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# Predictive value of early left ventricular end-diastolic volume changes for late left ventricular remodeling after ST-elevation myocardial infarction

Lei Yi*, Tianqi Zhu*, Xuezheng Qu*, Keremu Buayiximu, Shuo Feng, Zhengbin Zhu, Jingwei Ni, Run Du, Jinzhou Zhu, Xiaoqun Wang, Fenghua Ding, Ruiyan Zhang, Weiwei Quan, Xiaoxiang Yan

Department of Cardiovascular Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

## Abstract

**Backgroud:** *Left ventricular remodeling (LVR) is a major predictor of adverse outcomes in patients with acute ST-segment elevation myocardial infarction (STEMI). This study aimed to prospectively evaluate LVR in patients with STEMI who were successfully treated with primary percutaneous coronary intervention (PCI) and examine the relationship between early left ventricular dilation and late LVR.*

**Methods:** *Overall 301 consecutive patients with STEMI who underwent primary PCI were included. Serial echocardiography was performed on the first day after PCI, on the day of discharge, at 1 month, and 6 months after discharge.*

**Results:** *Left ventricular remodeling occurred in 57 (18.9%) patients during follow-up. Left ventricular end-diastolic volume (LVEDV) reduced from day 1 postoperative to discharge in the LVR group compared with that in the non-LVR group. The rates of change in LVEDV (ΔLVEDV%) were –5.24 ± ± 16.02% and 5.05 ± 16.92%, respectively ($p < 0.001$). LVEDV increased in patients with LVR compared with non-LVR at 1-month and 6-month follow-ups (ΔLVEDV% 13.05 ± 14.89% vs. –1.9 ± ± 12.03%; 26.46 ± 14.05% vs. –3.42 ± 10.77%, $p < 0.001$). Receiver operating characteristic analysis showed that early changes in LVEDV, including ΔLVEDV% at discharge and 1-month postoperative, predicted late LVR with an area under the curve value of 0.80 (95% confidence interval 0.74–0.87, $p < 0.0001$).*

**Conclusions:** *Decreased LVEDV at discharge and increased LVEDV at 1-month follow-up were both associated with late LVR at 6-month. Comprehensive and early monitoring of LVEDV changes may help to predict LVR.* (Cardiol J 2024; 31, 3: 451–460)

**Keywords: acute myocardial infarction, left ventricular remodeling, echocardiography, left ventricular end-diastolic volume, early left ventricular dilation**

Address for correspondence: Dr. Xiaoxiang Yan, MD, PhD; Dr. Weiwei Quan, MD, PhD; Dr. Ruiyan Zhang, MD, PhD, Department of Cardiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 197 Ruijin 2nd Road, Shanghai 200025, PR China, tel: 86-21-6445-7177, fax: 86-21-6445-7177, e-mail: cardexyanxx@hotmail.com; springqww@163.com; zhangruiyan@263.net

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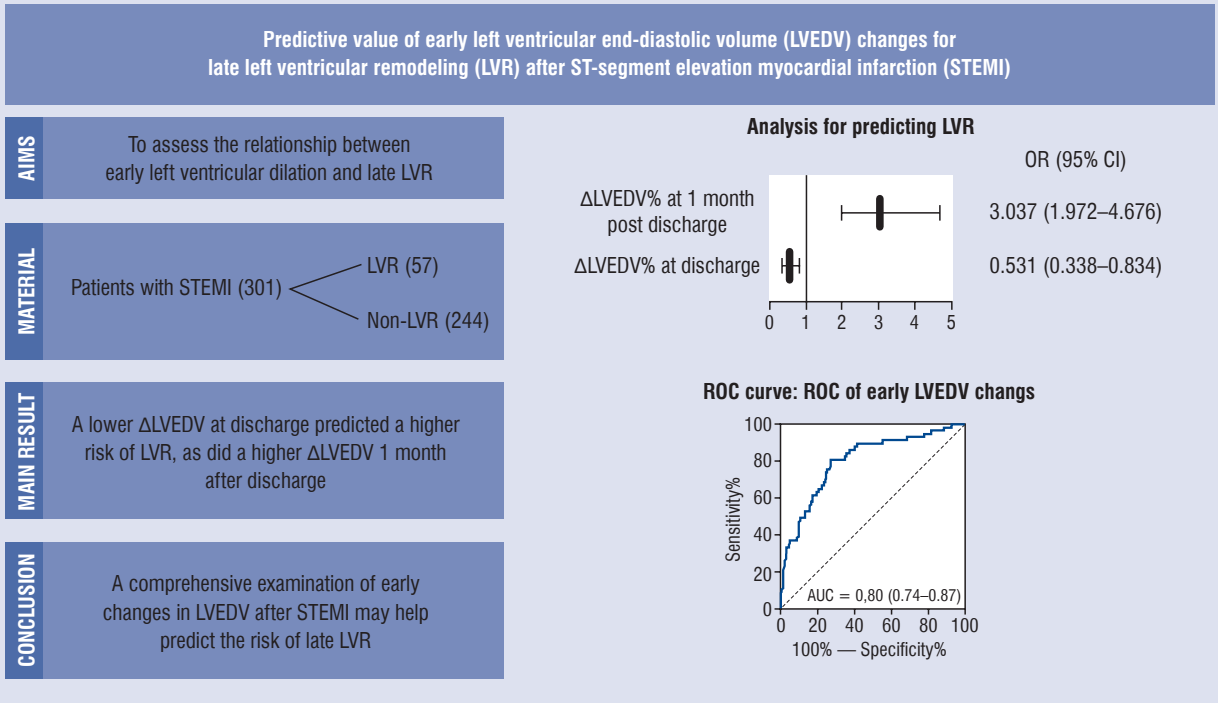
**These authors contributed equally to this work.*

## Graphical Abstract




## Introduction

The widespread use of primary percutaneous coronary intervention (PCI) has shifted the main adverse outcome in ST-segment elevation myocardial infarction (STEMI) from acute mortality to progressive left ventricular dysfunction and chronic heart failure [1]. Left ventricular remodeling (LVR) is regarded as a predictor of heart failure progression. LVR develops in 30% of patients after STEMI and is considered an important marker of poor prognosis [2, 3]. The risk of LVR needs to be assessed early after the onset of infarction, and patients at high risk need to be monitored more closely and undergo more aggressive treatment strategies. It is generally believed that the inflammatory reactions and neurohormonal pathways activated after acute myocardial infarction (AMI) ultimately result in mechanical and electrical remodeling of the myocardium, which leads to LVR [4–6]. Several biochemical markers of inflammation such as high-sensitivity C-reactive protein (hs-CRP) and soluble suppression of tumorigenicity 2 have been associated with LVR [4, 7]. Some conventional circulating biomarkers associated with myocardial injury such as creatine kinase (CK) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) have also been used to predict LVR [8, 9]. These markers are active at different phases of myocardial infarction (MI). However, these markers are not ideal indicators of remodeling given that LVR is a dynamic process [7, 9, 10].

During the process of ventricular remodeling, the area of the infarct scar grows, and there are subsequent regional ventricular expansion and functional changes [5, 11]. Cardiac magnetic resonance is commonly considered the gold standard for assessing infarct size and altered ventricular morphology [12]. Cardiac magnetic resonance and other techniques such as gated positron emission tomography, or dynamic gated single-photon emission computed tomography are seen as true "one stop shop" for cardiac imaging assessment, because these techniques allow molecular, metabolic, histological, structural, functional cardiac assessments. However, echocardiography is less time-consuming and costs less than these advanced techniques, thus becoming the default tool for serial follow-up of STEMI patients in most clinical settings [13].

Changes in left ventricular structure are not always linear at different stages in the remodeling process. Thus, static echocardiography parameters cannot accurately predict late LVR, and continuous measurements are more meaningful [10, 14, 15]. In this study, data was analyzed from patients with STEMI who were treated with primary PCI and optimal standard pharmacotherapy with a view to

detect the predictors of post-infarction LVR. In particular, the prognostic capability of early changes in left ventricular end-diastolic volume (LVEDV) as defined by dynamic echocardiography parameters was examined.

## Methods

### Study subjects

The study was comprised of 301 patients with STEMI who were admitted to hospital and underwent-primary PCI from September 2017 to March 2021. The inclusion criteria included the following: (1) typical chest pain lasting at least 30 minutes; (2) ST-segment elevation of 0.1 mV in 2 or more contiguous leads on electrocardiography; or (3) interval from onset of symptoms to admission being under 12 hours. The exclusion criteria included the following: (1) previous coronary angiography; (2) severe complications in hospital (death, reinfarction, acute heart failure with Killip class IV, or clinical instability); (3) complicated malignant disease; or (4) complicated severe valvular pathology or permanent atrial fibrillation. The study flow chart is shown in Figure 1.

The investigation conformed with the principles outlined in the Declaration of Helsinki. The study was approved by the Research Ethics Committee of Ruijin Hospital affiliated with Shanghai Jiao Tong University School of Medicine (2020CER152). All patients gave written informed consent.

### PCI and pharmacotherapy

All patients were pretreated before PCI with oral loading doses of acetylsalicylic acid (ASA, 300 mg), ticagrelor (180 mg), or clopidogrel (600 mg). In the catheterization laboratory, unfractionated heparin was administered according to patient weight (70–100 IU/kg). The diameter, length, and number of stents to be implanted were left to the discretion of the clinician. Coronary artery stenosis was measured by coronary angiography and intravascular ultrasound. Coronary flow was assessed by the thrombolysis in MI score. All patients were administered antiplatelet therapy (ASA combined with ticagrelor or clopidogrel) after the procedure. Patients without contraindications were administered statins, angiotensin converting enzyme inhibitors, angiotensin receptor blockers. and beta-receptor blockers.

### Echocardiography

Standard echocardiography was performed on the first day after PCI, on the day of hospital discharge, at 1 month and 6 months after discharge by a single and experienced echocardiography specialist, using a Philips Epic 7 machine and a 1.6/3.2 MHz probe. Echocardiography images were analyzed offline by the same echocardiography specialist.

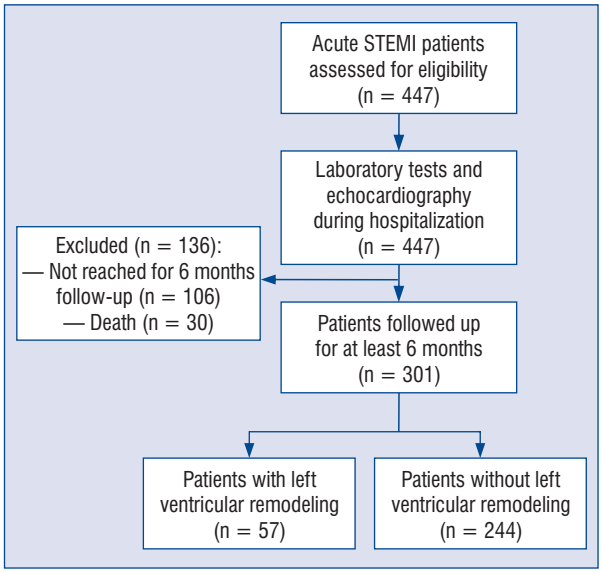



**Figure 1.** Study flow chart. Flow chart showing inclusion and exclusion criteria; STEMI — ST-segment elevation myocardial infarction.

Left ventricular end-diastolic volume, left ventricular end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF) were calculated using the Simpson method (**Suppl. Fig. 1**). Left atrial volume, left atrial volume index, and the E/E' ratio, where E is peak velocity flow in early diastole and E' is the average peak early diastolic mitral annulus velocity, were used to assess the diastolic function of the left ventricle.

Left ventricular remodeling was defined as a ≥ 15% increase in LVEDV from discharge to the 6-month follow-up [16, 17].

### Statistical analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8.0 (GraphPad Software, La Jolla, CA, USA) were used for statistical analysis. Data are presented as means ± standard deviations when they fit the normal distribution and as medians and the first and third quartiles in the case of non-normal distributions. P-values less than 0.05 were considered statistically significant. The Student t-test and the Mann-Whitney U test were applied depending on the normality of the data. Categorical variables were compared using the

$\chi^2$ test or the Fisher exact test. Binary logistic regression analyses with 95% confidence intervals (CIs) were used to assess predictors of LVR, including factors that may have had an effect on predicting LVR in previous univariate analysis (if p-values were less than 0.1).

Intra- and inter-observer measurement variability were quantified by calculating intraclass correlation coefficient (ICC). Intra-observer variability was based on two analyses of 20 patients' echocardiography by the same expert. Another expert's analysis of these images was used to calculate inter-observer variability. These observers were blinded to the previous measurements.

## Results

### Patient characteristics

Overall, 301 patients were included in this study and were divided into two groups: the LVR group (n = 57) and the non-LVR (n-LVR) group (n = 244). There were no significant differences in age, sex, body mass index, heart rate, blood pressure, hypertension status, diabetes mellitus prevalence, or smoking history between the two groups. The mean hospital stay of patients was 6.7 ± 3.7 days. The LVR group had a higher peak cardiac troponin I (cTNI) level (p = 0.023), a higher peak CK level (p = 0.009), and a higher peak creatine kinase isoenzyme MB (CK-MB) level (p < 0.001) compared with the n-LVR group (**Suppl. Fig. 2**). Lactic dehydrogenase (LDH) and aspartate aminotransferase (AST) levels were higher in the LVR group than in the n-LVR group (p = 0.006, p = 0.039) (**Suppl. Fig. 2**). There were no significant differences in peak NT-proBNP, serum lipid, and hs-CRP levels between the two groups. The frequency of the left anterior descending artery (LAD) being the main culprit vessel in the LVR group was higher than in the n-LVR group (p = 0.032). However, the frequencies of the right coronary artery or left circumflex artery being the culprit vessel were not statistically significant between the two groups (**Suppl. Fig. 3**). Both groups received similar medications at discharge, and the incidence of hospital complications and major adverse cardiovascular events was comparable between the two groups. The demographics and clinical characteristics of the study sample are presented in Table 1.

### Echocardiography characteristics

The intra-observer reliability and inter-observer reliability were good for LVEDV (ICC = 0.911 and 0.895, respectively), LVESV (ICC = 0.897 and 0.959, respectively) and LVEF (ICC = 0.724 and 0.680, respectively). **Supplemental Table 3** show the analysis of intra- and inter-observer reliability.

On the first day after PCI, there was no significant difference in LVEDV between the LVR group and n-LVR group (119.8 ± 28.14 mL vs. 124.16 ± ± 35.92 mL, p = 0.320). At discharge, the LVEDV in the LVR group was lower than that in the n-LVR group (116.09 ± 34.49 mL vs. 123.8 ± 26.1 mL, p = 0.014). However, at 1 month and 6 months after discharge, the LVEDV in the LVR group was higher than that in the n-LVR group (p = 0.037 vs. p < 0.001; Fig. 2A). Although LVEDV decreased in the LVR group at discharge compared with that on the first day after PCI (–5.24 ± 16.02%), it significantly increased in the LVR group by 13.05 ± ± 14.89% at the 1-month follow-up and increased by another 13.1 ± 14.41% from the 1-month to the 6-month follow-up. In contrast, LVEDV increased by 5.05 ± 16.92% in the n-LVR group at discharge but decreased to the level of day 1 post-PCI after 1 month and remained at that level at the 6-month follow-up (Fig. 2A, C). The same trend of change had been seen in the LVESV (Fig. 2D). At the time of discharge LVEF increased in both groups (p = = 0.035 in the LVR group, p = 0.019 in the n-LVR group). However, after discharge LVEF gradually increased in the n-LVR group (p = 0.002 at 1 month, p = 0.035 at 6 months), while it did not change significantly in the LVR group (Fig. 2B). Correspondingly, LVEF was significantly lower in the LVR group than in the n-LVR group at 1 month and 6 months post-discharge (p = 0.012 and p = = 0.004) (Fig. 2B). **Supplemental Table 1** show the echocardiography characteristics of all study participants.

### Follow-up biochemical characteristics

The levels of CRP and NT-proBNP, used to reflect inflammation as well as myocardial injury, were also measured in all patients. CRP levels were higher in the LVR group than in the n-LVR group 1 month after discharge (p = 0.040). However, they were at similar levels 6 months after discharge. There were no significant differences in NT-pro--BNP levels between the two groups at the 1-month follow-up, but NT-proBNP was higher in the LVR group at the 6-month follow-up (p = 0.006).

### Logistic regression analysis for predicting LVR

In univariate logistic regression analysis, CK, CK-MB, LDH, AST, hs-CRP at day 2 after PCI,

**Table 1.** Patient characteristics at baseline.

| | Non-LVR (n = 244) | LVR (n = 57) | P-value |
|---|---|---|---|
| Age [years] | 64.84 ± 11.28 | 62 ± 12.21 | 0.093 |
| Male gender | 200 (81.0%) | 46 (80.7%) | 0.938 |
| Body mass index [kg/m$^2$] | 24.49 ± 3.18 | 24.72 ± 3.63 | 0.632 |
| Heart rate [bpm] | 82.95 ± 14.69 | 82.19 ± 14.32 | 0.620 |
| Systolic pressure [mmHg] | 122.86 ± 18.99 | 124.47 ± 24 | 0.585 |
| Diastolic pressure [mmHg] | 75.68 ± 13.01 | 77.24 ± 14.73 | 0.688 |
| Hypertension | 146 (59.8%) | 36 (63.2%) | 0.644 |
| Diabetes mellitus | 71 (29.1%) | 16 (28.1%) | 0.877 |
| Smoker | 131 (53.7%) | 30 (52.6%) | 0.885 |
| Peak NT-proBNP [pg/mL] | 1126 (438.3–3209) | 882.3 (411.9–2459) | 0.432 |
| Peak cTNI [ng/mL] | 33.44 (11.71–111.78) | 68.88 (22.78–135.92) | 0.023* |
| Peak CK [U/L] | 1562.5 (570.3–2980.5) | 2353 (1214–4196) | 0.009* |
| Peak CK-MB [U/L] | 132.85 (45.93–265.05) | 243.3 (112.1–510.4) | 0.001* |
| Peak LDH [U/L] | 503.5 (307–807.25) | 676 (426.5–1014.5) | 0.006* |
| ALT [U/L] | 37 (20–56) | 47 (24–77.75) | 0.084 |
| AST [U/L] | 151 (55.25–301.25) | 235 (90–340) | 0.039* |
| TC [mmol/L] | 4.6 ± 1.2 | 4.69 ± 1.12 | 0.603 |
| TG [mmol/L] | 1.39 (1–1.89) | 1.38 (1.16–2.23) | 0.337 |
| HDL [mmol/L] | 1.06 ± 0.22 | 1.05 ± 0.27 | 0.725 |
| LDL [mmol/L] | 2.96 ± 1.1 | 2.97 ± 0.92 | 0.912 |
| APOB [mmol/L] | 0.92 ± 0.26 | 0.93 ± 0.24 | 0.720 |
| LP(a) [mmol/L] | 0.15 (0.08–0.32) | 0.13 (0.07–0.3) | 0.267 |
| hs-CRP [mg/L] | | | |
| Day 1 | 4.94 (2–12.27) | 5.96 (3.01–28.18) | 0.112 |
| Day 2 | 8.5 (3.95–18.86) | 12.08 (6.03–43.18) | 0.053 |
| Day 3 | 17.39 (7.58–49.78) | 17.39 (7.58–49.78) | 0.198 |
| Day 4 | 13.08 (6.39–41.54) | 13.56 (6.88–53.76) | 0.428 |
| WBC [10 ^ 9/L] | 9.71 ± 3.52 | 11.00 ± 3.54 | 0.016* |
| Neutrophil [%] | 78.8 (66.8–85.8) | 78.3 (68.48–85.93) | 0.608 |
| Hemoglobin [g/L] | 135.68 ± 19.19 | 139.20 ± 19.54 | 0.224 |
| Platelets [10 ^ 12/L] | 209.20 ± 68.68 | 211.07 ± 51.61 | 0.850 |
| HbA1c [%] | 6.41 ± 1.44 | 6.29 ± 1.38 | 0.600 |
| Scr [$\mu$mol/L] | 94.22 ± 107.23 | 92.19 ± 34.84 | 0.888 |
| eGFR [mL/min/1.73 m$^2$] | 80.90 ± 21.12 | 78.52 ± 22.44 | 0.452 |
| Main culprit vessel: | | | |
| LAD | 120 (49.2%) | 37 (64.9%) | 0.032* |
| RCA | 81 (33.2%) | 17 (29.8%) | 0.625 |
| LCX | 47 (19.3%) | 7 (12.3%) | 0.216 |
| Multivessel CAD: | | | 0.503 |
| 1-vessel | 53 (21.7%) | 16 (28.1%) | |
| 2-vessel | 84 (34.4%) | 16 (28.1%) | |
| 3-vessel | 107 (43.9%) | 25 (43.9%) | |
| TIMI flow grade: | | | 0.343 |
| 3 | 243 (99.6%) | 56 (98.2%) | |
| ≤ 2 | 1 (0.4%) | 1 (1.8%) | |
| MACE | 54 (22.1%) | 13 (22.85) | 0.912 |
| Hospital complications | 71 (29.1%) | 20 (35.1%) | 0.375 |
| Medication at discharge: | | | |
| Antiplatelet therapy | 240 (98.4%) | 57 (1005) | > 0.999 |
| Beta-blockers | 219 (89.8%) | 52 (91.2%) | 0.738 |
| ACEI/ARB/ARNI | 183 (75%) | 42 (73.75) | 0.837 |
| Aldactone | 20 (8.2%) | 9 (15.8%) | 0.080 |
| Statins | 235 (96.3%) | 56 (98.2%) | 0.694 |

Data were expressed as mean ± standard deviation for normal distribution, or median and the Me 25% and 75% quartiles for non-normal distribution. Dichotomous variables were presented as number (percentage). Hospital complications, including acute heart failure, arrhythmia, contrast-induced nephropathy and heart aneurysm; *statistical significance; NT-proBNP — N-terminal pro-B-type natriuretic peptide; cTNI — cardiac troponin I; CK — creatine kinase; CK-MB — creatine kinase-MB; LDH — lactic dehydrogenase; ALT — alanine aminotransferase; AST — aspartate aminotransferase; TC — serum total cholesterol; TG — triglycerides; HDL — high-density lipoprotein; LDL — low-density lipoprotein; APOB — apolipoprotein B; LP(a) — lipoprotein(a); hs-CRP — high-sensitivity C-reactive protein; WBC — white blood cells; HBA1c — glycated hemoglobin; Scr — serum creatinine; eGFR — estimated glomerular filtration rate; LAD — left anterior descending artery; RCA — right coronary artery; LCX — left circumflex artery; CAD — coronary heart disease; TIMI — thrombolysis in myocardial infarction; MACE — major adverse cardiovascular events; Antiplatelet therapy — acetylsalicylic acid combined with ticagrelor or clopidogrel; ACEI — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blockers; ARNI — angiotensin receptor enkephalinase inhibitor

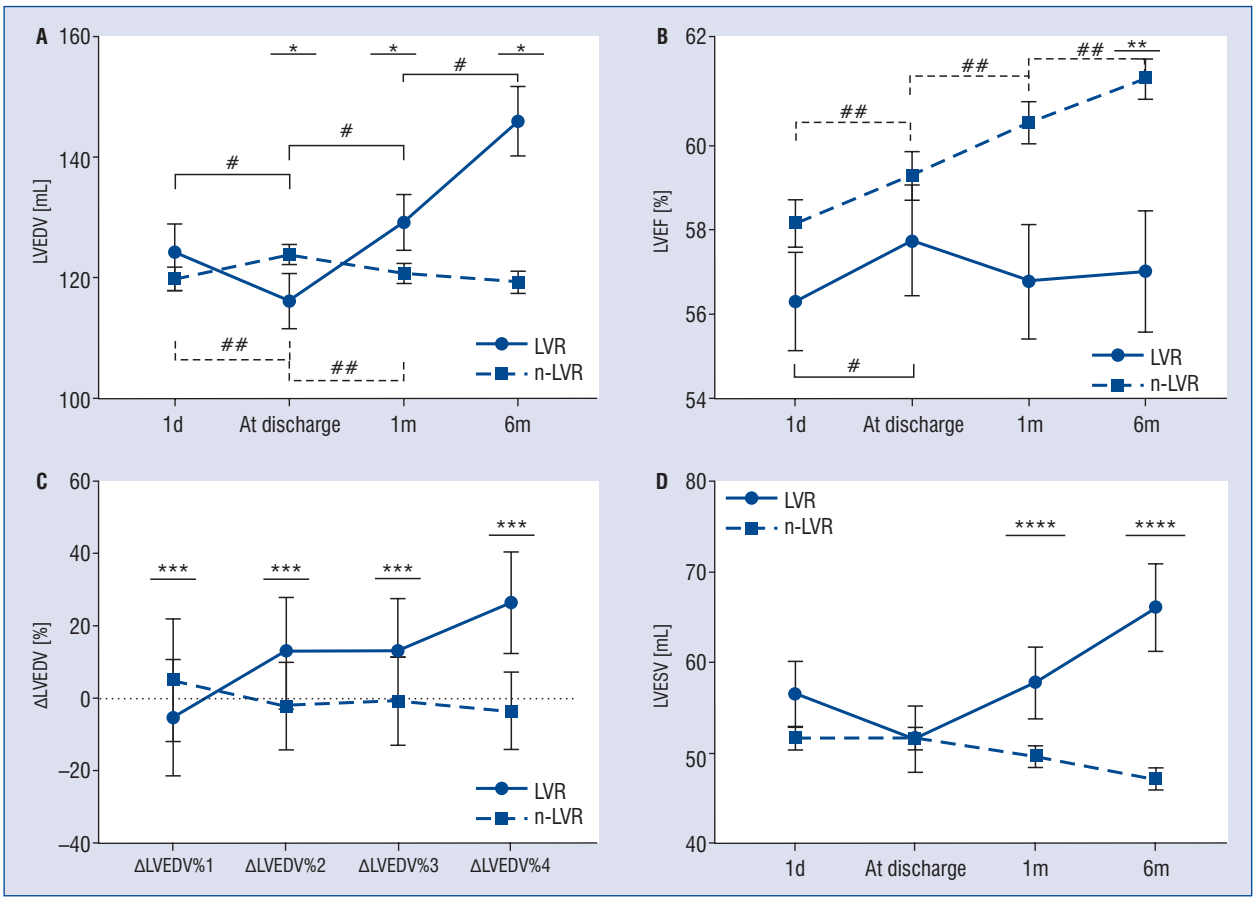



**Figure 2.** Echocardiography parameters: 1 day (1d) after percutaneous coronary intervention to 6 months (6m) post-discharge. Changes in left ventricular end-diastolic volume (LVEDV) (**A**), left ventricular ejection fraction (LVEF) (**B**) and left ventricular end-systolic volume (LVESV) (**D**) during 6 months of follow-up in the left ventricular remodeling (LVR) and non-LVR (n-LVR) groups. Comparison of LVEDV changes at different times (**C**); *p < 0.05 between LVEDV in LVR and n-LVR groups; **p < 0.05 between LVEF in LVR and n-LVR groups; ***p < 0.001 between LVEDV rate of change in LVR and n-LVR groups; ****p < 0.05 between LVESV in LVR and n-LVR groups; #p < 0.05 within LVR groups; ##p < 0.05 within n-LVR groups. ΔLVEDV%1 — increase in LVEDV from the first day after PCI to discharge; ΔLVEDV%2 — increase in LVEDV from discharge to 1 month after discharge; ΔLVEDV%3 — increase in LVEDV from 1 month to 6 months post-discharge; ΔLVEDV%4 — increase in LVEDV from discharge to 6 months post-discharge.

LAD involvement, LVEF at 1 month, rate of change in LVEDV from the first day after PCI to discharge (ΔLVEDV%1), and rate of change in LVEDV from discharge to the 1-month follow-up (ΔLVEDV%2) had more predictive value for LVR (p < 0.05). The results of the univariate logistic regression analysis are detailed in Table 2.

Multiple logistic regression analysis showed that peak CK-MB (odds ratio [OR] = 1.79, 95% CI 1.08–2.966, p = 0.024) and a positive ΔLVEDV%2 (OR = 3.037, 95% CI 1.972–4.676, p < 0.001) were independent risk factors for LVR in STEMI patients at the 6-month follow-up, whereas a positive ΔLVEDV%1 (OR = 0.531, 95% CI 0.338–0.834, p = 0.006) was a protective factor (Fig. 3A). Specificity and sensitivity of these variables was then analyzed for predicting adverse LVR. Model 1 showed that a high peak CK-MB level during hospitalization was accompanied by adverse LVR at 6 months post-discharge (area under the curve [AUC] = 0.64, 95% CI 0.56–0.72). Model 2 showed the predictive value of reduced LVEDV (during the very early stages after STEMI) for late LVR (AUC = 0.69, 95% CI 0.62–0.77). The predictive power of early left ventricular dilation at the 1-month follow-up was demonstrated in Model 3 (AUC = 0.79, 95% CI 0.72–0.85). Considering ΔLVEDV%1 and ΔLVEDV%2, Model 4 showed that early changes in the left ventricle may be a predictor of late LVR at 6 months (AUC = 0.80,

**Table 2.** Logistic regression analysis for left ventricular remodeling prediction.

| | Crude OR (95% CI) | P | Adjusted OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | 0.979 (0.955–1.004) | 0.094 | – | – |
| cTNI | 1.166 (0.907–1.5) | 0.232 | – | – |
| CK | 1.518 (1.034–2.229) | 0.033* | 1.303 (0.858–1.98) | 0.215 |
| CK-MB | 1.639 (1.245–2.158) | < 0.001* | 1.79 (1.08–2.966) | 0.024* |
| LDH | 1.485 (1.137–1.939) | 0.004* | 1.052 (0.53–2.086) | 0.885 |
| ALT | 1.125 (0.884–1.433) | 0.339 | – | – |
| AST | 1.337 (1.032–1.732) | 0.028* | 0.826 (0.455–1.499) | 0.53 |
| hsCRP day 2 | 1.311 (1.024–1.678) | 0.032* | 1.226 (0.869–1.729) | 0.245 |
| LAD culprit vessel | 1.881 (1.033–3.423) | 0.039* | 1.398 (0.685–2.851) | 0.357 |
| LVEF at 1 month | 0.667 (0.482–0.924) | 0.015* | 0.647 (0.400–1.047) | 0.077 |
| ΔLVDEV%1 | 0.437 (0.291–0.655) | < 0.001* | 0.531 (0.338–0.834) | 0.006* |
| ΔLVDEV%2 | 3.311 (2.277–4.816) | < 0.001* | 3.037 (1.972–4.676) | < 0.001* |

Datasets of cTNI, CK, CK-MB, LDH, ALT, AST and hsCRP were normalized; *statistical significance; OR — odds ratio; CI — confidence intervals; cTNI — cardiac troponin I; CK — creatine kinase; CK-MB — creatine kinase-MB; LDH — lactic dehydrogenase; ALT — alanine aminotransferase; AST — aspartate aminotransferase; hs-CRP — high-sensitivity C-reactive protein; LAD — left anterior descending artery; LVEF — left ventricular ejection fraction; ΔLVEDV%1 — the increase in LVEDV from first day after PCI to discharge; ΔLVEDV%2 — the increase in LVEDV from discharge to 1 month after discharge

95% CI 0.74–0.87). Model 5 combined peak CK-MB, ΔLVEDV%1, and ΔLVEDV%2 and showed good predictive power for LVR (AUC = 0.83, 95% CI 0.77–0.89) (Fig. 3B). However, the improvement in predictive power relative to Model 4 was not statistically significant (p = 0.071). Adjusted the LAD culprit vessel on the basis of the Model 5, the predictive power also did not improve significantly compared with Model 4 and Model 5 (p = 0.057 and p = 0.675, respectively) (**Suppl. Fig. 4**).

## Discussion

This study prospectively analyzed LVR in patients with STEMI who underwent primary PCI. The principal findings can be summarized as follows: (1) decreased LVEDV during the very early stages after STEMI may result in late ventricular dilation; (2) early left ventricular dilation at the 1-month follow-up predicted the occurrence of late LVR at 6 months; (3) early dynamic echocardiography may help detect late LVR.

### Predictive value of laboratory examinations

Compared with other cardiac biomarkers such as myoglobin and CK-MB, cardiac troponin is considered as a preferred and gold standard biomarker in the diagnosis of AMI due to its high sensitivity [18, 19]. Earlier appearance and peaking may mean that the peak cTNI value we observed during hospitalization do not fully represent the level of cTNI at the onset of AMI. In contrast, the time lag before CK-MB appearance allowed us to observe the process of its elevation [20]. It may be an explanation that peak CK-MB is a more powerful predictor than peak cTNI in this study.

### Changes in LVEF and LVEDV during hospitalization

The process of LVR is usually accompanied by an increase in left ventricular volume and a reduction in LVEF [17, 21]. The main factors that contribute to these changes are infarct size, ventricular wall pressure, and post-infarct healing [21]. The initial infarct size and ventricular wall pressure can be quickly controlled with the use of primary PCI and medications such as beta-receptor blockers and vasodilators. This results in patients with STEMI being discharged with improved cardiac function [22]. The present study demonstrated that patients in both the LVR and n-LVR groups had significant improvement in LVEF at discharge (p = 0.035, p = 0.019). However, changes in left ventricular morphology may be more related to the process of post-infarct healing.

In the very early post-infarction period, myocardial fibroblasts and effector cells recruit inflammatory cells to the infarct area to remove necrotic cells as well as extracellular matrix (ECM) in preparation for subsequent cell migration to the area of injury [23, 24]. Infiltration of inflammatory cells in the infarct area peaks between days 3 and 7 after infarction, and fibrosis progresses imme-

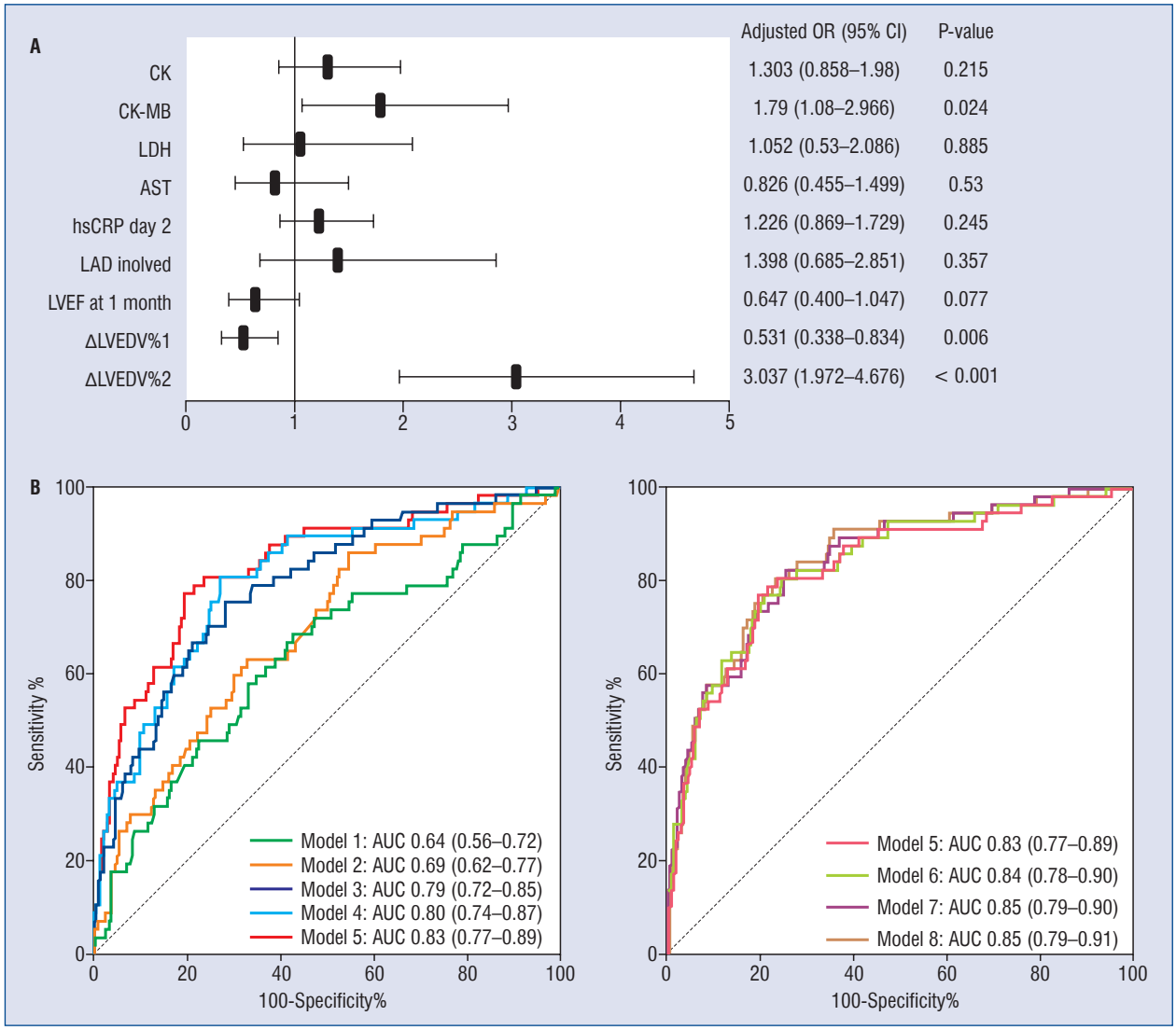



**Figure 3.** Relationship between ΔLVEDV% and late left ventricular remodeling (LVR). Multiple logistic regression analysis for predicting LVR (**A**). Receiver operating characteristic curve for risk prediction of LVR (**B**). Sensitivity and specificity were maximized at 0.68 and 0.57, respectively in Model 1 (peak CK-MB, cutoff value = 177.2 U/L, p = 0.001). Sensitivity and specificity were maximized at 0.46 and 0.86, respectively in Model 2 (ΔLVEDV%1, cutoff value = 3.09%. p < 0.0001). Sensitivity and specificity were maximized at 0.75 and 0.72, respectively in Model 3 (ΔLVEDV%2, cutoff value = 4.53%. p < 0.0001). Sensitivity and specificity were maximized at 0.81 and 0.73, respectively in Model 4 (ΔLVEDV%1 and ΔLVEDV%2, p < 0.0001). Sensitivity and specificity were maximized at 0.78 and 0.81, respectively in Model 5 (peak CK-MB, ΔLVEDV%1 and ΔLVEDV%2, p < 0.0001). Model 4 and Model 5 showed no significant difference in predictive power for late LVR (p = 0.071). Model 6 included Model 5 and left ventricular ejection fraction (LVEF) at 1 month, Model 7 incorporated all variables in multiple logistic regression analysis. Model 8 included Model 7 and age (p < 0.001 in these 3 models); OR — odds ratio; CI — confidence interval; CK-MB — creatine kinase isoenzyme MB; LDH — lactic dehydrogenase; AST — aspartate aminotransferase; hsCRP — high-sensitivity C-reactive protein; LAD — left anterior descending artery; ΔLVEDV% — rate of change in left ventricular end-diastolic volume; ΔLVEDV%1 — ΔLVEDV% from the first day after percutaneous coronary intervention to discharge; ΔLVEDV%2 — ΔLVEDV% from discharge to 1 month after discharge.

diately after the inflammatory response [24, 25]. Fibroblasts are the predominant cell type in the infarct area. They express and secrete ECM proteins at the border of the infarct and gradually migrate to the core infarct area along the newly synthesized ECM [26]. At the same time, the microvascular network formed by angiogenesis in the infarct area provides fibroblasts with the required oxygen for repair [24, 27]. Eventually, type III collagen produced by fibroblasts forms permanent scar tissue and replaces the necrotic cardiomyocytes. However, the excessive inflammatory response

further degrades the ECM, inhibits the progression of reparative fibrosis, interferes with early healing of the infarcted myocardium, and ultimately increases the risk of long-term ventricular remodeling [21, 28, 29].

Based on this, it is not difficult to explain why the two groups in this study had completely different LVEDV outcomes despite LVEF improvements in both groups. Mild ventricular dilatation at discharge is believed to be adaptive and physiological. It tends to indicate smooth healing of the infarcted myocardium in the initial post-infarction period and prevents further exacerbation of LVR. Conversely, a reduced LVEDV may imply that early collagen fiber repair in the injured area is impeded and that there is an increased risk of LVR, although it appears to be a good prognostic indicator.

### Development of LVR during the 6 months after discharge

Left ventricular ejection fraction continued to improve and left ventricular size remained stable during follow-up in the n-LVR group. There was no evidence to suggest dilation or remodeling (Fig. 2). In contrast, patients in the LVR group showed a significant increase in LVEDV 1-month post-discharge (Fig. 2). Left ventricular dilation usually becomes evident at 1 month and is the result of remodeling in the non-infarcted region. It represents pathological as well as maladaptive hypertrophy and fibrosis of the remote myocardium [3, 14].

Due to an excessive inflammatory response, patients with LVR fail to complete reparative fibrosis of the necrotic region early after AMI, which results in myocardial over function in the surviving non-infarcted area to maintain stroke volume. This in turn increases ventricular wall stress [3, 21]. This process contributes to the release of certain cytokines such as interleukin 6, interleukin 18, and tumor necrosis factor alpha, inducing a persistent inflammation in the remote myocardium [10, 30]. At the same time, the activation of the renin–angiotensin–aldosterone system accounts for the production of type I collagen and the activation of anti-apoptotic factors that drive the development of LVR. This ultimately manifests as an increase in LVEDV and a decrease in LVEF [31].

During the follow-up period, it was found that patients in the LVR group had a higher CRP level at the 1-month follow-up compared with patients in the n-LVR group (**Suppl. Table 2**), indicating that these patients remained in a chronic inflammatory state after the acute phase of MI.

### Predictive value of echocardiography parameters for LVR

This study demonstrates the predictive value of multiple follow-up echocardiography scans for post-infarction LVR. After adjusting for factors such as CK-MB, it was found that a lower ΔLVEDV at discharge predicted a higher risk of LVR, as did a higher ΔLVEDV 1 month after discharge (Fig. 3).

### Limitations of the study

This study was a single-center study with a small sample size and relatively short follow-up. Previous studies have found that the occurrence of adverse remodeling increases long-term mortality over a mean follow-up time of 3 to 5 years [31]. The same follow-up duration applies to the prediction of all-cause mortality as well as adverse clinical events by echocardiography parameters such as LVEF and LVEDV [32]. In the present study, the mean follow-up time was 7.4 ± 3.1 months. Therefore, the study was limited in the prediction of long-term LVR, and the predictive power of relevant data for longer-term adverse prognoses was not explored further. The details of PCI technique and pharmacotherapy management during the study period could also have been better described. Although the echocardiography specialist was experienced, intra-observer variability is unavoidable, which may have had an impact on these results.

## Conclusions

In patients with STEMI treated with primary PCI, decreased LVEDV at very early stages post--infarction and increased LVEDV at the 1-month follow-up were both associated with late LVR during 6 months of follow-up. A comprehensive examination of early changes in LVEDV after STEMI may help predict the risk of late LVR. Dynamic echocardiography is a useful and practical tool to detect LVR after STEMI.

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