratification and provide incremental predictive value.

## Materials and Methods

### Study Population

We retrospectively recruited consecutive patients who had symptomatic HF [New York Heart Association (NYHA) Class II–IV] with LVEF  $\leq 40\%$  measured by the latest preoperative echocardiography and had undergone CABG between January 2013 and July 2019 at Beijing Anzhen Hospital, Capital Medical University. The inclusion criteria included the following: 1) LVEF  $\leq 40\%$ , as assessed by their latest preoperative echocardiography; 2) symptomatic HF (NYHA class II–IV) and 3) underwent elective CABG. The exclusion criteria included the following: 1) emergency surgery; 2) combination with valve surgery; and 3)

cardiogenic shock. Ethical approval was obtained from the Institutional Ethics Committee of Beijing Anzhen Hospital.

### Data Collection

Clinical characteristics, echocardiographic parameters, laboratory results, and surgical characteristics were collected by trained physicians who were blinded to the aim of the study with a standard data collection form. Critical state was defined as a history of ventricular tachycardia, ventricular fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before anesthesia, preoperative inotropes, or end-organ damage. Recent myocardial infarction (MI) was defined as MI within 3 months. Increased serum creatinine was defined as serum creatinine measured before surgery  $>1.5$  mg/dl. The primary endpoint was postoperative death during hospitalization. Death was defined as any death occurring after a surgical procedure during the hospital stay.

### Echocardiographic Analysis

Transthoracic echocardiography was performed to evaluate LVH and LVE in each patient according to the recommendations for cardiac chamber quantification by echocardiography from the guidelines of the American Society of Echocardiography (ASE) and the European Association of Echocardiography (EAE).<sup>14,15</sup> Subjects without relevant echocardiographic information available were excluded from the present analysis. LV mass was calculated by left ventricular end-diastolic internal diameter (LVIDd), interventricular septum thickness at end-diastole (IVSTd), and posterior wall thickness at end-diastole (PWTd) with the following formula: LV mass (g) =  $0.8 \times (1.04 \times [(IVSTd + LVIDd + PWTd)^3 - LVIDd^3]) + 0.6$  g. LV mass index was calculated using the formula LV mass index (g/m<sup>2</sup>) = (LV mass)/[body surface area (BSA)], and LVIDd index was calculated using the formula LVIDd index (mm/m<sup>2</sup>) = (LVIDd)/(BSA). BSA was calculated by the Du Bois formula.<sup>16</sup> LVH was defined as LV mass index  $\geq 132$  g/m<sup>2</sup> in males and  $\geq 109$  g/m<sup>2</sup> in females, while LVE was defined as LVIDd index  $\geq 35$  mm/m<sup>2</sup> in both males and females, indicating a moderately or severely abnormal LV structure.<sup>14,15</sup> According to the above definitions and a previous study by Yamanaka,<sup>13</sup> we divided all patients into four LV structural types: (-)LVH/(-)LVE, (+)LVH/(-)LVE, (-)LVH/(+)LVE, and (+)LVH/(+)LVE.

### Statistical Analysis

Categorical variables are expressed as counts (percentages), and continuous variables are expressed as medians

(25th and 75th percentiles) or means  $\pm$  standard deviations (SDs). Among the 4 categories of LV structural types, continuous variables were compared by ANOVA or a Kruskal–Wallis test. The differences between the 2 groups were examined by the independent-sample *t*-test or the Mann–Whitney *U*-test. The chi-square test or Fisher's exact test was used to compare categorical variables. To determine the independent predictive value of LV structure for death, we used a multivariate logistic regression model. The baseline variables that were considered clinically relevant or associated with death in the univariate analysis ( $p < 0.05$ ) were adjusted and incorporated in the baseline model: age, critical state, stroke, recent MI, LVEF, and intervention on ventricular aneurysm. In addition, we also examined the independent predictive value of LV mass index or LVIDd index as continuous variables and LVH or LVE as binary variables in the multivariable analysis. The area under the curve (AUC), category-free net reclassification improvement (NRI), and integrated discrimination improvement (IDI) were calculated to evaluate the added predictive ability of new variables incorporated in the baseline model and EuroSCORE-2. DeLong's test was used to compare AUCs from each of the models. NRI and IDI were calculated with PredictABEL packages in R Programming Language. Statistical analysis was performed in R (version 4.0.2). A two-tailed  $p$  value  $< 0.05$  was regarded as statistically significant.

## Results

A total of 435 patients were ultimately enrolled in the present study. There were 102 patients (23.4%) with LVH and 95 patients (21.8%) with LVE. (-)LVH/(-)LVE was present in 288 (66.2%) patients, (+)LVH/(-)LVE in 52 (12.0%) patients, (-)LVH/(+)LVE in 45 (10.3%) patients, and (+)LVH/(+)LVE was present in 50 (11.5%) patients at baseline. The baseline characteristics stratified by LV structural types are summarized in Table 1.

## LV Structure and Mortality After CABG

A total of 29 (6.7%) patients died after CABG. Among them, 10 cases died of low cardiac output, 10 cases died of severe infection, 7 cases died of cardiac arrest caused by malignant arrhythmia, and 2 cases died of stroke. Thirteen (12.7%) and 15 (15.8%) patients died after CABG among patients with LVH and patients with LVE, respectively. (+)LVH had a significantly higher postoperative mortality than (-)LVH (12.7% vs 4.8%,  $p = 0.01$ ), likewise (+)LVE

(15.8% vs 4.1%,  $p < 0.001$ ) (Figure 1). The mortality rates of the 4 groups of LV structural types were 3.1%, 9.6%, 15.6%, and 16.0%, respectively. From (-)LVH/(-)LVE, (+)LVH/(-)LVE, (-)LVH/(+)LVE to (+)LVH/(+)LVE, the incidence of mortality progressively increased. The LV structural types were significantly associated with the risk of death ( $p < 0.001$ ). The mortality rates in (+)LVH/(-)LVE, (-)LVH/(+)LVE and (+)LVH/(+)LVE were all significantly higher than that in (-)LVH/(-)LVE (all  $p < 0.05$ ) (Figure 1). However, there was no significant difference in mortality among the last 3 groups of LV structure types (all  $p > 0.05$ ).

## Multivariable Analysis to Evaluate the Predictive Value of LV Structure

Table 2 shows the results of the logistic regression analysis in different variable models. The variables in the baseline model were adjusted, including age, critical state, stroke, recent MI, LVEF, and intervention for ventricular aneurysm. In multivariate analysis adjusted for covariates in the baseline model, (+)LVH/(+)LVE had a significant association with an increased risk of death ( $p < 0.001$ ), as did (+)LVH/(-)LVE ( $p = 0.004$ ) and (-)LVH/(+)LVE ( $p = 0.003$ ). In particular, patients with (+)LVH/(+)LVE had the highest risk of mortality (OR: 9.547; 95% CI: 2.726 to 34.805,  $p < 0.001$ ) (Table 2 and Figure 2). In addition, we further explored the predictive value of LVH and LVE as binary variables. In the baseline model simultaneously incorporating LVH and LVE, LVH and LVE were still independently associated with an increased risk of death (LVH,  $p = 0.032$ ; LVE,  $p = 0.020$ ). When separately incorporated in the baseline model alone, LVH ( $p = 0.001$ ) or LVE ( $p = 0.001$ ) remained an independent risk predictor of death. Similarly, as continuous variables, the LV mass index ( $p = 0.007$ ) and LVIDd index ( $p = 0.009$ ) were still independently associated with an increased risk of death when introduced to the baseline model (Table 2).

## Incremental Effect of LV Structure on the Predictive Value for Death

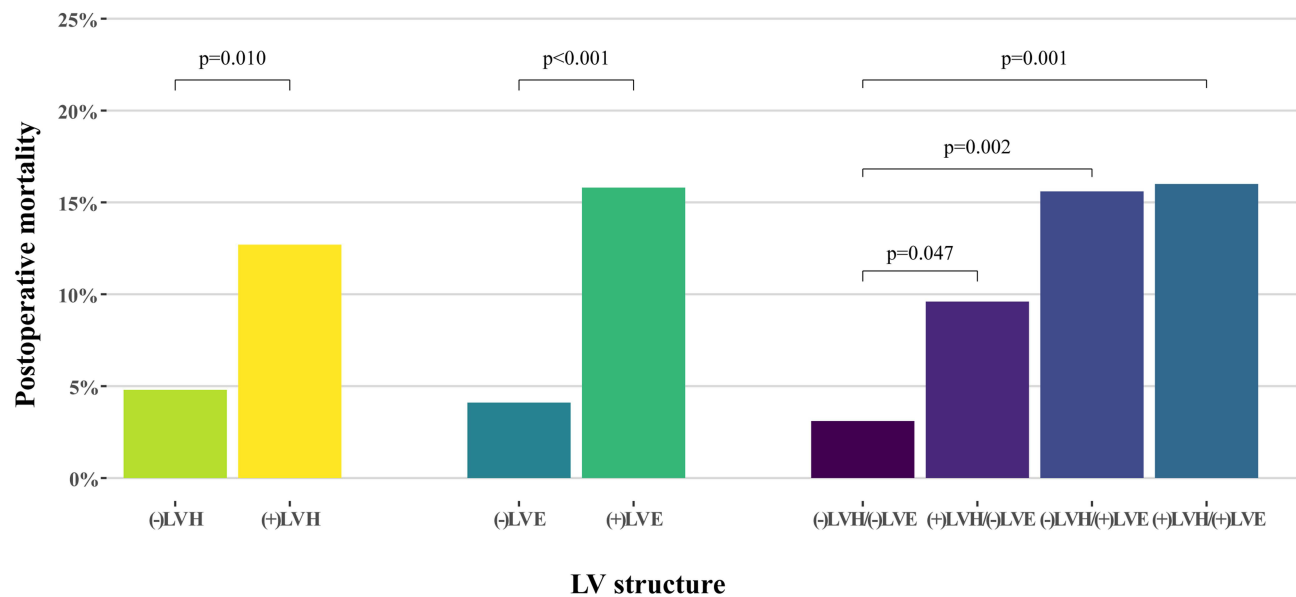
The addition of LV structural types had a significant incremental effect on the AUC obtained from the baseline model (AUC: baseline model, 0.838 vs baseline model + LV structural types, 0.901,  $p$  for comparison = 0.010). Moreover, the addition of LV structural types significantly improved the reclassification and discrimination abilities beyond the baseline model, with a category-free NRI of 0.764 ( $p < 0.001$ )

**Table 1** The Baseline Characteristics Stratified by LV Structural Types

Variable	Overall (n=435)	(-)LVH/(-)LVE (n=288)	(+)LVH/(-)LVE (n=52)	(-)LVH/(+)LVE (n=45)	(+)LVH/(+)LVE (n=50)	P value
Age (years)	59.4 (9.6)	59.4 (9.7)	57.9 (9.8)	61.0 (8.6)	59.4 (9.6)	0.489
Female	65 (14.9%)	30 (10.4%)	13 (25.0%)	5 (11.1%)	17 (34.0%)	<0.001
BMI (kg/m <sup>2</sup> )	25.3 (3.0)	25.6 (2.7)	26.4 (3.1)	23.2 (3.1)	24.9 (3.4)	<0.001
Critical State	13 (3.0%)	8 (2.8%)	1 (1.9%)	3 (6.7%)	1 (2.0%)	0.485
Hypertension	215 (49.4%)	136 (47.2%)	35 (67.3%)	17 (37.8%)	27 (54.0%)	0.018
Diabetes mellitus	202 (46.4%)	135 (46.9%)	30 (57.7%)	13 (28.9%)	24 (48.0%)	0.040
Hyperlipidemia	137 (31.5%)	89 (30.9%)	19 (36.5%)	15 (33.3%)	14 (28.0%)	0.798
Smoke	254 (58.4%)	181 (62.8%)	27 (51.9%)	23 (51.1%)	23 (46.0%)	0.060
Alcohol	92 (21.1%)	65 (22.6%)	6 (11.5%)	11 (24.4%)	10 (20.0%)	0.313
Chronic kidney disease	7 (1.6%)	3 (1.0%)	2 (3.8%)	0 (0.0%)	2 (4.0%)	0.147
Chronic pulmonary disease	16 (3.7%)	12 (4.2%)	1 (1.9%)	2 (4.4%)	1 (2.0%)	0.843
Stroke	69 (15.9%)	46 (16.0%)	5 (9.6%)	7 (15.6%)	11 (22.0%)	0.401
PCI	100 (23.0%)	68 (23.6%)	10 (19.2%)	15 (33.3%)	7 (14.0%)	0.140
Recent MI (past 3 months)	115 (26.4%)	79 (27.4%)	17 (32.7%)	10 (22.2%)	9 (18.0%)	0.329
NYHA class (%)	122 (28.0%)	80 (27.8%)	15 (28.8%)	11 (24.4%)	16 (32.0%)	0.872
Carotid artery stenosis	129 (29.7%)	83 (28.8%)	16 (30.8%)	17 (37.8%)	13 (26.0%)	0.600
LVEF (%)	36.8 (3.5)	37.4 (3.1)	37.1 (2.8)	34.3 (4.4)	35.3 (4.3)	<0.001
LVIDd (mm)	58.2 (6.3)	56.1 (5.2)	59.2 (5.1)	63.1 (4.7)	65.5 (6.2)	<0.001
IVSTd (mm)	9.0 (2.2)	8.8 (2.0)	11.2 (2.1)	7.3 (1.8)	9.5 (1.8)	<0.001
PWTd (mm)	8.4 (1.7)	8.2 (1.5)	10.1 (1.7)	7.4 (1.4)	9.2 (1.5)	<0.001
LVmass (g)	199.5 (54.7)	179.0 (37.4)	262.6 (47.4)	184.7 (36.7)	265.1 (59.3)	<0.001
LV mass index (g/m <sup>2</sup> )	110.3 (29.0)	97.2 (18.3)	143.2 (21.8)	107.6 (16.7)	153.8 (25.9)	<0.001
LVIDd index (mm/m <sup>2</sup> )	32.3 (3.9)	30.6 (2.8)	32.4 (2.1)	37.0 (1.8)	38.3 (2.8)	<0.001
LVH	102 (23.4%)	0 (0.0%)	52 (100.0%)	0 (0.0%)	50 (100.0%)	<0.001
LVE	95 (21.8%)	0 (0.0%)	0 (0.0%)	45 (100.0%)	50 (100.0%)	<0.001
Mitral regurgitation						0.046
None or Mild	358 (82.3%)	244 (84.7%)	46 (88.5%)	32 (71.1%)	36 (72.0%)	
Moderate	67 (15.4%)	39 (13.5%)	6 (11.5%)	11 (24.4%)	11 (22.0%)	
Severe	10 (2.3%)	5 (1.7%)	0 (0.0%)	2 (4.4%)	3 (6.0%)	
Ventricular aneurysm	126 (29.0%)	91 (31.6%)	12 (23.1%)	9 (20.0%)	14 (28.0%)	0.305
Serum creatinine>1.5 mg/dl	20 (4.6%)	13 (4.5%)	2 (3.8%)	1 (2.2%)	4 (8.0%)	0.602
Total number of distal anastomoses	3.3 (0.9)	3.3 (1.0)	3.3 (0.9)	3.2 (0.7)	3.2 (0.9)	0.871
Number of distal anastomoses						0.555
1	11 (2.53%)	9 (3.12%)	0 (0.00%)	0 (0.00%)	2 (4.00%)	
2–3	257 (59.1%)	163 (56.6%)	32 (61.5%)	31 (68.9%)	31 (62.0%)	
≥4	167 (38.4%)	116 (40.3%)	20 (38.5%)	14 (31.1%)	17 (34.0%)	
Arterial conduits ≥1	201 (46.2%)	146 (50.7%)	26 (50.0%)	10 (22.2%)	19 (38.0%)	0.002
Total number of conduit	2.1 (0.4)	2.1 (0.4)	2.2 (0.5)	2.1 (0.3)	2.1 (0.5)	0.784
Intervention on ventricular aneurysm	50 (11.5%)	37 (12.8%)	2 (3.8%)	5 (11.1%)	6 (12.0%)	0.317
CPB						–
OP	323 (74.3%)	219 (76.0%)	40 (76.9%)	32 (71.1%)	32 (64.0%)	
ONBEAT	71 (16.3%)	44 (15.3%)	7 (13.5%)	10 (22.2%)	10 (20.0%)	
ONSTOP	41 (9.4%)	25 (8.7%)	5 (9.6%)	3 (6.7%)	8 (16.0%)	
Euroscore-2 (%)	2.3 (2.5)	2.1 (2.1)	2.0 (2.0)	2.6 (2.7)	2.9 (4.4)	0.124

**Notes:** LVH was defined as LV mass index  $\geq 132 \text{ g/m}^2$  in males and  $\geq 109 \text{ g/m}^2$  in females, while LVE was defined as LVIDd index  $\geq 35 \text{ mm/m}^2$  in both males and females.

**Abbreviations:** BMI, body mass index; MI, myocardial infarction; PCI, percutaneous coronary intervention; NYHA, New York heart association; LVEF, left ventricular ejection fraction; LV, left ventricular; LVIDd, left ventricular end-diastolic internal diameter; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement; CPB, cardiopulmonary bypass; CABG, coronary artery bypass grafting; OP, off-pump CABG without CPB; ONBEAT, on-pump beating heart CABG; ONSTOP, on-pump CABG.



**Figure 1** Postoperative mortality after CABG in different LV structural groups.

**Abbreviations:** LV, left ventricular; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.

and an IDI of 0.061 ( $p = 0.007$ ) (Table 3 and Figure 3). Similarly, adding LVH and LVE simultaneously to the baseline model had significant incremental effects on mortality

risk prediction in terms of AUC, reclassification ability and discrimination ability (AUC: baseline model, 0.838 vs baseline model + LV structure, 0.890,  $p$  for comparison = 0.013;

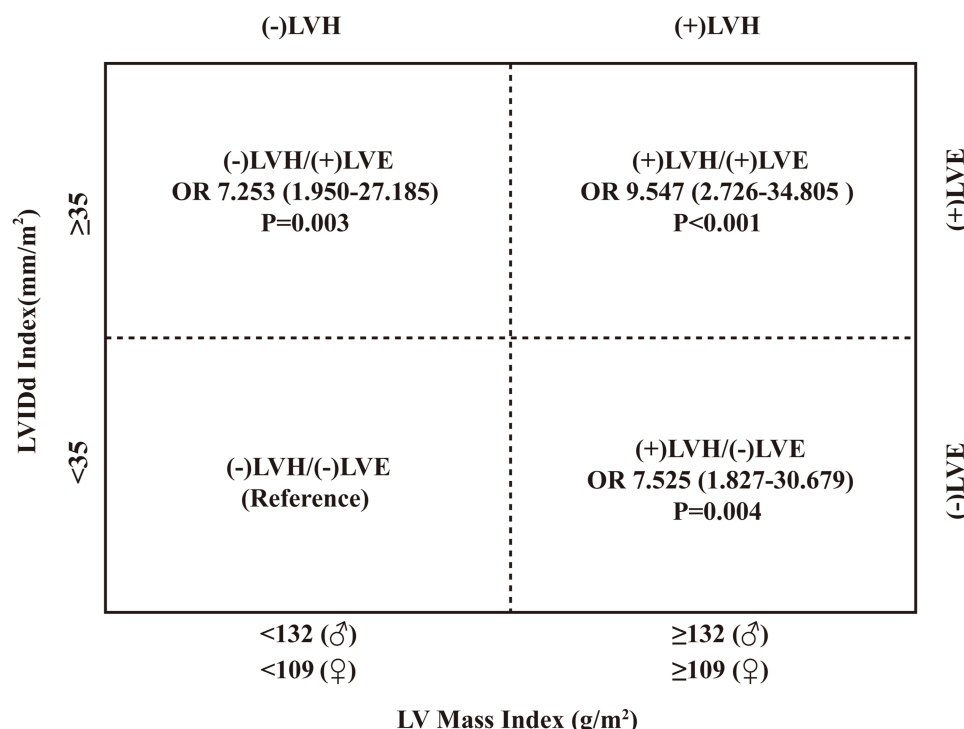
**Table 2** Predictive Value of LV Structure for Death After CABG and Each Component in Univariate and Multivariate Analysis

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Baseline model+ LV mass index				
LV mass index	1.014 (1.002–1.026)	0.018	1.020 (1.005–1.034)	0.007
Baseline model+LVId index				
LVId index	1.177 (1.073–1.294)	0.001	1.166 (1.040–1.312)	0.009
Baseline model+LVH				
(+)LVH vs (-)LVH	2.894 (1.321–6.237)	0.007	4.653 (1.844–12.124)	0.001
Baseline model+LVE				
(+)LVE vs (-)LVE	4.366 (2.018–9.511)	<0.001	5.100 (1.982–13.556)	0.001
Baseline model+LVH&LVE				
(+)LVH vs (-)LVH	2.894 (1.321–6.237)	0.007	2.990 (1.096–8.308)	0.032
(+)LVE vs (-)LVE	4.366 (2.018–9.511)	<0.001	3.400 (1.213–9.693)	0.020
Baseline model+LV structural types				
(-)LVH/(-)LVE	1.000 (Reference)		1.000 (Reference)	
(+)LVH/(-)LVE	3.298 (0.978–9.987)	0.040	7.525 (1.827–30.679)	0.004
(-)LVH/(+)LVE	5.711 (1.941–16.229)	0.001	7.253 (1.950–27.185)	0.003
(+)LVH/(+)LVE	5.905 (2.111–16.290)	0.001	9.547 (2.726–34.805)	<0.001
p for trend		<0.001		<0.001

**Notes:** The baseline model adjusted for variables with statistical significance ( $P < 0.05$ ) in univariate analysis, including age, critical state, stroke, recent myocardial infarction, LVEF and intervention on ventricular aneurysm.

**Abbreviations:** OR, odds ratio; CI, confidence interval; LV, left ventricular; LVId index, left ventricular end-diastolic internal diameter index; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.





**Figure 2** Multivariate odds ratio estimates (95% CI) for postoperative death after CABG. Adjusted for variables with statistical significance ( $p < 0.05$ ) in univariate analysis, including age, critical state, stroke, recent myocardial infarction, LVEF and intervention on ventricular aneurysm.

**Abbreviations:** CI, confidence interval; LV, left ventricular; LVIDd, left ventricular end-diastolic internal diameter; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.

category-free NRI: 0.680,  $p < 0.001$ ; IDI: 0.052,  $p = 0.022$ ). Although the addition of LVH or LVE to the baseline model did not have a significant incremental effect on the AUC (all  $p > 0.05$ ), incremental effects on the reclassification and discrimination ability were found (all  $p < 0.05$ ). Adding the LVIDd index to the baseline risk model had a significant incremental effect on AUC ( $p = 0.023$ ) and reclassification ability ( $p < 0.001$ ) but not on discrimination ability ( $p = 0.377$ ). Adding LV mass index to the baseline risk model only had a significant incremental effect on reclassification ability ( $p = 0.047$ ) (Table 3 and Figure 3).

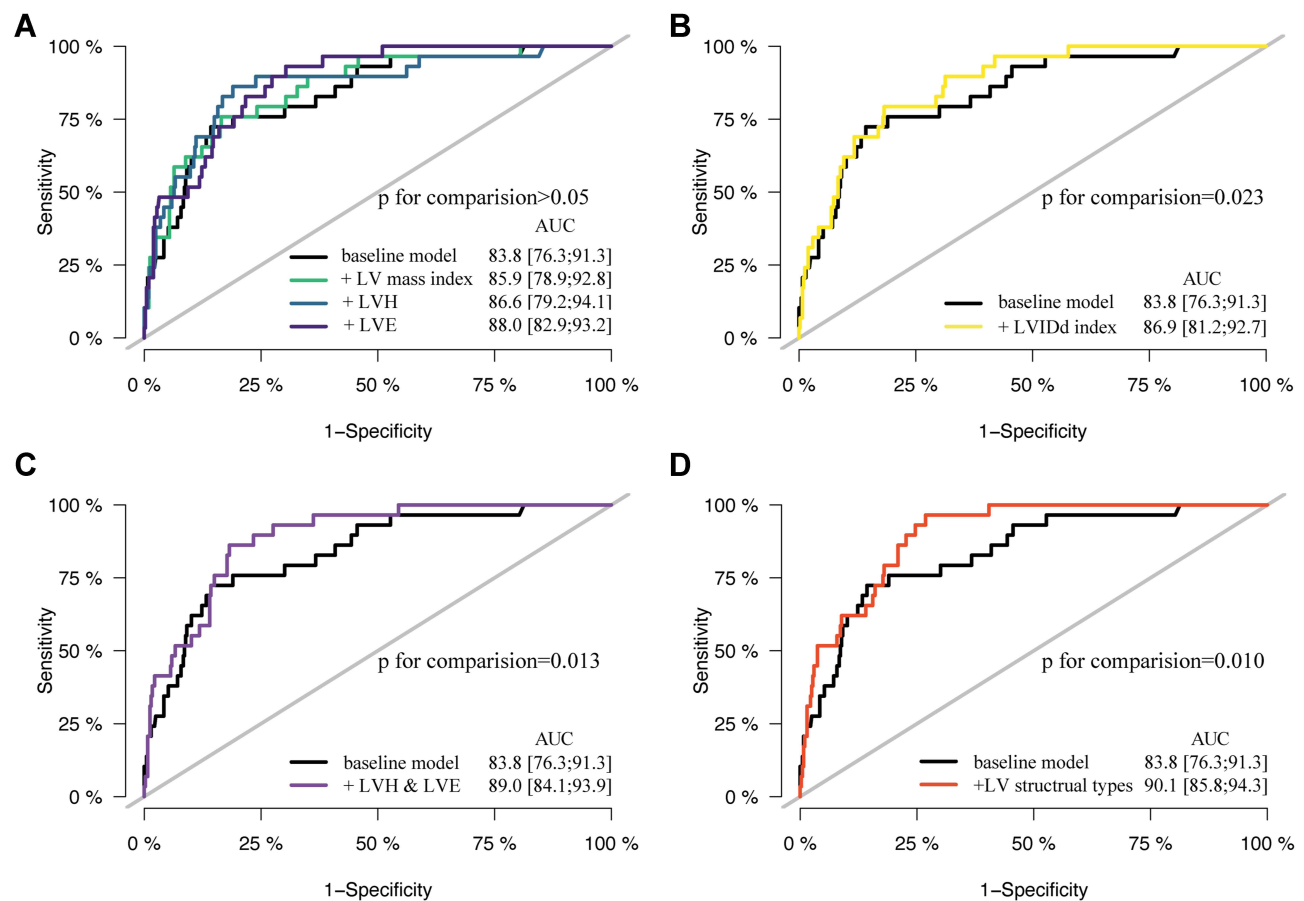
## Incremental Prognostic Value of LV Structure Over EuroSCORE-2

Adding LV structural types to EuroSCORE-2 had a significant incremental effect on mortality risk prediction in terms of NRI and IDI but not AUC (AUC: EuroSCORE-2, 0.790 vs EuroSCORE-2 + LV structural types, 0.830,  $p$  for comparison = 0.442; category-free NRI: 0.754  $p < 0.001$ ; IDI: 0.043,  $p = 0.002$ ) (Table 4). The reclassification and discrimination abilities (NRI and IDI) for death improved significantly after incorporating either LVH&LVE or LVE (all  $p < 0.05$ ). When adding the LVH,

**Table 3** The Incremental Predictive Values of Adding LV Structure to Baseline Model for Mortality After CABG

	AUC		Category-Free NRI		IDI	
	Index (95% CI)	p value	Index (95% CI)	p value	Index (95% CI)	p value
Baseline model	0.838 (0.763–0.913)	Reference	–	Reference	–	Reference
+ LV mass index	0.859 (0.789–0.928)	0.094	0.379 (0.004–0.754)	0.047	0.027 (–0.014–0.069)	0.199
+LVIDd index	0.869 (0.812–0.927)	0.023	0.611 (0.253–0.969)	0.001	0.013 (–0.016–0.042)	0.377
+LVH	0.866 (0.792–0.941)	0.153	0.527 (0.1545–0.899)	0.006	0.040 (7e-04–0.078)	0.046
+LVE	0.880 (0.829–0.932)	0.084	0.640 (0.269–1.012)	0.001	0.036 (0.002–0.069)	0.038
+LVH & LVE	0.890 (0.841–0.939)	0.013	0.680 (0.316–1.044)	<0.001	0.052 (0.007–0.097)	0.022
+LV structural types	0.901 (0.858–0.943)	0.010	0.764 (0.415–1.112)	<0.001	0.061 (0.017–0.106)	0.007

**Abbreviations:** AUC, area under the curve; NRI, net reclassification improvement; IDI, integrated discrimination improvement; CI, confidence interval; LV, left ventricular; LVIDd, left ventricular end-diastolic internal diameter; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.



**Figure 3** C-statistics evaluating the incremental effect of LV structure beyond the baseline model. **(A)** Baseline model vs +LV mass index/LVH/LVE; **(B)** baseline model vs +LVIDd index; **(C)** baseline model vs +LVH&LVE; **(D)** baseline model vs +LV structural types. The baseline model adjusted for variables with statistical significance ( $P < 0.05$ ) in univariate analysis, including age, critical state, stroke, recent MI, LVEF and intervention on ventricular aneurysm.

**Abbreviations:** LV, left ventricular; LVIDd, left ventricular end-diastolic internal diameter; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.

LVIDd index or LV mass index alone to EuroSCORE-2, only the reclassification ability (NRI) for death improved significantly (Table 4).

## Discussion

To our knowledge, our study is the first to examine the predictive value of LV structure in terms of LVH and LVE

for postoperative mortality among HFrEF patients with CABG. The main finding of the present study is that echocardiographically determined LVH, LVE, and LV structural types were all independently associated with death in patients with HFrEF undergoing CABG. This association remained significant even after adjustment for various potential confounding factors. In addition, our

**Table 4** Impact of Adding LV Structures to EuroSCORE-2 on Predicting Mortality

	AUC		Category-Free NRI		IDI	
	Index (95% CI)	p value	Index (95% CI)	p value	Index (95% CI)	p value
EuroSCORE-2	0.790 (0.697–0.882)	Reference	–	Reference	–	Reference
+ LV mass index	0.788 (0.700–0.876)	0.958	0.571 (0.207–0.936)	0.002	0.025 (–0.006–0.055)	0.115
+LVIDd index	0.817 (0.757–0.877)	0.502	0.596 (0.238–0.954)	0.001	0.027 (–0.001–0.055)	0.058
+LVH	0.788 (0.695–0.882)	0.970	0.458 (0.087–0.829)	0.015	0.019 (–0.001–0.039)	0.060
+LVE	0.829 (0.771–0.887)	0.410	0.640 (0.269–1.012)	0.001	0.032 (0.006–0.059)	0.016
+LVH & LVE	0.829 (0.767–0.892)	0.393	0.754 (0.405–1.102)	<0.001	0.036 (0.009–0.063)	0.008
+LV structural types	0.830 (0.764–0.896)	0.422	0.754 (0.405–1.102)	<0.001	0.043 (0.016–0.071)	0.002

**Abbreviations:** AUC, area under the curve; NRI, net reclassification improvement; IDI, integrated discrimination improvement; CI, confidence interval; LV, left ventricular; LV mass index, left ventricular mass index; LVIDd, left ventricular end-diastolic internal diameter; LVH, left ventricular hypertrophy; LVE, left ventricular enlargement.

results indicate that the combinatorial analysis of LVE and LVH provides incremental predictive value and added utility for surgical risk prediction in high-risk patients undergoing CABG. This strong significance of LV structure in HFrEF patients undergoing CABG suggests that LVH and LVE should be assessed during routine clinical practice to stratify the surgical risk of death.

## Prognostic Implications of LVH and Increased LV Mass Index

LVH results from increased hemodynamic load and increases the risk of cardiovascular disease, including CAD.<sup>17–19</sup> Only a few studies have investigated the association of LVH with early outcomes after CABG. Lin et al<sup>20</sup> found that in patients with triple vessel coronary artery disease, severe cardiac dysfunction (EF < 60%) and undergoing CABG, LVH was common and increased postoperative mortality and the incidence of hemodialysis following CABG surgery. Similarly, Christenson et al<sup>21</sup> reported that LVH was an independent predictor for mortality in patients with LVEF > 25% undergoing CABG. However, this increased risk was not apparent in all of the studies. Toumpoulis et al<sup>22</sup> reached a different conclusion: in general patients with CABG, LVH was not associated with postoperative mortality but was a detrimental risk factor for long-term survival, especially after the first 3 years. This association may be more predominant in high-risk patients with cardiac surgery whose abnormal LV structure is more severe and common. The present study examined the association of LVH with postoperative death and confirmed the hypothesis that LVH is an independent risk factor for postoperative mortality in HFrEF patients with CABG.

## Prognostic Implications of LVE and Increased LVIDd Index

CAD patients with HFrEF have a high prevalence of MI history. LVE following MI results from expansion of the infarct area, an increase in the surface area of the LV occupied by necrotic myocardium with concomitant thinning of the infarcted wall, cavity dilatation and distortion of the ventricle. This finding suggests that LVE reflects irreversible changes in ischemic patients and that LV size can be one parameter to predict outcomes.<sup>3,23</sup> LVE assessed by measurement of LV end-diastolic diameter has been recognized as a risk factor for adverse cardiovascular events in patients with reduced LVEF.<sup>10,11</sup>

Several studies confirmed the predictive value of LV volume on early and late death after CABG in patients with reduced LVEF.<sup>24–26</sup> Fukunaga et al<sup>27</sup> reported that LV size >5.5 cm affects postoperative mortality and major morbidity (OR 5.5 [2.0–15.7],  $p < 0.001$ ) in isolated CABG. In the present study, we further investigated and confirmed the predictive value of LVE and increased LVIDd index in patients with HFrEF undergoing CABG and found that LVE was significantly associated with postoperative death even after adjustment for other confounders.

## Prognostic Implications of LV Structure

Cardiac remodeling involves some changes in LV structure, including chamber enlargement (increased chamber size) and/or hypertrophy (increased LV mass).<sup>28</sup> It has been reported that the assessment of LVH in combination with LVE contributes to risk stratification for future CVD events in older adults and preserved HFpEF.<sup>12,13</sup> Even though the worse prognosis associated with LVH and LVE has been well confirmed in diverse patient groups, the predictive implication of a combination of LVH and LVE has not been clearly demonstrated in a high-risk cardiac surgery, such as CABG with HFrEF. Our study examined these findings in a high-risk population with HFrEF and demonstrated that LV structure, in terms of LVH and LVE, was associated with the risk of death after CABG. Notably, in our study, more than 30% of patients (33.8%) had an abnormal LV structure, with (-)LVH/(+)LVE, (+)LVH/(-)LVE and (+)LVH/(+)LVE accounting for approximately 10%. (+)LVH/(+)LVE carried the greatest risk of death (OR = 9.547), followed by (-)LVH/(+)LVE and (+)LVH/(-)LVE, with similar odds ratios for mortality. Moreover, the addition of the LV structure combination to the baseline model gained the largest predictive ability compared with the addition of LVH or LVE alone in AUC, NRI and IDI. The current risk score systems for cardiac surgery, such as EuroSCORE-2,<sup>29</sup> do not rely on information on LV structure. In the present study, we found that LV structural types significantly improved predictive ability in terms of NRI and IDI when incorporated in EuroSCORE-2. Therefore, LV structure in terms of LVH and LVE may be an additional risk factor to consider in HFrEF when risk-stratifying patients for postoperative death.

Our results clarify the strong relationship between LV structure and postoperative death, confirm the importance of LV structure in risk prediction, and emphasize the



clinical importance of its detection in CABG with HFrEF. As LV mass, LVIDd, LVH and LVE can be easily measured and assessed by transthoracic echocardiogram, we argue for their routine assessment in these high-risk patients with HFrEF undergoing CABG.

## Limitations

Our study had several limitations. The first is that this study is retrospective. Second, the power of this analysis may have been limited by small sample sizes and the number of events in the various subgroups. Further studies of LV structure in a large population are warranted to examine its ability to predict outcomes in HFrEF. Third, we acknowledge that there may be other echocardiographic parameters that may predict outcomes, especially LV volume. In addition, parameters determined by cardiac magnetic resonance imaging are more accurate and may have a better predictive ability for outcomes. However, we did not have these data available for analysis. Finally, patients recruited into the present study all had HFrEF; therefore, these results cannot be extrapolated to general patients with CABG.

## Conclusion

In this surgical high-risk cohort of patients with HFrEF, LVH and LVE were independently associated with an increased risk of postoperative mortality after CABG. (+) LVH/(+)LVE carried the greatest risk of death, and categorizing LV remodeling patterns with LVH and LVE contributes to risk stratification and provides incremental predictive ability. As LV structure has important predictive value, LVH and LVE should be assessed during routine clinical practice to provide a useful clinical tool for risk stratification for death after CABG in HFrEF patients.

## Ethical Statement

Written informed consent was approved by the Institutional Ethics Committee of Beijing Anzhen Hospital and this study was conducted in accordance with the Declaration of Helsinki.

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## Disclosure

The authors report no conflicts of interest in this work.

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