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The link between ventricular repolarization variables and arterial function

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Abstract

Aim: To assess the relationship between repolarization variables and arterial function.
Methods: A total of 54 participants, aged 33 ± 10 years, underwent arteriography and standard 12-lead electrocardiography (ECG). Arteriography was performed using a noninvasive automated oscillometric method, assessing: brachial (Aix Brach) and aortic augmentation index (Aix Ao), pulse wave velocity (PWV), arterial age (AA), diastolic reflection area (DRA) and diastolic area index (DAI). Standard 12-lead ECG enabled measurement of QT and Tpeak-Tend (TpTe) intervals and TpTe/QT ratios.
Results: QT interval was prolonged in patients with elevated blood pressure or body mass index. Significant associations were found between electrocardiographic repolarization parameters, such as QT intervals, TpTe and TpTe/QT and arteriography variables, such as Aix Brach, Aix Ao, PWV and AA.
Conclusion: Prolonged QTc and Tpe are associated with endothelial dysfunction, arterial stiffness, impaired coronary perfusion and accelerated arterial aging.

Keywords: QT interval; Tpeak-Tend interval; Arterial stiffness; Augmentation index; Endothelial dysfunction; Arterial age

Introduction

Several electrocardiographic (ECG) predictors of ventricular arrhythmia and sudden cardiac death risk have been described, including QT and Tpeak-Tend (TpTe) interval duration. The QT interval, the most used parameter in the electrocardiographic assessment of repolarization [1], is prolonged or borderline if it exceeds 460 and 450 ms, respectively, in women, and 450 and 430 ms, respectively, in men [2,3].

A prolonged Tpeak-Tend interval (TpTe), a readily available ECG measurement of dispersion of the end of repolarization [4,5], predisposes to life-threatening ventricular arrhythmias [6]. TpTe/QT ratio and TpTe/QTc ratio are used as indices of ventricular arrhythmogenesis [7–9]. Cardiovascular diseases continue to be the main mortality causes worldwide, and they are linked to atherosclerosis and its complications [10]. Arterial stiffness and endothelial dysfunction are markers of subclinical atherosclerosis, enabling cardiovascular risk screening [11]. Arterial age, the chronological age of a person with the same 10 years predicted risk but all risk factors at the normal levels [12], is a good predictor of cardiovascular disease.

The aim of the present study was to assess the relationship between repolarization variables such as: QT and TpTe intervals and TpTe/QT, and arterial function.

Material and methods

Study population and ethical aspects

A total of 54, apparently healthy participants, aged 33 ± 10 years, recruited from a general practitioners office, underwent arteriography and standard 12-lead ECG.

The most important *exclusion criteria* were: electrolyte imbalances, atrial fibrillation, and history of myocardial infarction, stroke or diabetes mellitus, the use of drugs known to influence the QT interval or arterial stiffness.

The investigations conformed to the principles outlined in the Declaration of Helsinki (Cardiovascular Research 1997; 35: 2–4) and were approved by the Ethics Committee of the University. A written informed consent was obtained from each patient.

The power analysis conducted to determine the number of participants needed for the present study showed a minimum sample size required for regression analysis of 54 (anticipated effect size: 0.15; desired statistical power level: 0.8; 0.05 probability level).

Arteriography

Arteriography was performed by the author using a noninvasive automated oscillometric analyzer (TensioMed

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Ltd, Budapest, Hungary). Brachial augmentation index (Aix Brach), aortic augmentation index (Aix Ao), pulse wave velocity (PWV), systolic blood pressure in the aorta (SBPAo), diastolic reflection area (DRA), diastolic area index (DAI) and arterial age (AA) were assessed. Pulse wave velocity (PWV) is the speed at which the pulse waveforms travel along the aorta and large arteries, calculated as the distance traveled by the pulse wave between two points, divided by the time taken to travel the distance [13], and depends on the elasticity of the arterial wall. Augmentation indices (aortic and brachial), markers of endothelial dysfunction, are calculated as the ratio of the difference between initial systolic and reflected pulse wave divided by the pulse pressure. DRA and DAI provide information about the quality of the coronary artery filling in diastole and were calculated using the mathematical model built in the software, analyzing the recorded diastolic pulse waves. Arterial age is investigated noninvasively through the measurement of arterial stiffness, central blood pressure and endothelial dysfunction. SBPAo is the central systolic blood pressure. The methodology for arteriography was previously described [14,15].

Arterial stiffness, endothelial dysfunction and early vascular aging were considered if the pulse wave velocity >10 m/s, the brachial augmentation index greater than −10%, and the vascular age was higher than the biological age, respectively [14]. Blood pressure values were classified according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [16].

Standard 12-lead ECG

Standard 12-lead ECG was performed at a paper speed of 25 mm/s, using a Rextra, multi-channel ECG unit. ECG measurements were made independently of the arteriography results, by the same investigator. The methodology for QT interval measurement was previously described [17]. The QT interval was corrected for heart rate using the Bazett formula [18]. The Tpeak-Tend interval was calculated in each lead as the difference between the QT interval and the QTpeak interval (from the beginning of the QRS complex to the peak of the T wave) [19,20]. All intervals were measured manually. QT and TpTe were measured in each lead and the longest value was used. QT and Tpeak-Tend intervals were not measured in leads with low amplitude T waves, in which the end of the T wave could not be assessed. TpTe/QTc and TpTe/QTmax ratios were also calculated. The longest values for TpTe and QT were used to obtain TpTe/QT ratios. Mean QT interval duration (QTm) was assessed as the mean of the QT intervals in all measurable leads.

Statistical analysis

Categorical variables are given in numbers (percentages); continuous data are given as means ± standard deviation. Linear and multiple regression analysis, Bravais–Pearson correlations, sensitivity, specificity, positive and negative predictive value were used as statistical methods. A $p < 0.05$ was considered statistically significant.

Results

The characteristics of the study population and the obtained ECG and arteriography variables are included in Table 1.

Prolonged QTc and Tpe

The patients with prolonged QTc were hypertensive, overweight, obese or with prehypertension. TpTe exceeded 100 ms in patients with elevated body mass index or increased blood pressure values. Considering the patients with a TpTe exceeding 100 ms, 38%, 34% and 14% had an impaired DRA, DAI or PWV. Most patients with a prolonged QTc had also an impaired diastolic reflection area (60%). Impaired DRA and DAI values were recorded in 48% and 35% study participants with borderline and prolonged QTc.

PWV was optimal (<7 m/s) only in 13 study participants (24%). Considering patients with a PWV exceeding 7 m/s (normal and elevated arterial stiffness), 17% (7) and 61% (25) had prolonged QTc and TpTe, respectively.

Table 1
Characteristics of the study population, electrocardiographic and arteriography variables.

Variable	Reference range (means ± SD) or N (%)
Chronological age (years)	33 ± 10
Gender (male)	23 (43%)
Body mass index (kg/m^2)	25 ± 6
Overweight (BMI ≥ 25 kg/m^2)	25 (46%)
Obesity (BMI ≥ 30 kg/m^2)	9 (17%)
Systolic blood pressure (SBP) (mmHg)	122 ± 13
Diastolic blood pressure (DBP) (mmHg)	71 ± 10
Hypertension	6 (11%)
Prehypertension	8 (15%)
Pulse pressure (PP) (mmHg)	51 ± 10
Mean arterial pressure (MAP) (mmHg)	88 ± 10
Heart rate (HR) (beats/minute)	76 ± 12
Brachial augmentation index (Aix Brach) (%)	−46 ± 23
Systolic blood pressure in the aorta (SBPAo) (mmHg)	111 ± 14
Pulse pressure in the aorta (PPAo) (mmHg)	40 ± 9
Aortic augmentation index (Aix Ao) (%)	14 ± 12
Diastolic reflection area (DRA)	52 ± 11
DRA <50	21 (39%)
Diastolic area index (DAI) (%)	52 ± 5
DAI <50%	15 (28%)
Pulse wave velocity (PWV) (m/s)	8 ± 1.4
PWV <7 m/s (optimal)	13 (24%)
PWV >9.7 m/s	7 (13%)
Arterial age (years)	41 ± 14
QTmax (maximal QT interval duration) (ms)	380 ± 25
QTc (heart rate corrected QT interval) (ms)	427 ± 28
Prolonged QTc	10 (19%)
Borderline and prolonged QTc	23 (43%)
QTm (mean QT interval duration in all measurable leads) (ms)	350 ± 24 ms
Tpeak-Tend interval (Tpe) (ms)	105 ± 38
Tpe >100 ms	29 (54%)
Tpe/QTmax	0.29 ± 0.08
Tpe/QTc	0.26 ± 0.07