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Original Article

Association between electrocardiographic parameters and collateral circulation in patients with chronic total occlusion

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Abstract

Aim: In patients with chronic total occlusion (CTO), negative cardiovascular outcomes (angina, more frequent ventricular arrhythmias, higher mortality) and reduced survival have been demonstrated. The association between several electrocardiogram (ECG) markers, revealing individuals at high risk for ventricular arrhythmia, and collateral has been investigated in different studies in coronary artery disease patients. In this study, we aimed to investigate the association between the electrocardiographic parameters between good coronary collateral group and poor coronary collateral group in CTO patients with PCI.

Material and Methods: Patients retrospectively implemented CTO PCI to those with symptomatic symptoms of myocardial ischemia or with the exact sign of ischemia in the CTO area. The patients were divided into 2 groups according to the Rentrop class: group 1 (Rentrop 0 and 1) and group 2 (Rentrop 2 and 3). Baseline characteristics, laboratory and ECGs, procedural data, and outcome data were retrospectively collected.

Results: In this study included 59 CTO patients undergoing PCI. Mean age was 61.0±10.3 years and 43 (72.9%) of patients were male, and PCI success was 69.4%. While 22 (37.2%) of the patients were poor collateral group 1 (Rentrop 0 and 1), the remaining 37 (62.3%) of them were good collateral group 2 (Rentrop 2 and 3). There was a significant difference, in poor and good collateral groups, QT dispersion (77.2±27.9 vs 66.5±22.5, p: 0.041, respectively), QTc dispersion (82.1±26.9 vs 70.4±23.9, p: 0.034, respectively), and the presence of fQRS (63.6% vs 43.2, p: 0.027, respectively). But there was no statistically difference in P wave dispersion (48.0±9.5 vs 47.2±11.3, p: 0.796). Correlation analysis reported the association between Rentrop classification and Syntax score (r: -0.397, p: 0.002), LDL-C (r: -0.198, p: 0.025), QT dispersion (r: -0.156, p: 0.045), QTc dispersion (r: -0.176, p: 0.037), and the presence of fQRS (r: 0.234, p: 0.021) were statistically significant.

Conclusion: We suggest that some ECG parameters are an important, easy, simple, and cost effective tool and can be beneficial in predicting the poor or good collateral in patients with CTO.

Keywords: Chronic total occlusion; fragmented QRS; P wave dispersion; Rentrop collateral; ventricular repolarization; QTc dispersion

INTRODUCTION

A coronary chronic total occlusion (CTO) is described as the total occlusion of a coronary artery, named as thrombosis in myocardial infarction (TIMI) grade 0 flow, present for at least 3 months (1). CTO is noticed in nearly 16% of patients underwent to the coronary angiography (2). Successful CTO percutaneous coronary intervention (PCI) points to a long-season survival advantage and may improve cardiac results confronted with the state in cases with a failed PCI (3). Normally, coronary collateral circulation (CCC) consists of possible arteries that cannot be diagnosed by conventional coronary angiography. However, when stenosis develops in the coronary vessels, the CCC expands due to carry more blood according to the pressure difference and become visible on angiography (4). The relationship between several markers, (QTc dispersion, fragmented QRS (fQRS), T wave peak to end period (TpTe), the TpTe/QT ratio) revealing people at high risk of arrhythmias of ventricular has been recognized applying 12-lead electrocardiogram (ECG), and collateral has been investigated in different studies in CTO patients (5-10). However, the study on the relationship between CTOs, conduction, and repolarization changes and the effects of successful PCI on these electrophysiological parameters is uncertain.

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In this study, we aimed to investigate the association between the electrocardiographic parameters between good CCC group and poor CCC group in CTO patients with PCI.

MATERIAL and METHODS

Study Design

Fifty-nine patients retrospectively implemented CTO PCI to those with symptomatic symptoms of myocardial ischemia or with the exact sign of ischemia in the CTO area at our hospital from January 2014 to December 2015. Baseline characteristics, laboratory and echocardiographic data, procedural data, and outcome data were retrospectively collected. A CTO has been identified as a total occluded lesion with TIMI 0 flow for more than 3 months, as recommended by the Euro CTO Club. (1). Collaterals were classified as Rentrop classification: grade 0, collateral arteries not fully fill; grade 1, collateral arteries filling the side branches of the CTO artery, excluding epicardial segments; grade 2, collateral arteries partial filling of epicardial arteries; grade 3, collateral arteries filling the epicardial arteries completely (11). The patients were divided into 2 groups according to the Rentrop class: group 1 (Rentrop 0 and 1) and group 2 (Rentrop 2 and 3). The Syntax score were evaluated by two experienced interventional cardiologists, using an online calculator (www.syntax score.com, version 2.1) and blinded to patients data. Patients were excluded for one of the following causes: patients with myocardial infarction within the three months or acute myocardial infarction, other rhythm than not sinus rhythm, atrial fibrillation, any degree of atrioventricular or left/right bundle block, severe valvular heart disease, irregular plasma electrolyte levels, taking antiarrhythmic medicines. Written informed consent of all patients was obtained before the procedure, and hospital ethical committee approved (2020/08) the present study.

ECG parameters

A regular twelve-lead resting ECG drawing at 10 mm/mV amplitude, and 25 mm/s paper speed was registered to utilizing a recorder (Nihon Kohden, Tokyo, Japan). All ECGs were examined by two specialist cardiologists, unaware of the patient's clinical status and angiographic result. The QT interval was measured as the distance from the first negative wave at the start of the QRS to the end of the T wave, based on the isoelectric line TP. The effect of heart rate on QT was corrected (QTc) using Bazett's formula. The dispersion of QT and QTc was recorded as the difference between the highest and lowest measurements recorded in precordial leads. The fQRS was defined as the presence of an extra R wave (R '), or the R or S wave notch, or the R' (multiple R ') in two consecutive leads that provide the area of the major coronary artery. Pmax in any of the 12-lead surface ECG was measured and accepted as a marker of the lengthened atrial conduction time. Pmax and Pmin were measured from the regular ECG, through sinus rhythm. P wave dispersion (PWD) is originated by subtracting the Pmin from Pmax in any of the 12 ECG leads. The P wave origin is defined as the first positive wave in the isoelectric baseline on which the T-P segment is based, and the P wave offset is defined as the re-arrival of the P wave into the baseline line. (12).

Statistical Analysis

All statistical analyses were applied in SPSS version 22.0 Windows (SPSS Inc, Chicago, Illinois). Categorical variables are presented as frequencies and percentages. Continuous variables are presented as mean ± SD. Categorical variables were analyzed using the chi-squared test and expressed as %. For continuous variables, Student's t test or a Mann-Whitney U test, as appropriate, was performed for comparison between two groups depending on the distribution pattern. A two-tailed P value <0.05 was considered statistically significant. Associations of Rentrop groups with ECG parameters, clinical, and laboratory outcomes were assessed by Pearson correlation coefficient.

RESULTS

Our study included 59 CTO patients undergoing PCI. Mean age was 61.0±10.3 years and 43 (72.9%) of patients were male. While 22 (37.2%) of the patients were poor collateral group 1, the remaining 37 (62.3%) of them were good collateral group 2. The baseline characteristics and procedural features of the patients are summary set in Table 1. While there was no significant difference between the two groups in terms of procedural features, hyperlipidemia (HL) and Syntax score were significantly higher in the poor collateral group (HL; 81.8% vs 54.1%, p: 0.031; Syntax score; 25.6±11.9 vs 18.3±8.7, p: 0.009, respectively). 89.3% of all patients had Canadian Cardiovascular Society (CCS) classes II-IV angina and no difference was observed between the two groups. The most common PCI performed in all 2 groups and all patients were RCA, and in 1 of 3 patients, CTO PCI was performed on LAD. Although there was no statistical difference in terms of PCI success (77.2% vs 64.8%), as in the volume of contrast usage (345.2±114.7 ml vs 298.7±114.0 ml), it was numerically higher in the poor group. In the laboratory parameters shown in Table 2, LDL-C (119.4±31.6 vs 96.5±39.8, p: 0.025) and hs-CRP levels (3.1±3.5 vs 1.1±1.0 p: 0.040) were statistically higher in the poor collateral group.

The comparison of ECG parameters of the good and poor collateral groups was shown in Figure 1. We found a significant difference, in poor and good collateral groups, QT dispersion (77.2±27.9 vs 66.5±22.5, p: 0.041, respectively), QTc dispersion (82.1±26.9 vs 70.4±23.9, p: 0.034, respectively), and the presence of fQRS (63.6% vs 43.2%, p: 0.027, respectively). But there was no statistically difference in P wave dispersion (48.0±9.5 vs 47.2±11.3, p: 0.796, respectively). In the follow-up results, were shown in Table 3, there was no statistical difference as clinical endpoint between both groups, at the end of the 2nd year, there were 2 mortality, 1 stroke and 3 revascularizations in the poor collateral group, and 1 mortality and 4 revascularizations were detected in the good collateral group. The associations between Rentrop collateral classification and baseline clinical,

Table 1. Baseline characteristics of the patients with good and poor collateral groups

Parameters	All Patients n=59	Poor Collateral n=22	Good Collateral n=37	p value
Age (years)	61.0±10.3	61.6±9.7	60.6±10.7	0.733
Gender (Male) n (%)	43 (72.9)	17 (77.3)	26 (70.3)	0.559
BMI (kg/cm2)	28.0±4.3	28.3±3.3	27.8±4.9	0.666
HT n (%)	36 (61.0)	15 (68.2)	21 (56.8)	0.384
HL n (%)	38 (64.4)	18 (81.8)	20 (54.1)	**0.031**
Current Smoker n (%)	36 (61.0)	14 (63.6)	22 (59.5)	0.750
DM n (%)	18 (30.5)	8 (36.4)	10 (27.0)	0.451
Syntax Score (%)	21.0±10.5	25.6±11.9	18.3±8.7	**0.009**
CCS Angina n (%)				
1	6 (10.2)	2 (9.1)	4 (10.8)	
2	28 (47.5)	12 (54.5)	16 (43.2)	0.531
3	22 (37.3)	8 (36.4)	14 (37.8)	
4	3 (5.1)	-	3 (8.1)	
Procedural Features				
Target Vessel n (%)				
LAD	22 (37.3)	8 (36.4)	14 (37.8)	
LCx	7 (11.8)	4 (18.1)	3 (8.1)	0.499
RCA	30 (50.8)	10 (45.5)	20 (54.1)	
Mean stent number	1.90±0.75	1.88±0.60	1.92±0.84	0.864
Mean Stent diameter mm	2.59±0.23	2.57±0.27	2.60±0.21	0.656
Mean Stent length mm	58.4±24.2	59.1±20.1	58.0±26.9	0.884
Procedure time (min)	68.1±29.4	64.1±34.3	70.5±27.5	0.663
Fluoroscopy time (min)	30.7±16.2	25.8±13.8	33.5±17.4	0.333
Contrast agent (ml)	315.6±115.5	345.2±114.7	298.7±114.0	0.142
Successful procedure n (%)	41 (69.4)	17 (77.2)	24 (64.8)	0.270

HT: Hypertension; HL: Hyperlipidemia; DM: Diabetes Mellitus; CCS: Canada Cardiovascular Society, LAD: left anterior descending, LCx: Left circumflex, RCA: right coronary artery

Table 2. Laboratory variables of the patients with good and poor collateral groups

Parameters	All Patients n=59	Poor Collateral n=22	Good Collateral n=37	p value
Serum glucose (mg/dl)	126.6±59.1	134.8±71.2	121.8±51.1	0.418
Serum creatinine (mg/dl)	1.08±0.24	1.03±0.18	1.11±0.27	0.233
Total cholesterol (mg/dl)	178.7±46.3	191.6±39.8	171.0±48.7	0.101
Triglyceride (mg/dl)	164.4±109.3	157.3±76.1	168.6±125.8	0.705
LDL cholesterol (mg/dl)	105.1±38.3	119.4±31.6	96.5±39.8	**0.025**
HDL cholesterol (mg/dl)	41.7±12.3	40.2±9.2	42.6±13.8	0.473
Hemoglobin g/dl	13.8±1.6	14.0±1.2	13.7±1.8	0.413
Platelet $\times 10^9$ /L	226.8±58.1	226.7±61.4	226.9±57.1	0.990
MPV (fL)	9.4±1.6	9.2±1.7	9.5±1.5	0.547
RDW (fL)	13.8±1.1	13.8±1.2	13.8±1.1	0.986
hs-CRP	2.7±3.2	3.1±3.5	1.1±1.0	**0.040**

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, hs-CRP: high sensitive C-reactive protein, MPV: mean platelet volume, RDW: red distribution width

Table 3. Follow-up outcomes

Parameters	All Patients n=59	Poor Collateral n=22	Good Collateral n=37	p value
30-Day MACE n (%)				
Mortality	1 (1.8)	1 (4.8)	-	
Stroke	1 (1.8)	1 (4.8)	-	0.271
Revascularization	1 (1.8)	-	1 (2.9)	
6th Month MACE n (%)				
Mortality	-	-	-	
Stroke	-	-	-	0.521
Revascularization	4 (7.8)	2 (11.1)	2 (6.1)	
1st Year MACE n (%)				
Mortality	1 (1.8)	1 (6.3)	-	
Stroke	-	-	-	
Revascularization	2 (4.6)	1 (6.3)	1 (3.7)	
2nd Year MACE n (%)				
Mortality	1 (3.8)	-	1 (7.1)	
Stroke	-	-	-	0.395
Revascularization	-	-	-	

MACE: Major Adverse Cardiac Events

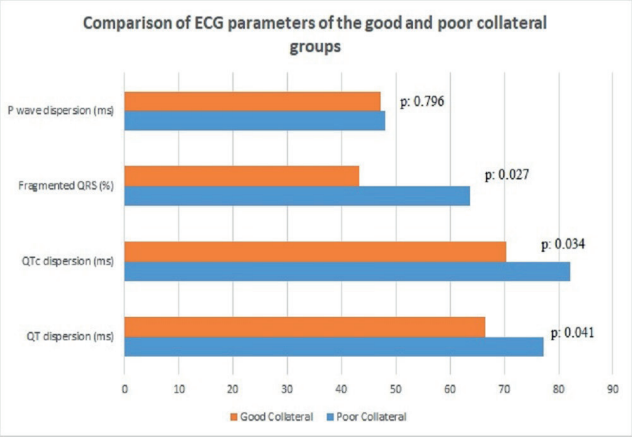

Figure 1. Comparison of electrocardiogram parameters of the good and poor collateral groups

Table 4. Correlation between the Rentrop classification and clinical variables

Parameters	r value	p value
Gender	-0.009	0.945
Age	-0.139	0.293
Syntax Score	-0.397	**0.002**
LDL-C	-0.198	**0.025**
Glucose	-0.129	0.330
QT dispersion	-0.156	**0.045**
QTc dispersion	-0.176	**0.037**
Fragmented QRS	0.234	**0.021**

ECG and, laboratory characteristics of the patients are shown in Table 4. Correlation analysis revealed that the association between Rentrop classification and Syntax score (r: -0.397, p: 0.002), LDL-C (r: -0.198, p: 0.025), QT dispersion (r: -0.156, p: 0.045), QTc dispersion (r: -0.176, p: 0.037), and the presence of fQRS (r: 0.234, p: 0.021) were statistically significant.

DISCUSSION

The major results of this study in patients with CTO undergoing PCI are that (1) in the consecutive CTO patient group, our PCI success was 69.4% in our center, (2) more than 1 in 3 of the patients had poor collateral, (3) at 2 years of follow-up, acceptable major adverse clinical events rates were determined, (4) QT dispersion, QTc dispersion, and the presence of fQRS were higher in poor collateral group but there was no significantly difference in P wave dispersion (5) we found statistically correlation between Rentrop collateral classification and Syntax score, LDL-C, QT dispersion, QTc dispersion, and the presence of fQRS.

The presence of CTO was correlated with adverse cardiovascular results (angina, greater occurrence of ventricular arrhythmias, higher mortality) and decreased survival in patients (13,14). CTO has been considered a classically demanding subset compared to non-CTO PCIs with low success rates, complex structure, increased procedural events compared to other PCIs. In current, the newest developments in dedicated CTO-PCI tools and methods have led to high rates of success and low complication rates in expert CTO clubs (14-16). No clear results are concerned from the outcomes of the studies directed on the impacts of Rentrop collateral on ECG

parameters in CTO patients. Sudden cardiac death is seen 5 times less in patients who have successfully undergone CTO PCI compared to patients receiving medical treatment with CTO (15). However, information on the etiology and associated mechanisms (arrhythmic or non-arrhythmic death) of poorer clinical outcomes in untreated CTO patients is limited (17). There are several studies on ECG parameters after successful CTO PCI (7-10). Cetin M. et al showed that the after PCI values of TpTe, the TpTe/QT ratio, and QTc dispersion were statistically reduced matched with the before PCI assessments after successful CTO PCI (8). In addition, they reported, in secondary results, that the patients in Rentrop grade 1 and patients with multi-coronary disease became higher before PCI assessments for TpTe and the TpTe/QT ratio than these in the opposite groups. Erdogan E et al. dedicated that QTd and QTcd reported significant change after successful CTO PCI (55.83±14.79 to 38.87±11.69; p<0.001 and 61.02±16.28 to 42.92±13.41; p<0.001) (9). Meta-analysis, which collected studies on ECG changes after successful recanalization of CTO, included 8 studies with a total of 467 patients (5). The findings obtained according to this meta-analysis are as follows: a significant decrease in mean QT dispersion and QTc dispersion of after successful CTO PCI and CABG, Tpe and the Tpe/QT ratio reduced significantly, and a decrease in heart rate variability (HRV) and baroreceptor sensitivity (BRS) parameters after CTO PCI. Besides, they concluded that this meta-analysis recommends a valuable consequence of successful PCI or CABG on several ECG factors that had been related to malignant ventricular arrhythmias and SCD in the background (5). While these studies mostly investigated the effect of CTO PCI on ECG parameters, our study examined the association between the pre-PCI collateral class and ECG parameters. Concerning the presence of fQRS, the parameter associated with arrhythmias, this retrospective observational study is included 56 patients with CTO (10). They reported that the association between the presence of fQRS on the ECG and poor collateral in patients with CTO, similar to our results.

The improvement of CCC can be a runner of the prognosis of patients with CTO. Coronary collateral is a reply to vascular occlusion damage in coronary arteries. Patients with CTO typically have collateral arteries of the distal artery, and these collaterals may add to the release of ischemia and angina and the protection of ventricular function (18). Previous studies have confirmed that good collateral is associated with less infarction, less ventricular aneurysm, improved ventricular function, less future cardiovascular events, and improved survival (19,20). Increased dispersion of repolarization is a perceived pathogenic factor in fatal ventricular arrhythmias (21). When we examine the studies evaluating ECG parameters with coronary collateral, it concludes that the Tpe and cTpe intervals and Tpe/QT and cTpe/QT ratios were lower in the patients with good collateral (22). Stable coronary artery disease (CAD) consecutive 203 patients, one of the coronary arteries with CTO, were included in this study. They reported that statistically correlations between the poor Rentrop grade and cTpe interval (r: -0.455, p <0.001), and they show that poor Rentrop grade (β = –0.228, p < 0.001) was independent predictors of a lengthened cTpe interval (22). But Tasolar et al. considered that the presence of collateral did not affect the QTd. In another study conducted by Tandogan et al in coronary artery disease patients including 100 non-CTO patients, they divided the patients into 2 groups as grade 0 and grade ≥1 collateral (23). The mean QTc dispersion was shown to be significantly higher in patients with collateral grade ≥1 than those with grade 0 and there was significantly correlation between collateral grade and QTc dispersion (23). In our study QTc dispersion was significantly higher in poor collateral group (Rentrop 0 and 1). Although there is no data in the literature regarding the P wave dispersion in the CTO patients we detected in our study, there was no statistical difference between both collateral groups, and two studies evaluated the relationship with CAD severity in stable CAD patients (24,25). Similarly in both studies, P wave dispersion is raised and associated with the severity of CAD in patients with stable CAD.

These ECG parameters will be useful in evaluating the revascularization method or with the knowledge of which patients have poor collaterals. The revascularization method should be chosen in CTO patients in line with current revascularization guideline indications. Bypass surgery may be more appropriate in patients whose ECG parameters suggest poor collateral in this decision. If revascularization is not performed, patients with these parameters should be given more aggressive medical therapy since they have a worse prognosis.

This study has several limitations. The main limitation of our study includes a small number of patients. Besides, we calculated ECG parameter with manually measures by the magnifying camera instead of the computer software program for ECG parameter calculations. Another limitation in our study is that the findings of ischemia evidence could not be reached.

CONCLUSION

This study suggests that higher QT dispersion, QTc dispersion, and the presence of fQRS were associated with a good coronary collateral grade in patients with CTO but there was no statistical difference in P wave dispersion. In addition, we conclude that significantly correlation between Rentrop collateral classification and Syntax score, LDL-C, QT dispersion, QTc dispersion, and the presence of fQRS. Larger study groups are needed to explain this correlation between coronary collateral improvement and ECG parameters.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: Medicana International Ankara Hospital, 2020/08.

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