Comparison of Transesophageal and Transthoracic Echocardiographic Measurements of Mechanism and Severity of Mitral Regurgitation in Ischemic Cardiomyopathy (from the Surgical Treatment of Ischemic Heart Failure Trial)

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Mitral regurgitation (MR) is common in ischemic heart disease and contributes to symptoms and mortality. This report compares the results of baseline transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) imaging of the mechanism and severity of functional MR in patients with ischemic cardiomyopathy in the Surgical Treatment for Ischemic Heart Failure (STICH) trial. Independent core laboratories measured both TTE and TEE images on 196 STICH participants. Common measurements to both models included MR grade, mitral valve tenting height and tenting area, and mitral annular diameter. For each parameter, correlations were assessed using Spearman rank correlation coefficients. A modest correlation was present between TEE and TTE for overall MR grade (n = 176, $r = 0.52$). For mechanism of MR, modest correlations were present for long-axis tenting height (n = 152, $r = 0.35$), tenting area (n = 128, $r = 0.27$), and long-axis mitral annulus diameter (n = 123, $r = 0.41$). For each measurement, there was significant scatter. Potential explanations for the scatter include different orientation of the imaging planes between TEE and TTE, a mean temporal delay of 6 days between TEE and TTE, and statistically significant differences in heart rate and blood pressure and weight between studies. In conclusion, TEE and TTE measurements of MR mechanism and severity correlate only modestly with enough scatter in the data that they are not interchangeable. **(Am J Cardiol 2015;116:913−918)**

In patients with heart failure due to ischemic cardiomyopathy, functional mitral regurgitation (MR) is common and has been shown to be associated with mortality.[1−5] The mechanism of functional MR is restricted leaflet closure by a combination of outward and apical tethering due to left ventricular (LV) dilation and/or regional wall motion abnormalities, reduced systolic closing force, and/or annular dilation.[6−10] In a substudy of the Surgical Treatment for Ischemic Heart Failure (STICH) trial, multiple measurements of MR mechanism, including leaflet tenting, annulus size, and LV end-systolic volume index, predicted MR severity.[11] This study was performed to compare measurements of MR mechanism and severity by transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in patients enrolled in the STICH Trial.

Methods

Of 2,136 patients enrolled in STICH, 2,006 (94%) had TTE studies measured by an independent Echocardiography Core Laboratory.[12] A TEE substudy enrolled 215 patients, of whom, 196 also had measureable TTE studies assessed by an independent TEE Core Laboratory.[11]

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Table 1
Comparison of demographic and clinical variables between patients in this mitral regurgitation substudy and the excluded STICH patients

Parameter	Excluded (n=1940)	Included (n=196)	P value
Age (years)	61.0 ± 9.5	58.9 ± 9.9	0.1690
Men	1680 (86.6%)	170 (86.7%)	0.9573
Region			<0.0001
USA	292 (15.1%)	15 (7.7%)	
Canada	257 (13.2%)	8 (4.1%)	
Europe	1040 (53.6%)	164 (83.7%)	
Asia	278 (14.3%)	9 (4.6%)	
South America	73 (3.8%)	0	
White	1490 (76.8%)	178 (90.8%)	<0.0001
Body Mass Index (kg/m^2)	27.4 ± 4.7	27.2 ± 3.9	0.7799
Myocardial infarction	1571 (81%)	171 (87.2%)	0.0311
Diabetes	738 (38%)	61 (31.1%)	0.0564
Stroke	125 (6.4%)	16 (8.2%)	0.3554
Hypertension	1160 (59.8%)	116 (59.2%)	0.8682
Hyperlipidemia	1257 (64.9%)	135 (68.9%)	0.2683
Current smoker	406 (20.9%)	39 (19.9%)	0.7325
Peripheral vascular disease	297 (15.3%)	24 (12.2%)	0.2526
Chronic kidney disease	165 (8.5%)	7 (3.6%)	0.0154
Atrial fibrillation	240 (12.4%)	20 (10.2%)	0.3765
Previous Coronary Artery Bypass	58 (3%)	2 (1%)	0.1118
Previous Percutaneous Coronary Intervention	297 (15.3%)	35 (17.9%)	0.3481
Current NYHA heart failure class			<0.0001
I	177 (9.1%)	40 (20.4%)	
II	913 (47.1%)	101 (51.5%)	
III	768 (39.6%)	51 (26%)	
IV	82 (4.2%)	4 (2%)	
Left ventricular ejection fraction	28.4 ± 8.8%	27.1 ± 8.5%	0.0604
Left ventricular end-diastolic volume index (ml/m^2)	116.6 ± 40.6	125.2 ± 42.6	0.0099
Left ventricular end-systolic volume index (ml/m^2)	83.2 ± 33.7	90.3 ± 34.4	0.0031
Mitral Regurgitation*			0.0002
None/trace	711 (36.8%)	57 (29.4%)	
Mild	892 (46.2%)	81 (41.8%)	
Moderate	278 (14.4%)	35 (18%)	
Severe	49 (2.5%)	21 (10.8%)	

* Mitral regurgitation as reported by sites.

Detailed echocardiographic measurements and results have been reported previously for both TTE and TEE findings in STICH.[11,12] All TEE studies were performed under conscious sedation; none were intraoperative. This report compares identical measurements of the mechanism and severity of MR by both TTE and TEE in the same patients. Specific measurements of MR mechanism that were common to TTE and TEE were mitral valve tenting height, mitral valve tenting area, and mitral annulus anteroposterior diameter, all performed in long-axis views. Specific measurements of MR severity were effective regurgitant orifice area (EROA) by the proximal isovelocity surface area method and overall MR grade which integrated multiple parameters, including jet size and eccentricity, EROA, mitral filling pattern, and pulmonary venous flow pattern. Because severe MR was rare, patients with moderate or severe MR were combined, giving 3 categories: none/trace, mild, and moderate/severe MR.

Data for 196 patients included in this study were descriptively summarized using the mean and standard deviation for the continuous variables and frequencies and percentages for the categorical variables. The distributions of continuous variables for the 196 patients and other STICH participants were compared using the Wilcoxon rank-sum test, and categorical variables were compared using the Pearson chi-square tests. Spearman rank correlation coefficients were used to assess the strength of association between TEE and TTE measurements on MR severity and MR mechanism. One-sample *t* tests were used to evaluate whether the mean differences of TEE and TTE measurements were significantly different from zero. All analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc., Cary, North Carolina).

Results

Table 1 lists the demographic and clinical characteristics of the patients in this MR substudy compared to the remainder of the STICH main trial population. There was a regional difference, with our patients being more likely white (90.8% vs 76.8%) and European (83.7% vs 53.6%; p <0.0001 for both). Our patients had slightly more previous myocardial infarctions (87.2% vs 81.0%, p = 0.0311) and less chronic kidney disease (3.6% vs 8.5%, p = 0.0154).

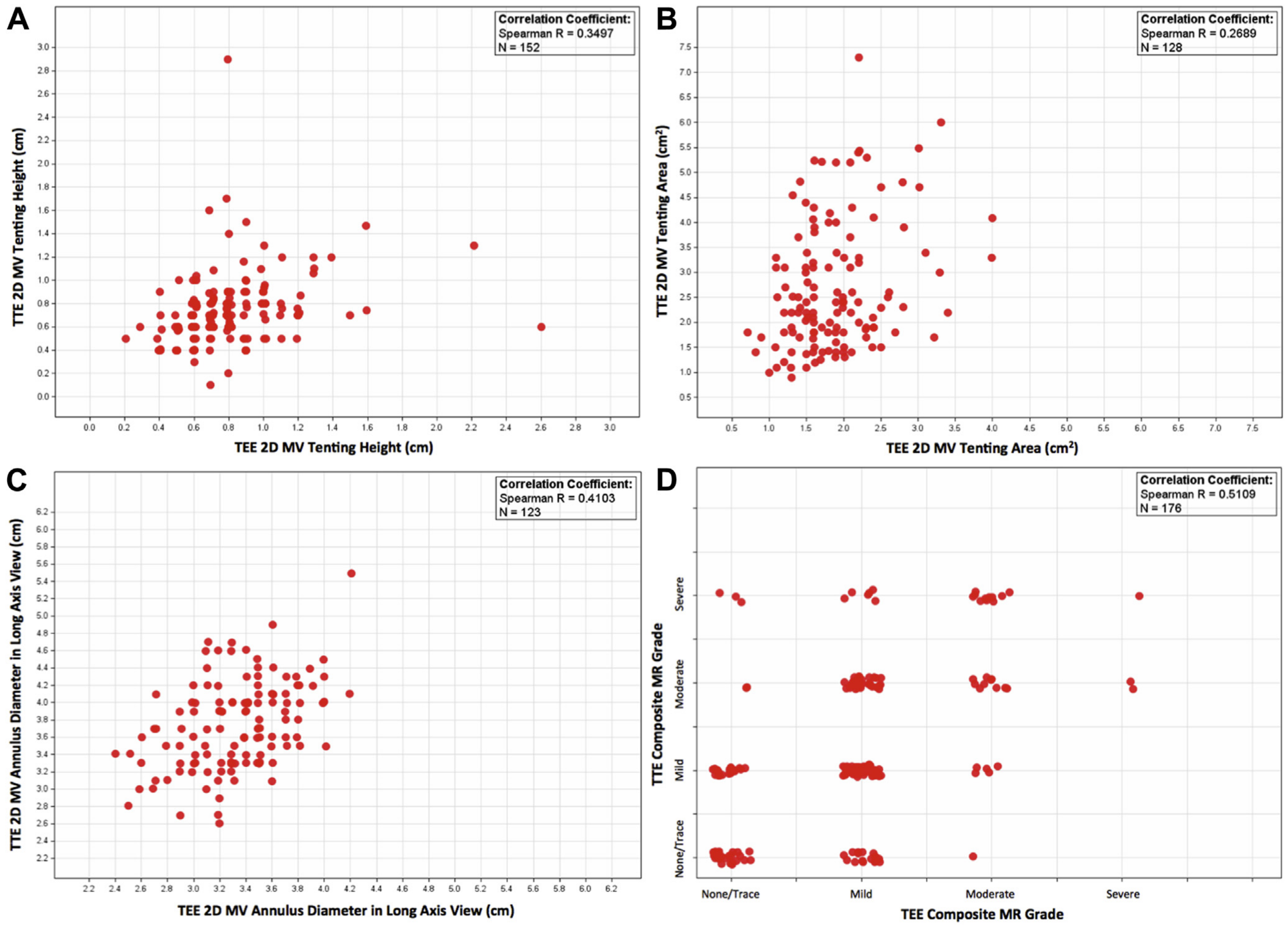

Figure 1. Scatterplots comparing TTE measurements (y-axis) to TEE measurements (x-axis) for mitral valve tenting height *(A)*, tenting area *(B)*, annulus diameter *(C)*, and MR severity grade *(D)*. Correlation coefficients are modest and there is a substantial amount of scatter present.

Table 2
Comparison of transesophageal and transthoracic echocardiographic values

Variables	N	TEE Measure (Mean ± Std)	TTE Measure (Mean ± Std)	Mean Difference (Mean ± Std)	95% Confidence Limit for Mean Difference	1-Sample T-test on Mean Difference	
						T-value	P-value
Mitral Regurgitation Grade	176	0.91 (0.70)	1.28 (0.96)	-0.37 (0.85)	(-0.50, -0.24)	-5.75	<0.0001
MV Tenting Area (cm^2)	128	1.88 (0.61)	2.70 (1.28)	-0.82 (1.24)	(-1.03, -0.60)	-7.44	<0.0001
MV Tenting Height (cm)	152	0.81 (0.31)	0.75 (0.31)	0.06 (0.37)	(0.01, 0.12)	2.11	0.0368
Long-axis Annulus Diameter (cm)	123	3.32 (0.38)	3.75 (0.51)	-0.42 (0.49)	(-0.51, -0.34)	-9.68	<0.0001
Systolic Blood Pressure (mmHg)	162	118.64 (17.47)	115.53 (16.66)	3.10 (16.41)	(0.56, 5.65)	2.41	0.0172
Diastolic Blood Pressure (mmHg)	163	75.29 (10.89)	73.10 (9.42)	2.19 (11.45)	(0.42, 3.96)	2.44	0.0157
Heart Rate (beats/minute)	167	75.37 (12.56)	71.26 (12.04)	4.11 (12.00)	(2.27, 5.94)	4.42	<0.0001
Weight (lbs)	169	172.97 (28.77)	171.71 (28.68)	1.26 (6.48)	(0.28, 2.25)	2.53	0.0124
Height (inch)	169	67.12 (3.09)	67.06 (3.16)	0.06 (1.19)	(-0.12, 0.23)	0.61	0.5394

New York Heart Association heart failure class was less severe ($p < 0.0001$), but LV volumes were larger (LV end-diastolic volume index 125.2 ± 42.6 vs 116.6 ± 40.6 ml/m^2, $p = 0.0099$; LV end-systolic volume index 90.3 ± 34.3 vs 83.2 ± 33.7 ml/m^2, $p = 0.0031$). MR severity (as graded by the sites) tended to be slightly worse in the patients in MR substudy (moderate/severe MR in 28.8% vs 16.9%, $p = 0.0002$).

Figure 1 displays the association of TEE and TTE measurements on MR grade (n = 176), tenting height (n = 152), tenting area (n = 128), and mitral annulus anteroposterior diameter (n = 123) on scatterplots. Only modest association

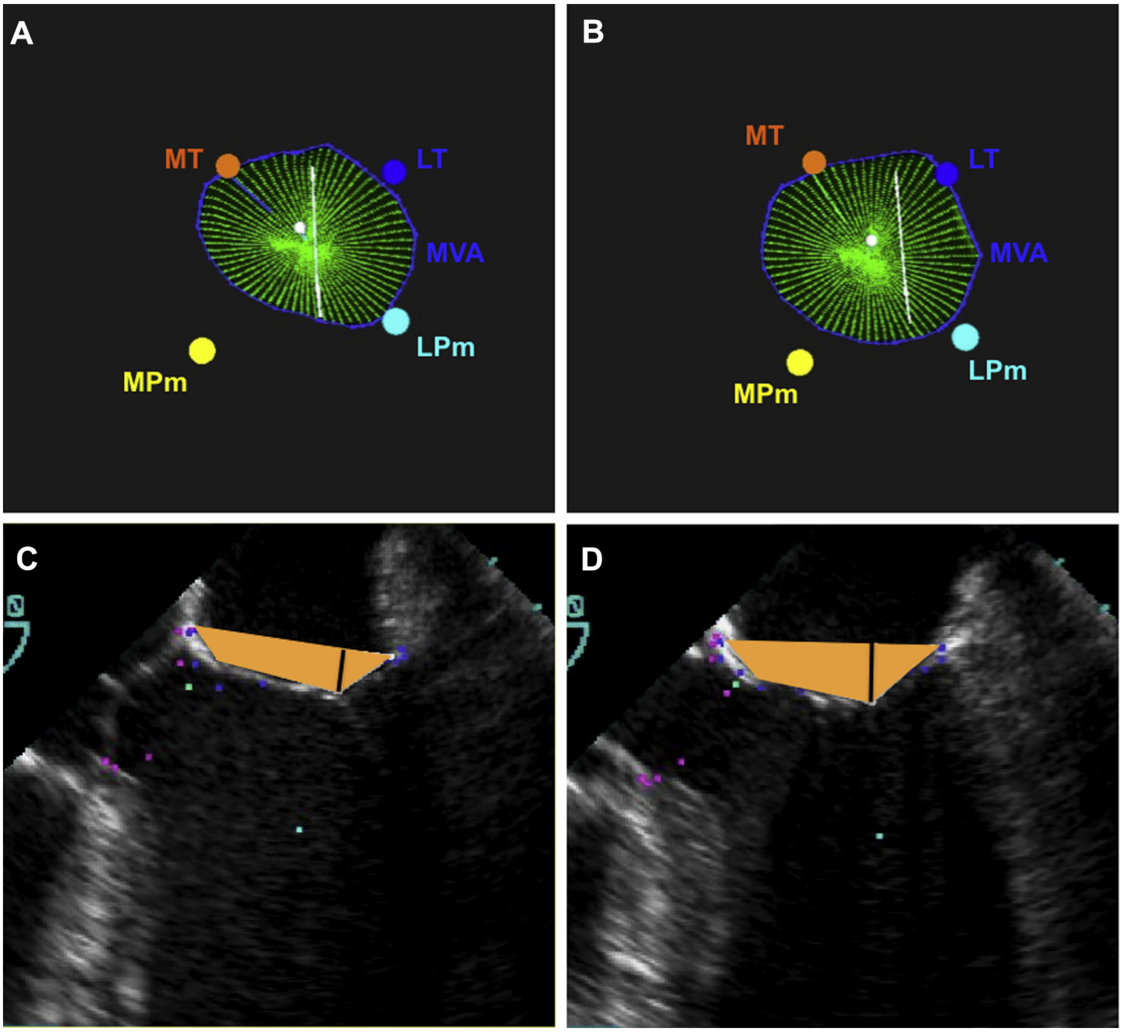

Figure 2. Three-dimensional TEE reconstruction of the mitral apparatus from a patient in this study illustrating potential malalignment and mismeasurement of tenting height and area due to off-axis imaging. *(A)* End-diastolic frame showing the mitral valve annulus (MVA) in *blue*, the medial and lateral trigones (MT and LT), and the medial and lateral papillary muscles (MPm and LPm). The *thin white line* shows that the 2D imaging plane is oriented through the center of the mitral annulus, as shown in *(C)* below. The tenting area in diastole is shown in *orange with a black line* illustrating tenting height. *(B)* End-systolic frame showing the mitral annulus to be more round than in end-diastole, but the imaging plane has moved off-center (*white line*) with the corresponding long-axis plane shown in *(D)*. Tenting area (*orange*) and tenting height (*black line*) can be affected by off-axis manual imaging using 2D technique.

between TEE and TTE measurements was observed on the scatterplots with the Spearman rank correlation coefficients ranged from 0.27 to 0.51, with considerable scatter present on the plots.

Furthermore, it was found the mean difference of all 4 TEE and TTE measures was statistically significantly different from zero by 1-sample *t* tests (Table 2). TEE measurements were significantly lower than TTE measurements on MR grade ($t = -5.75$, $p < 0.001$), tenting area ($t = -7.44$, $p < 0.001$), and mitral annulus anteroposterior diameter ($t = -9.68$, $p < 0.001$), whereas TEE measurement on tenting height was significantly greater than TTE measurement ($t = 2.11$, $p = 0.037$). EROA was not analyzed because only 16 patients had EROA by both TEE and TTE.

Given the significant differences between TTE and TEE measurements on MR grade and MR mechanism, the timing of TTE and TEE measurements was examined. TTE and TEE were performed at a mean of 6 days apart; median 1 day (interquartile range 0 to 4 days). The TTE and TEE measurements on other commonly used demographic and clinical factors were also compared. The agreement between TTE and TEE measurements on patients' body height is very strong ($n = 169$, Spearman correlation $= 0.93$), and no statistically significant difference was found between the TEE and TTE measurements on patients' height ($t = 0.61$, $p = 0.539$). However, there were statistically significant differences in systolic and diastolic blood pressure, heart rate, and body weight between TTE and TEE (Table 2).

Discussion

The primary finding of this study is that there is only modest correlation between TTE and TEE measurements of MR mechanism and severity with considerable scatter present. A number of potential explanations exist. First, imaging planes on 2-dimensional (2D) TTE or TEE may not be perfectly oriented along the same axis. This is illustrated in Figure 2, which shows a 2D and 3-dimensional (3D) image from a patient in the TEE substudy of STICH. Even slightly off-axis 2D images can result in different measurements of tenting height, tenting area, and annulus diameters. Although 3D echocardiographic imaging can properly align the imaging planes, it is not widely used in clinical practice and lacks the temporal and spatial resolution of 2D echocardiography. Second, studies were performed a median of 1 day apart, and there were significant differences in heart rate and blood pressure and weight as measured when the TTE and TEE studies were obtained. Functional MR is known to be dynamic and can vary substantially during systole and with changes in loading conditions.[13,14] Third, only 8% of patients in the STICH trial had measureable EROA by the proximal isovelocity surface area method on TTE.[12] As a result, only 16 patients had EROA by both TTE and TEE. Reasons for this included absence of a proximal flow convergence region in patients with no MR or only mild MR, inability to measure the radius due to use of variance maps or failure to properly adjust the aliasing velocity to obtain a hemispheric shape, and failure to obtain a continuous Doppler velocity profile of the MR jet. It is possible that greater use and availability of EROA may have improved the correlation in MR grading. In contrast, the low prevalence of EROA measurement in STICH, despite a TTE protocol mandating it, implies that using EROA to define severity of functional MR may not be achievable in most patients in clinical practice.

Our data support a growing consensus that MR grading is difficult by TTE. Biner et al[15] showed poor reproducibility in expert readers for measuring EROA, vena contracta width, and MR jet area to left atrial area ratio. Uretsky[16] recently showed that compared to cine magnetic resonance imaging, TTE tends to overestimate MR severity. These problems are likely to be worse in functional MR, in part because intrinsic leaflet abnormalities are absent. For example, flail leaflet is a reliable sign of severe degenerative MR but is absent in functional MR by definition. Adjunctive findings, such as left atrial enlargement and pulmonary vein flow patterns, are not as useful in functional MR as in degenerative MR because it is not clear whether observed abnormalities are due to the MR, the underlying cardiomyopathy, or a combination of both. Moreover, the regurgitant orifice in functional MR is often crescent shaped rather than circular, which can lead to significant underestimation of EROA by the proximal isovelocity surface area method.[10,17–23] Use of 3D imaging to directly measure EROA may be helpful in functional MR but was not available for use in the present study.

This study shows considerable scatter in MR grading between core laboratory expert reads of TTE and TEE data in STICH. Similar scatter was present between quantitative EROA and integrative MR grading in the STICH TTE substudy.[12] These findings underscore the need for more precise and reproducible methods for determining severity of functional MR.

Disclosures

The authors have no conflicts of interest to disclose.

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