



ECG changes and markers of increased risk of arrhythmia in patients with myocardial bridge

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ABSTRACT

Background: The clinical significance and prognosis of myocardial bridge (MB) is still a matter of debate.

Objectives: To assess the novel ECG markers of T peak-to-end (Tp-e) interval, transmural dispersion of repolarization (TDR), is assessed by Tp-e/QT ratio, and index of electrophysiological index (iCEB), is defined by QT/QRS ratio and changes (ST-T changes) in MB patients.

Patients and methods: Forty one patients who were diagnosed as having MB (MB group) and other 41 patients without MB (non-MB group) at multi-detector CT (MDCT) exam matched by age, sex were enrolled in the study. **Results:** iCEB was significantly increased in MB group in comparison to non-MB group particularly in patients with no coronary atherosclerosis (5.3 Vs 4.5, $p = 0.04$). Tp-e and TDR values were decreased in MB in comparison to non-MB patients particularly in patients with coronary atherosclerosis (69 Vs 80, $p = 0.003$ and 0.18 Vs 0.2, $p = 0.01$ respectively). Isolated T inversion in V1 was observed more in MB compared to non-MB patients (58% Vs 5%, $p \leq 0.0001$) particularly in patients without coronary atherosclerosis.

Conclusion: MB patients have shown decreased Tp-e and TDR markers particularly in MB patients with coronary atherosclerosis.

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Introduction

Myocardial bridge (MB) is an anatomical variant of coronary artery course occurs when a segment of the artery is enclosed partially or completely by band of myocardial muscle fibers most commonly in the left anterior descending artery leading to systolic compression of the bridged segment and hemodynamic changes. [1,2]

In the literature, several case reports linked MB presence with angina, myocardial infarction, malignant arrhythmias and sudden death [1,3].

However, the clinical significance and long term adverse events occurrence of MB presence is still a matter of debate.

Recently, several novel ECG markers including the T peak-to-end (Tp-e) interval, transmural dispersion of repolarization (TDR), is assessed by Tp-e/QT ratio, and index of electrophysiological index (iCEB), is defined by QT/QRS ratio, are used as a novel markers to predict the risk of malignant ventricular arrhythmias and sudden cardiac death in several cardiovascular diseases. [3,5,6]

Increased TDR and decreased or increased iCEB are associated with elevated risk of malignant arrhythmias and sudden death [5].

This study aimed to investigate ECG markers of depolarization and repolarization disturbances (Tp-e, TDR and iCEB) and changes (ST-T changes) in MB patients in comparison with non-MB controls.

Patients and methods

This cross-sectional study was carried out at the Cardiology Center at Al-Sader Teaching city between January 2016 and December 2018.

Patients recruited in this study were consecutive patients with suspected coronary artery disease who underwent 64-slice MDCT angiography examination to exclude coronary artery disease. Forty one patients who were diagnosed as having MB (MB group) (92.5% involved

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left anterior descending artery) at MDCT exam and other 41 patients without MB(non-MB group) matched by age, sex were enrolled in the study.

Using standard physician-based questionnaires, a history of conventional cardiac risk factors for coronary artery disease was obtained from each patient at the time of coronary MDCT angiography examination including a positive family history of premature coronary artery disease (occurring before the age of 55 years in men and before 65 years in women), current smoking history (>10 cigarettes per day in the last year), a history of hypertension or use of anti-hypertension medications, hyperlipidaemia (defined as levels of total cholesterol $\geq 200 \text{ mg dl}^{-1}$ or triglyceride $\geq 150 \text{ mg dl}^{-1}$) or use of lipid-lowering drugs, a history of diabetes mellitus or use of insulin or diabetes lowering drugs and measurement of body weight and height to calculate body mass index (BMI) [5].

Verbal informed consent was obtained from all patients enrolled in the study. The study was approved by our medicine college board.

MDCT scan protocol

CT coronary angiography was performed with a 64-slice scanner (Aquilion 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan). The MDCT data analyses were assessed as per our previous study [5].

The analysis of MDCT images were performed by two independent radiologists with >5 years' experience in coronary MDCT angiography data interpretation.

ECG examination

The 12 lead ECGs were obtained for all patients at the time of MDCT examination with a paper speed of 25 mm/s and voltage of 10 mm/mV by using standard ECG system (Marquette Electronics, Milwaukee, WI) while the patient was resting in the supine position. ECG readings were measured manually by two cardiologists blinded to MDCT results, using calipers and a magnifying glass. QRS duration in ms was calculated from the end of PR to the end of S wave. The Tp-e interval was calculated from the peak of the T wave to the end of the T wave in the precordial leads. The mean value of the measurements was used in the analysis [5].

The QT interval was calculated from the beginning of the QRS complex to the end of the T [3,5].

The Tp-e/QT, and QT/QRS were calculated from these measurements. Inter-observer variability was <5%.

With the regard of ECG changes, ST-segment deviation was defined as an elevation or depression of >0.1 mV at 80 milliseconds after the J point in all leads. T wave inversion was defined as T wave >1 mm below TP segment in all leads. Diffuse ST-T changes were defined when ≥ 2 contiguous and noncontiguous leads showed ST depression or elevation or T inversion.

Statistical analysis

Data are presented as mean \pm standard deviation or as median (interquartile range (IQR)). Categorical data are expressed as frequencies and were compared with Pearson's Chi-square test. Continuous variables were compared using Student's *t*-test. All data were collected and analyzed with SPSS for MAC version 17 (IBM, Somers, NY, USA). A probability (P) value of <0.05 was considered statistically significant.

Results

The statistical analysis is performed in two steps:

First we studied the differences in the ECG markers and changes distribution between MB and non-MB groups (82 patients). The clinical characteristics of the patients enrolled in the study are shown in Table 1.

Second, we classified the patients into two groups according to CAC values: patients without coronary atherosclerosis or normal coronary

Table 1
Patients characteristics.

Variables	MB N = 41	Non-MB N = 41	P
Age(years)	56 \pm 10	55 \pm 8	0.4
Male	56%	56%	1
Hypertension	53%	65%	0.2
Diabetes mellitus	24%	20%	0.5
Smoking	27%	20%	0.4
Dyslipidemia	36%	36%	1
Family history	10%	12%	0.8
BMI	29 \pm 5	30 \pm 3	0.2
CAC(median(IQR))	3(0–54)	0(0–67)	0.9
ECG markers and changes			
Tp-e	72 \pm 12	77 \pm 11	0.1
QRS	77 \pm 22	89 \pm 28	0.03
QT	396 \pm 61	388 \pm 35	0.4
iCEB	5.6 \pm 2	4.6 \pm 1	0.009
TDR	0.18 \pm 0.0	0.19 \pm 0.0	0.04
T inversion, diffuse	27%	5%	0.01
T inversion,V1	58%	5%	<0.0001

arteries (CAC = 0) group (containing 22 non-MB patients and 19 MB patients) and patients with coronary atherosclerosis (CAC > 0) group (containing 22 MB patients and 19 non-MB patients). The distribution of ECG markers and changes among MB and non-MB patients was analyzed in each group separately.

In first step analysis, there was no significant difference in the distribution of conventional cardiac risk factors between MB and non-MB groups. iCEB was significantly increased in MB patients in comparison to non-MB patients (5.6 Vs 4.6, $p = 0.009$) while QRS duration and TDR were significantly decreased in MB in comparison to non MB patients (77 Vs 89, $p = 0.03$ and 0.18 Vs 0.19, $p = 0.04$ respectively). No significant difference was observed in Tp-e and QT interval between MB and non-MB patients ($p > 0.05$) as in Table 1.

With regard to ST and T changes, T wave inversion was significantly observed in MB in comparison to non-MB patients (the percentage of isolated T inversion in V1 was 58% Vs 5%, $p \leq 0.0001$ and the percentage of diffuse T inversion was 27% Vs 5%, $p = 0.01$) as in Table 1. There were no ST segment depression or elevation reported in MB and non-MB patients of this study.

Patients with normal coronary arteries (CAC = 0) group

iCEB was significantly increased in MB group in comparison to non-MB group (5.3 Vs 4.5, $p = 0.04$). Also, isolated T inversion in V1 was observed more in MB group compared to non-MB group (74% Vs 9%, $p \leq 0.0001$).

There was no statistically significant difference in the distribution of Tp-e, QRS, QT, TDR and diffuse T inversion occurrence between MB and non-MB groups as in Table 2.

Table 2
distribution of ECG markers between MB and non-MB groups in patients with normal coronary arteries (CAC = zero).

ECG markers	MB N = 19(46%)	Non-MB N = 22(54%)	P
Tp-e	76 \pm 13	74 \pm 12	0.5
QRS	74 \pm 20	88 \pm 33	0.1
QT	408 \pm 80	384 \pm 41	0.2
iCEB	5.9 \pm 2	4.7 \pm 1	0.04
TDR	0.19 \pm 0	0.19 \pm 0	0.6
T inversion, diffuse	12%	9%	0.1
T inversion,V1	74%	9%	<0.0001

Patients with coronary atherosclerosis (CAC > 0) group

Tp-e and TDR values were decreased in MB in comparison to non-MB patients (69 Vs 80, $p = 0.003$ and 0.18 Vs 0.2, $p = 0.01$ respectively). Isolated T inversion in V1 was observed more in MB compared to non-MB patients (45% Vs 5%, $p = 0.04$).

There was no statistically significant difference in the distribution of QRS, QT, iCEB and diffuse T inversion between MB and non-MB patients as in Table 3.

Discussion

In this study, a significantly decreased TDR and Tp-e values and increased iCEB values were found in MB patients compared to non-MB controls and this difference in the distribution of ECG markers was more significant in patients with coronary atherosclerosis.

In the recent years, Tp-e interval, TDR and iCEB, as new emerging ECG markers of increased risk of malignant arrhythmias and sudden death, are proposed to have a substantial predictive value of increased mortality in patients with cardiovascular disease in addition to established ECG risk factors [5,6].

iCEB is hypothesized to reflect the potential balance and imbalance in the depolarization and repolarization of cardiac cycle and increased or decreased values of iCEB are associated with increased risk to malignant arrhythmia [6,7].

According to our knowledge, there were no clinical studies about the role of iCEB changes in MB patients in the medical literature.

On the other hand, increased QT dispersion, Tp-e interval and TDR, which are markers of heterogeneous repolarization, are reported to be important risk factors for the potential development of malignant arrhythmias and sudden death secondary to repolarization disturbances [5,7].

Previous studies reported a significant increase of repolarization abnormalities in MB patient compared to non-MB controls [3,7,8,9].

The results of the present study are in discordance with previous studies probably because these studies had enrolled persons with normal coronary arteries as a control groups with no additional tests to exclude the possibility of MB presence in controls or lack the match between MB and non-MB groups [3,9,10].

Moreover, some authors in the previous studies had used exercise echocardiography to diagnose MB presence of MB, but the accuracy of the exercise echocardiography for the diagnosis of MB is not yet known [8], whereas other authors had used interventional coronary angiography, rather than MDCT modality, to assess MB presence [3,9,10].

The pitfall of interventional coronary angiography, in comparison to MDCT, relay in the fact that detection of MB depends on the presence of systolic narrowing in vessel caliber and proximal stenosis. Therefore, interventional coronary angiography fail to detect thin and superficial MB that don't show systolic narrowing leading to much higher prevalence of coronary atherosclerosis and ischemia in patients with MB detected by interventional coronary angiography than that seen in patients detected by MDCT [3,9,10].

Table 3
distribution of ECG markers between MB and non-MB groups in patients with coronary atherosclerosis (CAC > 0).

ECG markers	MB N = 22(54%)	Non-MB N = 19(46%)	P
Tp-e	69 ± 11	80 ± 9	0.003
QRS	79 ± 24	90 ± 23	0.1
QT	386 ± 36	392 ± 27	0.5
iCEB	5.3 ± 1	4.5 ± 1	0.7
TDR	0.18 ± 0	0.2 ± 0	0.01
T inversion, diffuse	27%	5%	0.06
T inversion,V1	45%	5%	0.04

Although MB was associated with cardiac ischemia and sudden death in multiple case reports, there are several evidences about the benign nature of MB presence. [1,11–13]

It has been reported that the bridged segment of left anterior descending artery is protected from atherosclerosis when compared with other vessels of the same heart that do not form bridges and MB may have a protective role against progressive atherosclerosis in the whole coronary artery system [11].

Moreover, most of reported cases of MB showed no adverse clinical outcomes following ischemic heart disease with long term benign prognosis [11].

Some authors looks to MB as a complex coronary variant with diverse pathophysiological mechanism causing variable clinical manifestations and is generally associated with an excellent survival rate of 97% at 5 years suggesting that not all MB are the same, some MB are benign whereas others have the tendency to cause malignant arrhythmias or sudden death and certain MB morphologies and characteristics may pay a role in the occurrence of morbidity and mortality.[7,12].

However, the electrophysiological changes and arrhythmogenic potential of MB characteristics on the coronary flow and occurrence of adverse cardiac events are not clearly understood.[3].

Generally, MB patients with suspected coronary artery disease showed nonspecific ECG changes of coronary ischemia or conduction abnormalities in the resting state although some patients may report ST-T changes during exercise [14].

Isolated T wave inversion can occur in healthy persons with no structural heart disease or in rarely in athletes. [15]

It has been suggested that an isolated precordial T wave inversion in patients with suspected coronary artery disease is associated with lesions in the left anterior descending artery. [16]

There are several limitations in this study. First, controlling for all possible factors or residual confounding that might affect ECG markers was difficult. Second, the clinical relevance of our results relative to cardiac arrhythmogenesis may be speculative due to the lack of long term follow-ups to assess the clinical significance of our results in correlation to patient's outcome in our population study.

However, the results of this study may provide new insight, which could be used in large-scale, follow up studies to assess the prognostic significance of these ECG markers in correlation to future adverse outcome as 50% of patients suffer sudden cardiac death as a first manifestation of their illness with increased mortality without earlier detection [5,17].

Conclusion

MB patients, as compared to non-MB controls, have shown decreased Tp-e and TDR markers particularly in MB patients with coronary atherosclerosis, suggesting that MB patient may be less susceptible for increased risk of malignant arrhythmias and sudden death than non-MB controls. A follow up studies linking the predictive value of these ECG parameters to adverse cardiac outcome are required to confirm these results and highlight the precise nature of MB as a benign coronary variant.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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