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Myocardial bridging is associated with exercise-induced ventricular arrhythmia and increases in QT dispersion

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Background: A myocardial bridge (MB) has been associated with ventricular arrhythmia and sudden death during exercise. QT dispersion (QTd) is a measure of abnormal repolarization and may predict ventricular arrhythmia. We investigated the frequency of ventricular arrhythmias during exercise and the QTd at rest and after exercise, in patients with an MB compared to a normal cohort.

Methods: We studied the rest and stress ECG tracings of patients with an MB suspected by focal septal buckling on exercise echocardiography (EE) (Echo-MB group, N = 510), those with an MB confirmed by another examination (MB group, N = 110), and healthy controls (Control group, N = 198).

Results: The frequency of exercise-induced premature ventricular contractions (PVCs) was significantly higher in the Echo-MB and MB groups compared with the Control group (both $p < .001$). In all, 25 patients (4.9%) in the Echo-MB group, seven patients (6.4%) in the MB group and no patients in the Control group had exercise-induced nonsustained ventricular tachycardia (NSVT). There was no difference in the baseline QTd between the groups. In the Echo-MB and MB groups, QTd postexercise increased significantly when compared with baseline (both $p < .001$). Patients with NSVT had a higher frequency of male gender and an even greater increase in QTd with exercise compared with the non-NSVT group.

Discussion: There is an increased frequency of exercise-induced PVCs and NSVT in patients with MBs. Exercise significantly increases QTd in MB patients, with an even greater increase in QTd in MB patients with NSVT. Exercise in MB patients results in ventricular arrhythmias and abnormalities in repolarization.

KEYWORDS
myocardial bridging, QT dispersion, ventricular arrhythmia

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1 | INTRODUCTION

A myocardial bridge (MB) is a congenital coronary variant, mostly affecting the left anterior descending artery (LAD). It is defined as a segment of the epicardial coronary artery that is covered by myocardium. Autopsy reports have shown the prevalence of myocardial bridging to be 5%–86%, with a mean of 25% (Mohlenkamp, Hort, Ge, & Erbel, 2002). The rate of detection of MBs varies depending on the cohort studied and the type of imaging test performed. Coronary angiography (CA) is the least sensitive test, with a prevalence of 0.5%–12% (Soran, Pamir, Erol, Kocakavak, & Sabah, 2000). Intravascular ultrasound (IVUS) is a gold standard, with a detection rate of 20%–25%, demonstrating systolic compression and a specific echolucent "half-moon" sign (Ge et al., 1999). Coronary computed tomography angiography (CCTA) utilizing multi-slice scanners can detect intramyocardial segments at a rate similar to IVUS (Ishikawa et al., 2006). Exercise echocardiography (EE) is a noninvasive examination where the presence of an MB is associated with a characteristic focal buckling of the septum with apical sparing during the end-systolic to early-diastolic phase (Lin et al., 2013; Siciliano, Migliore, & Piovesana, 2014). Although MBs are often considered benign and most patients with MBs are asymptomatic, MBs have been associated with ventricular arrhythmias and sudden death during exercise (Cutler & Wallace, 1997; Feld et al., 1991; Ishikawa, Kawawa, Kohda, Shimada, & Ishii, 2011). This may be a result of local ischemia, as suggested by the reduction in diastolic fractional flow reserve (dFFR) demonstrated during dobutamine stress testing (Escaned et al., 2003; Lin et al., 2013). Prior studies in patients without an MB have suggested that QT dispersion (QTd) reflects abnormal repolarization of the myocardium and an increased QTd may predict ventricular arrhythmia (de Bruyne et al., 1998; Okin et al., 2000; Stoletniy, Pai, Platt, Torres, & Pai, 1999). Previous studies have reported a significant increase in QTd and repolarization abnormalities during exercise in patients with MB when compared with a control group (Aksan et al., 2015; Barutcu et al., 2004). The aim of this study was to investigate the frequency of premature ventricular contractions (PVCs) and nonsustained ventricular tachycardia (NSVT), as well as changes in QTd, during exercise in patients with an MB compared with healthy controls.

2 | METHODS

2.1 | Study population

We retrospectively identified all patients with a suspected MB on EE performed in the Stanford Hospital Echocardiography Laboratory from January 2011 to December 2013. The MB patients were referred for evaluation of chest pain, dyspnea on exertion, or palpitations. We excluded patients with left ventricular dysfunction (left ventricular ejection fraction (LVEF) <50%), resting wall motion abnormalities, inducible wall motion abnormalities suggestive of fixed coronary artery disease, valvular heart disease, pulmonary hypertension, prior cardiac surgery, left ventricular hypertrophy, bundle branch block, atrial fibrillation, a paced rhythm, congenital heart disease, a history of coronary artery disease, use of antiarrhythmic drugs (Class I and Class III), and poor quality ECGs. All echocardiographic studies of the remaining MB patients were re-reviewed by a senior echocardiographer (IS) to confirm the initially reported finding. In the case of disagreement between the initial interpreting echocardiographer and the re-reviewer, a consensus between the two readers was established. Subsequently, we defined the following study groups: Patients with a suspected MB on EE by the presence of focal septal buckling (Echo-MB group, 510 patients) and patients with a suspected MB on EE (124 patients) who underwent a second imaging study (CA, IVUS, or CCTA) in which the MB was confirmed (MB group, 110 patients). Normal exercise echocardiograms from consecutive patients with structurally normal hearts, from the same Echo Lab data base were re-reviewed by one echocardiographer (IS) and if disagreement with the initial reader, a consensus was established. These patients were asymptomatic but referred for stress testing as a screening test for cardiovascular disease, family history of heart disease, or as prospective donors of kidney transplantation (Control group, 198 patients). None of the patients in the control group had focal septal buckling on EE. For further analysis, we also combined the patients in the Echo-MB and MB groups, and then divided them by the presence or absence of NSVT (32 and 588 patients, respectively) (Figure 1). The retrospective review of the records was approved by the Stanford Institutional Review Board.

2.2 | Exercise echocardiography (EE)

EE was performed according to the American Society of Echocardiography (ASE) recommendations (Pellikka, Nagueh, Elhendy, Kuehl, & Sawada, 2007). All subjects performed the Bruce treadmill protocol test, with a target heart rate of 85% of maximum predicted for age (Bruce & Lovejoy, 1949). The blood pressure (BP) was noninvasively recorded with an automated BP monitor before, during, and after exercise.

Standard echocardiographic views, including parasternal long and short axes, and apical 2-, 3-, and 4-chamber views, were obtained in two-dimensional (2D) scan planes. LVEF was derived from the modified Simpson method according to the ASE guidelines (Lang et al., 2015). An MB was defined as present when there was stress-induced focal septal buckling with apical sparing during the end-systolic to early-diastolic phase (Lin et al., 2013). All echocardiographic studies were performed using an iE33 echo system (Philips Healthcare, Andover, MA). An average of 5–10 beats per loop was recorded at rest and immediately after stress.

During exercise treadmill testing, 12-lead ECGs were monitored continuously and recorded at 1 min intervals. The ECGs were recorded with a standard digital recorder at a paper speed of 25 mm/s and amplitude 10 mm/mV. All patients were monitored postexercise until their vital signs reached baseline.

2.3 | Measurement of ventricular arrhythmia

We examined the frequency of PVCs and NSVT during exercise in each patient. In patients who had PVCs, we defined frequent PVCs as
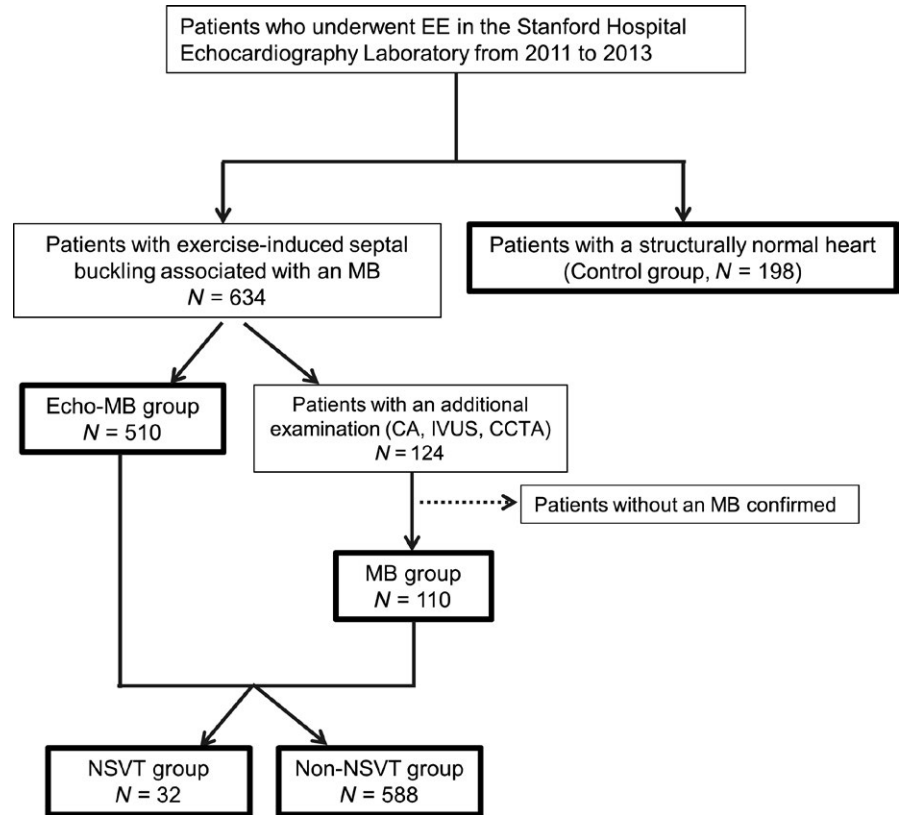
FIGURE 1 Study population. The study patients were divided into the following groups; (1) Echo-MB group, (2) MB group, and (3) Control group. Additionally, the patients of Echo-MB group and MB group were divided into an NSVT group and non-NSVT group. CA, coronary angiography; CCTA, coronary computed tomography angiography; EE, exercise echocardiography; IVUS, intravascular ultrasound; MB, myocardial bridge; NSVT, nonsustained ventricular tachycardia

PVCs >0.22/min and infrequent PVCs as PVCs ≤0.22/min (Morshedi-Meibodi, Evans, Levy, Larson, & Vasan, 2004). NSVT was defined as ≥3 consecutive ventricular beats at a rate ≥120 beats/min.

2.4 | Measurement of QT interval duration and dispersion (QTd)

The QT interval duration in all leads of a surface 12-lead ECG was measured at baseline and after treadmill exercise at 1 min of recovery in each group. All measurements were performed manually with digital calipers and a magnifying glass. The QT interval duration was measured from the beginning of the QRS complex to the end of the T wave in each lead. The maximum slope intercept method was used to define the end of the T wave. QT dispersion (QTd) was defined as the maximum minus the minimum QT interval. The corrected QT dispersion (QTcd) was measured according to Bazett's formula (Ahnve, 1985). We also compared the change in QTd (ΔQTd) with exercise, defined as the QTd postexercise minus the QTd at rest, in each group. In the same way, we compared the change in QTcd (ΔQTcd) with exercise, defined as the QTcd postexercise minus the QTcd at rest.

The ECG measurements of QTd were performed by one observer (M.N.). A random sample of 10% from each of the three study groups was re-measured by a second observer (V.P.) who was unaware of the first observer's results. In addition, both observers were blinded to which study group the patients belonged. Interobserver variability of QTd measurement was 19%, similar to previous reports (Malik & Batchvarov, 2000).

2.5 | Statistical analysis

Statistical analyses were performed using SPSS statistical software (Version 22.0; IBM Corporation, Armonk, NY). Data are expressed as mean value ± standard deviation (SD) or number (%). For comparison of categorical variables, the chi-square test or the Fisher's exact test was performed as appropriate. Continuous variables between two groups were analyzed by the unpaired Student t-test or Mann–Whitney U-test. We analyzed the difference in QTd between the pre- and post-exercise ECGs using paired t-test or Wilcoxon signed-rank test in each group. A p value <.05 was considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

The clinical characteristics of each group are summarized in Table 1. There were no significant differences between the groups except that compared with controls, there were more women in the Echo-MB and MB groups, and the patients in the MB group were younger. In the Control group, there were no patients who complained of symptoms during exercise. However, in the Echo-MB group and MB groups, 195 patients (38%) and 67 patients (61%), respectively, complained of symptoms during exercise.

3.2 | Ventricular arrhythmia

The exercise treadmill test results of each group are described in Table 2. There were no differences between the three groups in

TABLE 1 Patient characteristics

Variables	Echo-MB group N = 510	p value	MB group N = 110	p value	Control N = 198
Age	53.5 ± 14.4	.009*	47.6 ± 16.9	.434	52.6 ± 13.8
Male gender, n (%)	247(48.4)	<.001*	38(34.5)	.030*	114 (57.6)
BMI	26.1 ± 5.0	.054	25.5 ± 5.8	.090	26.8 ± 4.4
SBP (mm Hg)	123.0 ± 18.0	.169	119.6 ± 16.6	.614	122.2 ± 15.6
DBP (mm Hg)	73.4 ± 11.5	.561	72.0 ± 9.2	.450	72.7 ± 11.4
MBP (mm Hg)	89.9 ± 12.1	.304	87.8 ± 10.2	.467	89.2 ± 11.6
Beta-blocker	83(16.3)	.507	18(16.4)	.420	27 (13.6)
CCB	47(9.3)	.276	10(9.1)	.101	27 (13.6)
ACE-I/ARB	97(19.2)	.179	26(23.6)	.591	34 (17.2)
LVEF (%)	62.2 ± 4.3	.053	62.0 ± 4.0	.058	62.9 ± 3.6

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; CCB, calcium channel blocker; ACE-I/ARB, angiotensin-converting-enzyme inhibitor/angiotensin receptor blocker; LVEF, left ventricular ejection fraction.

*Statistically significant to $p < .05$. p values represent difference between Echo-MB or MB group and control group.

TABLE 2 Exercise testing, ventricular arrhythmia, and QT interval duration/dispersion results

Variables	Echo-MB group N = 510	p value	MB group N = 110	p value	Control N = 198
Maximum heart rate (beats/min)	159.2 ± 19.5	.517	163.2 ± 20.4	.183	161.5 ± 21.4
% heart rate achieved	95.7 ± 9.9	.146	94.8 ± 9.3	.403	96.4 ± 9.3
Peak SBP (mm Hg)	166.1 ± 23.6	.828	163.6 ± 22.6	.116	163.0 ± 22.2
Peak DBP (mm Hg)	75.7 ± 14.3	.222	76.2 ± 15.4	.159	74.1 ± 14.0
Peak MBP (mm Hg)	105.4 ± 14.6	.341	105.9 ± 14.6	.080	103.7 ± 14.3
PVCs, n (%)	254 (49.8)	<.001*	50 (45.5)	<.001*	11 (5.6)
NSVTs, n (%)	25 (4.9)	.001*	7 (6.4)	<.001*	0 (0)
Baseline					
Heart rate (bpm)	73.3 ± 13.3	.003*	73.8 ± 13.8	.06	76.9 ± 14.1
QT max (ms)	383.6 ± 29.7	.213	382.5 ± 31.1	.087	380.3 ± 26.5
QT min (ms)	356.3 ± 28.4	.417	354.4 ± 29.6	.115	353.0 ± 26.5
QTd (ms)	27.3 ± 8.7	.190	28.2 ± 12.6	.576	27.3 ± 5.6
QTcd (ms)	30.3 ± 10.1	.350	31.1 ± 14.6	.778	30.6 ± 7.0
Postexercise					
Heart rate (bpm)	122.2 ± 18.1	<.001*	123.7 ± 18.9	.008*	129.9 ± 20.8
QT max (ms)	312.0 ± 24.9	.002*	307.8 ± 26.8	<.001*	299.8 ± 24.4
QT min (ms)	275.5 ± 22.9	.968	270.9 ± 24.8	.021*	271.2 ± 23.7
QTd (ms)	36.5 ± 10.2	<.001*	36.8 ± 11.2	<.001*	28.6 ± 7.2
QTcd (ms)	51.4 ± 14.5	<.001*	52.0 ± 16.1	<.001*	37.4 ± 9.1

bpm, beats per minute; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.

*Statistically significant to $p < .05$. p values represent difference between Echo-MB or MB group and control group.
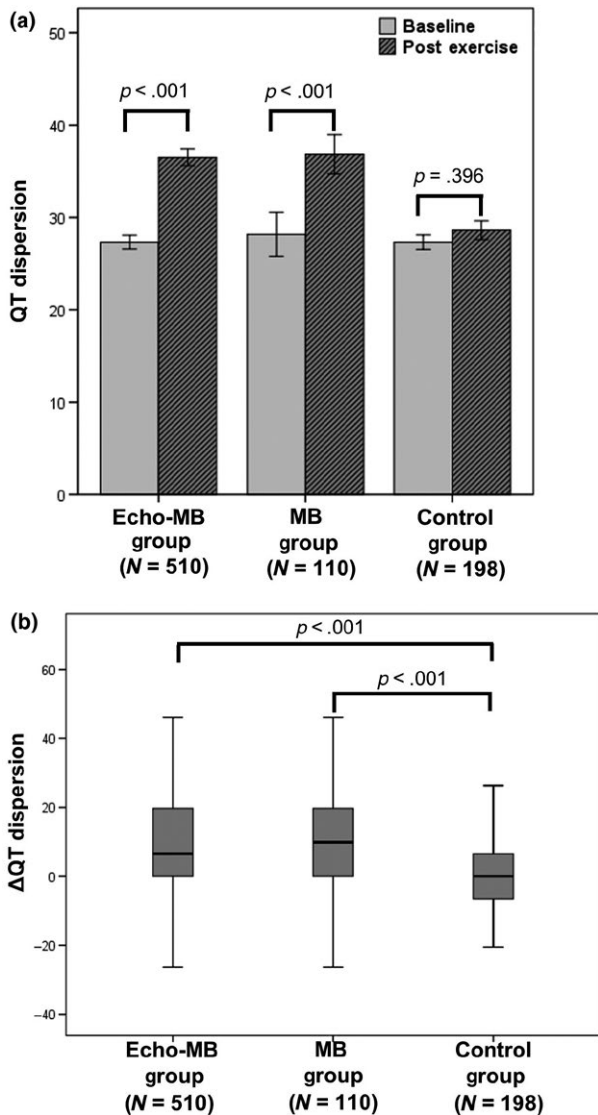
FIGURE 2 (a) Change in QTd (ΔQTd) with exercise in each group. Patients in the Echo-MB and MB groups both had a significant increase in their QTd from baseline to postexercise (p < .001), whereas there was no significant change in the QTd with exercise in the Control group. Error bars represent mean with a 95% confidence interval. (b). Comparison of ΔQTd between the groups. The ΔQTd was significantly greater in the Echo-MB group compared with the Control group and in the MB group compared with the Control group (both p < .001). ΔQTd = postexercise QTd − baseline QTd

TABLE 3 Clinical characteristics of patients with NSVT and without NSVT in the combined Echo-MB and MB groups

Variables	NSVT N = 32	Non-NSVT N = 588	p value
Age	57.2 ± 12.7	52.2 ± 15.1	.067
Male gender, n (%)	23 (71.9)	262 (44.6)	.003[*]
BMI	26.7 ± 3.6	26.0 ± 5.2	.434
SBP (mm Hg)	126.4 ± 18.0	122.2 ± 17.7	.183
DBP (mm Hg)	71.6 ± 8.9	73.2 ± 11.3	.313
MBP (mm Hg)	89.9 ± 9.6	89.5 ± 11.9	.884
Beta-blocker	9 (29.0)	92 (15.7)	.076
CCB	4 (12.9)	53 (9.0)	.517
ACE-I/ARB	9 (29.0)	114 (19.5)	.246
LVEF (%)	61.7 ± 4.1	62.2 ± 4.3	.475

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; CCB, calcium channel blocker; ACE-I/ARB, angiotensin-converting-enzyme inhibitor/angiotensin receptor blocker; LVEF, left ventricular ejection fraction.
[*]Statistically significant to p < .05.

terms of the maximum heart rate achieved, the percentage of maximal predicted heart rate achieved, and the peak blood pressures. The frequency of exercise-induced PVCs was significantly higher in the Echo-MB and MB groups (49.8% and 45.5%, respectively) compared with the Control group (5.6%). In the Echo-MB group, 127 patients (25%) had frequent PVCs, including 25 with bigeminy and 14 with trigeminy, and 127 patients (25%) had infrequent PVCs. In the MB group, 23 patients (21%) had frequent PVCs, including four with bigeminy and two with trigeminy, and 27 patients (25%) had infrequent PVCs. In the Control group, only two patients (0.5%) had frequent PVCs, with no bigeminy or trigeminy, and nine patients (4.5%)

had infrequent PVCs. Likewise, 25 patients (4.9%) in the Echo-MB group and seven patients (6.4%) in the MB group had exercise-induced NSVT, whereas no patient in the Control group had NSVT.

3.3 | QT dispersion and corrected QT dispersion

The baseline QTd and QTcd were not different between the groups, whereas the postexercise QTd and QTcd were significantly higher in the Echo-MB and MB groups compared with the Control group (Table 2). With exercise, the Echo-MB and MB groups had a significant increase in QTd (p < .001), whereas QTd did not significantly change from baseline to postexercise in the Control group (Figure 2a). Compared with the Control group, the ΔQTd with exercise was significantly greater in the Echo-MB (9.2 ± 12.7 vs. 1.3 ± 7.0, p < .001) and MB (8.6 ± 16.5 vs. 1.3 ± 7.0, p < .001) groups (Figure 2b). The ΔQTcd with exercise was significantly greater in the Echo-MB (21.1 ± 17.0 vs. 6.8 ± 8.1, p < .001) and MB groups (20.9 ± 21.7 vs. 6.8 ± 8.1, p < .001) compared with the Control group.

3.4 | Comparing patients with NSVT and without NSVT in the Echo-MB and MB groups

The combined Echo-MB and MB groups were divided into two groups based on whether or not they developed NSVT with exercise. There were no significant differences between the NSVT and the non-NSVT groups except there were a higher proportion of men in the NSVT group (Table 3). The maximum heart rate achieved, the percentage of maximal predicted heart rate achieved, and the peak blood pressures were not significantly different between the groups. Additionally, the incidence of symptoms and ST-segment depressions during exercise treadmill testing was not different between the groups (Table 4).

TABLE 4 Exercise testing and QT interval duration/dispersion results of patients with NSVT and without NSVT in the combined Echo-MB and MB groups

Variables	NSVT N = 32	Non-NSVT N = 588	p value
Maximum heart rate (beats/min)	155.0 ± 21.1	160.2 ± 19.7	.147
% heart rate achieved	95.6 ± 14.0	95.6 ± 9.6	.967
Peak SBP (mm Hg)	166.2 ± 20.7	165.6 ± 23.6	.902
Peak DBP (mm Hg)	75.7 ± 17.3	75.8 ± 14.3	.956
Peak MBP (mm Hg)	105.8 ± 16.2	105.8 ± 14.5	.976
Symptoms during exercise testing	10 (31.3)	252 (42.9)	.270
ST segment depression ≥1 mm during exercise testing	4 (12.5)	93 (15.8)	.804
Baseline			
QT max (ms)	391.2 ± 24.9	383.0 ± 30.1	.129
QT min (ms)	363.5 ± 24.2	355.9 ± 28.6	.145
QTd (ms)	27.8 ± 9.0	27.5 ± 9.6	.863
QTcd (ms)	29.9 ± 10.1	30.1 ± 11.1	.786
Postexercise			
QT max (ms)	321.3 ± 27.5	310.7 ± 25.0	.021[*]
QT min (ms)	275.3 ± 25.8	274.7 ± 23.2	.888
QTd (ms)	46.1 ± 9.6	36.0 ± 10.2	<.001[*]
QTcd (ms)	64.3 ± 14.7	50.8 ± 14.5	<.001[*]

SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.

[*]Statistically significant to $p < .05$.

While there were no significant differences in the baseline QTd and QTcd between the groups, the QTd and QTcd postexercise were significantly higher in the NSVT group compared with the non-NSVT group (Table 4). In both groups, QTd postexercise increased significantly when compared to baseline values (Figure 3a). However, the ΔQTd with exercise was significantly greater in the NSVT group compared with the non-NSVT group (18.3 ± 12.9 vs. 8.5 ± 13.4, $p < .001$) (Figure 3b). The ΔQTcd with exercise was significantly greater in the NSVT group compared with the non-NSVT group 34.4 ± 16.7 vs. 20.7 ± 17.7, $p < .001$).

4 | DISCUSSION

The major findings of the present study are as follows: (1) Patients with an MB have a significantly higher frequency of exercise-induced PVCs and NSVT than patients without an MB; (2) Patients with an MB have a significantly higher postexercise QTd and a significantly greater ΔQTd with exercise than patients without an MB; (3) Patients with an MB and NSVT during exercise are more often men, and have a
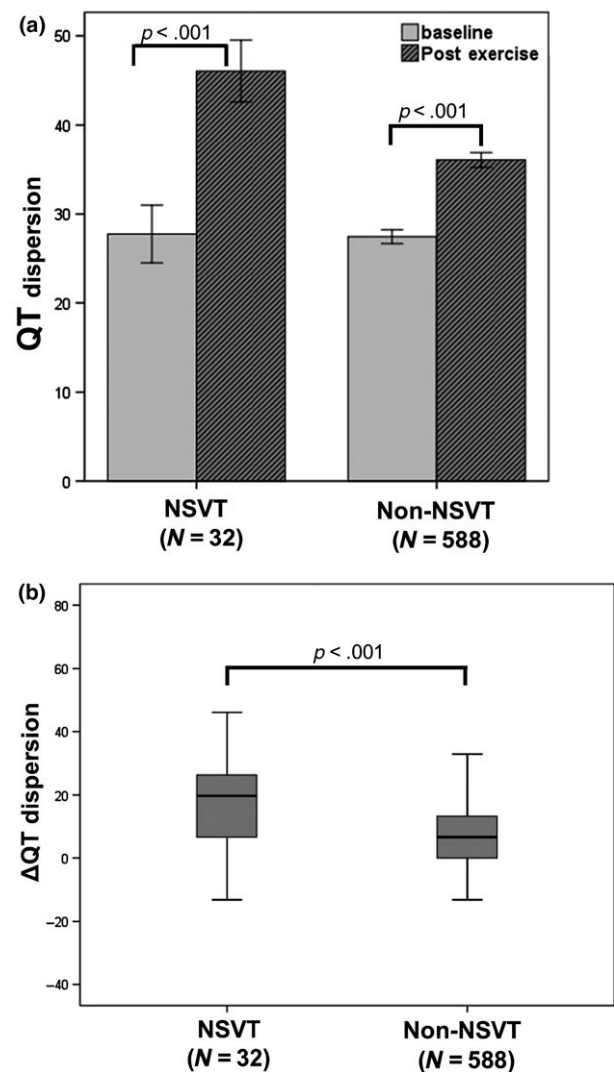

FIGURE 3 (a) Change in QTd (ΔQTd) with exercise in patients with NSVT and without NSVT. In both groups, QTd was significantly increased postexercise when compared with baseline values ($p < .001$). Error bars represent mean with a 95% confidence interval. NSVT, nonsustained ventricular tachycardia. (b) Comparison of ΔQTd in patients with NSVT and without NSVT. The ΔQTd was significantly greater in those with NSVT compared with those without NSVT ($p < .001$). NSVT, nonsustained ventricular tachycardia; ΔQTd, postexercise QTd – baseline QTd

significantly higher postexercise QTd and a significantly greater ΔQTd with exercise, than patients with an MB who do not have NSVT during exercise.

Previous studies have reported adverse clinical outcomes in patients with exercise-induced frequent PVCs (Dewey et al., 2008; Lee, Hemingway, Harb, Crake, & Lambiase, 2012). Our study demonstrated that the frequency of exercise-induced PVCs and NSVT is significantly increased in patients with an MB. Nearly, half of the patients in the Echo-MB and MB groups had exercise-induced PVCs (49.8% and 45.5%, respectively), and NSVT was commonly present (4.9% and 6.4%, respectively), whereas 5.6% of patients in the Control group had PVCs, and none had NSVT.

The main angiographic finding of an MB is systolic narrowing of a coronary artery, or the "milking effect." However, it has been shown by IVUS that this systolic narrowing extends into diastole and can take up to half of the diastolic filling period, at resting heart rates, before the vessel reaches maximal cross-sectional area (Ge et al., 1994), leading to inadequate blood flow during the time of the cardiac cycle when the majority of coronary flow occurs. Tachycardia will further decrease diastolic filling time and potentially increase regional variation in ventricular repolarization, making MB patients particularly vulnerable to develop ventricular arrhythmia during exercise. In addition, other mechanisms of myocardial ischemia leading to ventricular arrhythmia, such as endothelial dysfunction and atherosclerotic plaque in the LAD upstream from the MB, with or without thrombus formation, have been reported in patients with an MB (Alegria, Herrmann, Holmes, Lerman, & Rihal, 2005; Bourassa, Butnaru, Lespérance, & Tardif, 2003; Yamada et al., 2016).

The QTd is a simple noninvasive measurement and an effective marker of heterogeneous repolarization. An increased QTd reflects regional variations in ventricular repolarization and is believed to be an important risk factor for fetal ventricular arrhythmia and sudden death (de Bruyne et al., 1998; Tavernier, Jordaens, Haerynck, Derycke, & Clement, 1997). Similar to previous reports (Aksan et al., 2015; Barutcu et al., 2004), we demonstrated that QTd is significantly increased by exercise in patients with an MB. In addition, we present in this study the first evidence of the increased frequency of exercise-induced ventricular arrhythmias and the relationship between QTd and NSVT in MB patients. Specifically, we have shown that patients with an MB who develop NSVT during exercise have a significantly higher postexercise QTd, as well as a greater ΔQTd with exercise compared not only to control patients, but even to patients with an MB who do not develop NSVT during exercise.

The finding that there are more significant changes in QTd in patients with MBs who develop NSVT during exercise compared with MB patients who do not, supports the concept that not all myocardial bridges are the same. Some are clearly benign, whereas others have the potential to cause life-threatening arrhythmia. Our data suggest that in patients with a known MB undergoing exercise testing, it is preferable to note the frequency of PVCs and NSVT, and to measure the postexercise QTd and ΔQTd regardless of the presence or absence of symptoms during exercise. Moreover, in patients undergoing an exercise treadmill test, suspicion of an MB should be raised by the presence of frequent PVCs and/or NSVT, as well as a large increase in QTd. In this situation, septal buckling with apical sparing on stress echocardiography might provide additional information that could subsequently be confirmed with another imaging test, such as CCTA. In particular, close follow-up might be needed for male patients who have a significant increase in their postexercise QTd compared to baseline, due to an increased vulnerability to develop exercise-induced NSVT.

The observation that QTd was increased in MB patients who developed NSVT during exercise treadmill testing despite a lack of consistent clinical findings suggestive of cardiac ischemia, such as symptoms of angina or ST-segment depressions of ≥1 mm, is worth noting. A previous report suggested a peak exercise QTd >60 ms is diagnostic of significant coronary artery disease in women (sensitivity of 70% and specificity of 95%) (Stoletniy & Pai, 1997). In our study, the QTd in the NSVT group was 38.6 ms postexercise and the QTcd was 52 ms postexercise. We likely had a lower value than the previous report because of differences in our study population, as well as our methodology. We included men, and measured postexercise QTd at 1 min of recovery rather than at peak exercise. In addition, ischemia from MBs is thought to be focal and, therefore, may affect a smaller territory than a fixed coronary lesion. This may also explain why there was a lack of ST-segment depressions in most of our patients. At the same time, the diagnostic accuracy of ischemia with standard exercise treadmill testing criteria is not ideal, and it is known that patients with an MB who do not have significant ST-segment depressions may still have myocardial ischemia (Gawor et al., 2011). We suspect that even patients without significant ST-segment changes have abnormal repolarization and an increased QTd due to focal ischemia (Koide, Yotsukura, Yoshino, & Ishikawa, 2000). In the future, the development of formal cutoff values for QTd and ΔQTd may be helpful. Nevertheless, ECG-based QT dispersion is a temporal measurement of heterogeneity and does have recognized limitations in determining the end of the T wave. Measurement of the T-peak to T-end period is another time-based interval; however, it has similar shortcomings in determining the end of the T wave, resulting in less than ideal reproducibility. Vector-cardiographic approaches to assess heterogeneity of the R- and T waves represent a morphologic technique and may prove to have superior accuracy; however, more studies that are clinical are needed to determine its value in predicting vulnerability to lethal cardiac arrhythmias (Verrier & Huikuri, 2017).

Our study has several limitations. First, we used focal septal buckling with apical sparing on EE as a marker for the presence of an MB, but the accuracy of this screening test is not yet known. In those patients who had another imaging modality, 89% of the Echo-MBs were confirmed. While this is a substantial percentage, it suggests that some of the patients in the Echo-MB group likely did not have an MB. Still, given the similarity in data between the Echo-MB and MB groups, we are confident that the Echo-MB group captured a high percentage of patients with an MB and that the findings would have only been strengthened by the ability to confirm MBs in those patients. Further studies will be necessary to establish the sensitivity and specificity of EE to diagnose an MB. Second, the patients in the control group also did not have additional imaging studies to exclude the presence of an MB. However, their very normal EE suggests that even if an MB was present, it is inconsequential. Third, although the MB patients and the control patients appeared to be similar on multiple variables, there was no matching performed because of the limited sample size. Therefore, there could be unappreciated confounding factors present. Fourth, with regard to QT dispersion, the interobserver variability may seem high but it is in the range of previously published papers and the interobserver variability was spread equally in all groups. Finally, development of myocardial ischemia from an MB depends on several factors, including the length and depth of the MB, as well as the force of cardiac contractility (Ge et al., 1994). We did not investigate these

parameters, nor did we directly demonstrate ischemia in the MB patients. Therefore, we cannot demonstrate with certainty that all PVCs are due to an MB. Further investigation into the relationship between the degree of myocardial ischemia from an MB and the development of ventricular arrhythmias is needed.

5 | CONCLUSION

In this study, there was an increased incidence of exercise-induced PVCs and NSVT in patients with an MB. Exercise significantly increases QTd and ΔQTd in patients with an MB, and this increase is most notable in MB patients who develop NSVT with exercise. Evaluating the frequency of PVCs and NSVT, as well as the QTd and ΔQTd, during exercise stress testing, even in the absence of symptoms and ST-segment depressions, may help risk stratify patients with an MB.

DISCLOSURES

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