Evaluation of left ventricular systolic function in patients with acute ST segment elevation myocardial infarction treated by Tongxinluo after percutaneous coronary intervention by tissue mitral annulus displacement technique

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Research Article

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Abstract

Purpose: We aimed to investigate the value of the tissue mitral annular displacement (TMAD) technique in evaluating left ventricular systolic function in patients with acute ST segment elevation myocardial infarction (STEMI) treated by Tongxinluo after percutaneous coronary intervention (PCI).

Methods: Sixty patients with acute STEMI who underwent emergency PCI were randomly assigned to either the conventional group or the Tongxinluo group. Conventional echocardiography, two-dimensional speckle tracking imaging (2D-STI) and TMAD were performed 72 hours and 12 months after PCI. The following parameters were obtained: left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), stroke output (SV), left ventricular ejection fraction (LVEF-Simpson), global longitudinal strain of left ventricle (GLS), left ventricular global circumferential strain (GCS), septal displacement (TMAD-sep), lateral displacement (TMAD-lat), midpoint displacement (TMAD-midpt) and the percentage of TMAD to LV length from the midpoint of the mitral annulus to the apex at end-diastolic (TMAD-midpt%). And LVEF was measured by three-dimensional automated cardiac function quantification (3DQA) (LVEF-3DQA). Statistical analysis was used to analyze the differences in the above indicators among the groups and their correlations.

Results: 12 months after PCI, compared with the conventional group, LVEDD, LVESD and SV decreased, LVEF-Simpson, LVEF-3DQA, GLS, GCS and TMAD parameters increased in the Tongxinluo group ($P < 0.05$). Correlation analysis showed that TMAD parameters were positively correlated with GLS and LVEF-3DQA, and TMAD-midpt% had the highest correlation with GLS and LVEF-3DQA ($r = 0.829$ $P < 0.01$ $r = 0.754$ $P < 0.01$), and TMAD-midpt% had good repeatability and good repeatability.

Conclusion: TMAD can be used to evaluate the protective effect of Tongxinluo on left ventricular systolic function in patients with acute STEMI after PCI.

Introduction

Percutaneous coronary intervention (PCI) is currently an effective treatment for acute myocardial infarction (AMI) reperfusion, and greatly reduces mortality [1]. However, due to the presence of hibernating myocardium and stunned myocardium, the recovery of systolic function in patients with coronary heart disease, even after PCI, is often delayed or cannot be fully recovered [2]. The lack of full recovery of systolic function after PCI seriously limits the survival rate, prognosis, and quality of life of patients [3]. Thus, improving the prognosis of patients after acute ST segment elevation myocardial infarction (STEMI) treated by PCI is urgently needed in clinical practice. Studies have shown that Tongxinluo can prevent myocardial ischemia-reperfusion injury after AMI, thereby improving the prognosis of these patients [4]. Tongxinluo is a capsule preparation made from traditional Chinese medicines according to the Chinese medical theory of collateral disease [5]. It has anti-inflammatory, anti-oxidative stress, anti-apoptosis, anti-myocardial ischemia and anti-cardiomyocyte edema properties [5, 6]. Tissue mitral annular displacement (TMAD) is a new ultrasound technology that can quickly and accurately evaluate left ventricular systolic function [7]. TMAD has great potential in clinical applications due to its low image quality requirements, lack of angle dependence, and ease of operation [7, 8]. The purpose of this study was to investigate the value of the TMAD in evaluating left ventricular systolic function in patients with acute STEMI treated by Tongxinluo after PCI.

Subjects And Methods

Research subjects, treatment groups and medications

Sixty patients with acute STEMI admitted to the First Affiliated Hospital of Shihezi University School of Medicine from 2019 to 2020 were selected as research subjects. All patients were confirmed by coronary angiography to have ≥75% coronary artery stenosis or occlusion. Emergency PCI was successfully performed on all subjects. Patients who received conventional drug treatment after PCI were assigned to the conventional group (n=30). Patients who received Tongxinluo in addition to conventional drug treatment after PCI were assigned to the Tongxinluo treatment group (n=30). The conventional group was administered ticagrelor tablets, enteric-coated aspirin tablets, statins and betaloc after PCI. For the Tongxinluo treatment group, an initial dose consisting of 8 capsules of Tongxinluo, taken orally, was administered prior to emergency PCI. After surgery, these patients received 8 capsules of Tongxinluo, 3 times per day for 12 months, in addition to the same medications as the conventional group. At the same time, based on the patient’s medical condition, other drugs, such as diuretics, hypoglycemic drugs, β-receptor blockers, angiotensin-converting enzyme inhibitors (ACEI), and angiotensin II receptor antagonists (ARB) were administered.

Inclusion and exclusion criteria

Inclusion criteria:

(1) patients who had acute STEMI onset within 24 hours;

(2) patients who undergone emergency PCI;

(3) patients who signed a written informed consent.

Exclusion criteria:

(1) patients with life-threatening conditions such as severe infection, severe weakness, severe liver or kidney disease, or severe coagulation abnormalities;

(2) non-ST-segment elevation myocardial infarction;

(3) allergies to any drugs used in this study;

(4) previous participation in another clinical research study.

This clinical study has been approved by the hospital ethics committee of the First Affiliated Hospital of Shihezi University School of Medicine. Informed written consent was received from the patients and their families in the study.

Echocardiography

Conventional echocardiography and 2D-STI were performed 72 hours and 12 months after PCI. A Philips EPIQ 7C echocardiograph configured with an X5-1 probe, a frequency range of 1-5 MHz, and Qlab offline analysis software was employed for the study. A sonographer at the deputy director level or above collected and analyzed the images. Firstly, the subject was asked to breathe calmly and lie down on their left side; then the electrocardiogram was recorded. The parasternal left ventricular long axis, apical four-chamber, apical three-chamber, and apical two-chamber views, as well as the mitral valve level, papillary muscle level, and apical level left ventricular short-axis views were collected. The dynamic images for 4 consecutive cardiac cycles were stored. The image was copied to the hard disk in DICOM format, imported into the Qlab offline software and analyzed to obtain the relevant parameters.

Routine parameters

On the parasternal left ventricular long axis view, the left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), and stroke volume (SV) were measured. According to the guidelines of the American Society of Echocardiography, the left ventricular ejection fraction (LVEF-Simpson) was measured using the biplane Simpson method on the apical four-chamber and apical two-chamber views.

2D-STI parameters

In the apical four-chamber, three-chamber, two-chamber, and left ventricular short-axis views, after manually tracing the left ventricle, the software automatically identified the left ventricular endocardium and epicardium. After the software generated a region of interest (ROI), we manually adjusted the ROI to obtain a satisfactory tracing point, which allowed the automatic tracking function of the software to obtain the left ventricular global longitudinal strain (GLS) and left ventricular global circumferential strain (GCS).

LVEF-3DQA

Instruct the patient to hold his breath at the end of the expiration and obtain a full volume image in the apical four-chamber view in the "Full Volume" mode, and then copy the acquired image to the hard disk in DICOM format, and import it into the Qlab software for analysis, and follow the prompts at the end of diastole Mark the reference point and repeat this step during systole to calculate LVEF-3DQA.

TMAD parameters

In the apical four-chamber view, we selected "AP4" in the TMAD mode. The software automatically located the cardiac cycle, and sequentially traced three tracking points: mitral annulus ventricular septum point, mitral annulus sidewall point and left ventricular apex. We manually adjusted the position of the tracking point. Subsequently, the following data were obtained: septal displacement (TMAD-sep), lateral displacement (TMAD-lat), midpoint displacement (TMAD-midpt), and the percentage of TMAD to LV length from the midpoint of mitral annulus to the apex at end-diastolic (TMAD-midpt%).

Statistical analyses

The Statistical Package for the Social Sciences software (version 22) was used for statistical analysis. The data conforming to normal distribution were expressed as mean ± standard deviation ($\bar{X} \pm s$). If the data did not conform to the normal distribution, they were expressed as median ± quartile spacing to enable the use of single-factor one-way analysis of variance to compare between the means in each group. For the comparison between the two groups, LSD t-test was used. The Pearson method was used to analyze the correlation between TMAD parameters and GLS and LVEF-3DQA. The intra-group correlation coefficient (ICC) was used for a repeatability test: the images of 10 patients were randomly selected and TMAD was used by 2 sonographers at the deputy director level or above to obtain relevant parameters. We then randomly selected the images of 10 patients and repeated the measurement twice on the same patient by the same physician. ICC > 0.75 indicated high reproducibility. $P < 0.05$ indicated that the difference is statistically significant.

Results

Basic characteristics

There was no significant difference in the basic data between the conventional group and the Tongxinluo group ($P > 0.05$). (Table 1)

Table 1
Comparison of basic characteristics

	conventional group (n = 30)	Tongxinluo group (n = 30)	χ^2/t	*P*
Gender (Male/Female)	28/2	29/1	0.35	0.55
Age (years)	53.20 ± 6.73	53.30 ± 9.43	0.05#	0.96
BMI (kg/m^2)	26.77 ± 1.95	27.11 ± 2.05	0.66#	0.51
HR (bpm)	70.37 ± 8.43	72.00 ± 9.91	0.69#	0.50
SBP (mmHg)	121.37 ± 7.84	118.13 ± 8.71	1.51#	0.14
Risk factors (example)				
Diabetes	7	4	1.00	0.32
Hypertension	15	10	1.71	0.19
Hyperlipidemia	5	2	1.46	0.23
Smoke	22	24	0.37	0.54
Drinking wine	10	11	0.07	0.79
Auxiliary medication situation (example)				
ACEI/ARB	13	16	0.60	0.44
β-receptor blocker	12	19	3.27	0.07
Diuretic	10	9	0.08	0.78
Hypoglycemic drugs	7	4	1.00	0.32
Pathological changes (example)				
Left trunk	2	3	0.22	0.64
Left anterior descending branch	14	17	0.60	0.44
Left circumflex branch	15	13	0.27	0.61
Right coronary artery	7	9	0.34	0.56

Note: #: the value of T; BMI: body mass index, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin II receptor antagonists, HR: heart rate, SBP: systolic blood pressure

Routine parameters and 2D-STI parameters

72 h after PCI, there was no significant difference in routine parameters and 2D-STI parameters between the conventional group and the Tongxinluo group ($P > 0.05$). 12 months after PCI, compared with the conventional group, LVEDD, LVESD and SV decreased, LVEF, GLS and GCS increased in the Tongxinluo group ($P < 0.05$). In addition, 12 months after PCI, LVEDD, LVESD and SV decreased, while LVEF, GLS and GCS increased in both the conventional group and the Tongxinluo group compared to the values 72 h after PCI ($P < 0.05$). (Table 2, Figs. 1–3)

Table 2
Comparison of routine parameters and strain parameters between conventional group and Tongxinluo group ($\chi \pm s$, n = 30)

	conventional group		**Tongxinluo group**	
	72 h after PCI	12 months after PCI	72 h after PCI	12 months after PCI
LVEDD (mm)	57.20 ± 4.57	55.85 ± 4.22	58.21 ± 4.58	53.46 ± 4.15*#
LVESD (mm)	35.08 ± 2.51	33.68 ± 2.43*	34.86 ± 2.51	31.53 ± 2.51*#
SV (mL)	55.40 ± 3.10	57.39 ± 2.96*	54.26 ± 3.09	61.67 ± 2.91*#
LVEF-Simpson (%)	49. 74 ± 3.53	52.67 ± 3.51*	50.68 ± 5.49	55.12 ± 5.67*#
LVEF-3DQA (%)	46.30 ± 5.56	50.30 ± 4.12*	46.81 ± 5.99	54.16 ± 4.55*#
GLS (%)	10.60 ± 3.40	12.85 ± 2.61*	10.86 ± 2.90	15.69 ± 2.91*#
GCS (%)	11.72 ± 3.56	15.19 ± 3.26*	12.24 ± 4.12	17.40 ± 4.51*#

Note: *: compared with the values 72 h after PCI, $P < 0.05$; #: Compared with the conventional group 12 months after PCI, $P < 0.05$; LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter, SV: stroke output, LVEF-Simpson: Left ventricular ejection fraction measured by Simpson method, LVEF-3DQA: Left ventricular ejection fraction measured by three-dimensional automated cardiac function quantitative method, GLS: global left ventricular overall longitudinal strain, GCS: left ventricular global circumferential strain

TMAD parameters

72 h after PCI, there was no significant difference in TMAD parameters between the conventional group and the Tongxinluo group ($P > 0.05$). 12 months after PCI, compared with the conventional group, TMAD-sep, TMAD-lat, TMAD-midpt and TMAD-midpt% increased in the Tongxinluo group ($P < 0.05$). In addition, 12 months after PCI, TMAD-sep, TMAD-lat, TMAD-midpt and TMAD-midpt% increased in both the conventional group and the Tongxinluo group compared to the values 72 h after PCI ($P < 0.05$). (Table 3, Fig. 4)

Table 3
Comparison of TMAD parameters between the conventional group and the Tongxinluo group ($\chi \pm s$, n = 30)

	conventional group		Tongxinluo group	
	72 h after PCI	12 months after PCI	72 h after PCI	12 months after PCI
TMAD-sep (mm)	9.78 ± 1.98	10.98 ± 1.79*	9.97 ± 2.14	11.86 ± 1.88*#
TMAD-lat (mm)	10.31 ± 2.09	11.44 ± 2.07*	10.50 ± 2.32	12.58 ± 2.13*#
TMAD-midpt (mm)	10.30 ± 2.11	11.35 ± 1.91*	10.44 ± 2.36	12.38 ± 1.87*#
TMAD-midpt% (%)	11.39 ± 2.01	12.55 ± 1.68*	11.42 ± 2.01	13.85 ± 1.48*#

Note: *: compared with the values 72 h after PCI, $P < 0.05$; #: Compared with the conventional group 12 months after PCI, $P < 0.05$, TMAD: tissue mitral annular displacement, TMAD-sep: septal displacement, TMAD-lat: lateral displacement, TMAD-midpt: midpoint displacement, TMAD-midpt%: the percentage of TMAD to LV length from the midpoint of mitral annulus to the apex at end- diastolic

Correlation analysis

correlation between LVEF-3DQA and 2D-STI parameters

GLS and GCS were significantly positively correlated with LVEF-3DQA in the Tongxinluo group ($P < 0.01$), and the absolute values were as follows: GLS > GCS. (Fig. 5)

Correlation Analysis between TMAD parameters and GLS

TMAD parameters were significantly positively correlated with GLS in the Tongxinluo group ($P < 0.01$), and the absolute values were as follows: TMAD-midpt% > TMAD-midpt > TMAD-sep > TMAD-lat. (Fig. 6)

Correlation Analysis between TMAD parameters and LVEF-3DQA

TMAD parameters were significantly positively correlated with LVEF-3DQA in the Tongxinluo group ($P < 0.01$), and the absolute values were as follows: TMAD-midpt% > TMAD-midpt > TMAD-sep > TMAD-lat. (Fig. 7)

Repeatability test

The intra-observer ICC of LVEF-3DQA, GLS and TMAD-midpt% were 0.839, 0.828 and 0.827, respectively; and the inter-observer ICC were 0.822, 0.819 and 0.802, indicating that the reliability and repeatability of TMAD-midpt%, respectively are relatively high. (Fig. 8)

Discussion

Acute STEMI is a cardiovascular disease with a rapid onset, high morbidity, and mortality, which seriously threatens human health [9]. PCI can quickly restore coronary blood supply, reduce the area of myocardial infarction, and restore the patient's myocardial contractility, thereby improving the patient's clinical symptoms and clinical prognosis [10]. However, even if patients with acute STEMI undergo PCI successfully, it is possible that myocardial infarction or myocardial reperfusion injury may occur again, due to damage to endothelial cells and increased vascular resistance [11]. Therefore, it is extremely important to improve the prognosis of patients with acute STEMI after PCI to reduce the risk of postoperative death. Most patients with acute STEMI after PCI require adjuvant drug therapy to effectively prevent re-infarction and in-stent thrombosis and improve existing damage of myocardial function [12]. At present, relevant studies have shown that Tongxinluo has the effect of protecting vascular endothelial function and relieving vasospasm [13]. And tongxinluo plays an important role in protecting the integrity of micro-vessels, reducing the area of myocardial infarction, preventing reperfusion injury, and improving patient prognosis [14]. TMAD is based on speckle tracking imaging, which automatically tracks the displacement of the mitral valve annulus relative to the apex of the left ventricle to obtain parameters reflecting the systolic function of the left ventricle [15]. This technique is not affected by whether the endocardium is clear or not, it takes a short time to complete, and is relatively simple to conduct [15]. Therefore, it can more effectively evaluate the left ventricular systolic function.

The results of our study showed that there was no statistical difference in the 2D-STI parameters between the conventional group and the Tongxinluo group 72 h after PCI. This suggests that the myocardium of patients with acute STEMI has been severely damaged, causing a decrease in left ventricular systolic function. Short-term use of Tongxinluo after PCI is not yet effective in treating the myocardium. This may be due to the Tongxinluo's lack of short-term efficacy and a failure to detect its protective effect on the myocardium by ultrasound imaging. 12 months after PCI, LVEDD, LVESD and SV decreased, while LVEF-Simpson and LVEF-3DQA increased in both the conventional group and the Tongxinluo group compared to the values 72 h after PCI. This may be because PCI and thrombolytic therapy can open the diseased blood vessels, improve the blood supply of myocardial cells and inhibit local myocardial cell contraction, thereby improving the patient's heart function and prognosis [16]. 12 months after PCI, compared with the conventional group, LVEDD, LVESD and SV decreased, LVEF-Simpson and LVEF-3DQA increased in the Tongxinluo group. This shows that the addition of Tongxinluo to conventional treatment for patients with acute STEMI after PCI is more conducive to the recovery of left ventricular systolic function. This may be due to Tongxinluo's long acting time, which can fully protect the structure, function, and barrier of vascular endothelial cells; improve myocardial ischemia; reduce the myocardial infarction area; and further restore the patient's left ventricular systolic function [17]. However, in clinical work, we mainly use changes in LVEF to reflect changes in patients' left heart function [18]. In the study, we found that although the difference in LVEF between the Tongxinluo group and the conventional group at 12 months after PCI is statistically significant, the difference is small and it is not easily identified in clinical work. Studies have shown that the three-dimensional automated cardiac function quantification method is currently the clinically recommended method for more accurate measurement of cardiac function, which shows that LVEF-3DQA can be used as a sensitive indicator of patients' cardiac function [19].

In this study, 12 months after PCI, GLS and GCS increased in both the conventional group and the Tongxinluo group compared to the values 72 h after PCI. What's more, 12 months after PCI, compared with the conventional group, GLS and GCS increased in the Tongxinluo group. And the results of correlation analysis showed that GLS and GCS are significantly correlated with LVEF-3DQA, and GLS is the major factor. Thus, both GLS and GCS can reflect the recovery of left ventricular systolic function in patients with acute STEMI after PCI plus Tongxinluo treatment. GLS can more sensitively reflect changes in left ventricular systolic function than GCS and LVEF, which is consistent with the results of Teraguchi I, et al [20]. This may be because the inner myocardium is more sensitive to myocardial injury, it is located at the distal end of the coronary artery, with abundant microvessels and less effective collateral circulation, and the longitudinal myocardium is easily damaged after PCI [21]. Therefore, since hypokinesia of the long axis of the myocardium becomes the first manifestation, GLS can sensitively reflect the changes in left ventricular systolic function [22]. However, in our study, we found that most patients tested after acute STEMI PCI have poor image quality, due to additional medical conditions such as obesity. Since GLS and GCS have higher requirements for patient image quality, we developed a new examination method during our study.

In our study, 12 months after PCI, TMAD parameters increased in both the conventional group and the Tongxinluo group compared to the values 72 h after PCI. What's more, 12 months after PCI, compared with the conventional group, TMAD parameters increased in the Tongxinluo group. And the results of correlation analysis showed that the TMAD parameters were positively correlated with GLS and LVEF-3DQA. TMAD-midpt% had the highest correlation with GLS and LVEF-3DQA. And TMAD-midpt% was found to have good repeatability. This may be because the longitudinal movement of the myocardium accounts for more than 70% of the maintenance of myocardial function, so TMAD can reflect the overall systolic function of the left ventricle and can be applied to patients with multiple medical conditions to reflect the overall systolic function of the left ventricle [23]. TMAD-midpt% is the displacement of the midpoint of the mitral valve annulus ventricular septum-side wall point as a percentage of the left ventricular long diameter, which is corrected for the left ventricular long diameter, including TMAD and left ventricular size changes [24]. TMAD is not affected by changes in the size of the left ventricle, it is a standardized indicator that can more accurately reflect the systolic function of the left ventricle, which is consistent with the results of Asada D et al [25]. At the same time, TMAD is automatically tracked by the software, which eliminates human error, is not affected by the angle, and has low image quality requirements [26]. Since it only needs to clearly display the mitral valve annulus and apex, patients with poor acoustic windows can also obtain more accurate results [26].

The limitations of this study are: (1) human factors have a greater impact on ultrasound image acquisition and post-processing; (2) the sample size of our study is small.

Conclusion

In summary, TMAD can be used as a quick, simple and accurate technique to assess the changes in left ventricular systolic function of patients with acute STEMI after PCI. TMAD can be used to assess the prognosis of patients with acute STEMI, and TMAD-midpt% has the highest predictive value. The addition of Tongxinluo to conventional treatment for patients with acute STEMI after PCI is conducive to the recovery of left ventricular systolic function.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose

Author Contributions

All authors contributed to the study conception and design. Material preparation was performed by Wenjuan Qin and Zijing Zhai. Data collection was performed by Jia Feng and Ruimeng Tian. Analysis weas performed by Zhen Wang and Lei Huang. The first draft of the manuscript was written by Wenjuan Qin, Zijing Zhai and Jia feng. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

Ethics approval

The study has passed an ethical review and the approval number is 2019-124-01. The study has been approved for clinical trial registration with the registration number chiCTR2000035226, and the registration date of 2020.08.04

Consent to participate

Informed consent was obtained from all individual participants included in the study

Consent to publish

The authors affirm that human research participants provided informed consent for publication of the images in Figures 1 - 4.

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Figures

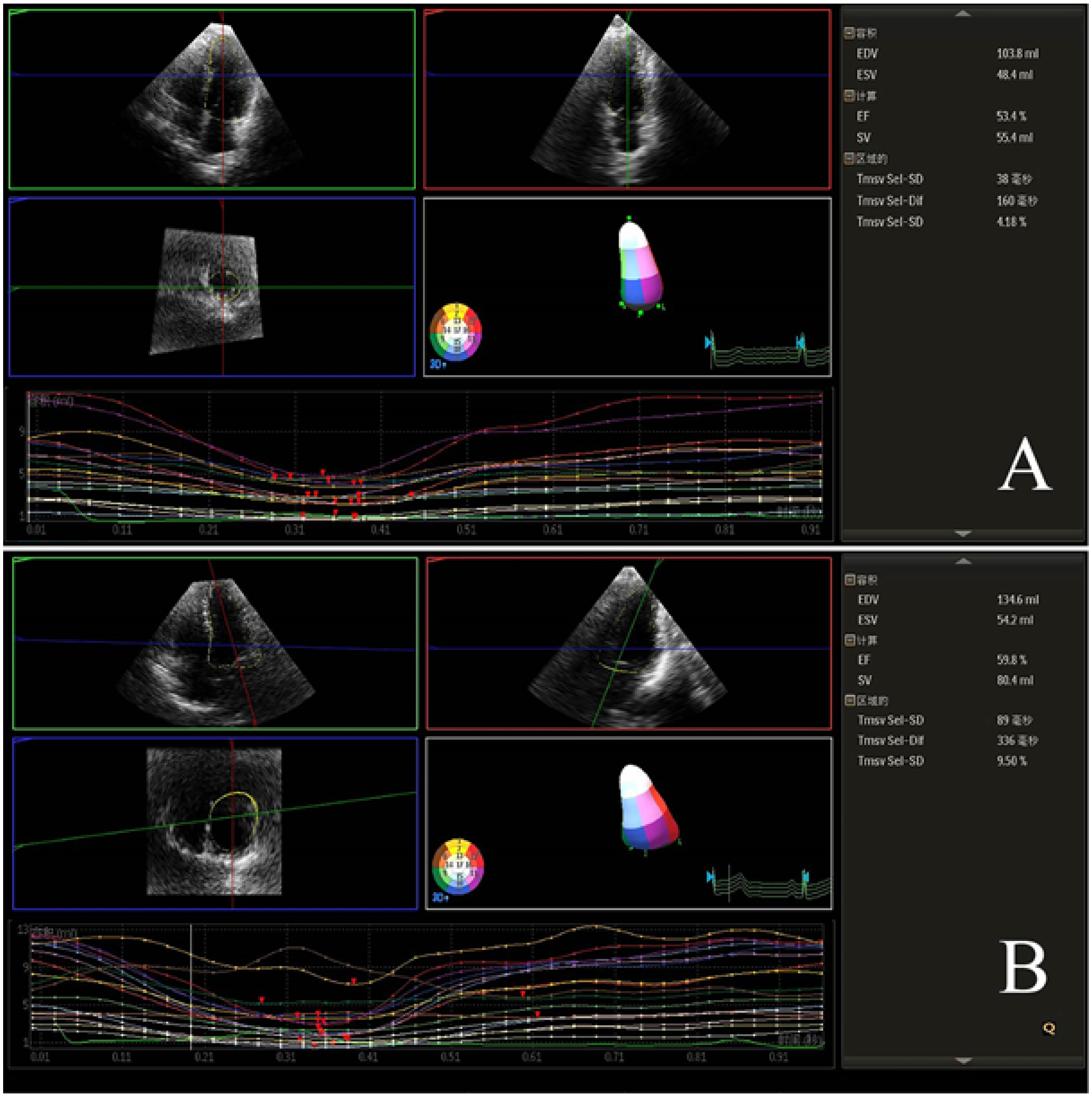

Figure 1

Comparison of LVEF-3DQA in the Tongxinluo group (This is a representative image of 30 patients examined)

A: 72 hours after PCI, B: 12 months after PCI

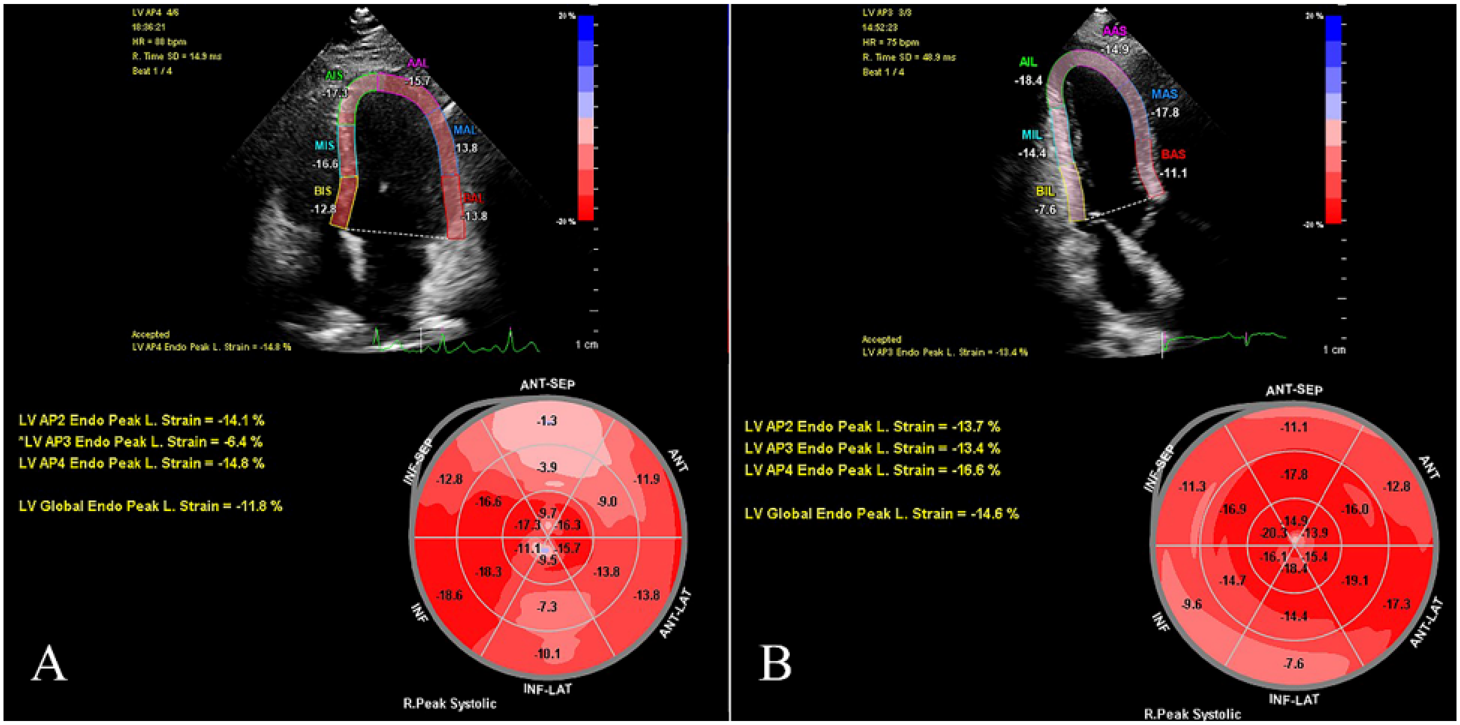

Figure 2

Comparison of GLS in the Tongxinluo group (This is a representative image of 30 patients examined)

A: 72 hours after PCI, B: 12 months after PCI

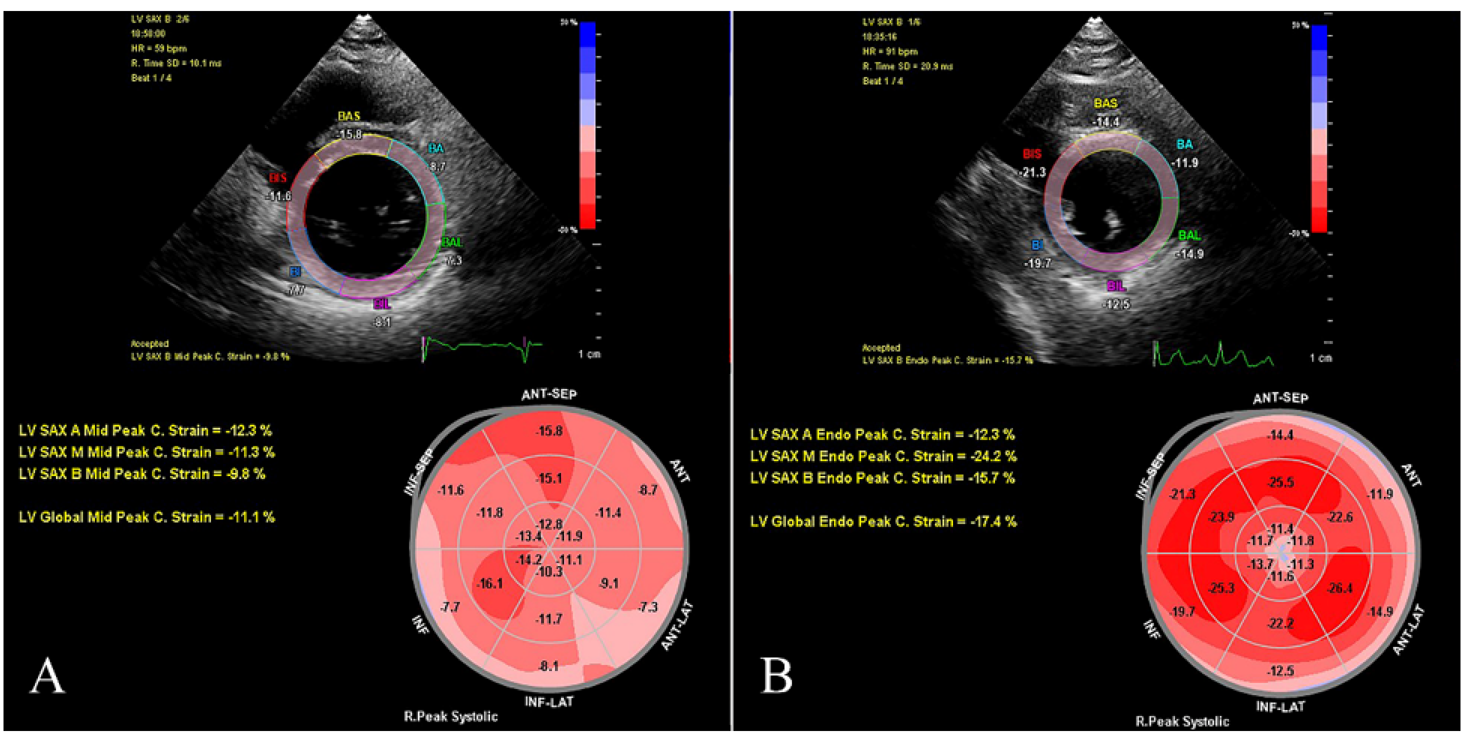

Figure 3

Comparison of GCS in the Tongxinluo group (This is a representative image of 30 patients examined)

A: 72 hours after PCI, B: 12 months after PCI

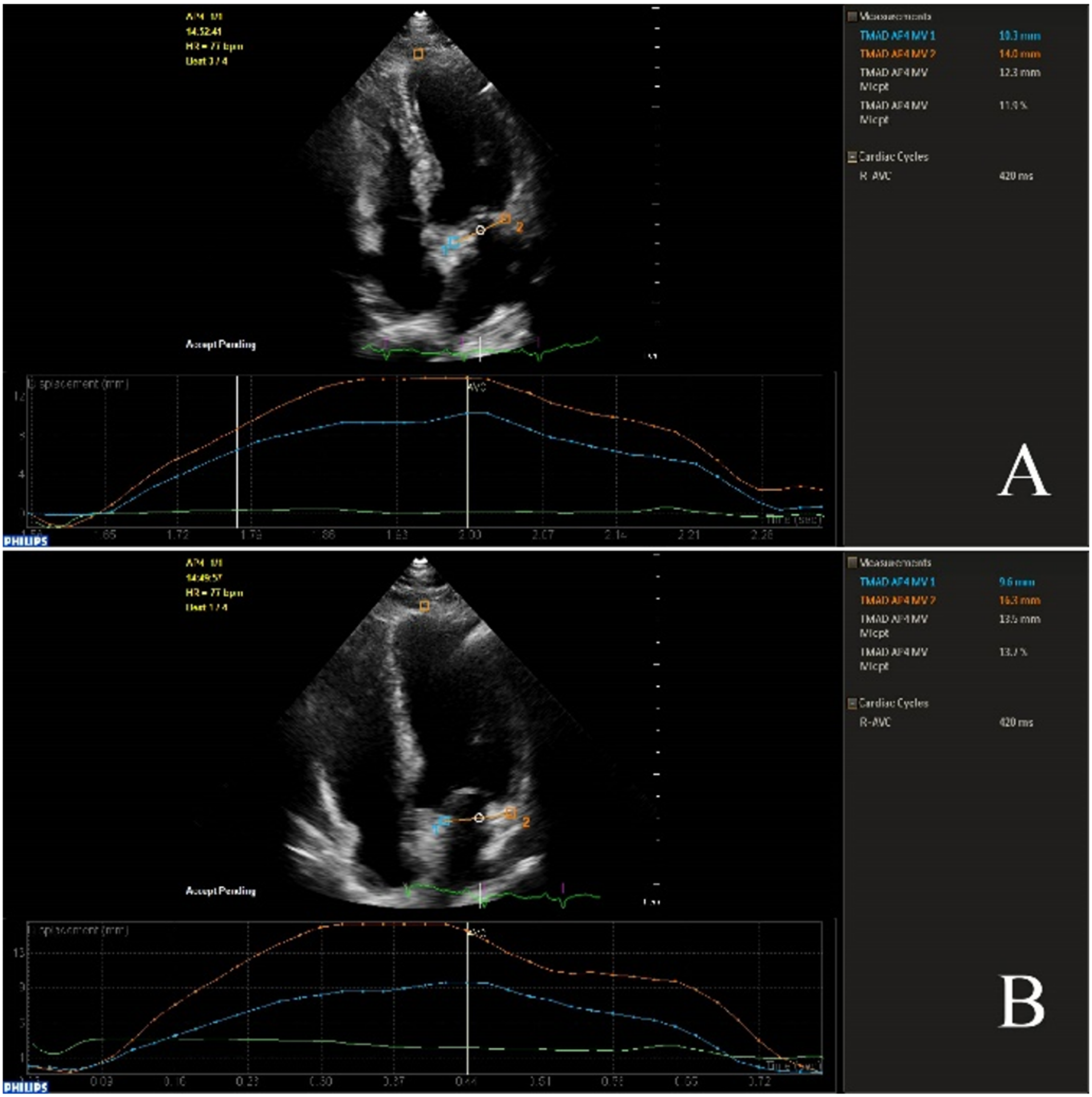

Figure 4

Apical four-chamber mitral annulus displacement in the the Tongxinluo group (This is a representative image of 30 patients examined)

A: 72 hours after PCI, B: 12 months after PCI

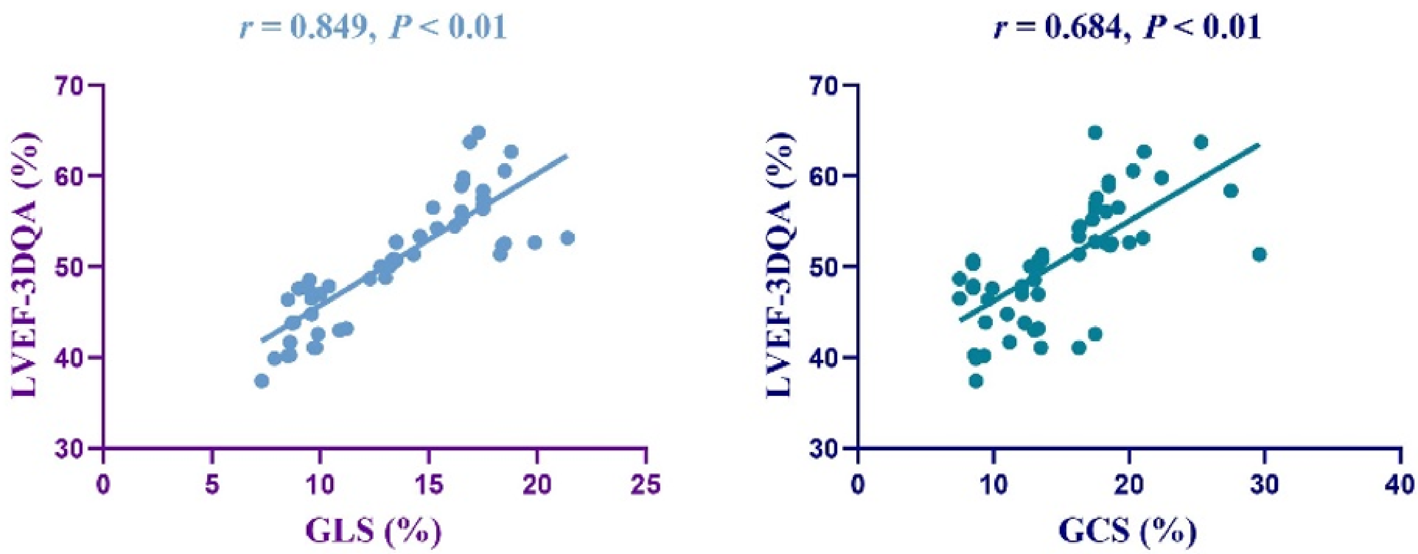

Figure 5

correlation between LVEF-3DQA and 2D-STI parameters in the Tongxinluo group

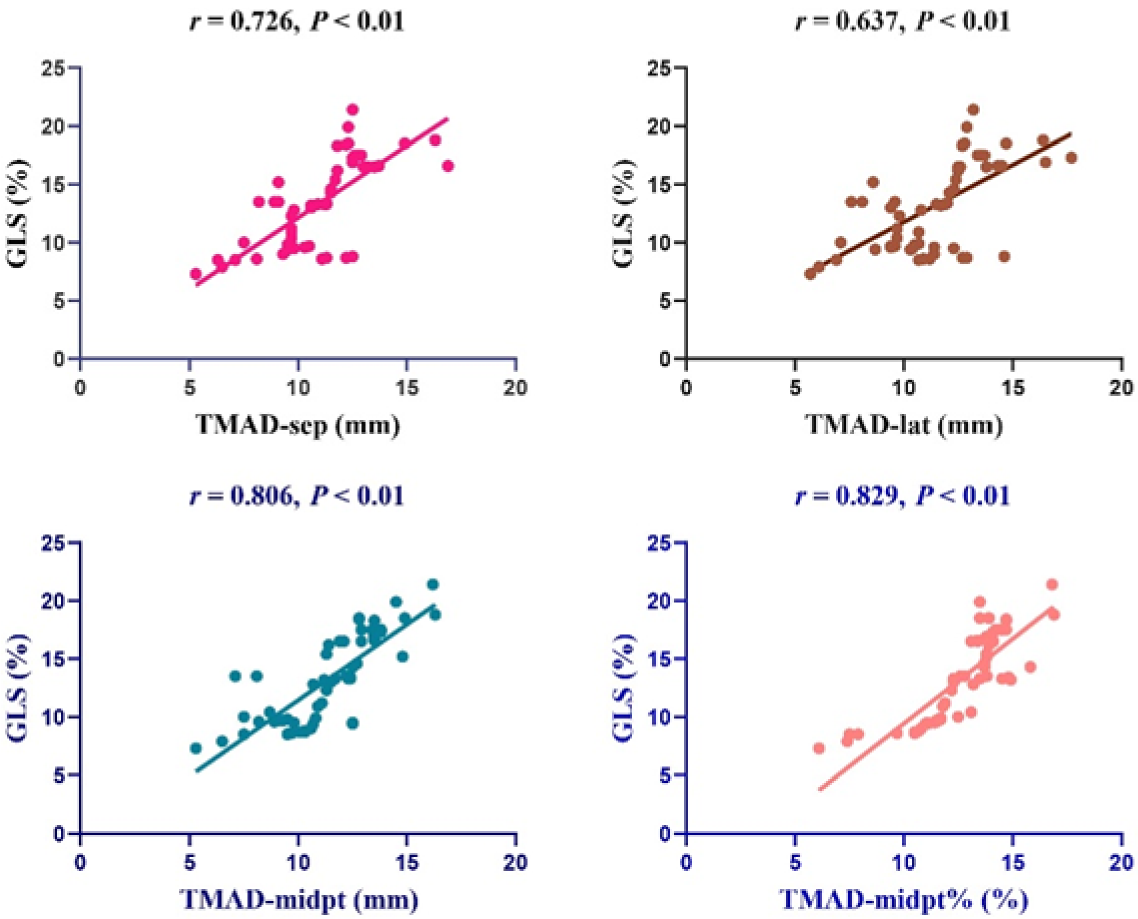

Figure 6

correlation between TMAD parameters and GLS in the Tongxinluo group

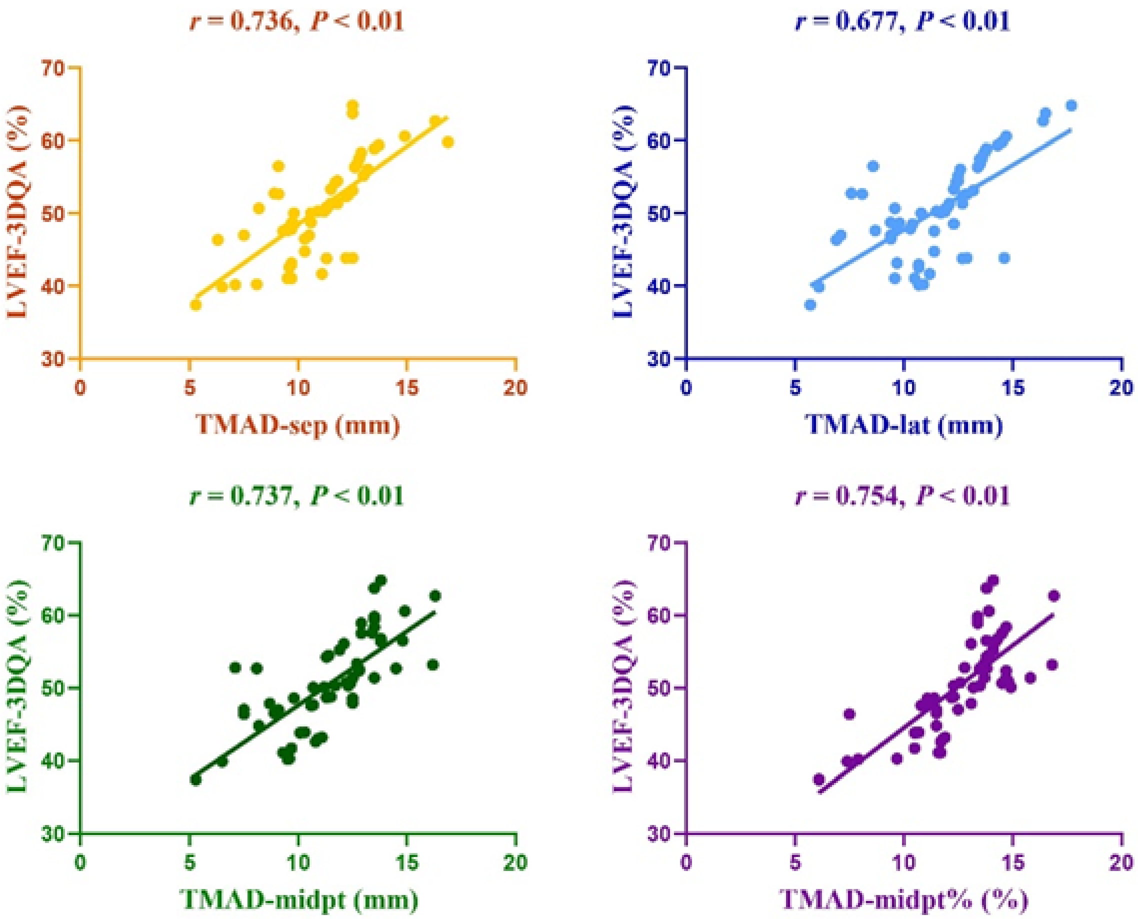

Figure 7

correlation between TMAD parameters and LVEF-3DQA in the Tongxinluo group

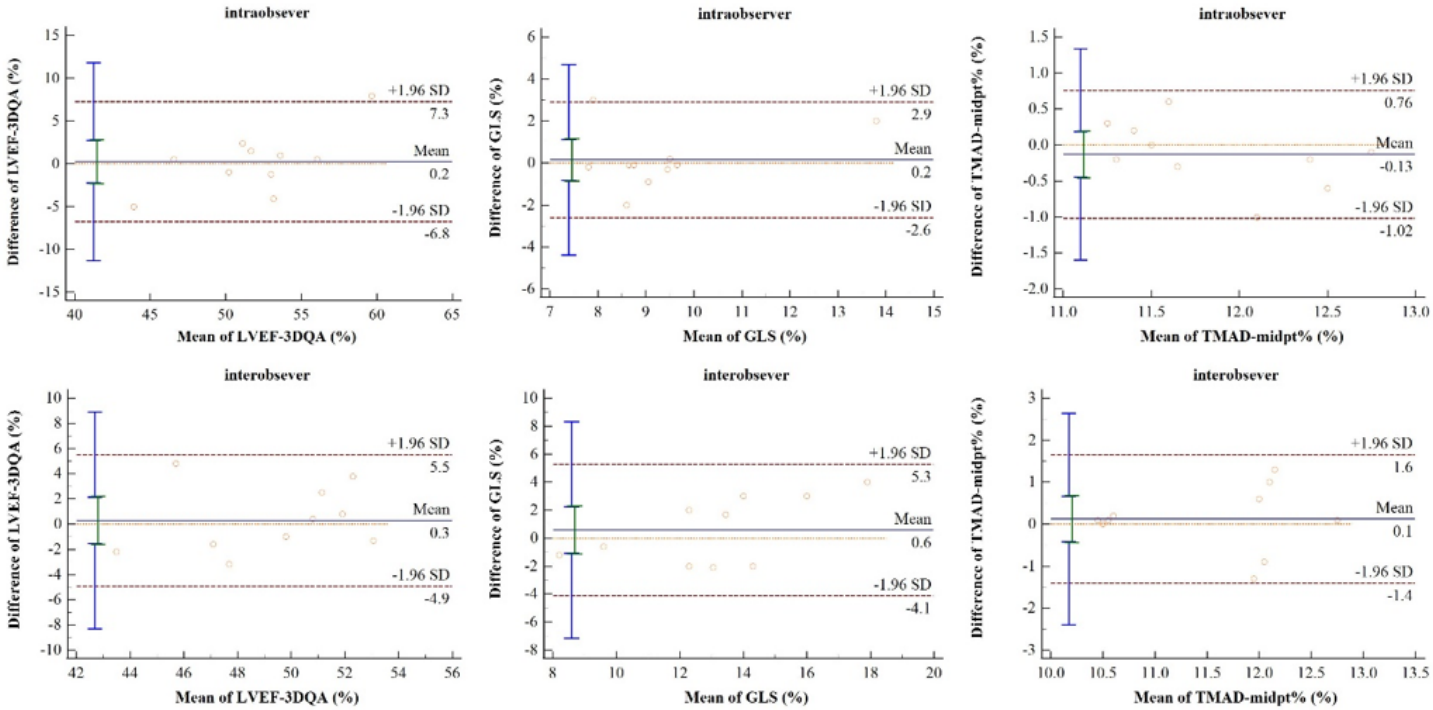

Figure 8

Bland Altman analyses of intra- and inter-observer reliability in LVEF-3DQA, GLS and TMAD-midpt%