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Assessment of Left Atrial Function in Patients with Non-ST-Segment Elevation Myocardial Infarction Using Two-Dimensional Speckle Tracking Echocardiography

Mansour M. Mostafa*, Wael M. Attia*, Mohamed O. Taha, and *Mohamed N. Mahmoud**

***Cardiology Department, Faculty of Medicine, Al-Azhar University and **National Heart Institute (NHI), Cairo, Egypt**

Corresponding author: Mohamed Nasem Mahmoud, E-mail: dr.mohamednassim@gmail.com

ABSTRACT

Background: the left atrium (LA) plays a major role in Left ventricular (LV) performance. LA function is a surrogate marker of LV diastolic dysfunction. LA mechanical dysfunction occurs in LV systolic and diastolic dysfunction, coronary artery disease, myocardial infarction (MI), hypertension, aortic stenosis and cardiomyopathies. In the MI process, the contribution of the LA to LV function may increase if the cardiac myocytes are not affected by direct ischemia. However, myocyte necrosis or ischemia of the LA or significant LV systolic/diastolic dysfunction affects this booster effect. Assessment of LA size and function provides prognostic data for the outcome of patients with MI or ischemia. **Aim of the Study**: was to evaluate LA function in patients with non-ST-segment elevation myocardial infarction (NSTEMI) by two-dimensional speckle tracking echocardiography (2D STE). **Patient and Methods:** 60 patients with NSTEMI and 20 age-matched normal control individuals were enrolled in this study. Conventional echocardiographic parameters and global longitudinal strain rate (GLSR) were measured at left ventricular (LV) and LA segments. **Results:** Compared with healthy subjects, patients with NSTEMI had significantly increased LA volumes but significantly decreased LA emptying fraction and GLSR. LA-GLSR had significant correlations with the 2D Doppler echocardiographic parameters of LA function. In particular, global LA peak negative strain rate during early ventricular diastole (LA-GLSRe) was significantly correlated with both LA 2D Doppler echocardiographic parameters and LV contractile function. This could be suggested as a better indicator to evaluate LA function as a preferred parameter of STE. **Conclusion:** It could be concluded that two-dimensional speckle tracking echocardiography represented a non-invasive, relatively simple and reproducible technique to assess left atrial myocardial function in patients with NSTEMI.

Keywords: two-dimensional speckle tracking echocardiography, strain rate, non-ST-segment elevation myocardial infarction, left atrial function

INTRODUCTION

Myocardial infarction is a major cause of death and disability worldwide. MI may be the first manifestation of coronary artery disease (CAD) or it may occur, repeatedly, in patients with established disease[(1)]. Left atrial function is one of the most important clinical parameters of two-dimensional speckle tracking echocardiography (2D STE), which is an innovative tool for more comprehensive and reliable echocardiographic evaluation of myocardial function[(2)].

LA function has been conventionally divided into three phases first, as a reservoir, the LA stores pulmonary venous return during LV contraction and isovolumetric relaxation. Secondly, as a conduit, the LA transfers blood passively into the LV. Thirdly, the LA actively contracts during the final phase of diastole and contributes between 15 and 30% of LV stroke volume. As a continuum of the LV, especially during diastole, its size and function are very much influenced by the compliance of the LV[(3)].

Traditionally, assessment of LA function has been performed by measuring LA size or volume with two-dimensional (2D) echocardiography. Doppler echocardiographic measurements such as transmitral and pulmonary venous flow can also be used [(4,5)]. Currently, a method known as strain imaging is used for the quantitative assessment of myocardial deformation [(6)]. It has been shown that non-Doppler strain imaging is a feasible and reproducible method to assess LA function [(7,8)].

The LA function is closely related to the ventricular function throughout the cardiac cycle. During ventricular systole, the

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longitudinal shortening of the ventricular base increases the filling of the LA from the pulmonary veins. In diastole, the LA contributes to the filling of the LV through both active and passive emptying. Moreover, the LA emptying function might be strongly affected by LV diastolic properties due to the direct interaction of ventricular pressures through the open mitral valve during diastole[9].

Compared with Doppler and 2D echocardiography, 2D STE has the advantages of angle independence, and is also less affected by reverberations, side lobes or drop-out artifacts. While this novel echocardiographic method has been frequently used to assess LV function[10], it has been used to evaluate atrial function in normal subjects and in conditions with atrial dysfunction[11,12].

The aim of the current work was to evaluate LA function in patients with non-ST-segment elevation myocardial infarction (NSTEMI) by two-dimensional speckle tracking echocardiography (2D STE).

PATIENTS AND METHODS

This study included 60 patients with NSTEMI and 20 healthy individuals as control group attending at Al-Azhar University Hospitals. Approval of the ethical committee and a written informed consent from all the subjects were obtained. This study was conducted between Jan 2016 to September 2017.

Inclusion criteria: patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Exclusion criteria: Patients with atrial fibrillation or flutter, valvular heart disease (of mild or greater severity), and poor left atrial images were excluded.

Data regarding age, gender, body mass index (BMI) were obtained from all patients. **All patients were subjected to:**

A. Clinical evaluation including: History taking, General & local examinations.
B. Laboratory investigations including: Lipids profile and plasma glucose level.
C. Conventional 2D and Doppler echocardiography studies were performed using the Philips IE33 equipped with a 3S phased-array transducer (frequency range of 1.7–3.4 MHz). Echocardiographies of patients were performed within 48 hr. after NSTEMI. Cardiac dimensions were measured in accordance with recommendations of the American Society of Echocardiography. M-mode echocardiography was used to measure LV end-diastolic and end-systolic diameters. LV ejection fraction (LVEF) was calculated from apical four- and two-chamber views, using the modified Simpson's rule. LA volumes were measured using the area–length method from apical four- and two-chamber views, according to the guidelines of the American Society of Echocardiography[13]. Left atrial maximum volume (LAVmax) was measured at the end of LV systole, just before the opening of the mitral valve, LA minimum volume (LAVmin) was measured at the end of LV diastole, right after the closure of the mitral valve, and LA reservoir volume (LAVres), (LAVres.): LAVmax. – LAVmin and LA ejection fraction (LAEF): (LAVmax)-(LAmin.)/ (LAVmax)[14]. For 2D STE analysis, we obtained 2D gray-scale harmonic images in three apical planes (long axis of LV, four- and two-chamber). Three consecutive heart cycles were recorded and averaged. The frame rate was set between 60 and 90 frames per second[15]. Echocardiograms were digitally stored and later analysed off-line using PHILPS Q Lab 8 A 16-segment LV model was obtained from the four- and two-chamber, and long-axis recordings[16]. Two-dimensional strain software identified the endocardial border, and after tracing myocardial motion, was automatically tracked in each imaging view. Strain rate measurements from 16 segments were averaged to assess a LV global longitudinal parameter based on peak systole (LV-GLSRs), early diastole (LV-GLSRe), and late diastole (LV-GLSRa). The LA myocardium was divided into six equidistant regions from apical four- and two-chamber views, while only three were analysed in the apical long-axis view because the remaining three in this view are part of the aortic valve and ascending aorta and not LA myocardium. The software generates

strain rate curves for each atrial segment. Global strain and strain rate were also calculated by averaging values from 15 atrial segments.

RESULTS

This study included 60 patients with NSTEMI (mean age 54.42 ± 9.24 years, 38 males and 22 females) and 20 healthy individual as control group (mean age 36.35 ± 9.95 years, 14 males and 6 females).

The main clinical features and 2D Doppler echocardiography data of the controls and NSTEMI patients are summarized in Table 1.

Table 1: Clinical features of patients with NSTEMI and controls

Parameters	Cases (n=60)	Controls (n=20)	p-value
Male, n (%)	38 (63.3)	14 (70.0)	0.588
Female, n (%)	22 (36.7)	6 (30.0)	0.588
Age (years)(Mean ± SD)	54.42 ± 9.24	36.35 ± 9.95	<0.001*
Weight (kg)Mean ± SD.	90.97 ± 10.41	87.65 ± 8.95	0.206
Height (cm)Mean ± SD.	173.17 ± 9.57	174.60 ± 5.93	0.433
BMI (kg/m2)Mean ± SD.	30.65 ± 4.70	28.56 ± 2.43	0.013*
Hypertension, n (%)	48 (80.0)	6 (30.0)	<0.001*
DM, n (%)	33(55)	4 (20.0)	0.007*
Hyperlipidemia, n (%)	43 (71.7)	7 (35.0)	0.007*
Smoking, n (%)	31(51.7)	11 (55.0)	0.796

There were significant differences in clinical features, such as hypertension, diabetes and hyperlipidaemia between patients and healthy subjects Patients with NSTEMI had significantly increased LAVmax (56.33 ± 10.60vs 44.50 ± 10.36ml, p <0.001), LAVmin (26.39 ± 7.21vs 17.75 ± 5.62ml, p <0.001), and LAV res (30.62 ± 7.0vs 26.65 ± 6.21ml, p = 0.001), but significantly lower in LAEF (50.81 ± 9.11 vs 60.30 ± 6.38%, p <0.001), and LVEF (56.22 ± 6.29vs 60.40 ± 3.99%, p = 0.001). 20 healthy subjects and 60 patients with NSTEMI were randomly selected for the assessment of LA-GLSRs, LA-GLSRe, LA-GLSRa, LV-GLSRs, LV-GLSRe and LV-GLSRa, respectively as seen in figures (1,2)

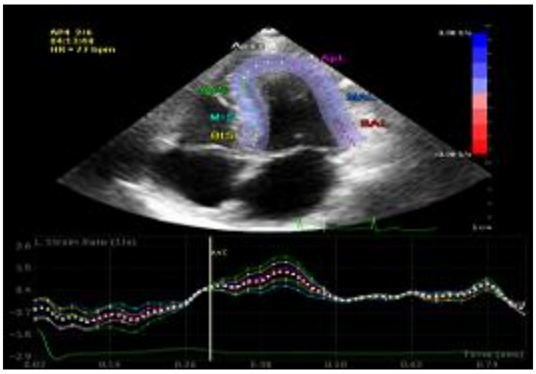

Figure 1: Measurement of global longitudinal left ventricular strain rate from an apical 4 camber view.

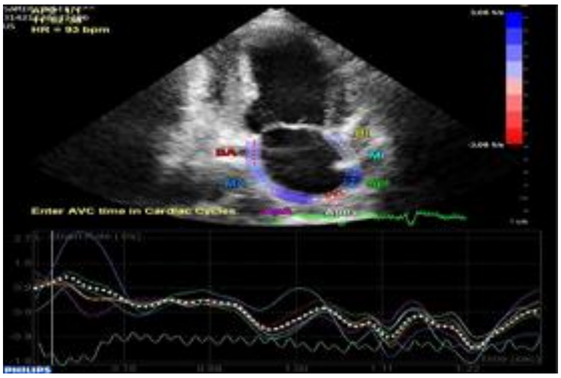

Figure 2: left atrial strain rate from an apical 2 chamber view.

The SR imaging echocardiographic variables of the normal and NSTEMI groups. Compared with the controls, patients with NSTEMI had significantly decreased LAGLS (p<0.001), LA-GLSRs (p <0.001), LA-GLSRe (p < 0.001), LV-GLSRs (p < 0.001), and LV-GLSRe (p = 0.001), as seen in table 2 and figures (3,4)

Table 2: 2D STE parameters in patients with NSTEM and the controls

	Cases (n=60)	Control (n=20)	p
LAGLSs (%)	22.53 ±5.20	32.75 ±4.05	<0.001*
LA-GLSRs	1.36 ±0.45	1.99 ±0.26	<0.001*
LA-GLSRe	-1.21 ±0.30	-2.10 ±0.40	<0.001*
LA-GLSRa	-1.91 – 0.57	-2.11 ±0.48	0.168
LV-GLSRS	-0.85 ±0.15	-1.10 ±0.32	<0.001*
LV-GLSRe	1.05 ±0.54	1.27 ±0.22	0.001

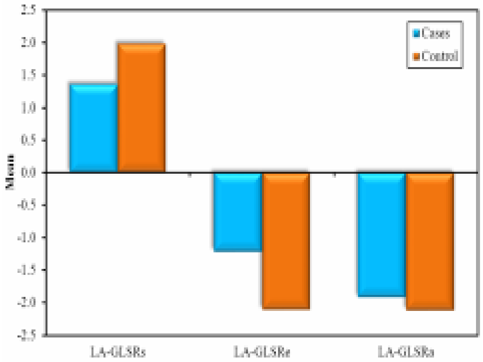

Figure 3: Comparison between the two studied groups according to LA-GLSRs, LA-GLSRe and LA-GLSRa

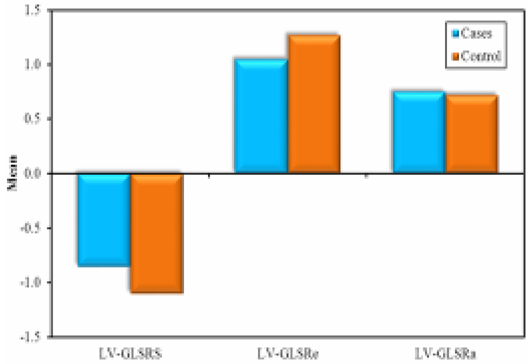

Figure 4: Comparison between the two studied groups according to LV-GLSRS, LV-GLSRe and LV-GLSRa

Correlations of LA-GLSRs, LA-GLSRe, LA-GLSRa, LV-GLSRs, LV-GLSRe and LV-GLSRa with parameters of LA volume and function in NSTEMI patients were performed (Table 3).

Table 3: Correlation of global LA/LV strain rate parameters with LA volume and function parameters in patient with NSTEMI

		LAVmax(ml)	LAVmin(ml)	LAV res	LAEF(%)	LVEF(%)
LA-GLSRs	r	-0.350*	-0.339	-0.259	-0.260*	-0.288*
	p	0.006*	0.008*	0.046*	0.044*	0.026*
LA-GLSRe	r	0.494	0.464	0.302	-0.427	-0.305
	p	<0.001*	<0.001*	0.019*	0.001*	0.018*
LA-GLSRa	r	0.387	0.346	0.259	-0.102	-0.063
	p	0.002*	0.007*	0.045*	0.439	0.633
LV-GLSRs	r	0.052	0.172	-0.045	-0.029	-0.243
	p	0.691	0.188	0.735	0.826	0.062
LV-GLSRe	r	-0.037	-0.063	0.107	0.150	0.109
	p	0.778	0.631	0.416	0.253	0.409
LV-GLSRa	r	-0.002	0.076	-0.108	0.092	0.203
	p	0.988	0.564	0.413	0.484	0.120

LA-GLSRs showed modest correlations with parameters of LA volume and function, including LAVmax (r = –0.350, p =0.006), LAVmin (r = –0.339, p = 0.008), LAVres (r = –0.259, p = 0.046), LAEF (r = 0.260, p = 0.044), and LVEF (r = –0.288, p =0.029). LA-GLSRe significantly correlated with LAVmax (r = 0.494, p < 0.001), LAVmin (r = 0.464, p < 0.001), LAVres (r = 0.302, p = 0.019), LAEF (r = 0.427, p =0.001), and LVEF (r = –0.305, p < 0.001). LA-GLSRa had significant correlations with the following echocardiographic variables: LAVmax (r = 0.387, p = 0.002), LAVmin (r = 0.346, p < 0.007), LAVres (r = 0.259, p = 0.045), LAEF (r = –0.102, p < 0.439). and LVEF (-0.063, p=0.633) LV SR parameters had no significant correlation with the following LA echocardiographic variables: LAVmax, LAVmin, LAVres and LAEF. In addition, LVEF was significantly correlated with LA-GLSRs (r = –0.288, p =0.026) and LA-GLSRe (r = –0.305, p = 0.018) (Fig. 5), but not significantly correlated with LA-GLSRa (r = 0.063, p = 0.633). LA-GLSRe correlated significantly with LV-GLSRe (r = –0.226, p = 0.04) (Fig. 6).

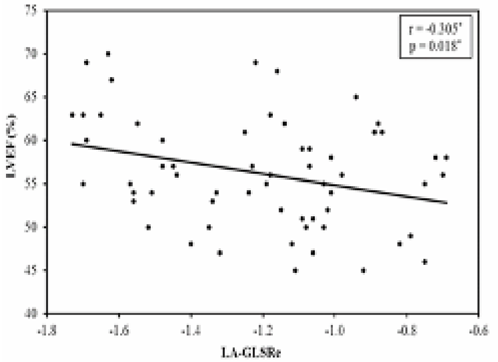

Figure 5: Correlation between left ventricular ejection fraction(LVEF) and peak early diastolic strain rate of the left atrium (LA-GLSRe) in patients with NSTEMI.

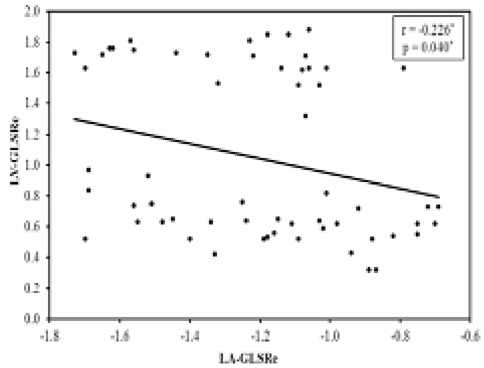

Figure 6: Correlation between peak early diastolic strain rate of the left ventricle (LV-GLSRe) and peak early diastolic strain rate of the left atrium (LA-GLSRe) in patients with NSTEMI.

However, both LA-GLSRs and LA-GLSRa showed no such significant correlation with LV-GLSRs (Fig. 7) and LV-GLSRa (Fig. 8), respectively.

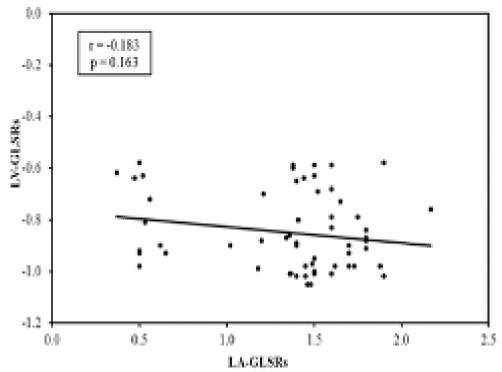

Figure 7: Correlation between peak early diastolic strain rate of the left ventricle (LV-GLSRs) and peak early diastolic strain rate of the left atrium (LA-GLSRs) in patients with NSTEMI

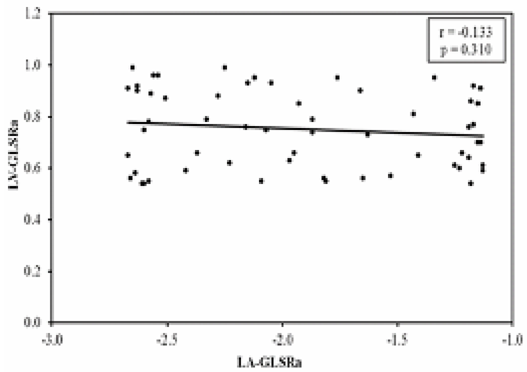

Figure 8: Correlation between peak early diastolic strain rate of the left ventricle (LV-GLSRa) and peak early diastolic strain rate of the left atrium (LA-GLSRa) in patients with NSTEMI.

DISCUSSION

After several decades of investigations, current consensus recommendations state that LA function plays an important role in optimizing overall cardiac function, and the changes in LA size and function are associated with cardiovascular disease and are risk factors for atrial fibrillation, stroke and death[(17),(18)].

The left atrium serves as a blood reservoir during ventricular systole and a conduit for the passage of blood from the pulmonary veins into the left ventricle during early and middle ventricular diastole, as well as a booster pump increasing LV filling during late diastole[(19)].

In subjects with normal diastolic function, the relative contribution of the reservoir, conduit and pump function of the LA to the filling of the LV is approximately 40, 35 and 25%, respectively[(20)].

Determined by conventional 2D echocardiography, LA function has been mainly evaluated using LA volumetric parameters and LA emptying fraction which may be used to evaluate the reservoir, conduit and booster pump components of LA function[(13),(21)].

Parameters that evaluate LA function may have prognostic potential. LA reservoir function may predict the first atrial fibrillation or flutter episode in elderly subjects, and LA systolic force may predict cardiovascular events in a population with a high prevalence of hypertension and diabetes[(22),(23)]. However, all these echocardiographic parameters and others that evaluate LA function are influenced by LV dynamics and geometry and/or rely on measurements that are subjected to error[(24),(25)]. Therefore, new methodologies that can evaluate LA function by analysis of LA myocardial deformation may be of potential clinical interest. Two strain imaging methods are based on different principles and can potentially give different results. Tissue Doppler imaging (TDI)-derived strain is limited to the measurement of movement parallel to the ultrasound beam. Non-Doppler 2D strain imaging derived from speckle tracking is a newer echocardiographic technique for obtaining SR measurements. The advantage of this method is that it tracks in two dimensions, along the direction of the wall, not along the ultrasound beam, and thus is angle independent, which is a great advantage of non-Doppler 2D strain imaging in comparison to TDI-derived strain data[(2)]. Previous studies show that 2D STE with its latest applications such as strain rate imaging may represent promising techniques to better evaluate LA function[(8)]. With the use of strain rate imaging, ***Inaba et al.*** found that SRs corresponded to reservoir function and SRe corresponded to conduit function, while SRa corresponded to booster pump function[(26)]. In patients with AMI, left ventricular stroke volume is relatively maintained despite the impairment of left ventricular function caused by myocardial ischaemia and necrosis. With increased stiffness or reduced compliance of the LV, LA pressure rises to maintain adequate LV filling, and the increased atrial wall tension leads to chamber dilatation and stretch of the atrial myocardium[(27)]. Therefore, the left atrium works harder and transports more blood to the left ventricle during left ventricular diastole. This function of the left atrium can be attributed to the Frank-Starling mechanism. LA pump function augmentation is therefore due to the increased left atrial volume before active atrial emptying, but not to the increased contractility of the left atrium[(28)]. In our study protocol, patients with NSTEMI showed increased LA volumes (LAVmax, LAVmin and LAVres). Moreover (LA total EF) was significantly impaired and compared with healthy controls. In accordance with the conventional echocardiographic parameters mentioned above, we found LA reservoir function assessed by SR imaging (LA-GLSRs) and LA conduit function assessed by SR imaging (LA-GLSRe) were significantly reduced in patients with NSTEMI (Table 2), but LA booster function assessed by SR imaging (LA-GLSRa) showed no significant difference. This may be explained by when the LA is well stretched longitudinally, and consequently a high LA positive peak is present, the LV then relaxes rapidly, generating a high E wave, as blood rushes into the LV, generating a high passive LA emptying fraction. Therefore, LA-GLSRs and/or LA-GLSRe have significant correlations with LV diastolic function, which are impaired in patients with NSTEMI. In our study protocol, a good correlation was found between LA global strain rate and LA functional parameters (Table 3). The present study extends previous results and describes changes in LA function after AMI, combining LA volumes, LA emptying fraction, and LA strain in patients with NSTEMI. The results show that speckle tracking-derived strain rate is a promising technique to assess LA function as well as LA volumes and LA emptying fraction. Global strain is a relatively new parameter for assessment of LV function[(29)] and tends to predict the infarct mass better than established indices of global function such as LVEF and WMSI. LVEF can be regarded as the sum of all LV systolic deformation.

In ***Wakami et al.***'s study, peak LA strain rate during LV systole, which corresponds to our measured LA-GLSRs, correlated inversely with LV end-diastolic pressure and LV end-systolic volume and positively with LVEF[(30)]. In a recent study by ***Vartdal et al.*** global strain measured by TDI immediately after PCI was found to be superior to LVEF for predicting final infarct mass in patients with acute MI[(30)]. Comparing with tagged magnetic resonance imaging (the current 'gold standard' for deformation analysis), STE measurements correlated well with data obtained by magnetic resonance imaging, both in normal myocardial segments and infarcted areas ($r = 0.87$, $p < 0.001$)[(30)]. The findings of our present study are in accordance with previous studies. There was significant correlation between LVEF and global LA-GLSRs (r = –0.334, $p < 0.05$) or LA-GLSRe (r = –0.477, $p < 0.001$). In particular, LA-GLSRe was strongly correlated with LV-GLSRe (r = –0.644, p = 0.001), while LA-GLSRs and LA-GLSRa were not significantly correlated with LV strain rate parameters (LV-GLSRs and LV-GLSRa). These findings support the idea that LA-GLSRe can serve as an important new marker of LA and LV function in the acute MI. Therefore, speckle tracking echocardiography was found to be a feasible and reproducible method to assess LA longitudinal strain in healthy subjects and patients with NSTEMI. The reproducibility of measurements was good, with lower variability of intra- and inter-observer. In particular, we found LA-GLSRe was significantly correlated with both LA 2D Doppler echocardiographic parameters and LV contractile function, and could be an optimal parameter of 2D STE in assessing the degree of impairment of heart function in patients with NSTEMI.

These data suggest that speckle tracking echocardiography may be considered a promising tool to explore LA myocardial deformation dynamics

Study limitations

A number of obvious limitations of our study should be noted. First, the 2D STE analysis software that was originally designed for the left ventricle was applied to the left atrium in our study. Second, echocardiography in this study was not performed in the emergency room but on arrival at the coronary care unit or one to two days later. Third, the relatively small number of patients eligible for analysis in the present study may render it difficult to generalise the results and apply them to other patient populations. Further larger, prospective studies are required to determine the cost effectiveness of this new technique to evaluate LA function in NSTEMI patients. Lastly, this was a cross-sectional study, and therefore no clinical outcomes were examined.

CONCLUSIONS

Our study demonstrated that two-dimensional speckle tracking echocardiography represented a non-invasive, relatively simple and reproducible technique to assess left atrial myocardial function in patients with NSTEMI. The reservoir and conduit function of the left atrium were impaired in these patients, compared with controls, LA-GLSRe was significantly correlated with both LA 2D Doppler echocardiographic parameters and LV contractile function and could be suggested as a better indicator to evaluate LA function as a preferred parameter of STE.

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