

# Relationship between Color-Coded Anatomical M-Mode, Strain Imaging, and Tissue Doppler Imaging in Assessing Myocardial Asynchrony in Normal Subjects

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## Abstract

**Background:** This study aimed to compare the time-to-peak systolic contraction time ( $T_c$ ) by color-coded anatomical M-mode (AMM), the time-to-peak systolic strain ( $T_{st}$ ) by strain rate imaging (SRI), and the time-to-peak systolic velocity ( $T_s$ ) by tissue Doppler imaging (TDI) in the left (LV) and right (RV) ventricular segments of normal subjects. We also sought to determine the relationship between these methods for defining asynchrony indices in normal subjects.

**Methods:** Conventional echocardiography, color-coded AMM, SRI, and TDI were performed on 44 healthy adult volunteers (at the Tehran Heart Center and Shariati Hospital) to measure  $T_c$ ,  $T_{st}$ , and  $T_s$  for 12 LV and 2 RV segments at mid and basal levels. Additionally, delays and standard deviations (SDs) were measured in all 12 LV segments.

**Results:** In the assessed segments,  $T_c$  by AMM and  $T_{st}$  by SRI were significantly greater than  $T_s$  by TDI ( $P < 0.001$ ). No significant differences were noted between  $T_c$  and  $T_{st}$  in 8 LV and 2 RV segments ( $P < 0.05$ ). For the septal basal segment, the respective values were  $T_s = 170.43 \pm 36.76$  ms,  $T_{st} = 372.34 \pm 72.21$  ms, and  $T_c = 374.19 \pm 42.76$  ms. A moderate correlation was observed between AMM and SRI in assessing asynchrony and SD for all LV segments, but no correlation existed between AMM and TDI.

**Conclusion:**  $T_c$  by AMM and  $T_{st}$  by SRI were significantly higher than  $T_s$  by TDI in the LV and RV segments. There was no correlation between AMM and TDI in defining asynchrony indices.

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**Keywords:** Echocardiography; Methods; Anatomical M-mode; Tissue doppler imaging; Myocardial asynchrony; Strain rate imaging

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## Introduction

Mechanical dyssynchrony can predict the outcome of cardiac resynchronization therapy (CRT).<sup>1, 2</sup> Different echocardiographic modalities have been used to assess the presence and severity of dyssynchrony in patients suffering from cardiomyopathy. Tissue Doppler imaging (TDI) was once known as a good candidate to screen patients who might benefit from CRT; however, multicenter studies have since revealed that TDI-derived parameters fail to predict CRT responders.<sup>3, 4</sup>

Regarding the current guidelines for echocardiographic indices in decision-making about cardiac resynchronization therapy (CRT) implantation, both the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) recommend CRT as a Class I intervention. This recommendation applies to patients with left bundle branch block (LBBB) who have symptomatic heart failure classified as functional class II, III, or IV, a left ventricular (LV) ejection fraction of  $\leq 35\%$ , and a QRS duration of  $\geq 150$  milliseconds. Additionally, CRT is classified as a Class IIa recommendation for symptomatic heart failure patients with LBBB and a QRS duration between 130 and 150 milliseconds, as well as for non-LBBB patients with a QRS duration of  $\geq 150$  milliseconds. However, symptomatic heart failure patients who have an LV ejection fraction of  $\leq 35\%$ , a non-LBBB ECG pattern, and a QRS duration between 130 and 149 milliseconds fall into Class IIb for CRT eligibility (ESC Guidelines 2021, ACC/AHA 2022). Approximately 20% of CRT patients do not respond to the treatment (BAX 2003). Therefore, echocardiographic indices may become crucial in future patient selection for CRT.

Anatomical M-mode (AMM), based on high-frame-rate 2D echocardiography, is a new post-processing technique for quantitatively assessing myocardial function, offering high measurement reproducibility among independent observers.<sup>5-7</sup> AMM is a modification to the standard M-Mode used in 2D echocardiography and allows the user to lead the sample volume to any angle of interest, rather than have the sample volume in only a vertical position. M-mode's most predominant advantages are its high resolution, independence from the orientation of the ultrasound beam, and the precise estimation of diastolic and systolic time intervals.<sup>8</sup> Tissue harmonic imaging in AMM reduces errors compared with B-Mode echocardiography.<sup>9</sup> Color-coded AMM is a new imaging modality that allows the use of AMM and TDI in the same echocardiographic frame.

In the present study, we sought to compare the time-to-peak systolic contraction (Tc) by color-coded AMM as a trustworthy representation of myocardial contraction, the time-to-peak systolic strain (Tst) by strain rate imaging (SRI), and the time-to-peak systolic velocity (Ts) by TDI in 12 LV segments and 2 right ventricular (RV) segments in normal subjects.

## Methods

The study population was examined using standard 2D and M-mode echocardiography. The sample size was selected consecutively by performing regular echocardiography on healthy subjects referred to the echocardiographic department. Patients were excluded from the study if they exhibited wall motion abnormalities, more-than-mild valvular regurgitation, or valvular stenosis.

Echocardiographic data were obtained using a digital ultrasound machine commercially available (VIVID 7, Vingmed-General Electric, Horten, Norway, and EPIQ 7 Philips Medical System, Andover, MA), equipped with 3.5 and 4 -MHZ phased array transducers, respectively. Patients were guided to lie in the left decubitus position to optimize echocardiographic images. All measurements complied with the guidelines of the American Society of Echocardiography. The LV ejection fraction was assessed via the eyeball appraisal and the Simpson method using the multi-plane modality of a 4D probe. The study received approval from the Research Committee of the Tehran Heart Center.

The parasternal long-axis view was applied to record the conventional M-mode tracing. A cluster of digital data, including parameters such as direction, position, and timing of any single echo received from any single point of the tissue, was gathered using AMM. Hence, the operator managed to perform the AMM analysis in any direction. AMM affords a wider spectrum analysis of the LV and RV walls than traditional M-mode. More precisely, examining individual LV wall segments is considered the most significant goal of this new technique. To that end, TDI was performed on the study population in the apical 4-, 2-, and 3-chamber views.

Color-coded AMM cursor was placed at basal and mid-portion levels under TDI guidance in the apical 4-, 2-, and 3-chamber views. Thereafter, the AMM cursor was adjusted at the basal and mid-portions of each wall, at the septal and lateral walls in the apical 4-chamber view (Figure 1A), at the anterior and inferior walls in the apical 2-chamber view, and at the anteroseptal and posterior walls in the apical 3-chamber view. The cursor of AMM for the RV was placed in the apical 4-chamber view. Next, Tc was measured from the initiation point of the QRS complex to the peak contraction of each LV and RV segment by AMM with simultaneous use of color-coded TDI through offline analysis (Figure 1B). Tst was assessed in 6 basal and 6 mid-portion LV and RV segments using tissue velocity imaging aided by tissue synchronization imaging from the apical 4-, 3-, and 2-chamber views. Tst was measured in 6 basal and 6 mid-portion LV segments and 2 basal and mid-portion RV segments using tissue strain imaging in the apical 4-, 3-, and 2-chamber views. Adjustments were made to gain and filters to eliminate background noise, resulting in a clear spectral display. The sweep speed was set to 100 millimeters per second, and measurements were digitally reserved. Offline

analysis of 3 beats in a row at the end of expiration was performed, and the average of the results was calculated.

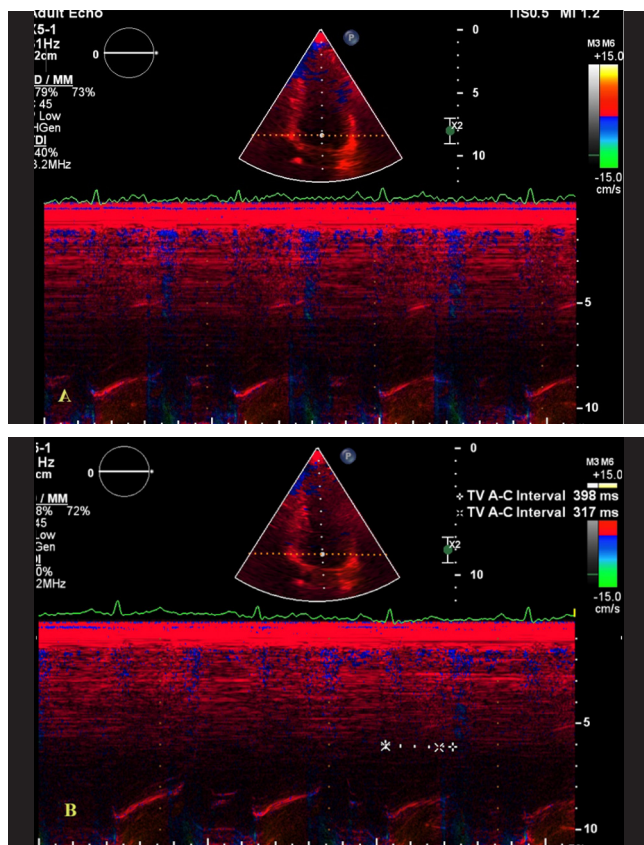


Figure 1. A) Color-coded AMM in the apical 4-chamber view in the basal segments of the septal and lateral walls. Notably, the maximum excursion of the walls occurs concomitantly with the change of color from red to blue at the end of the T wave in the lateral wall and the peak of the T wave in the septal wall.

B) Time-to-peak systolic contraction by AMM in the septal basal and lateral basal segments (317 and 398 ms, respectively).

AMM, Anatomical M-mode

The following parameters, formerly reported as LV dyssynchrony indices by the 3 different methods of TDI, SRI, and AMM, were calculated:

- 1) All segments delay: the interval between the shortest and longest Ts, Tst, and Tc in 12 LV segments
- 2) Four basal segments delay: the interval between the shortest and longest Ts, Tst, and Tc in the LV basal segments
- 3) SD calculated for all segments (Ts, Tst, and Tc-SD all segments): SD of the Ts, Tst, and Tc of 12 LV basal and mid-segments
- 4) Four basal segments SD: (Ts, Tst, and Tc-SD basal segments): SD of the Ts, Tst, and Tc of 6 LV basal segments
- 5) Septal-lateral interval: the maximum interval between peak Ts, Tst, and Tc between the interventricular septum and the lateral wall
- 6) Anteroseptal-posterior interval: absolute difference of

Ts, Tst, and Tc indices between the posterior and anteroseptal segments

The inter- and intraobserver variabilities for Ts in our lab were  $13.00 \pm 11.00\%$  and  $18.00 \pm 20.00\%$ , respectively.<sup>9</sup>

The Statistical Software Package (IBM SPSS for Windows, version 22, SPSS Inc, and Chicago, Illinois, USA) was elected to perform statistical analyses. Mean  $\pm$  SD was employed to indicate continuous variables, and categorical variables were expressed in percentages. Wherever required, continuous variables were compared using the Student t-test or the Mann-Whitney test. Categorical variables were compared using the  $\chi^2$  or the Fisher exact test. Statistically significant indices were determined by a P value of  $\leq 0.05$ . To assess the reproducibility of the data, the second observer randomly took 27 measurements for interobserver variability control. Additionally, the first observer evaluated intraobserver variability after 2 weeks. Dividing the mean gap between observations by their mean measurements allowed for calculating inter- and intraobserver variabilities.<sup>10</sup>

## Results

The average age of the subjects was  $52.17 \pm 9.80$  years, and 17/44 (41.7%) were male. The mean LV ejection fraction was  $55.05 \pm 2.22$ . The demographic, clinical, and echocardiographic characteristics of the study population are presented in Table 1.

In 12 basal and mid-portion segments of the LV and 2 RV segments, the mean Tc by AMM was significantly higher than the mean Ts by TDI ( $P < 0.001$ ) (Table 2). In 12 LV and 2 RV segments, the mean Tst was significantly higher than the mean TS by TDI ( $P < 0.001$ ) (Table 2). The mean Tc by AMM was significantly higher than the mean Tst in the anterior and inferior LV walls ( $P < 0.05$ ). In the other 8 LV and 2 RV segments, there were no significant differences between Tc and Tst.

There was a weak correlation between TDI and SRI concerning asynchrony in all LV segments, asynchrony in the basal LV segments, and the SD of all 12 LV segments (Table 3). No correlation existed between TDI and SRI regarding the anteroseptal-to-posterior wall delay and the septal-lateral wall delay (Table 3), nor was there any correlation between AMM and TDI (Table 3). A moderate correlation was observed between AMM and SRI for asynchrony in all 12 LV segments and the SD of all 12 LV segments ( $r = 0.5-0.6$ ) (Table 3).

For AMM measurements, intra- and interobserver variabilities were  $3.32 \pm 2.55$  milliseconds and  $3.43 \pm 2.40$  milliseconds (mean  $\pm$  SD). The intra- and interobserver variabilities for TDI and SRI at our center were reported previously.<sup>10,11</sup>



Table 1. Demographic, clinical, and echocardiographic characteristics of the study subjects\*

Demographic Characteristics	
Mean age (y)	52.17±9.80
Male sex	20 (41.7)
Diabetes mellitus	9 (18.8)
Hypertension	22 (45.8)
Hyperlipidemia	29 (60.4)
Cigarette smoking	4 (8.3)
Echocardiography Findings	
LV ejection fraction (%)	55.05±2.22
Left atrial size (mm)	36.06±3.55
LV end-diastolic diameter (mm)	46.02±5.04
LV end-systolic diameter (mm)	29.57±8.96
Septal wall thickness (mm)	9.74±1.03
RV diameter, mm	27.82±3.82
Mitral Regurgitation	
No	14 (29.2)
Mild	34 (70.8)
Tricuspid Regurgitation	
No	11 (22.9)
Mild	37 (77.1)
RV peak systolic velocity, cm/s	11.83±1.63
TAPSE, mm	20.77±2.84
Pulmonary artery systolic pressure, mm Hg	27.90±4.54

\*Data are presented as mean±SD or n (%).

LV, Left ventricle; RV, Right ventricle; TAPSE, Tricuspid annular plane systolic excursion

Table 2. Ts, Tst, and Tc in 12 LV and 2 RV segments\*

	TDI	SRI	AMM	TDI vs SRI	TDI vs AMM	SRI vs AMM
Septal basal	170.43±36.76	372.34±72.21	374.19±42.76	<0.001	<0.001	0.172
Septal midportion	172.17±37.53	365.19±73.55	359.48±33.04	<0.001	<0.001	0.610
Lateral basal	179.78±52.98	365.74±62.65	367.37±35.12	<0.001	<0.001	0.980
Lateral midportion	180.65±54.05	365.53±58.41	362.77±33.25	<0.001	<0.001	0.549
Anterior basal	177.33±50.15	358.72±48.48	370.46±37.23	<0.001	<0.001	0.040
Anterior midportion	177.78±48.24	351.49±43.59	363.25±32.41	<0.001	<0.001	0.041
Inferior basal	178.26±37.38	354.68±52.87	372.35±40.67	<0.001	<0.001	0.018
Inferior midportion	182.83±41.13	342.98±47.64	364.71±33.87	<0.001	<0.001	0.002
Anteroseptal basal	173.48±45.28	359.36±52.06	367.40±32.85	<0.001	<0.001	0.046
Anteroseptal midportion	172.39±50.65	352.98±50.04	361.10±34.15	<0.001	<0.001	0.230
Posterior basal	180.43±50.33	355.96±60.49	361.71±35.15	<0.001	<0.001	0.409
Posterior midportion	176.96±48.57	351.91±60.71	362.52±36.78	<0.001	<0.001	0.391
Right ventricular free wall basal	171.30±35.50	346.52±64.26	361.40±37.68	<0.001	<0.001	0.114
Right ventricular free wall mid	171.96±37.16	341.09±58.47	356.46±35.04	<0.001	<0.001	0.057

\*Data are presented as mean±SD or n (%).

Ts, Time-to-peak systolic velocity; Tst, Time-to-peak systolic strain; Tc, Time-to-peak systolic contraction time; LV, Left ventricle; RV, Right ventricle; TDI, Tissue Doppler imaging; SRI, Strain rate imaging; AMM, Anatomical M-mode

Table 3. Linear correlations between the 3 different echocardiographic methods in measuring the time-to-peak systolic velocity of the left myocardium\*

	TDI (ms)	SRI (ms)	AMM (ms)	TDI vs SRI		TDI vs AMM		SRI vs AMM	
				r	P value	r	P value	r	P value
Septal lateral delay	20 (10, 30)	20 (10, 40)	20 (10, 30)	0.204	0.190	-0.108	0.492	0.101	0.521
Anteroseptal posterior delay	20 (10, 40)	30 (20, 50)	20 (10, 40)	-0.012	0.940	-0.056	0.719	0.107	0.493
Dys all	60 (40, 80)	90 (50, 120)	50 (40, 70)	0.447	0.003	0.064	0.684	0.534	<0.001
Dys basal	50 (30, 70)	70 (40, 90)	60 (50, 80)	0.379	0.012	0.228	0.142	0.508	<0.001
SD all	19 (13, 30)	25 (16, 35)	20 (14, 25)	0.352	0.020	0.140	0.371	0.590	<0.001
SD basal	19 (14, 29)	25 (16, 36)	20 (15, 27)	0.362	0.017	0.286	0.063	0.558	<0.001

\*Data are presented as the median (25%–75% percentile).

Correlations were achieved using the Spearman correlation coefficient test.

TDI, Tissue Doppler imaging; SRI, Strain rate imaging; AMM, Anatomical M-mode



## Discussion

The results of our study revealed that in 12 LV and 2 RV segments, Tc by AMM and Tst by SRI were significantly higher than Ts by TDI. This finding may be explained by the fact that Ts by TDI reflects only time-to-peak systolic velocity and not contraction. Tc by AMM is a direct measurement of the time-to-peak systolic contraction of that segment, and Tst by SRI is close to Tc by AMM and may reflect a time near the true contraction of a segment.

Further, our results yielded a significant moderate correlation between Tc by color-coded AMM and Tst by SRI for asynchrony markers among our normal subjects. We also found that the mean Tc by AMM was significantly higher than the mean Tst in the anterior and inferior LV walls, whereas, in the other 8 LV and 2 RV segments, there was no significant difference between Tc and Tst.

Further, our results yielded a significant moderate correlation between Tc by color-coded AMM and Tst by SRI for asynchrony markers among our normal subjects. We also found that the mean Tc by AMM was significantly higher than the mean Tst in the anterior and inferior LV walls, whereas, in the other 8 LV and 2 RV segments, there was no significant difference between Tc and Tst.

AMM was used recently by Sakamaki et al<sup>12</sup> in patients with LBBB to predict their response to CRT. If an early septal point was not detected by the current M-mode because of septal to posterior wall motion delay, AMM was used to visualize an early septal displacement expanding from the scanned area to the inferoseptal wall.

Burgess et al<sup>13</sup> compared real-time 3D echocardiography and TDI for the prediction of intraventricular dyssynchrony in 100 patients suffering from ischemic cardiomyopathy and reported a poor relationship between the period from the initiation of QRS to the peak sustained systolic tissue velocity by TDI and the minimal systolic volume by real-time 3D echocardiography ( $r=0.11$ ,  $P=\text{nonsignificant}$ ). Taking into consideration the outcome of their study, real-time 3D echocardiography predicted the validation of the two techniques using AMM as an indicator of radial timing better than TDI ( $\chi^2=11.8$ ,  $P=0.001$ ).

The debate over whether the time-to-peak systolic velocity measured by TDI reflects Tc has persisted for years. As noted, systolic velocities by TDI occur during the first third of systole, while systolic strain happens in late systole, potentially serving as a better indicator of contraction. AMM is a reliable marker of actual contraction. Additionally, when utilized in color-coded TDI, AMM can more effectively visualize Tc across different LV segments, particularly in the mid segments. Consequently, we compared this method with Tst and found a moderate correlation between the two. Tc by AMM is an accurate contraction index and can significantly aid in assessing dyssynchrony before CRT implantation in patients with cardiomyopathy. Future studies pre- and post-CRT implantation are needed to evaluate the efficacy of Tc by AMM in predicting response to CRT.

Tc by AMM may be used in upcoming studies to define dyssynchrony in patients with heart failure. Tc by AMM serves as a true indicator of the contraction of the LV and RV segments and may be utilized in patients with heart failure to assess dyssynchrony. Future studies are needed to compare

the predictive value of Tc, Tst, and Ts for dyssynchrony in heart failure patients, who may benefit from CRT.

Our relatively small study population is a possible limitation of the present investigation.

## Conclusion

In 12 LV and RV segments, Tc by AMM and Tst by SRI were significantly higher than Ts by TDI. There was a significant moderate correlation between Tc and Tst for the LV asynchrony markers among our normal subjects. No correlation was observed between AMM and TDI in defining asynchrony indices. There was a weak correlation between TDI and SRI regarding asynchrony in all 12 LV segments and the SD of all 12 LV segments.

According to our study results, the evaluation of time-to-peak systolic contraction using AMM closely aligns with the time-to-peak systolic strain but diverges from the time-to-peak systolic velocity measured by TDI. Future studies may explore the role of dyssynchrony assessment through the time-to-peak systolic contraction by AMM and time-to-peak systolic strain in decision-making for CRT implantation in borderline cases. Some studies have utilized strain and speckle imaging as dyssynchrony markers before CRT (Bertolla 2006 Goresan III 2008).

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