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Predictive value of acoustic cardiography for post-PCI early ventricular remodeling in acute myocardial infarction

Weiwei Wang^{1,5}, Haizhen Hao^{2,5}, Tingting Fan¹, Jia Yue¹, Mingyang Wang³, Moshui Chen², Guolan Deng⁴, Liangyi Si^{1✉} & Fuwei Zhang^{1✉}

Acoustic cardiography is a completely new technology, it has great advantages in the rapid diagnosis of cardiovascular diseases. The purpose of this study was to investigate the clinical value of the fourth heart sound (S₄), cardiac systolic dysfunction index (SDI), and the cardiac cycle time-corrected electromechanical activation time (EMATc) in the prediction of post-percutaneous coronary intervention (PCI) early ventricular remodeling (EVR) in patients with acute myocardial infarction (AMI). We recruited 161 patients with AMI of 72-h post-PCI, including 44 EVR patients with left ventricular ejection fraction (LVEF) < 50% and 117 Non-EVR patients (normal left ventricular systolic function group, LVEF ≥ 50%). EMATc, S₄, and SDI were independent risk factors for post-PCI early ventricular remodeling in patients with AMI [S₄ (OR 2.860, 95% CI 1.297–6.306, *p* = 0.009), SDI (OR 4.068, 95% CI 1.800–9.194, *p* = 0.001), and EMATc (OR 1.928, 95% CI 1.420–2.619, *p* < 0.001)]. The area under the receiver operating characteristic curve for EMATc was 0.89, with an optimal cutoff point of 12.2, EMATc had a sensitivity of 80% and a specificity of 83%. By contrast, an optimal cutoff point of 100 pg/ml, Serum brain natriuretic peptide had a sensitivity of 46% and a specificity of 83%. Our findings suggest the predictive value of EMATc for the occurrence of EVR in these patients was also identified; EMATc may be a simple, quick, and effective way to diagnose EVR after AMI.

Acute myocardial infarction (AMI) is a common cardiovascular disease that poses a serious threat to human health. Percutaneous coronary intervention (PCI) and standardized drug therapy can effectively treat most patients, but many patients still develop ventricular remodeling, which can contribute to heart failure post-PCI¹. A strong relationship has been demonstrated among disease prognosis, heart failure, and ventricular remodeling after AMI. Ventricular remodeling is an independent predictor of the development of heart failure². Many guidelines for the management of cardiovascular diseases refer to the importance of ventricular remodeling after AMI and its treatment modalities^{3,4}. Ventricular remodeling after AMI can be divided into early ventricular remodeling and late ventricular remodeling, with various clinical manifestations, such as enlarged left ventricle, reduced left ventricular ejection fraction (LVEF), and abnormal ventricular wall motion^{5,6}. Asymptomatic left ventricular systolic dysfunction (LVSD) is a major manifestation of early ventricular remodeling, with an occurrence of up to 30–60% in patients after AMI⁷. Early detection of ventricular remodeling after AMI is key to effective treatment. Although B-type brain natriuretic peptide (BNP) and echocardiography can be utilized in the diagnosis of LVSD, they carry several disadvantages, including increased cost, need for specialized technicians, and difficulty in achieving dynamic monitoring. Therefore, acoustic cardiography is gaining attention as a simple, rapid, non-invasive, and effective diagnostic modality for LVSD.

Many clinical studies have confirmed the diagnostic value of acoustic cardiography in a variety of cardiovascular diseases, especially in the diagnosis of heart failure. Some studies have shown that cardiac cycle time-corrected electromechanical activation time (EMATc), left ventricular systolic time (LVST), and third heart sound (S₃) are superior to serum BNP levels in the diagnosis of heart failure. EMAT is related to left ventricular systolic function. Furthermore, S₃ and S₄ are less affected by age, which increase their utility in evaluating

¹Division of Cardiology, Third Affiliated Hospital of Chongqing Medical University, Chongqing, China. ²Department of Neurology, Haikou People's Hospital, Central South University, Haikou, China. ³Department of Critical Care Medicine, Peoples Hospital of Jiangbei District, Chongqing, China. ⁴Division of Cardiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China. ⁵These authors contributed equally: Weiwei Wang and Haizhen Hao. ✉email: doctorstly@126.com; zhangfuwei@163.com

cardiac systolic and diastolic function^{8–10}. However, acoustic cardiography has been rarely used in the diagnosis of coronary artery disease. Several studies have shown improved sensitivity and specificity using standard ST-T changes combined with $S_4 > 3.6$ as diagnostic criteria for coronary artery disease¹¹. Additionally, our previous study confirmed the clinical significance of acoustic cardiography in the diagnosis of coronary artery disease and ventricular remodeling¹².

The present study investigated the relationship between parameters of acoustic cardiography and early ventricular remodeling and examined the predictive value of each parameter for early ventricular remodeling after PCI in patients with AMI.

Methods

Study population and study design. A total of 183 inpatients from the Departments of Cardiology of the Third Affiliated Hospital of Chongqing Medical University and Haikou People's Hospital were enrolled in the study from March 05, 2019 to June 30, 2021 [22 patients were excluded due to poor quality electrocardiograms (ECGs)]. 161 patients with asymptomatic acute anterior wall MI after emergency PCI were included (all occurring within 24 h, with increased serum troponin I levels, ST segment elevation and pathological Q wave on ECG, and angiography showing severe stenosis or occlusion of the anterior descending branch of the coronary artery). Serum BNP, acoustic cardiography (AUDICOR, Inovise Medical, Inc., Portland, OR, USA; Henan Shanren Medical Technology Co, SR-X12Y1), and Color Doppler echocardiography were performed pre-operatively. Color Doppler echocardiography was also performed after 72 h, and $LVEF\% < 50\%$ ($LVEFs\%$ were normal before operation) 72-h post-PCI was defined as early ventricular remodeling. The study subjects were divided into two groups: early ventricular remodeling group ($EF\% < 50\%$ EVR, 44 cases) and normal left ventricular systolic function group ($EF\% \geq 50\%$, Non-EVR, 117 cases).

The exclusion criteria were: (1) atrial fibrillation, pre-excitation syndrome, and intraventricular block; (2) severe liver and kidney disease; (3) patients on mechanical ventilation; (4) inferior wall MI; and (5) patients with pacemaker. Before participation, written-informed consent was obtained from each patient. We calculated the sample size through Power and Sample Size online; the website is <https://powerandsamplesize.com/Calculators/>. We calculated sample size between Non-EVR group and EVR group with regard to EMATc. With power equal to 0.9, we chose a ratio of 3:1 for the Non-EVR and EVR groups, the total sample size needed is 120. We have a sufficient number of cases. The study was approved by the Third Affiliated Hospital of Chongqing Medical University in the participating institutions (protocol number 202133), and was conducted in accordance with the Declaration of Helsinki.

Echocardiography. Echocardiography (Vivid 7, Vingmed-General Electric, IE33, Phillips, Andover) was performed in all patients. The biplane Simpson's method was used to calculate both end-diastolic and end-systolic volumes. These volumes were employed to calculate LVEF.

Acoustic cardiography. Each patient underwent an acoustic cardiography examination in the supine position. For the measurement of heart sounds, acoustic cardiography raw data were analyzed by a computerized algorithm. At least 3 examinations were performed on each study subject, and the average values of each variable were used for analysis. In this study, the following acoustic cardiography parameters were evaluated:

- (1) Electromechanical activation time (EMAT), the time from Q wave onset to the mitral component of the first heart sound (S_1) (Fig. 1). Time-corrected electromechanical activation time (EMATc) indicates the proportion of the cardiac cycle occupied by EMAT.
- (2) Fourth heart sound (S_4) score: measurement of the intensity of S_4 based on timing, persistency, intensity, and frequency of the sound (Fig. 1); one value between 0 and 10 is reported.
- (3) Third heart sound (S_3) score: measurement of the intensity of S_3 based on timing, persistency, intensity, and frequency of the sound (Fig. 1); one value between 0 and 10 is reported.
- (4) Systolic dysfunction index (SDI): $SDI = \exp(S_3 \text{ score}/10) \times \text{QRS duration} \times \text{QR interval} \times \text{EMAT}/RR$. The SDI value undergoes a nonlinear transformation and is mapped into a scale of 0–10.

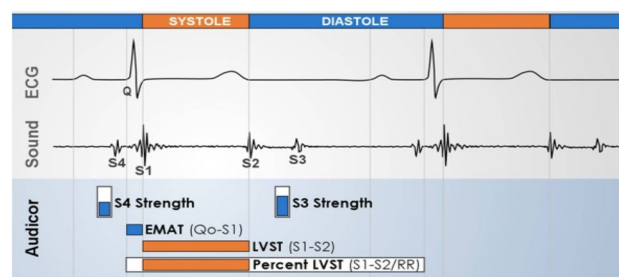


Figure 1. Acoustic cardiography parameters (Courtesy of Inovise Medical, Inc.). S_3 third heart sound, S_4 fourth heart sound, EMAT electromechanical activation time, LVST left ventricular systolic time.

Statistical analysis. SPSS, version 20, was used for statistical analyses (SPSS, Inc., Chicago, Illinois). A two-sided P value <0.05 was considered statistically significant. Continuous variables with a normal distribution were expressed as mean \pm standard deviation (SD). For predicting EVR, the receiver operating characteristic (ROC) curves were generated to determine the area under the curve (AUC), sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR-). Multivariate logistic regression analysis was used to analyze the independent risk factors of EVR. In addition, comparisons between groups were tested by using both Student's t test for normally distributed data and Mann-Whitney U test for skewed data.

Results

Characteristics of study subjects. A total of 161 patients were enrolled into this study. Table 1 summarizes the demographic and clinical data, medical history, and medications of our study subjects.

Compared with Non-EVR patients, those EVR patients had higher EMATc, S4 score, SDI, and BNP and lower LVEF.

Diagnostic characteristics of acoustic cardiography and BNP for detecting EVR. By using ROC curve analyses, the value of a variety of acoustic cardiographic parameters and BNP were determined for the prediction of EVR. As shown in Fig. 2 and Table 2, the area under the ROC curve (AUC) for EMATc was 0.9 (95% confidence interval CI 0.8–0.9, $p < 0.001$). With an optimal cutoff point of 12.2, EMATc produced a sensitivity of 80% and a specificity of 83%. The AUC for S4 was 0.7 (95% CI 0.6–0.8, $p = 0.001$). With an optimal cutoff point of 4.3, S4 strength produced a sensitivity of 56% and a specificity of 75%. The AUC for SDI was 0.8 (95% CI 0.7–0.9, $p = 0.001$). With an optimal cutoff point of 3.9, SDI strength produced a sensitivity of 91% and a specificity of 54%. The AUC for BNP was 0.8 (95% CI 0.7–0.9, $p = 0.001$). In addition, with an optimal cutoff point of 92.5 pg/ml, BNP produced a sensitivity of 73% and a specificity of 72%, whereas, with an optimal cutoff point of 100 pg/ml, BNP produced a sensitivity of 46% and a specificity of 83%. As can be seen in Fig. 3, there was a better linear correlation between LVEF and EMATc than LVEF and BNP.

Determination of independent risk factors for EVR. As shown in Table 3, many parameters (SDI, HR, S4, S3, BNP, age, sex, diabetes, and EMATc) were analyzed for statistically significant differences by multivariate logistic regression. The parameters, EMATc (OR 2.3, 95% CI 1.4–3.7, $p < 0.001$), SDI (OR 15.9, 95% CI 3.6–69.5, $p = 0.001$), and BNP (OR 1.1, 95% CI 1.0–1.1, $p = 0.009$), were independent risk factors for EVR. There were no statistical differences in the parameters of S3, S4, HR, sex, diabetes, and age.

Discussion

Although the widespread use of PCI has improved the prognosis of patients with AMI, many patients still develop heart failure. Ventricular remodeling after AMI is an independent predictor of the development of HF and is one of the major factors affecting prognosis but without uniform and clear criteria¹. It has suggested that $>15\%$ increase in left ventricular end systolic volume, measured by echocardiography, 6 months after PCI for AMI, is evidence of ventricular remodeling¹³. However, a meta-analysis of data from Medline and Embase showed that the LVEF was below 50% in patients with asymptomatic LVSD after AMI¹⁴. In a prospective study of 284

Variables	Non-EVR (n = 117)	EVR (n = 44)	P
Age (years)	65.1 \pm 7.9	64.0 \pm 10.4	0.47
Male, n (%)	63 (54%)	26 (59%)	0.60
Heart rate (bpm)	79.2 \pm 10.4	83.3 \pm 6.1	0.02
SBP (mmHg)	141 \pm 18.9	145 \pm 15.44	0.20
DBP (mmHg)	77.4 \pm 11.7	79.84 \pm 6.9	0.19
Hypertension, n (%)	51 (43%)	17 (39%)	0.60
Diabetes, n (%)	29 (25%)	13 (29%)	0.12
ACEI/ARB, n (%)	51 (44%)	18 (41%)	0.48
Beta-blockers, n (%)	42 (36%)	14 (32%)	0.59
CCB, n (%)	43 (36%)	15 (34%)	0.47
S3	3.4 \pm 0.9	3.5 \pm 1.0	0.71
S4	3.7 \pm 0.7	4.2 \pm 1.0	0.002
EMATc	10.3 \pm 1.8	13.6 \pm 1.8	<0.001
SDI	3.8 \pm 0.8	4.7 \pm 0.7	<0.001
BNP(pg/ml)	82.0 \pm 18.7	105.5 \pm 21.9	<0.001
LVEF	56.2 \pm 4.5	41.6 \pm 2.9	<0.001

Table 1. Demographics and clinical characteristics. ACEI/ARB angiotensin converting enzyme inhibitor/angiotensin II type 1 receptor blocker, CCB calcium channel blocker, SBP systolic blood pressure, DBP diastolic blood pressure, Non-EVR acute AMI with normal ejection fraction, EVR acute anterior MI with ventricular remodeling.

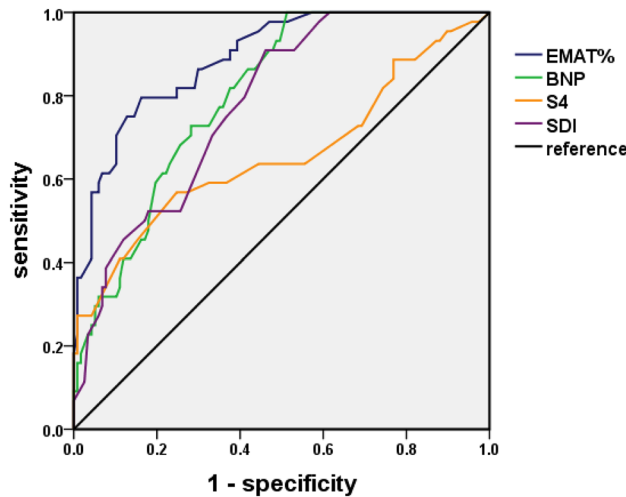


Figure 2. Receiver operating characteristic curves for S4 strength, EMATc, SDI, and BNP for defining EVR. The green curve represents BNP; the blue curve represents EMATc; the yellow curve represents S4 strength; the purple curve represents SDI; EMATc (EMATc): electromechanical activation time divided by the cardiac cycle length.

Parameter	Cutoff value	Sensitivity	Specificity	LR+	LR-
EMATc	12.2	35/44 (80%)	20/117 (83%)	4.7	0.2
S4	4.3	19/44 (56%)	29/117 (75%)	2.2	0.6
SDI	3.9	40/44 (91%)	54/117 (54%)	2.1	0.2
BNP (pg/ml)	92.5	32/44 (73%)	33/117 (72%)	2.6	0.4
BNP (pg/ml)	100	20/44 (46%)	97/117 (83%)	2.8	0.7

Table 2. Performance of acoustic cardiographic parameters and serum BNP levels to detect EVR.

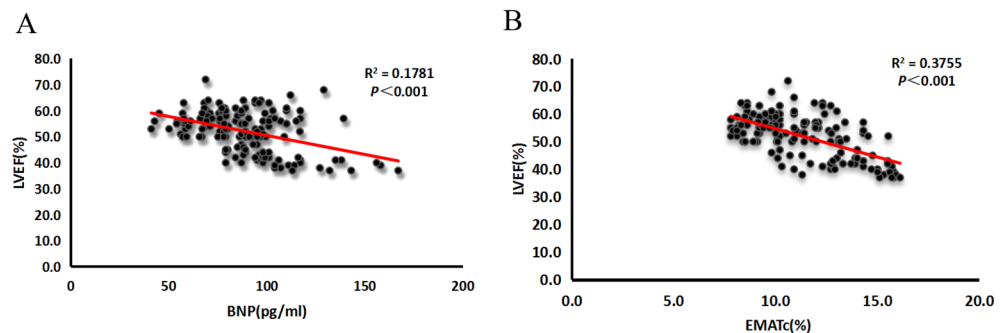


Figure 3. The linear correlations of LEVE, BNP and EMATc. (A) The linear correlations of LVEF% and BNP; (B) the linear correlations of LVEF% and EMATc.

patients with AMI treated with PCI, 30% had ventricular remodeling after 6 months¹⁵. Early ventricular remodeling usually occurs 24–72 h after AMI and presents clinically as asymptomatic LVSD, but is underdiagnosed^{5,7}. There are a number of clinical indicators that predict LVSD; copeptin was shown to be a valid indicator¹⁶; heart rate-corrected QT interval prolongation to the Global Registry of Acute Coronary Events risk score improves the predictive value for early mortality in patients with acute coronary syndrome¹⁷; Of course, there are many other methods of prediction, such as BNP, echocardiography, and magnetic resonance imaging, but these approaches are expensive, cumbersome and cannot be monitored systematically. Moreover, many patients refused these tests to be performed. Therefore, acoustic cardiography is gaining attention as a simple, rapid, non-invasive, and effective diagnostic modality for asymptomatic LVSD which leads to HF. The practical value of acoustic cardiography, with EMATc, as the main parameter, in the clinical diagnosis of heart failure has also been reported. Dillier et al.¹⁰ showed that in healthy subjects there was no circadian rhythm variation in EMAT, no significant change from

Variables	OR	95% CI	P
S3	1.2	0.5–2.9	0.67
S4	2.4	0.8–7.4	0.13
EMATc	2.3	1.4–3.7	<0.001
SDI	15.9	3.6–69.5	0.001
BNP	1.1	1.0–1.1	0.009
HR	1.4	0.9–2.0	0.23
Age	0.9	0.9–1.1	0.53
Sex	2.5	0.5–13.4	0.29
Diabetes	0.4	0.07–2.0	0.24

Table 3. Determination of independent risk factors for EVR.

wake-to-sleep state, and no change with age. However, prolonged EMATc in patients with HF is associated with LVSD, poor HF prognosis, and rehospitalization, independent of serum BNP levels and LVEF^{9,18}. Roos et al.¹⁹ reported that in 108 patients who underwent elective diagnostic cardiac catheterization, EMAT > 110 ms had a high specificity for LVEF (~ 50%) patients with LVSD. In a study of 433 patients, Kosmicki et al.⁸ found that EMAT, LVST, and S3 were better than serum BNP in the diagnosis of LVSD; acoustic cardiography alone and acoustic cardiography combined with BNP had equivalent clinical value in the diagnosis of LVSD; in the "gray zone" of serum BNP (100 ng/L to ≤ 500 ng/L), acoustic cardiography was superior to BNP. Many other studies have found the clinical applications of EMATc in disease prediction. Zhang et al. reported that the elevated EMATc measured on admission was an independent risk factor for major adverse cardiovascular events in hospitalized patients with congestive heart failure. Acoustic cardiography measured on admission may provide a simple, non-invasive method for risk stratification of patients with congestive heart failure²⁰. Chao et al. found that EMAT-guided post-discharge management was superior to traditional symptom-driven therapy in patients hospitalized for acute heart failure in terms of 1-year outcomes¹⁸. There are few clinical studies on the value of acoustic cardiography in the diagnosis of AMI. Some studies have shown that STT changes combined with S4 as the standard for the diagnosis of coronary heart disease have a sensitivity and specificity of 68% and 84% respectively; S3 or S4 combined with ECG increases the detection rate of myocardial ischemia by 32%^{11,21}.

In the present study, we identified three parameters, EMATc, S4, and SDI, as independent risk factors for post-PCI early ventricular remodeling in patients with AMI and their predictive value for the occurrence of early ventricular remodeling. We determined the value of various acoustic cardiographic parameters and serum BNP levels for predicting early ventricular remodeling and showed that the AUC of EMATc was 0.89, the optimal threshold was 12.2, the sensitivity of EMATc was 80%, and the specificity was 83%. By contrast, when the optimal threshold of serum BNP was set at 100 pg/ml, the sensitivity of BNP was 46% and the specificity was 83%. Therefore, our results suggested that EMATc was superior to serum BNP levels.

We believe that acoustic cardiography is a simple, quick, and effective way to diagnose early ventricular remodeling after AMI. However, there are some limitations of the present study that need to be addressed. First, the sample size was small (n = 161). Therefore, more subjects are needed to determine the clinical value of acoustic cardiography in the diagnosis of AMI. Second, we selected only the patients with anterior MI. Third, echocardiography data were limited to EF% values and therefore, did not provide additional information on other echocardiography variables that may have led to the discovery of other significant correlations. A better way to determine early ventricular remodeling should be the decrease in LVEF after PCI compared with pre-PCI LVEF. However, echocardiography is often overlooked in order to complete the procedure as quickly as possible pre-PCI. Therefore, it was difficult for us to obtain complete information. Finally, we only studied the early ventricular remodeling rather than the relationship between acoustic cardiography and late ventricular remodeling, which would take a long time.

Conclusions

We identified three parameters, EMATc, S4, and SDI, as independent risk factors for post-PCI early ventricular remodeling in patients with AMI and also identified the predictive value of these parameters for the occurrence of early ventricular remodeling in these patients. Acoustic cardiography can be a simple, quick, and effective way to diagnose early ventricular remodeling after AMI.

Data availability

The datasets generated and analyzed in the present study are available from the corresponding author upon reasonable request.

Received: 12 October 2022; Accepted: 28 April 2023

Published online: 03 May 2023

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Acknowledgements

We gratefully thank the patients who participated in our study. We gratefully also thank Jose PA, Jian Yang, and other research staff of the Division of Cardiology, Third Affiliated Hospital of Chongqing Medical University and Haikou people's Hospital for their assistance; This study was supported by a research grant from the Chongqing Medical University.

Author contributions

F.Z., L.S. conceived and designed the study. W.W., H.H., T.F., J.Y., M.W. recruited patients and performed the assays. W.W., H.H. wrote the manuscript. F.Z., G.D. performed the statistical analysis and revised the manuscript. L.S., M.C. critically revised the study protocol and the manuscript. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to L.S. or F.Z.

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