Original Article
Clinical evaluation of left ventricular systolic dyssynchrony among patients with coronary heart disease using two-dimensional speckle tracking imaging and three-dimensional echocardiography

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Abstract: The present study aimed to quantify left ventricular (LV) systolic dyssynchrony in patients with LV systolic dysfunction using a combined method of two-dimensional speckle imaging (2D-STI) and real-time three-dimensional echocardiography (RT-3DE). Totally, 26 myocardial infarction patients, 24 myocardial ischemia patients and 30 normal subjects were retrospectively reviewed. Their echocardiographic images were acquired by 2D-STI and RT-3DE. Time parameters of LV wall mechanics including times to peak longitudinal strain of 16 segments (Tls-16), to peak radial strain of 12 segments (Trs-12), to peak circumferential strain of 12 LV segments (Tcs-12), to peak rotation of 12 LV segments (Trot-12), and to peak rotation strain at the basal (Tbase) and apical (Tapex) levels were obtained from 2D-STI. Time to minimum systolic volume of 16 LV segments (Tmsv-16) was obtained from RT-3DE. Time differences between Tls and Tmsv (Tlsv), Trs and Tmsv (Trsv), Tcs and Tmsv (Tcsv), Trot and Tmsv (Trotv) and the time interval of rotation between apex and base (Tabrot) were calculated. The Tls-16, Tmsv-16 and Tlsv were prolonged in ischemia patients than control (*P* < 0.05). Compared with ischemia and control groups, all the time parameters were prolonged in infarction patients (*P* < 0.05). Tlsv, Trsv, Tcsv, Trotv and Tabrot had negative correlation with LV ejection fraction (LVEF) in infarction group. The relationship of LV wall mechanics with volume-time parameters could be used to evaluate LV systolic dys-synchrony in myocardial infarction. Besides, Tlsv could be applied on early detection of LV systolic dys-synchrony in ischemia patients.

Keywords: Left ventricle, speckle tracking imaging, three-dimensional, echocardiology, synchronization, mechanical motion

Introduction

Coronary heart disease (CHD) also called coronary artery disease (CAD), is a narrowing of the small blood vessels that supply blood and oxygen to the heart, usually caused by fatty deposition, a process known as atherosclerosis [1]. It remains the leading cause of mortality worldwide and is responsible for 502,000 deaths in the United States and > 700,000 deaths in China annually [2]. CHD has two principal forms, angina and myocardial infarction, both of which will cause the part of heart muscle deprived of oxygen and dead as well as subsequently systolic dysfunction due to the insufficient blood-supply [1].

As all known that left ventricular (LV) contraction and rotation in a synchronous pattern is of the essence to achieve an efficient pumping blood [3]. A growing number of current researches have focused on the synchrony in myocardial mechanical motion [4-6]. With the introduction of speckle tracking imaging [7], two-dimensional speckle tracking imaging (2D-STI) and real-time three-dimensional echocardiology (RT-3DE) have become the commonly used echocardiographic techniques for the quantitative assessment of systolic synchronization [8-11]. Wu has reported the relationship of myocardial mechanics and regional volume change in patients with left ventricular systolic dysfunction [12]. Hence, this study was aimed to assess
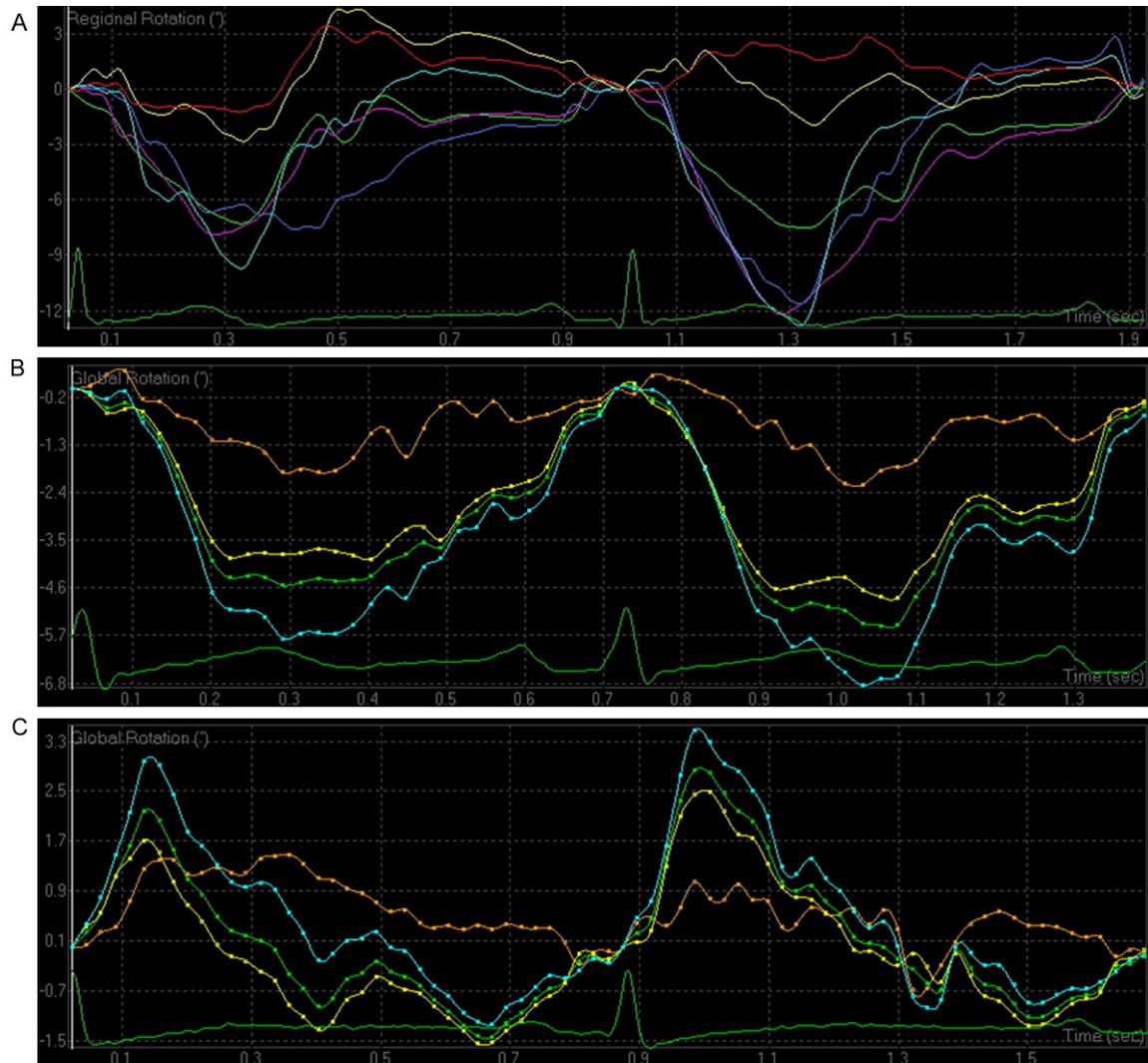
Figure 1. The LV regional rotation-time curve from the parasternal short axis view at the papillary muscles of left ventricle level (A), and the global rotation curves at cardiac base (B, green color) and apex (C, green color) levels were obtained.

LV systolic synchronization in patients with LV systolic dysfunction using the relationship between myocardial segmental mechanics and regional volume changes, and to establish a combined method of 2D-STI and RT-3DE for the assessment of left ventricular systolic synchronization.

Patients and methods

Subjects

This study retrospectively reviewed a total of 50 Chinese patients diagnosed with CHD (32 males and 18 females, mean age: 61.0 ± 2.3 years, age range: 32-82 years old) who were

admitted to our hospital from March 2014 to June 2015. Among the total patients, there were 24 patients diagnosed with myocardial ischemia and 26 patients diagnosed with myocardial infarction, based on the medical history, clinical manifestation, electrocardiogram examination, myocardial enzyme and routine echocardiography. All the patients were confirmed with stenosis of at least one vessel of main coronary ≥ 50% by coronary angiography. Patients with organic heart disease, serious cardiac arrhythmias, chronic obstructive pulmonary diseases and other serious complications, and who had previous implantation of coronary artery supporter or coronary artery bypass surgery, as well as who had unclear
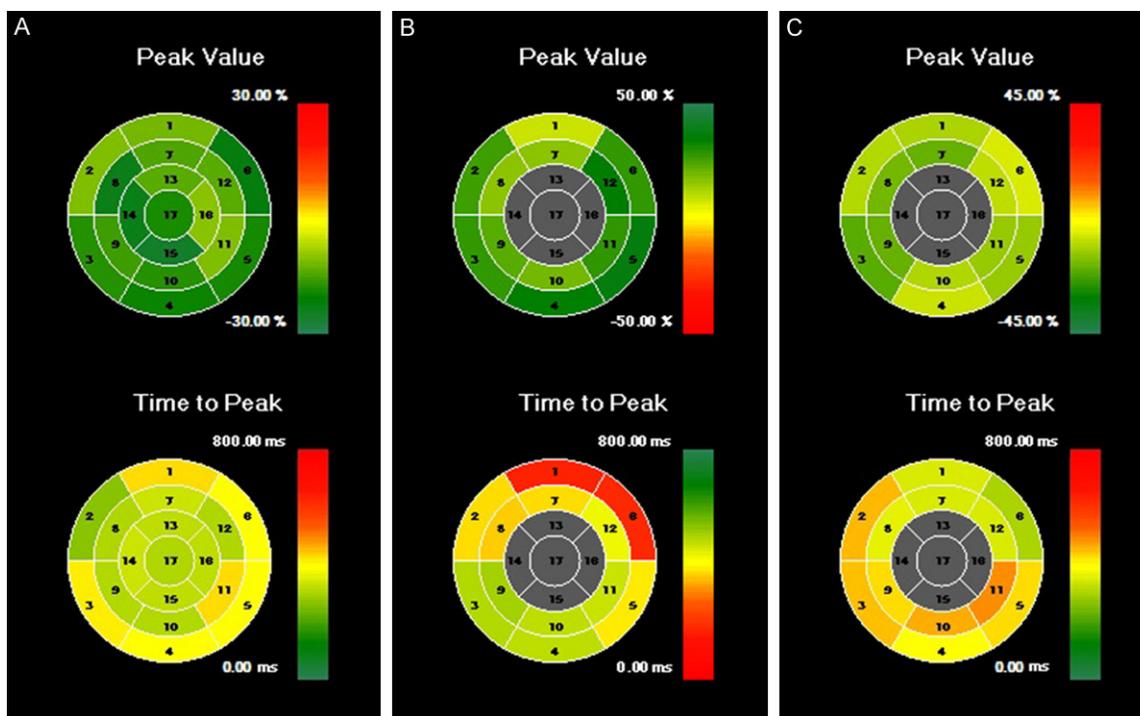
Figure 2. The LV global longitudinal strain (A), radial strain (B) and circumferential strain (C) data were obtained by using two-dimensional speckle tracking imaging (2D-STI).

images, were excluded. The demographic and clinical data of the patients were recorded. They were divided into myocardial ischemia group and myocardial infarction group based on the medical history, clinical manifestation, electrocardiogram (ECG) examination, myocardial enzyme and routine echocardiography.

Besides, a total of 30 subjects with negative coronary angiography (no stenosis or stenosis diameter < 50%) were enrolled from all hospitalized patients homochronously admitted to our hospital, which were regarded as control group. They were confirmed with no heart disease by physical examination, ECG and echocardiography examinations. This research protocol was approved by the Ethics Committee of our hospital and informed consents were signed by all patients.

Echocardiographic image acquisition

Acquisition of 2D-STI and RT-3DE data sets and off-line analysis were performed as previously described [13, 14]. Subjects were investigated in a left-lateral position. Standard 2-dimensional echocardiography (Simpson's biplane method of disks) was performed with iE33 (Philips,

Guildford, Surrey, UK) and a 1-5 MHz transducer (S5-1) to measure the left ventricular ejection fraction (LVEF). Then subjects hold their breath, and echocardiographic views, including the LV parasternal short-axis view (at mitral, papillary muscle and cardiac apex levels) and cardiac apex long-axis view (apical four-chamber, three-chamber and basal two-chamber views), were obtained in dynamic 2D tissue imaging modes. Four consecutive cardiac cycles of the images were recorded with optimization of depth, focal range, and high frame rate (> 100 HZ) to ensure optimal border delineation. Thereafter, the transducer was changed to X3-1 matrix array transducer (S1-3). The optimized apical four-chamber view was obtained during the full volume acquisition. Full-volume acquisition was performed during breathholding and requires a stable duration of one cardiac cycle (R-R) interval to minimize the stitch artifacts. Four consecutive cardiac cycles were saved in digital format for off-line analysis.

Image analysis

LV end-diastolic and end-systolic volumes were measured from the apical four- and two-chamber views using the biplane methods, then left
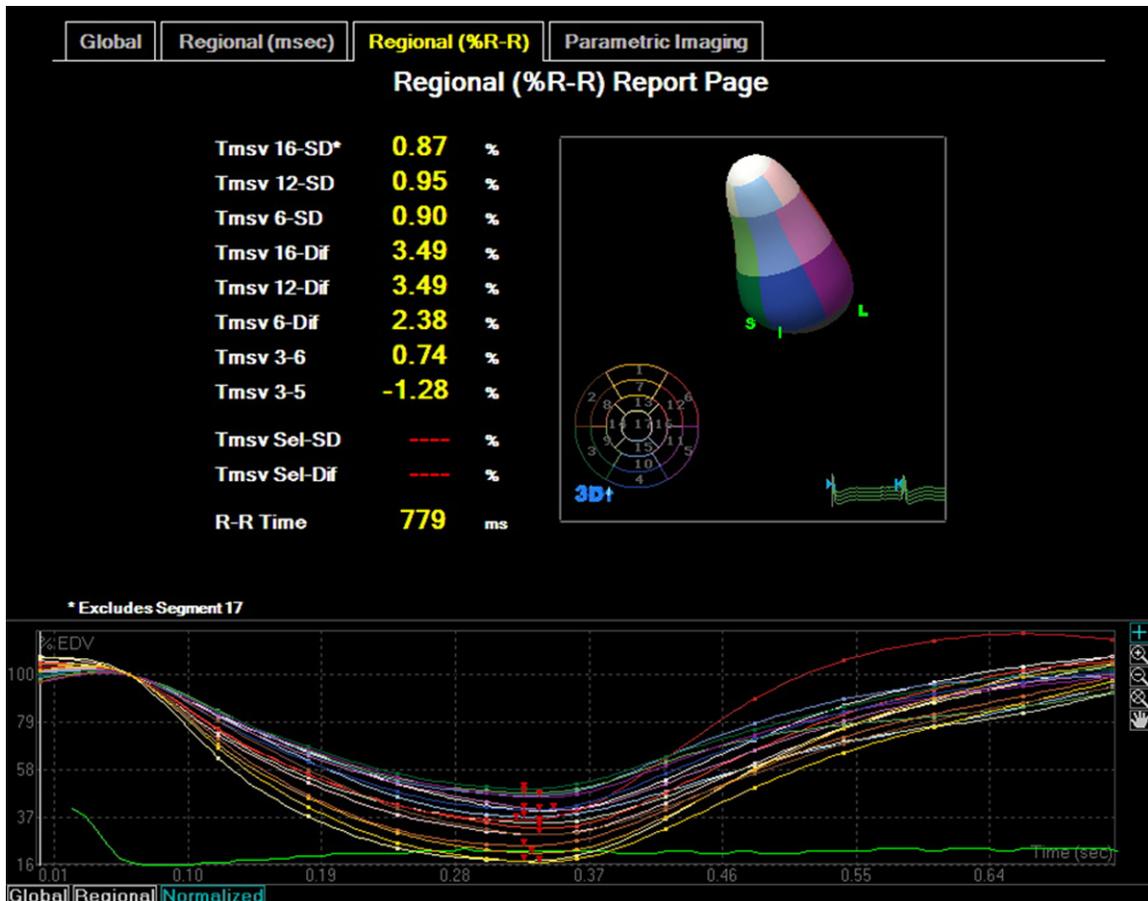
Figure 3. The LV regional volume-time curve and systolic synchronization parameters were obtained by using real-time three-dimensional echocardiolograph (RT-3DE).

ventricular ejection fraction (LVEF) was calculated [15]. The 2D strain analysis was performed using Philips QLAB CMQ software (v8.1, Philips Medical Systems, Zurich, Switzerland). The regional rotation-time curve of 12 LV segments were obtained from the parasternal short axis view at the papillary muscles level (**Figure 1A**), as well as the global rotation curve at cardiac base (**Figure 1B**) and apex (**Figure 1C**) levels, and the global longitudinal strain, radial strain and circumferential strain data of 12 LV segments and 16 LV segments (**Figure 2A-C**). The index of times to peak longitudinal strain of 16 LV segments (Tls-16), to peak radial strain of 12 LV segments (Trs-12), and to peak circumferential strain of 12 LV segments (Tcs-12) were calculated from the above strain figures. Time-to-peak rotation of 12 LV segments (Trot-12) was recorded from the onset of the QRS interval to the time of peak rotation strain of 12 LV segments at the short axis view, as well as the time from the onset of the QRS interval to the time of peak rotation strain at the basal (Tbase) and apical (Tapex) levels. Then the time interval of rotation between apex and base (Tabrot) was calculated.

Analyses of RT3DE datasets were performed with a QLAB workstation using the 3D-Advanced quantification software package (QLAB 3DQ-Advanced, Philips Healthcare) as described previously [16, 17]. The LV regional volume-time curve and systolic synchronization parameters were obtained (**Figure 3**). Time to minimum systolic volume of 16 LV segments (Tmsv-16) was recorded from the onset of the QRS interval to the time of minimum systolic volume of 16 LV segments. Then the time differences between Tls and Tmsv (Tlsv), between Trs and Tmsv (Trsv), between Tcs and Tmsv (Tcsv), and between Trot and Tmsv (Trotv) were calculated. To eliminate the effect of individual difference in heart rates, the aforementioned time parameters were all corrected for R-R interval and

Table 1. Baseline characteristics of patients among the three groups

Items	Control group (n = 30)	Ischemia group (n = 24)	Infarction group (n = 26)	P-value
Age (years)	61.82 ± 2.40	61.30 ± 2.52	60.51 ± 2.81	0.60
Gender (male/female)	17/13	16/8	16/10	0.68
BMI (kg/m^2)	23.90 ± 0.72	24.20 ± 0.67	24.30 ± 0.69	0.15
Systolic pressure (mmHg)	129.30 ± 11.78	131.44 ± 10.26	132.03 ± 10.04	0.21
Diastolic pressure (mmHg)	78.28 ± 10.14	76.38 ± 13.40	77.60 ± 12.81	0.24
Heart rate (beat/min)	69.34 ± 5.87	71.03 ± 8.29	72..01 ± 6.24	0.29

$P < 0.05$ was considered as statistically significant.

Table 2. The LV wall mechanics and volume-time parameters of the Control myocardial ischemia and myocardial infarction groups

Parameters, %	Control (n = 30)	Myocardial ischemia group (n = 24)	Myocardial infarction group (n = 26)
Tls-16	40.49 ± 6.26	50.91 ± 6.42*	68.74 ± 6.18**,#
Trs-12	39.81 ± 7.50	44.18 ± 6.95	9.46 ± 5.24**,##
Tcs-12	40.64 ± 5.23	45.23 ± 7.04	69.07 ± 7.56**,#
Trot-12	42.35 ± 7.41	47.26 ± 4.32	68.71 ± 8.86**,#
Tmsv-16	42.28 ± 3.65	51.30 ± 5.27*	59.49 ± 8.56**,#

LV, left ventricle; Tls-16, time-to-peak longitudinal strain of 16 LV segments; Trs-12, radial strain of 12 LV segments; Tcs-12, and circumferential strain of 12 LV segments; Trot-12, time-to-peak rotation of 12 LV segments; Tmsv-16, time to minimum systolic volume of 16 LV segments. *$P < 0.05$ compared with control group, **$P < 0.01$ compared with control group; #$P < 0.05$ compared with myocardial ischemia group, ##$P < 0.01$ compared with myocardial ischemia group. $P < 0.05$ was considered as statistically significant.

(heterogeneity of variance). Meanwhile, the correlations of LVEF with LV wall mechanics and volume-time parameters (Tlsv, Trsv, Tcsv, and Trotv) and LV rotation time parameter (Tabrot) were assessed using the Spearman'rho correlation coefficient for the myocardial infarction group. Subsequently, Bland-Altman analysis was used to assess repeatability/consistency of the performed measurements. $P < 0.05$ was considered as statistically significant.

expressed as percentage. The above data was measured three times by two experienced radiologists and the average value was obtained.

Repeatability test

After a period of one week, an intra-observer repeatability test was conducted by one observer, using 15 randomly selected cases of ultrasonic images which have been analyzed by him. Then these ultrasonic images were all evaluated by the other observer who was blinded to the analysis results for inter-observer repeatability test.

Statistical analysis

All statistical analyses were performed using SPSS 20.0 (SPSS Inc, Chicago, IL, USA). Data are expressed as mean ± standard deviation (SD). The one-way analysis of variance (ANOVA) was used to test the differences among the three groups followed by post hoc pairwise comparisons using Tukey's least significant difference (LSD, homogeneity of variance) or Dunett-C tests were used for post hoc comparisons

Results

Among the 26 patients with myocardial infarction, there were 10 cases of acute myocardial infarction (AMI) and 16 cases of remote myocardial infarction, and 3 cases were accompanied with ventricular aneurysm. Patients in the myocardial ischemia and myocardial infarction groups were well matched with control group regarding the demographics data at admission, with no significant differences in terms of the age, gender, BMI, blood pressure and heart rate (**Table 1**).

Table 2 presented the LV wall mechanics and volume-time parameters of the Control, myocardial ischemia and myocardial infarction groups. Compared with Control, Tls-16 and Tmsv were longer in myocardial ischemia group (both $P < 0.05$), whereas Tls-16, Trs-12, Tcs-12, Trot-12, and Tmsv-16 were significantly prolonged in myocardial infarction group (all $P < 0.01$). Besides, patients with myocardial infarction also had longer Tls-16, Trs-12, Tcs-12, Trot-12, and Tmsv-16 than that of those with myo-

Table 3. The LV wall mechanics and volume-time parameters and LV rotation time parameter of the Control myocardial ischemia and myocardial infarction groups

Parameters, %	Control (n = 30)	myocardial ischemia group (n = 24)	myocardial infarction group (n = 26)
Tlsv	4.36 ± 1.23	2.31 ± 0.81*	11.20 ± 5.81**,##
Trsv	4.67 ± 2.20	5.12 ± 3.21	17.12 ± 3.21**,##
Tcsv	3.69 ± 1.81	4.72 ± 2.38	10.72 ± 2.38**,##
Trotv	2.86 ± 1.36	3.21 ± 2.15	7.21 ± 2.15*,#
Tabrot	5.57 ± 1.07	5.79 ± 1.63	9.90 ± 6.15**,#

LV, left ventricle; Tls-16, time-to-peak longitudinal strain of 16 LV segments; Trs-12, radial strain of 12 LV segments; Tcs-12, and circumferential strain of 12 LV segments; Trot-12, time-to-peak rotation of 12 LV segments; Tmsv-16, time to minimum systolic volume of 16 LV segments; Tabrot, time interval of rotation between apex and base; Tlsv, time difference between Tls and Tmsv; Trsv, time difference between Trs and Tmsv; Tcsv, time difference between Tcs and Tmsv; Trotv, time difference between Trot and Tmsv. *$P < 0.05$ compared with control group, **$P < 0.01$ compared with control group; #$P < 0.05$ compared with myocardial ischemia group, ##$P < 0.01$ compared with myocardial ischemia group. $P < 0.05$ was considered as statistically significant.

Table 4. The correlations of LVEF with LV wall mechanics and volume-time parameters and LV rotation time parameter

Parameters, %	r	P-value
Tlsv	-0.76	< 0.01
Trsv	-0.82	< 0.01
Tcsv	-0.64	< 0.01
Trotv	-0.49	< 0.05
Tabrot	-0.65	< 0.01

LV, left ventricle; Tls-16, time-to-peak longitudinal strain of 16 LV segments; Trs-12, radial strain of 12 LV segments; Tcs-12, and circumferential strain of 12 LV segments; Trot-12, time-to-peak rotation of 12 LV segments; Tmsv-16, time to minimum systolic volume of 16 LV segments; Tabrot, time interval of rotation between apex and base; Tlsv, time difference between Tls and Tmsv; Trsv, time difference between Trs and Tmsv; Tcsv, time difference between Tcs and Tmsv; Trotv, time difference between Trot and Tmsv. $P < 0.05$ was considered as statistically significant.

cardial ischemia ($P < 0.01$ for Trs-12; $P < 0.05$ for others).

As shown in **Table 3**, patients with myocardial ischemia had only longer Tlsv ($P < 0.05$) than control, but there was no difference in Trsv, Tcsv, Trotv, and Tabrot between the two groups (all $P > 0.05$). However, compared with control and myocardial ischemia groups, all the aforementioned parameters were longer in patients with myocardial infarction (both $P < 0.01$ for Tlsv, Trsv and Tcsv; both $P < 0.01$ for Trotv; $P < 0.01$ and $P < 0.05$ for Tabrot). Furthermore,

Table 4 revealed negative correlations of LVEF with LV wall mechanics and volume-time parameters (Tlsv, Trsv and Tcsv, $P < 0.01$; Trotv, $P < 0.05$) and LV rotation time parameter (Tabrot, $P < 0.01$).

The analyses for intra-observer and inter-observer variability revealed that both 2D-STI and RT-3DE measurements of the LV wall mechanics and volume-time parameters show good consistency and correlation. The reproducibility of the measurements for Tmsv was most satisfactory, with r = 0.983 for intra-observer variability and r = 0.979 for inter-observer variability.

Discussion

Patients with CHD generally had LV systolic dyssynchrony, which might be a neo- direct repression of LV function and ultimately lead to LV distension and heart failure [18]. Recently, LV torsion has recently attracted a great deal of attention to LV mechanics and is believed to be a sensitive indicator of LV systolic and diastolic performance [19]. Among the several assessment methods of LV torsion, 2D-STI and RT-3DE were two novel echocardiographic technologies tool which can be used for the quantitative assessment of systolic synchronization [8-10]. However, until now there have been no uniform evaluation criteria of LV mechanical motion in a synchronous mode. This study assessed LV systolic synchronization in patients with LV systolic dysfunction using analyzing the relationship between myocardial segmental mechanics and regional volume changes, and provided a combined method of 2D-STI and RT-3DE for the assessment of LV systolic synchronization.

In this study, no abnormality was seen in the segmental wall motion and Simspon's LVEF of patients with myocardial ischemia, however, the 2D-STI and RT-3DE displayed a prolonged Tls-16, Tmsv-16 and Tlsv compared with control. This suggested that although myocardial ischemia patients had normal LV systolic function in the resting state, the systolic function of the involved cardiac muscle has been impaired, with the presence of intraventricular dyssyn-

chrony, consistent with previous study [20]. This might be explained by the fact that myocardial ischemia start with endocardium and the subendocardial myofibers had greatest impact on longitudinal motion, whereas the twisting motion in subendocardial myofibers still played a compensatory role to maintain the LV systolic function when the left heart dysfunction is not obvious; however, this compensation would be decreased under the occurrence of obviously impaired left heart function [21, 22]. Besides, the prolonged Tlsv, Trsv, Tcsv, and Trotv in patients with myocardial infarction than that of control and ischemic groups was in accordance with the work by Wu et al. [12].

The LV torsion is the twisting motion of the heart around its long axis [23], due to the oppositely directed myofibers rotation between the subendocardial and subepicardial layers [7, 24]. It is essential for the maintenance of the heart blood-pumping function [25], and has been proposed as a sensitive parameter of hemodynamics and myocardial contractility [26, 27]. In this study, the analysis of Tabrot, a LV torsion synchronization parameter, showed that both the base and apical rotation angles reached the peak at the end-systole in the control group, achieving the LV torsion synchronization. In myocardial infarction group of patients, apart from the significantly decreased ability of myocardial fibers to deform, the concordance of the LV "twisting towel" motion was also damaged severely, and the peak time of the base and apical rotation angles was not synchronized. As in the ischemia patients, despite twisting notion didn't differ from that of the control group despite a slight decrease, in agreement with previous studies [20, 28]. Furthermore, the results also showed well negative correlations of LVEF with Tlsv, Trsv, Tcsv, Trotv and Tabrot in infarction group. The high degree of dyssynchrony was associated with the poor LV systolic function, suggesting that dyssynchrony notion could lead to the damage of LV systolic dysfunction, supporting the results of a previous research [29].

This study has several limitations. Firstly, the number of cases was not sufficient. Secondly, RT-3DE was used to analyze the mechanical motion of each segmental in the same cardiac cycle, whereas 2D-STI was applied on the analysis of myocardial segmental in different cardiac cycles. Thirdly, the Philips QLAB CMQ software (v8.1) could only supply the systolic synchronization parameters of 12 segments at the parasternal short axis view.

Conclusions

Not with standing its limitation, this study did support that the relationship between the LV wall mechanics and the volume could be used for the evaluation of LV systolic dyssynchrony in patients with myocardial infarction, and the LV wall mechanics and volume-time parameters were negative correlated with Simspon's LVEF. Besides, Tlsv (%) could be applied on early detection of LV systolic dyssynchrony in patients with myocardial ischemia.

Disclosure of conflict of interest

None.

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