

# Evaluation of the Tp-Te Interval, QTc and P-Wave Dispersion in Patients With Coronary Artery Ectasia

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## Abstract

**Background:** Coronary artery ectasia (CAE) is defined as a diffuse dilatation of the diameter of the ectatic segment of the coronary artery, 1.5 times greater than that of the adjacent segment. The Tp-Te interval, P-wave and QTc dispersions are relatively new electrocardiographic markers associated with an increased risk of developing arrhythmias. Despite CAE increasing in prevalence in recent years, there is a sparsity of data available about its arrhythmogenic effect. The aim of the study was to evaluate QTc, P-wave dispersion and Tp-Te and Tp-Te/QT ratio in patients with CAE.

**Methods:** A retrospective comparative study was designed for consecutive age- and sex-matched patients. Twenty patients with isolated CAE (group 1) and 20 control subjects (group 2), with normal coronary arteries, were included. All patients presented with chest pain and coronary angiogram was indicated. Outcome measures included Tp-Te interval, Tp-Te/QT ratio, QTc dispersion and P-wave dispersion. Measurement of electrocardiogram (ECG) parameters was conducted using standardized digital online software. Descriptive and inferential statistics were performed.

**Results:** Mean Tp-Te ( $95.5 \pm 9.01$  ms) and Tp-Te/QT ratio ( $0.22 \pm 0.02$ ) were significantly prolonged in CAE group (Tp-Te:  $84 \pm 5.62$  ms,  $P = 0.00009$ ; Tp-Te/QT ratio:  $0.20 \pm 0.01$ ,  $P = 0.00004$ ). In addition, QTc ( $31.2 \pm 3.71$  ms) and P-wave dispersion ( $31.9 \pm 5.46$  ms) were significantly increased in comparison to the control group (QTc:  $27.6 \pm 2.82$  ms,  $P = 0.00532$  and  $20 \pm 3.77$  ms,  $P = 0.00003$  respectively). However, there was no difference in ventricular activation time (VAT) between groups.

**Conclusions:** CAE ECGs were found to be associated with increased Tp-Te, Tp-Te/QT ratio, QTc intervals and P-wave dispersions. This may suggest that CAE existence has a pro-arrhythmogenic nature.

**Keywords:** Coronary artery ectasia; Tp-Te interval; QTc dispersions; Arrhythmia; P-wave dispersions; Tp-Te/QT ratio

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## Introduction

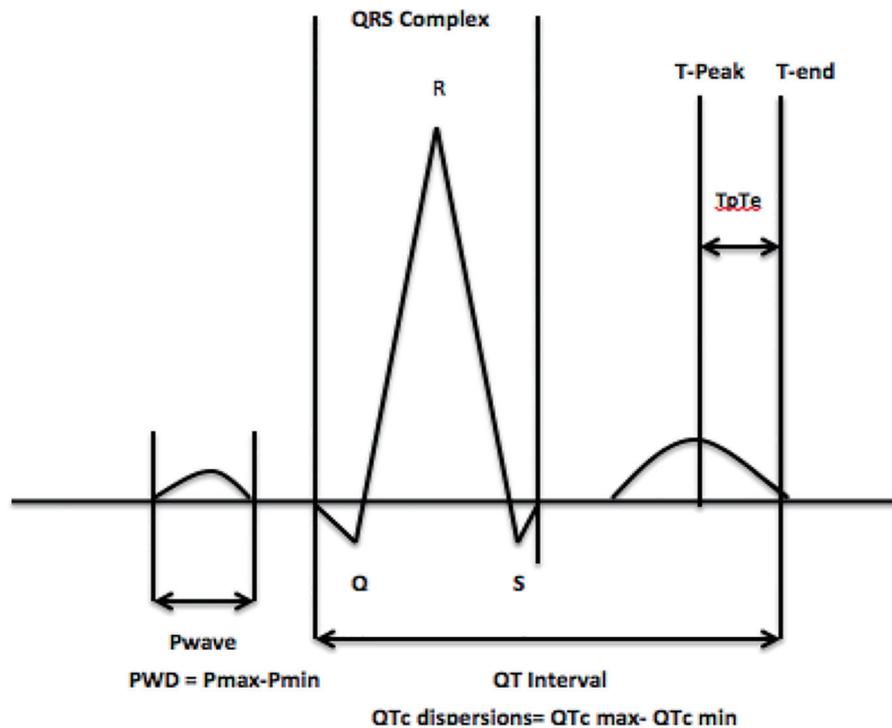
Coronary artery ectasia (CAE) has been defined dilatation of a coronary vessel segment up to 1.5 times the diameter of the adjacent vessel and including more than a third of the total length of the vessel [1]. The pathophysiology and clinical significance of CAE is poorly understood. Suggested etiologies include atherosclerosis, congenital abnormalities, inflammatory and/ or connective tissue diseases [2, 3].

The interval from the peak of the T wave to the end of the T wave (Tp-Te interval), on a standard 12-lead electrocardiogram (ECG), is a measure of transmural dispersion of repolarization in the left ventricle [4-6], with prolongation representation a period of possible susceptibility to ventricular arrhythmias [7, 8]. A prolonged Tp-Te interval has been associated with an increased risk of mortality in hypertrophic cardiomyopathy, in patients undergoing primary percutaneous coronary intervention for myocardial infarction, and in congenital and acquired long-QT syndromes [9-11]. Limited data are available with regard to the effect that CAE has on the Tp-Te interval, which is important given its potential arrhythmogenic effect (Fig. 1).

Other ECG parameters such as QTc dispersion, which has been defined as the difference between the longest and shortest QT interval and P-wave dispersion (PWD), which is calculated by subtracting the minimum P-wave duration from the maximum in a 12-lead ECG (Fig. 1), are important measurements and have been implicated in the development of both ventricular and atrial arrhythmias respectively [12-14]. In the present study, we examine the Tp-Te interval, QTc and PWD in patients with CAE, to assess whether an apparently benign disease has a pro-arrhythmogenic effect.

## Materials and Methods

A retrospective chart review of 1,650 consecutive angiograms, between January 2014 and January 2017, was conducted to identify patients with CAE [15]. Patients with known previous myocardial infarction (MI), atrial fibrillation, bundle branch blocks, ventricular preexcitation and atrioventricular conduction abnormalities were excluded from the study. Also, patients on any antiarrhythmic drugs that may have an effect on ECGs parameters were excluded. A total of 20 patients with isolated CAE (group 1) were identified and compared to 20 control subjects (group 2), with normal coronary arteries. All



**Figure 1.** The Tp-Te interval, QTc and P-wave dispersion.

patients presented with chest pain and following non-invasive tests for risk stratification, for ischemic heart disease a coronary angiogram was indicated. Both groups were matched for age and sex as well as cardiovascular risk factors including: hypertension, family history of ischemic heart disease, diabetes mellitus, smoking history and dyslipidemia.

All ECGs were measured at rest, using a 12-lead high resolution ECG (GE, MAC 5000, New York) with 1 mV/cm amplitude and 25 mm/s rate. Outcome measures included Tp-Te interval, Tp-Te/QT ratio, QTc dispersion, PWD and VAT.

### **Tp-Te interval and Tp-Te/QT ratio**

The Tp-Te interval was measured from the peak of the T wave to the end of the T wave. The end of the T wave was defined as the intersection of the tangent to the down slope of the T wave and the isoelectric line [16]. The QT interval was measured from the earliest onset of the QRS complex to the end of the T wave (Fig. 1). When a U wave interrupted the T wave prior to returning to baseline, the interval was measured to the nadir of the curve between the T and U waves.

The Tp-Te/QT ratio was calculated as the ratio of Tp-Te in lead V5 to the corresponding QT interval in the same lead [9]. The Tp-Te and QT interval were measured in lead V5 [9, 17].

### **QTc dispersion**

QTc dispersion was defined as the difference between the long-

est and shortest QT intervals and rate corrected using Bazett's formula, as the heart rate was found to be under 100 bpm in all ECGs [12].

### **PWD**

PWD was calculated by subtracting the minimum P-wave duration from the maximum in any of the 12 ECG leads (Fig. 1). The beginning of the P wave was defined as the point where the initial deflection of the P wave crossed the isoelectric line and the end was defined as the point where the final deflection of the P wave crossed the isoelectric line.

### **Ventricular activation time (VAT)**

VAT was defined as the average measurement from the onset of the Q wave to the peak of the R wave. The measurements from V6 were comparable with the mean value calculated from 12 leads as previously validated [18].

### **ECG measurements**

Measurement of ECG parameters was conducted manually using digital online software (Cardio Calipers, Iconico, New York, NY), by a blinded observer. A second blinded observer repeated all ECG measurements using the same technique and

**Table 1.** Demographics and Cardiovascular Risk Factors: Group 1 Versus Group 2

Variables	Group 1 (n = 20)	Group 2 (n = 20)	P value
Age	63.2 ± 10.2	60 ± 8.8	0.58
Gender (female, %)	14/6	15/5	0.77
Hypertension (%)	12 (60%)	11 (55%)	0.31
FHx of CAD (%)	6 (30%)	4 (20%)	0.71
Diabetes mellitus (n, %)	4 (20%)	3 (15%)	0.40
Smoking history (n, %)	14 (70%)	10 (50%)	0.94
Dyslipidemia (n, %)	16 (80%)	13 (65%)	0.98

FHx: family history; CAD: coronary artery disease.

the two subsets of data were compared to ensure there was no inter-observer variability ( $P > 0.05$ ).

### Statistical analysis

Descriptive and inferential statistics were performed using Stata 13 (StataCorp CP, College Station, TX). An unpaired *t*-test was used to compare groups. Statistical significance was set at  $P < 0.05$ .

## Results

### Demographics

Baseline demographics of age, gender and cardiovascular risk factors including: hypertension, family history of ischemic heart disease, diabetes mellitus, smoking history and dyslipidemia were all listed in Table 1. There was no significant difference between both groups. Hypertension was defined in accordance with the JNC-7 guidelines as a systolic blood pressure  $\geq 140$  mm Hg, diastolic blood pressure  $\geq 90$  mm Hg and/or use of antihypertensive medications. Family history of CAD was noted if a male first-degree relative developed CAD before the age of 55 or a female first-degree related before 65. Diabetes was defined as overnight fasting blood glucose  $\geq 7$  mmol/L (126 mg/dL), postprandial blood glucose  $\geq 11$  mmol/L (200 mg/dL) or use of insulin or oral hypoglycemic agents. Patients were classified as smokers if they had smoked during the last month. Dyslipidemia was defined as a total cholesterol  $\geq$

6.2 mmol/L (240 mg/dL), low-density lipoprotein cholesterol  $\geq 4.14$  mmol/L (160 mg/dL) or use of lipid-lowering medications [19].

### CAE/ECG comparison with control

In Table 2, all the predefined intervals were compared and showed results as follows.

#### *Tp-Te interval and Tp-Te/QT ratio*

Mean Tp-Te ( $95.5 \pm 9.01$  ms) and Tp-Te/QT ratio ( $0.22 \pm 0.02$ ) were significantly prolonged in group 1, compared to group 2 (Tp-Te:  $84 \pm 5.62$  ms,  $P = 0.00009$ ; Tp-Te/QT ratio:  $0.20 \pm 0.01$ ,  $P = 0.00004$ ).

#### *QTc dispersion and PWD*

CAE/ECG measurements of QTc ( $31.2 \pm 3.71$  ms) and PWD ( $31.9 \pm 5.46$  ms) were significantly higher in comparison to group 2 (QTc:  $27.6 \pm 2.82$  ms,  $P = 0.00532$ ; PWD:  $20 \pm 3.77$  ms,  $P = 0.00003$ ).

#### *VAT*

There was no significant difference in VAT duration between groups (group 1:  $42 \pm 2.63$  ms, group 2:  $43.72 \pm 3.23$  ms,  $P = 0.22$ ).

**Table 2.** Comparison of ECG Intervals Between CAE Group and Control Group

Variables	CAE group (n = 20), mean ± SD	Control group (n = 20), mean ± SD	P value
Tp-Te (ms)	$95.5 \pm 9.01$	$84 \pm 5.62$	$< 0.001$
Tp-Te/QT ratio	$0.22 \pm 0.02$	$0.20 \pm 0.01$	$< 0.001$
QTc dispersions (ms)	$31.2 \pm 3.71$	$27.6 \pm 2.82$	$< 0.01$
P-wave dispersions (ms)	$31.9 \pm 5.4$	$20 \pm 3.77$	$< 0.001$
VAT (ms)	$42 \pm 2.63$	$43.72 \pm 3.23$	0.22

Tp-Te: peak T wave duration to the end of T wave; QTc: corrected QT dispersions; VAT: ventricular activation time.

## Discussion

The present study represents an assessment of pertinent ECG markers associated with arrhythmias in patients with CAE. CAE was found to be associated with a prolonged Tp-Te interval, QTc and PWD. These findings suggest that CAE, an apparently benign disease, may in fact have a pro-arrhythmogenic effect.

CAE is a relatively rare coronary anomaly, found in approximately 5% of patients undergoing coronary angiography [2]. Ectatic coronary arteries have been found to be associated with myocardial ischemia, thrombosis, spasm, dissection and rupture [20-22]. In addition, they have been associated with electrical instability, ventricular fibrillation and sudden death [22, 23].

### Tp-Te interval

Tp-Te interval is a measure of transmural dispersion of repolarization in the left ventricle, with prolongation representing a period of possible susceptibility to ventricular arrhythmias [7, 8]. A proposed mechanism for this phenomenon was suggested by Antzelevitch and coworkers [24, 25]. Three electrophysiological distinct cell types exist in the ventricular myocardium, which include the endocardial, epicardial and subendocardial M cells (Masonic mid-myocardial Moe cells). The action potential of the M cells is the most susceptible to prolongation [6], likely because of a combination of larger late-sodium and sodium/calcium exchange currents as well as a weaker slowly activation delayed rectifier current [26]. The Tp-Te interval corresponds with transmural dispersion of repolarization in the ventricular myocardium, a period where the epicardium has fully repolarized but the M cells are still in the process of repolarization, making them more vulnerable to early after-depolarizations [16, 17]. These early after-depolarizations can lead to reentry, which could result in a polymorphic ventricular tachycardia or ventricular fibrillation, hence why a prolonged Tp-Te likely corresponds to an extended period of vulnerability that could increase the risk of ventricular arrhythmogenesis [7, 27-29].

In the present study, the Tp-Te interval was found to be longer in the CAE group. Our results were consistent with another study conducted by Karaagac et al [30], where the Tp-Te interval was found to be significantly increased in patients with isolated CAE. In their study, the mean Tp-Te interval was found to be  $97.71 \pm 8.7$  ms in patients with CAE, compared to  $85.23 \pm 7.1$  ms in the group with normal coronary arteries [30].

A disproportionate increase in transmural dispersion of repolarization relative to the total duration of repolarization (Tp-Te/QT ratio) has previously been shown to have a pro-arrhythmic effect [31]. It has been proposed as a marker of arrhythmogenesis for long QT-syndrome as well as hypertrophic cardiomyopathy [9, 32]. In the present study, mean Tp-Te/QT ratio was significantly greater among patients with CAE compared to controls.

### QTc dispersion

QTc dispersion is emerging as an important clinical tool as

it is known to be an important factor in the development of ventricular arrhythmias in patients with chronic heart failure, mitral valve prolapse, MI and familial long QT syndrome [13, 33-35]. In the present study, isolated CAE was associated with a significantly increased QTc in comparison to the control group. Our findings are consistent with another study, which also found QTc dispersion to be increased in patients with CAE [36].

### PWD

PWD is thought to reflect prolongation of both intra-atrial and interatrial conduction time and the inhomogeneous propagation of sinus impulses, which are known electrophysiological features in patients with atrial arrhythmias [14]. A prolonged PWD time has been reported to increase the risk of developing atrial fibrillation in patients with no underlying heart disease [37, 38]. Our results were consistent with another study, which demonstrated a statistically significant increase in PWD time in patients with CAE [36].

### Conclusions

CAE was found to be associated with prolongation of the Tp-Te interval, QTc and PWD. Our data suggest that these patients may be more susceptible to developing both ventricular and atrial arrhythmias. Routine measurement of the aforementioned ECG parameters in clinical practice may be useful in risk stratifying these patients. Further prospective studies are warranted to quantify arrhythmia burden in CAE patients.

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