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# The Evaluation of Lesion Localization and Ischemic Myocardial Mass Via Arrhythmia Parameters in Stable Coronary Artery Patients with Myocardial Ischemia

# Miyokart İskemisi Olan Kararlı Koroner Arter Hastalarında Lezyon Lokalizasyonunun ve İskemik Miyokart Kitlesi Büyüklüğünün Aritmi Parametreleri ile Değerlendirilmesi

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**Öz**

Kararlı koroner arter hastalığında, hangi koroner arterdeki kritik darlığın daha aritmik olduğunu ve darlık bulunan arterin mi yoksa darlığa bağlı iskemi altında kalan miyokart dokusunun büyüklüğünün mü malign ventriküler aritmiler açısından daha önemli olduğunu elektrokardiyografi üzerinde hesaplanan aritmi öngördürücüleri yardımıyla değerlendirmektir. Çalışmamız retrospektif gözlemsel çalışma olarak tasarlanmıştır. Ocak 2013-2016 tarihleri arasında koroner anjiyografisinde tek damar hastalığı saptanmış ve bu damara perkütan koroner girişim uygulanmış 183 hasta incelendi. Girişim öncesi ve sonrası çekilen elektrokardiyografilerde aritmi öngördürücülerinden TpTe intervali, QTc intervali ve TpTe/QT oranı hesaplandı. İskemi altındaki miyokart dokusu yüzdesi APPROACH skoru kullanılarak, koroner anjiyografi görüntüleri yardımı ile hesaplandı. Sol ön inen arter lezyonlarının iskemi altında bıraktığı sol ventrikül miyokart dokusu yüzdesinin (34±10); sirkumflex arter (17±11) ve sağ koroner arter (21±5)'in iskemi altında bıraktığı miyokart dokusu yüzdelerinden anlamlı bir şekilde fazla olduğu görüldü (p<0.001). Perkütan koroner girişim öncesi ve sonrası TpTe intervali ve TpTe/QT oranı farkı sol ön inen arter lezyonu olan grupta sirkumflex arter ve sağ koroner arter lezyonu olan gruplardan anlamlı bir şekilde yüksek bulundu (p<0.001). Kararlı koroner arter hastalığında, iskemik miyokart büyüklüğü arttıkça aritmojenitenin artabileceği saptandı. Elektrokardiyografi üzerinden hesaplanan aritmi parametreleri açısından revaskülarizasyondan en fazla fayda görebilecek grubun kritik sol ön inen arter darlığına sahip kararlı koroner arter hastaları olduğu görüldü.

**Anahtar Kelimeler:** Elektrokardiyografi, Koroner Arter Hastalığı, Perkütan Koroner Girişim

**Abstract**

The aim of this study was to evaluate which critical coronary artery stenosis is more arrhythmogenic in stable coronary artery disease and whether the involved stenotic artery or the size of the myocardial tissue under ischemia due to stenosis is more important in terms of malignant ventricular arrhythmias by using arrhythmia predictors calculated on electrocardiography. This was a retrospective observational study. We scanned patients who underwent percutaneous coronary intervention for single vessel stable coronary artery disease between January 2013 and 2016. Assigned indicators of increased arrhythmogenic risk as TpTe interval, QTc interval and TpTe/QT ratio were calculated on electrocardiography before and after the percutaneous coronary intervention. We also calculated the anatomical myocardial area at risk of ischemia as a percentage of the left ventricular myocardium volume for a given site of lesion with APPROACH score by assessing coronary angiography images. The percentage of left ventricular jeopardized myocardium in left anterior descending artery lesions (34±10) was significantly higher than those in circumflex artery (17±11) and right coronary artery (21±5) lesions (p<0.001). Furthermore, the differences between TpTe intervals and TpTe/QT ratios measured before and after the percutaneous coronary intervention were significantly higher in patients with left anterior descending artery lesions than patients with circumflex artery and right coronary artery lesions (p<0.001). In patients with stable coronary artery disease, the size of the ischemic myocardium was associated with increased arrhythmogenesis. Patients with left anterior descending artery lesions may get the greatest benefit from revascularization in terms of arrhythmia predictors calculated on electrocardiography.

**Keywords:** Electrocardiography, Coronary Artery Disease, Percutaneous Coronary Intervention

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## Introduction

Coronary artery disease (CAD) is a progressive disease caused by reduced coronary blood flow at rest or during exercise due to anatomical and pathophysiological changes in the epicardial coronary arteries and is manifests with a variety of symptotblems and signs ranging from angina pectoris to acute coronary syndromes (1). It is an important public health problem in developed and developing countries and its prevalence is gradually increasing (2). Coronary arteriography remains the

gold standard for the detection and evaluation of CAD (3).

QT interval, corrected QT (QTc) interval and QT dispersion have been shown to be indicators calculated by electrocardiography (ECG) which are effective in the development of arrhythmic events (4). T-peak T-end (TpTe) interval, defined as the interval between the peak and the end of the T wave, represents the disper¬sion of repolarization. The TpTe interval has been proposed as indicator of regional and transmural heterogeneity of cardiac repolarization (5). Abnormal repolarization and prolonged TpTe interval are associated with increased malignant ventricular ar¬rhythmias and sudden cardiac death (SCD) in many acquired and congenital heart diseases (6). The TpTe/QT ratio, can be used to show the distribution of ventricular repolarization without being affected by changes in heart rate and QT interval variations (7).

Various methods have been used to calculate the myocardial tissue under ischemia on coronary angiographic images according to the location of the lesion (8). It is known that the percentage of ischemic myocardium is more important for prognosis than the number of lesions detected on coronary angiography (9). The APPROACH lesion score, which predicts one-year mortality in patients undergoing percutaneous coronary intervention (PCI), has been reported to be superior to other scoring systems (9).

The aim of this study was to evaluate which critical coronary artery stenosis is more arrhythmogenic in stable CAD and whether the involved stenotic artery or the size of the myocardial tissue under ischemia due to stenosis is more important in terms of arrhythmia by using arrhythmia predictors calculated on the ECG. By calculating the change in the patient's values before and after PCI, it is possible to determine which coronary revascularization procedure is associated with the greatest change. With these results, it may be possible to predict which coronary artery has a higher risk of developing malignant ventricular arrhythmias. In addition, it may be possible to predict which epicardial coronary critical lesion intervention will most reduce the risk of arrhythmia development according to the change in arrhythmia predictors calculated on the ECG.

## Material and Method

Between January 2013 and January 2016, 183 patients (54 women, 129 men) who underwent PCI after detecting myocardial ischemia by non-invasive methods [positive exercise stress test, ischemia greater than 5% on myocardial perfusion scintigraphy, stress echocardiography demonstrating regional systolic wall-thickening abnormalities (1)] and detecting single-vessel disease by coronary angiography were scanned. A total of 155 patients (38 women, 117 men) who did not meet the exclusion criteria and had the Canadian Cardiovascular Society (CCS) angina score of 2 or 3 were included in the study.

The study was approved by the Ethics Committee of Istanbul Medipol University Faculty of Medicine on 10/08/2016 with number E.13015. Written consent was obtained from all patients.

Exclusion criteria included; patients over 80 years of age, with acute coronary syndromes, chronic liver failure, chronic renal failure, advanced valvular disease, dilated, hypertrophic and restrictive cardiomyopathy, chronic obstructive pulmonary disease, malignancy, advanced atrio-ventricular block, bundle branch block, pacemaker rhythm, atrial fibrillation, presence of pre-excitation on ECG, detection of over 50% stenosis in the coronary artery where the target lesion is located or in others, whose baseline ECG was not suitable for TpTe interval measurement.

The 12-lead surface ECGs of all patients were scanned retrospectively. RR interval, QT interval, TpTe interval were calculated manually using a magnifying glass. The QT interval was defined as the distance from the beginning of the QRS complex to the end of the T wave, the point where it turns to the isoelectric line. RR interval was found by calculating the distance between the peaks of the R waves in two consecutive QRS complexes. QTc was calculated using the Bazzet formula [$QTc=QT/\sqrt{RR}$].

The TpTe interval was measured as the distance between the peak point of T wave and the end point of the T wave (5). The TpTe/QT ratio was calculated from these measurements. Measurements were taken from precordial leads. These values were recalculated in the ECGs of all patients 24 hours after PCI. Δ TpTe, Δ QTc and Δ TpTe/QT values were obtained by subtracting the pre-procedure values from the post-procedure values.

All coronary angiographies and PCIs were performed using standardized methods on a Philips Allura FD 10 angiography device by interventional cardiologists with experience of ≥100 interventional procedures per year. Stenosis ≥70% was considered significant and PCI was performed. Patients without >50% stenosis in coronary vessels other than the target lesion were included in the study.

The percentage of myocardial tissue under ischemia potentially caused by each target lesion was calculated using the modified APPROACH score (10). In the modified version shown in Table 1, vessel dominance, localization of the culprit lesion and the size of the major side branches were taken into consideration (10). For example, a lesion of the proximal circumflex (Cx) artery with a medium-sized posterior descending artery and small posterolateral arterial branches in the left dominant system was estimated to produce an ischemic area of 29.50% in myocardial tissue (Table 1).

**Table 1.** Percentage of ischemic myocardium caused by the target lesion* (10)

| Culprit lesion location | Target artery side branches ⇩ | ⇨ Diagonal for LAD, Posterolateral for all others | | | |
|---|---|---|---|---|---|
| | | | Small or absent | Medium | Large |
| LAD (Right or left dominant) | | Distal | 13.75 | 14.80 | 15.90 |
| | | Mid | 27.50 | 29.70 | 31.80 |
| | | Proximal | 41.25 | 44.50 | 47.75 |
| Proximal Cx (Right Dominant) | OM | Small or absent | 9.25 | 12.50 | 15.75 |
| | | Medium | 15.25 | 18.50 | 21.75 |
| | | Large | 21.25 | 24.50 | 27.75 |
| Proksimal Cx (Left Dominant) | PDA | Small or absent | 23.50 | 28.00 | 32.50 |
| | | Medium | 29.50 | 34.00 | 38.50 |
| | | Large | 35.50 | 40.00 | 44.50 |
| Mid Cx (Left Dominant) or RCA (Right Dominant) Mid Cx (Right Dominant) | PDA | Small or absent | 9.25 | 12.50 | 15.75 |
| | | Medium | 15.25 | 18.50 | 21.75 |
| | | Large | 21.25 | 24.50 | 27.75 |
| | | | 3.25 | 6.50 | 9.75 |

Cx:Circumflex artery, LAD:Left anterior descending artery , RCA:Right coronary artery, PDA:Posterior descending artery, OM:Obtuse marginal artery.

*Statistical Analysis*

Demographic data, pre- and post-procedural ECGs, coronary angiography and PCI images were obtained by retrospective scanning. Data were analysed using IBM SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA). The normal distribution of the data was analysed using the Kolmogrov Similrov test. Normally distributed continuous variables were expressed as mean ± standard deviation and non-normally distributed variables were expressed as median (25th percentile-75th percentile). Categorical variables were expressed as numbers (percentages). Chi-square test was then used for categorical variables and an Anova test or Kruskal-Wallis test was used for more than two variables. Post-hoc analysis of variance was performed using Tukey's b or Dunnett's T3 test, depending on homogeneity of variances. Pearson and Spearman correlation analyses were performed for the relationship between numerical data. For P values, <0.05 was considered significant and <0.001 was considered highly significant. According to the two-independent Pearson correlation analyses using the G-power program with 95% confidence (1-α), 80% test power (1-β) and d=0.5 effect size, the minimum number of samples required were 132. The power of this study, which included 183 patients, was >90% (G-power version 3.1, Dusseldorf, Germany).

## Results

The mean age of the patients included in the study was 62±10 years and 76% were male. Sixty patients had isolated left anterior descending artery (LAD) lesions, 54 patients had isolated Cx lesions, 41 patients had isolated right coronary artery (RCA) lesions and PCI was performed in these lesions.

When the patients were divided into three groups according to the target lesion, no significant differences were observed between the groups in terms of gender, age, creatinine, hemoglobin, hypertension, diabetes mellitus, smoking, use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and use of beta blockers. Although the mean left ventricular ejection fraction was slightly lower in the group of patients with LAD lesions and this decrease was not statistically significant (Table 2). The percentage of left ventricular myocardial tissue under ischemia by LAD lesions (34±10) was significantly higher than the percentage of myocardial tissue under ischemia by Cx (17±11) and RCA (21±5) (p<0.001). The difference between the percentages of myocardial tissue under ischemia in Cx and RCA was not statistically significant (Table 2). Preoperative TpTe interval, preoperative QTc interval and preoperative TpTe/QT ratio were higher in the group with LAD lesion compared to the groups with Cx and RCA lesion groups (p<0.001). However, the difference in these values between the groups with Cx and RCA lesions was not statistically significant (Table 2).

The difference in TpTe interval before and after PCI was significantly higher in the LAD lesion group [0.02 (0.01-0.04)] than in the Cx [0.01 (0.00-0.02)] and RCA [0.01 (0.00-0.02)] lesion groups (p<0.001). Similarly, the difference in TpTe/QT ratio before and after PCI was significantly higher in the LAD lesion group than in the Cx and RCA lesion groups (p<0.001). When comparing the Cx lesion group with the RCA lesion group, no statistical significance was observed between the changes in TpTe interval and TpTe/QT ratio before and after the procedure (Table 3).

The relationship between the percentage of myocardium under ischemia and arrhythmia predictors in patients with single-vessel stable CAD was investigated. Correlation analysis showed a significant correlation between the percentage of myocardium under ischemia and preoperative TpTe interval (r=0.845, p<0.001), QTc interval (r=0.465, p<0.001) and TpTe/QT ratio (r=0.751, p<0.001) in stable CAD patients with LAD lesion (Table 4, Figure 1).

**Table 2.** Comparison of patients divided into groups according to target lesions

| | LAD | Cx | RCA | p |
|---|---|---|---|---|
| Gender (female), n (%) | 19 (32) | 11 ((20) | 8 (20) | 0.252* |
| Current Smoker, n (%) | 23 (38) | 21 ( 39) | 15 (37) | 0.971* |
| Hypertension, n (%) | 37 (62) | 36 (67) | 28 (68) | 0.751* |
| Diabetes Mellitus, n (%) | 24 (40) | 25 (46) | 19 (46) | 0.741* |
| ACEi/ARB, n (%) | 35 (58) | 34 (63) | 26 (63) | 0.832* |
| Beta Blocker, n (%) | 33 (55) | 24 (44) | 16 (39) | 0.252* |
| Age (years), (mean; SD) | 62±10 | 60±11 | 62±9 | 0.383** |
| Creatinine (mg/dl; SD) | 0.9±0.1 | 0.8±0.1 | 0.9±0.1 | 0.091** |
| Hemoglobin (g/dL; SD) | 14±1 | 14±1 | 14±1 | 0.921** |
| Left ventricular ejection fraction (%; SD) | 59±5 | 60±5 | 60±5 | 0.792** |
| Ischemic myocardial tissue (%; SD) | 34±10 | 17±11 | 21±5 | **<0.001**** |
| Preoperative TpTe interval (sec) | 0.098±0.01 | 0.077±0.01 | 0.076±0.01 | **<0.001**** |
| Preoperative QTc interval (sec) | 0.416±0.03 | 0.387±0.02 | 0.39±0.02 | **<0.001**** |
| Preoperative TpTe/QT ratio | 0.237±0.03 | 0.201±0.03 | 0.196±0.02 | **<0.001**** |
| Δ TpTe (sec) | 0.02 (0.01-0.04) | 0.01 (0.00-0.02) | 0.01 (0.00-0.02) | **<0.001***** |
| Δ QTc (sec) | 0.02 (0.00-0.02) | 0.01 (0.00-0.02) | 0.01 (0.00-0.02) | 0.191*** |
| Δ TpTe/QT | 0.03 (0.01-0.09) | 0.02 (0.00-0.04) | 0.002 (0.001-0.04) | **<0.001***** |

Variables are reported, Mean±standard deviation; Median (25th percentile-75th percentile) and Number (%). Abbreviations: ACEi: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, Cx: Circumflex artery, LAD: Left anterior descending artery , RCA: Right coronary artery, Δ TpTe: Difference in Tp-Te intervals before and after revascularization, Δ QT: Difference in QT interval before and after revascularization, Δ TpTe/QT: Difference in Tp-Te/QT rates before and after revascularization. *The p-value was calculated using the Chi-squared test, ** The p-value was calculated using the Anova test, ***The p value was calculated using the Kruskal-Wallis test.

**Table 3.** Post-hoc analysis results for the data with statistical significance between the target lesion groups

| | | | p |
|---|---|---|---|
| Ischemic Myocardial Tissue (%)* | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.082 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.082 |
| Preoperative TpTe interval (sec)* | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.963 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.963 |
| Preoperative QTc interval (sec)* | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.891 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.891 |
| Preoperative TpTe/QT ratio* | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.784 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.784 |
| Δ TpTe (sec)** | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.714 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.714 |
| Δ TpTe/QT** | LAD | Cx | **<0.001** |
| | | RCA | **<0.001** |
| | Cx | LAD | **<0.001** |
| | | RCA | 0.267 |
| | RCA | LAD | **<0.001** |
| | | Cx | 0.267 |

Cx: Circumflex artery, LAD: Left anterior descending artery , RCA: Right coronary artery, Δ TpTe: Difference in Tp-Te intervals before and after revascularization, Δ TpTe/QT: Difference in Tp-Te/QT rates before and after revascularization, *Tukey's b test was used for post-hoc analysis of variance, ** Dunnett's T3 test was used for post-hoc analysis of variance.

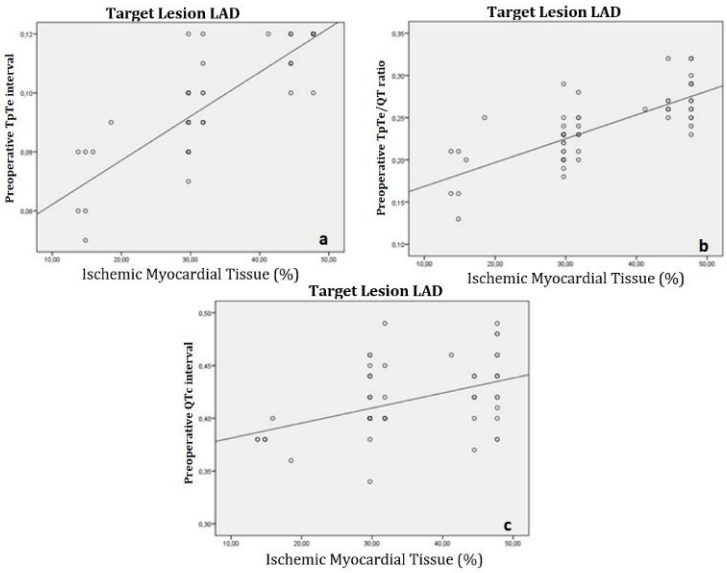


**Figure 1.** Correlation analysis plots showing the relationship between the percentage of ischemic myocardium and electrocardiographic arrhythmia predictors for LAD

For each lesion group, the relationship between the percentage of myocardium under ischemia and the change in arrhythmia predictors before and after revascularization was evaluated. Correlation analysis showed a significant correlation between the percentage of myocardial tissue under ischemia and the change in TpTe interval ($r=0.81$, $p<0.001$) and TpTe/QT ratio ($r=0.83$, $p<0.001$) in the LAD lesion group (Table 4, Figure 2).

## Discussion

In our study, we found that the percentage of myocardial tissue under ischemia, TpTe interval, QTc interval and TpTe/QT ratio were higher in patients with stable CAD with isolated LAD lesions than in patients with Cx and RCA lesions. Similarly, we found that the change in TpTe interval and Tp-Te/QT ratio after revascularization was greater in patients with stable CAD with LAD lesions than in patients with Cx and RCA lesions. Furthermore, in LAD lesions, we found a significant correlation between myocardial tissue under ischemia and TpTe interval, QTc interval, TpTe/QT ratio and the change in TpTe interval, Tp-Te/QT ratio after revascularization.

In a study by Arbustini et al. investigating myocardial ischemia and arrhythmia potential, it was mentioned that the appearance of an area of ischemic tissue adjacent to tissue with normal perfusion significantly alters the electrophysiological properties of the myocardium and may cause life-threatening arrhythmias. (11) The electrophysiological substrate (heart rate, QT duration, transmural dispersion of repolarization measured by TpTe duration) is also very important in the context of arrhythmia induction (12). A recent study by Thomsen et al. showed an increased risk of ventricular tachyarrhythmias in patients with incomplete revascularization. They hypothesized that residual ischemia acts as an arrhythmic trigger, with local electrophysiological changes, especially during exercise (13).

**Table 4.** Correlation analysis of the percentage of ischemic myocardium with changes in the electrocardiographic predictors of arrhythmia.

| | | r | p |
|---|---|---|---|
| **LAD** | Preoperative TpTe interval | 0.845 | **<0.001** |
| | Preoperative QTc interval | 0.456 | **<0.001** |
| | Preoperative TpTe/QT ratio | 0.751 | **<0.001** |
| | Δ TpTe (sec) | 0.81 | **<0.001** |
| | Δ QTc (sec) | 0.07 | 0.614 |
| | Δ TpTe/QT | 0.83 | **<0.001** |
| **Cx** | Preoperative TpTe interval | 0.135 | 0.341 |
| | Preoperative QTc interval | 0.055 | 0.713 |
| | Preoperative TpTe/QT ratio | 0.073 | 0.621 |
| | Δ TpTe (sec) | 0.08 | 0.543 |
| | Δ QTc (sec) | 0.14 | 0.312 |
| | Δ TpTe/QT | 0.09 | 0.491 |
| **RCA** | Preoperative TpTe interval | 0.165 | 0.332 |
| | Preoperative QTc interval | 0.236 | 0.113 |
| | Preoperative TpTe/QT ratio | 0.252 | 0.121 |
| | Δ TpTe (sec) | 0.01 | 0.962 |
| | Δ QTc (sec) | 0.03 | 0.851 |
| | | 0.04 | 0.831 |

r: Spearman Correlation Coefficient, Cx: Circumflex artery, LAD: Left anterior descending artery, RCA: Right coronary artery. Δ TpTe: Difference in Tp-Te intervals before and after revascularization, Δ QT: Difference in QT interval before and after revascularization, Δ TpTe/QT: Difference in Tp-Te/QT rates before and after revascularization.

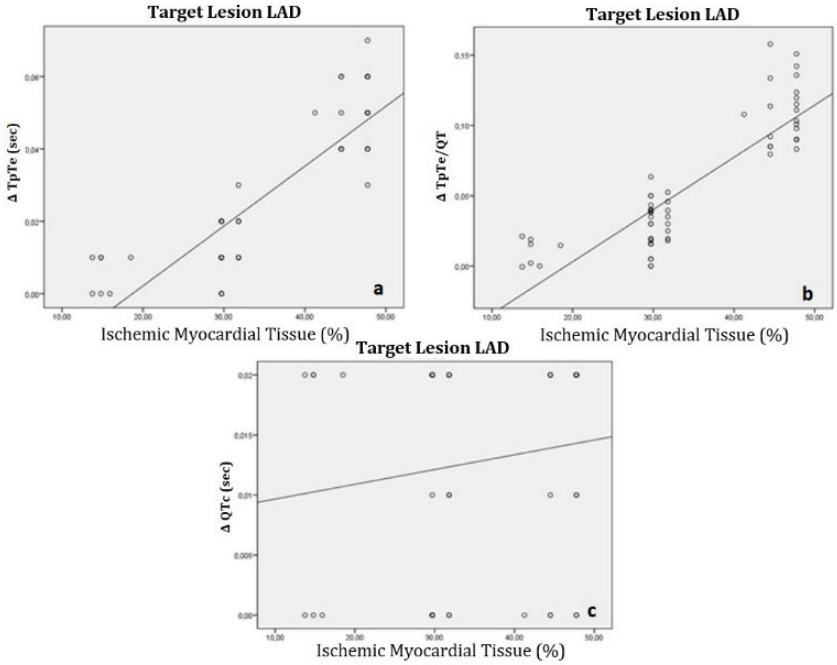


**Figure 2.** Correlation analysis plots showing the relationship between the percentage of ischemic myocardium and the change in electrocardiographic arrhythmia predictors before and after revascularization

In the setting of ischemia, the action potential duration (APD) changes and there was a trend for further prolongation of the TpTe interval. The prolongation of the TpTe interval is a consequence of the conduction rate slowing and magnifying the difference in APD duration between myocardial layers. Therefore, Okninska et al. reported that the TpTe interval is a good predictor of increased risk of malignant ventricular arrhythmias. (12)

A prolonged TpTe interval, which is one of the parameters associated with repolarization heterogeneity and ventricular arrhythmogenesis, leads to re-entrant ventricular tachycardia. In patients with sepsis, hypertrophic cardiomyopathy, obstructive sleep apnea and ST- elevation myocardial infarction undergoing PCI, a prolonged TpTe interval was associated with an increased risk of mortality (14-17).

Juki et al. showed the TpTe interval and TpTe/QT ratio increased significantly during maximal exercise in patients with stable CAD, whereas they remained constant or decreased in patients without CAD (18). In patients with stable CAD, exercise-induced ischemia and increased sympathetic activity widen the ventricular repolarization distribution and lead to triggering ventricular tachycardia/fibrillation by intraventricular re-entry phenomenon. After rest or revascularization, the repolarization distribution returns to normal due to improved blood flow and the risk of cardiac arrhythmia decreases (18).

Carrizo et al. showed that the most common target lesion was the LAD in a retrospective study of 46 patients presenting with SCD due to acute coronary syndrome (19). Kwofie et al. developed proximal LAD occlusion in experimental animals and found fatal ventricular arrhythmias in about 70% of cases (20).

Graham et al. showed that the APPROACH lesion score, one of the scoring systems indicating the percentage of ischemic myocardial tissue on coronary angiographic images, was superior to other scores in terms of prognosis in patients undergoing revascularization (9). In retrospective studies, the fact that it does not require additional investigations or images other than classic angiographic images enhances the usability of this scoring system (10). Similarly, the ease of calculation compared to other scoring systems suggests that its use will increase, especially in retrospective studies. Although Petousis et al. in a recent study stated that cardiac magnetic resonance imaging (CMR) is the most commonly used method for determining jeopardized myocardium, in their study they assessed the myocardial ischemic area by calculating it with APPROACH score (21). De Palma et al. emphasized that the jeopardized myocardium calculated by the APPROACH score correlated very well with the values obtained by CMR. (22)

TpTe interval, QTc interval and TpTe/QT ratio were significantly higher in the LAD lesion group compared to the Cx or RCA lesion groups. In the light of these findings, critical LAD stenoses may be more arrhythmogenic than other coronary artery stenoses in patients with stable CAD. It is also known that the area supplied by the LAD in the left ventricle is greater than the area supplied by any of the other vessels. When the percentage of myocardial tissue under ischemia and the target lesions were compared individually, the percentage

of myocardial tissue under ischemia in LAD lesions was significantly higher than the other lesions. There was no significant difference between the groups with Cx and RCA lesions in terms of both the arrhythmia parameters calculated from the ECG and the percentage of myocardial tissue under ischemia. Therefore, we could not comment on the arrhythmogenicity of lesions in these vessels.

Δ TpTe and Δ TpTe/QT, the differences between the arrhythmia parameters we calculated on ECGs before the procedure and at 24 hours after revascularization, were significantly higher in the LAD lesion group compared with the other target lesion groups. Compared with the other two coronary vessel lesions, LAD lesions were the group with the greatest benefit from revascularization in terms of change in arrhythmia parameters.

For LAD lesions, the relationship between the percentage of myocardial tissue under ischemia and Δ TpTe and Δ TpTe/QT was significant. This was interpreted as a possible predisposition to arrhythmia in stable CAD patients with LAD lesions and may be an indicator of the beneficial effect of LAD lesion revascularization on mortality.

It has been shown that not all revascularization procedures performed in stable CAD contribute equally to the development of arrhythmias, in particular, the localization of the re-perfused lesion and the percentage of ischemic myocardial tissue corresponding to this localization may be related to the reduction in arrhythmia risk after revascularization.

*Study Limitations:*

First, this is a retrospective observational study with a small sample size in a single center. Patient records and angiographic images were reviewed retrospectively. If the study had been prospective, it would have allowed long-term follow-up of patients. This would have provided information on the development of arrhythmia and survival. Second, the ECG measurements were taken by a single observer. Performing these measurements in a computer environment using newly developed software packages would have given us more accurate results. Third, the APPROACH score is based on a typical heart structure and ignores coronary anatomical variations and non-critical plaques. Since myocardial tissue under ischemia cannot be quantified by magnetic resonance or nuclear perfusion imaging techniques, the mean values provided by the APPROACH score were used. As angiographic jeopardy scores are based on anatomical assumptions, there remains uncertainty in scoring systems for predicting clinical outcomes. Fourth, the large number of exclusion criteria and the small number of patients with single-vessel coronary lesions resulted in a small sample size. Our results should be confirmed by prospective and long-term follow-up studies with larger numbers of patients. Finally, due to the small study population and the retrospective design of our study, it is not expected to change our daily management approach in stable CAD. Changes in our clinical approach may be expected with the results of prospectively designed multicenter trials with larger numbers of patients.

## Conclusion

TpTe, QTc and TpTe/QT values calculated on ECG were found to be higher in patients with critical LAD lesions in stable CAD and therefore critical LAD lesions may be more arrhythmogenic than other lesions. There was a significant correlation between the percentage of myocardial tissue under ischemia and arrhythmogenicity. It was also shown that arrhythmogenicity may increase with an increase in the percentage of ischemic myocardium. In terms of arrhythmia parameters calculated on ECG, stable CAD patients with critical LAD stenosis may benefit the most from revascularization.

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## Conflict of interest statement

The authors have no conflicts of interest to declare.

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Istanbul Medipol University Faculty of Medicine on 10/08/2016 with number E.13015. The study was conducted in accordance with the principles of the Declaration of Helsinki and written consent was obtained from all patients. Artificial intelligence technology was not used in our study.

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