

An indicator of sudden cardiac death during brief coronary occlusion: electrocardiogram QT time and the role of collaterals

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Aims

The coronary collateral circulation has a beneficial role regarding all-cause and cardiac mortality. Hitherto, the underlying mechanism has not been clarified. The aim of this prospective study was to assess the effect of the coronary collateral circulation on electrocardiogram (ECG) QTc time change during short-term myocardial ischaemia.

Methods and results

A total of 150 patients (mean age 63 ± 11 years, 38 women) were prospectively included in this study. An ECG was recorded at baseline and during a standardized 1 min coronary balloon occlusion. QT interval was measured before, during, and after balloon occlusion and was corrected for heart rate (QTc). Simultaneously obtained collateral flow index (CFI), expressing collateral flow relative to normal anterograde flow, was determined based on intracoronary pressure measurements. During occlusion of the left anterior descending coronary artery mean QTc interval increased from 422 ± 33 to 439 ± 36 ms ($P < 0.001$), left circumflex occlusion led to an increase from 414 ± 32 to 427 ± 27 ms ($P < 0.001$). QTc was not influenced by occlusion of the right coronary artery (RCA) (417 ± 35 and 415 ± 34 ms, respectively; $P = 0.863$). QTc change during occlusion of the left coronary artery was inversely correlated with CFI ($R^2 = 0.122$, $P = 0.0002$).

Conclusion

Myocardial ischaemia leads to QT prolongation during a controlled 1 min occlusion of the left, but not the RCA. QT prolongation is inversely related to collateral function indicating a protective mechanism of human coronary collaterals against cardiac death.

Keywords

Coronary collateral circulation • Protective effect • QT interval • QT dispersion • Ischaemia

Introduction

The coronary collateral circulation refers to the anastomotic network of blood vessels, existent even in the healthy human heart, which are an alternative source of blood supply to cardiac regions jeopardized by myocardial ischaemia.^{1,2} Several studies have indicated that the presence of collaterals in coronary artery disease (CAD) plays a beneficial role in reducing major adverse events including all-cause and cardiac mortality.^{3,4} This protective effect of coronary collaterals seems plausible; however, its underlying mechanisms has not been elucidated yet.

It is beyond doubt that myocardial ischaemia can provoke electrical instability.^{5,6} Electrical myocardial changes during ischaemia are measurable even on the surface electrocardiogram (ECG). As Kenigsberg *et al.* demonstrated, abrupt coronary vessel occlusion during percutaneous coronary intervention may increase ECG QT interval.⁷ The QT interval represents the onset of completion of ventricular repolarization. A growing body of evidence has suggested that QT prolongation and QT time variability are markers or even triggers for electrical instability and sudden cardiac death.^{8–13} A recent analysis based on the Oregon Sudden Unexpected Death Study (Ore-SUDS) has confirmed an

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increased mortality risk even for QT prolongation of unknown reason and independent of other factors.¹⁴

From animal experiments, it has been known for a long time that a well-developed collateral circulation mitigates electrical instability and arrhythmogenic vulnerability during impaired epicardial blood flow.¹⁵

Since respective data from studies in humans are not available, the current clinico-pathophysiological study was designed to investigate whether the function of coronary collaterals is related to QT interval prolongation during vessel occlusion.

Methods

Patients

One-hundred and fifty adult patients (>18 years of age) with suspected CAD who presented at our institution for elective coronary angiography due to chest pain or positive stress test were included in this prospective study. Patients with acute coronary syndromes were not considered. Patients with previous Q-wave infarction in the area of collateral assessment, those with atrial fibrillation, as well as those with baseline ECG ST-segment abnormalities or conduction abnormalities or paced rhythm were excluded from the study. The Ethics Committee of the Kanton of Bern, Switzerland approved the present investigation and the patients gave written informed consent to participate in the study.

Even if angiography did not reveal any significant coronary artery stenosis, patients were enrolled in the study. After coronary angiography, participants were divided into two groups depending on the site of collateral flow index (CFI) measurement. In the left coronary artery (LCA) group, measurements were performed in the left anterior descending (LAD) coronary artery or left circumflex (LCX) coronary artery. In the right coronary artery (RCA) group, measurements were performed in the RCA. The rationale of grouping was based on the previous work by de Marchi et al.¹⁶ demonstrating differential sensitivity to ischaemia of myocardial regions supplied by the LCA and RCA.

Cardiac catheterization and coronary angiography

Patients underwent left heart catheterization from the femoral artery approach. Biplane coronary angiography was performed. The projection showing the most severe narrowing was chosen for monoplane assessment of coronary artery diameter stenosis by quantitative coronary angiography (Philips DCI/ Integris systems). Left ventricular end-diastolic pressure (LVEDP) was obtained and a left ventricular angiogram was performed in each patient, ejection fraction and regional wall motion abnormalities were assessed visually by the operator.

Collateral function assessment

For collateral measurement in patients with CAD, the vessel and the vessel site of tightest stenosis were selected. In the 55 participants without significant coronary obstruction, a non-diseased large-calibre vessel with minimal tortuosity was chosen.

In all patients, recruitable coronary collateral flow during the first 1 min vascular balloon occlusion relative to normal flow through the non-occluded coronary artery (CFI) was determined quantitatively based on simultaneous pressure measurements. A sensor-tipped pressure wire (Radi, Upsala, Sweden) was positioned distal to the site of balloon occlusion. Collateral flow index was determined by simultaneous measurements of mean aortic (P_{ao} , mmHg, via angioplasty

guiding catheter), distal coronary occlusive pressure (P_{occl} , mmHg), and central venous pressure (CVP, measured at right atrial level through femoral vein access): $CFI = (P_{occl} - CVP) / (P_{ao} - CVP)$. This method has been validated and described previously in detail.^{17,18}

If patients had a significant stenosis, the vessel with the tightest stenosis was selected for measurements; balloon occlusion was performed at the location of the stenosis. For patients in whom no significant stenosis was found, the proximal segment of a normal vessel was chosen for balloon occlusion. The vessel selection was at operator's discretion; generally a large-size non-tortuous vessel was selected.

Blinding

The investigator (P.M.) measuring the QT intervals and heart rate on the ECG tracing was blinded to patients' characteristics, details on the invasive measurements such as CFI, vessel, and site of measurement. Electrocardiogram tracings were labelled with patient identification numbers exclusively. Each patient finally had three ECG tracings (baseline, during balloon occlusion, and after balloon deflation). The tracings were labelled with A, B, or C by a study nurse, Hélène Steck (HS). For each individual patient, assignment of balloon occlusion status to A, B, or C was at her discretion and directly performed during measurements. HS was exclusively involved in CFI measurements and labelling. Two separate databases were maintained, Database 1 to fill in the ECG measurements for time points A, B, and C; Database 2 for all other measurements (baseline characteristics, invasive measurements, CFI, assignments of time-point labels A, B, or C to vessel occlusion status). In both databases, patients were identified by the unique patient identification number. The two databases were merged for statistical analysis by a merge data step in SAS.

Electrocardiogram QT measurements

Electrocardiogram QT time and cycle length (RR interval) were measured manually using calipers. Leads II, aVL, and aVF were recorded before, during, and after the vessel occlusion at an ECG sweep of 25 mm/s and amplitude calibration at 10 mm/mV. These leads usually show less prominent U waves compared with precordial leads (especially V2 and V3). U waves represent a population of sub-epicardial cells with unique activation properties and complicate QT interval measurements. Time intervals (QT and RR) were measured in at least five consecutive cardiac cycles and mean values were calculated. Cycles within the last minute before vessel occlusion, at the very end of vessel occlusion and 1 min after occlusion were selected for interval measurements. The investigator was blinded to patients' characteristics. QT intervals were measured from the earliest onset of the QRS complex (beginning of the Q-wave or R-wave if there was no Q-wave present) to the end of the T-wave. Intraindividually, the same lead was used consistently for all measurements. The point of T-wave offset was defined as the return of the T-wave to baseline. If T-wave was followed by a distinct U-wave, the T-wave offset was identified when the descending limb of the T-wave returned to the TP baseline. When T-wave deflections of equal or near-equal amplitude resulted in a biphasic T-wave, the QT interval was measured to the time of final return to baseline. If an U-wave interrupted the terminal portion of the T-wave, offset was measured at the nadir between the two waves.¹⁹ Baseline and occlusion measurements have been performed in the same lead.

QT interval correction

All QT intervals were adjusted for corresponding heart rates. Of note, QT time is prolonged at slower heart rates and shortened at faster

heart rates. This represents a potentially critical confounding factor: the aim of our study was to evaluate the independent influence of vessel occlusion and of coronary collaterals on QT intervals rather than any indirect effect via heart rate changes.

Corrections were performed using different formulae: square or cube root correction according to Bazett²⁰ and Fridericia,²¹ linear correction according to Framingham²² and according to Hodges.²³

Bazett: $QTc(B) = QT/RR^{0.5}$ (QT and RR in s)
 Fridericia: $QTc(F) = QT/RR^{0.33}$ (QT and RR in s)
 Framingham: $QTc(FH) = QT + 0.154(1000 - RR)$ (QT and RR in ms)
 Hodges: $QTc(H) = QT + 1.75(HR - 60)$ (QT in ms, HR per min)

The effectiveness of the different approaches was evaluated by assessing the correlation between HR and the corrected QT. An optimal correction would eliminate any residual correlation completely. The Framingham formula performed best and thus, Framingham-corrected QT intervals were used for all analyses.

Statistical analysis

All continuous data are presented as mean and standard deviation. Baseline characteristics between the three groups were analysed by factorial analysis of variance for continuous data (*post hoc* analysis by Scheffé) and by χ^2 /Fisher's exact tests for categorical data. To evaluate change of continuous data at different time points in the different coronary vessels, non-parametric repeated measures ANOVA²⁴ were performed. Here, the analysis of primary interest was the interaction of time point (baseline and vessel occlusion) and vessel (RCA or LCA). Wilcoxon signed-rank tests were then performed for paired comparisons between two consecutive time points within the same vessel group. Here, the analysis of primary interest was change A = difference between QTc during balloon occlusion and QTc at baseline. Difference B (=QTc after recovery - QTc during balloon occlusion) was used to further confirm the direct effect of balloon occlusion on QTc and of accuracy of measurements but was not a measure of primary interest. Non-parametric tests were preferred, as QT and RR interval data were right-skewed. In contrast, changes of QTc were approximately normally distributed. Influence of coronary collateral function on Difference A was evaluated with a linear regression analysis; model assumptions were verified (linear relationship, homoscedasticity, and normal distribution of residuals). To avoid influence of confounding variables, a multivariate linear regression analysis was performed to control for the following covariables: cardiac medication (beta-blocker, acetylsalicylate, statins, ACE-inhibitors/ARB, diuretics, clopidogrel), age, diabetes, hypertension, smoking, gender, vessel diameter stenosis. All covariables were included in the multivariate model irrespective of their significance level. These covariates were selected by our group for inclusion in the model based on prior literature and a priori considerations of potential confounding. Evaluation of the effectiveness of the different approaches to correct QT intervals for HR was performed by linear correlation analyses. To test for the influence of QT correction algorithms on the results, re-analyses were done with uncorrected QT intervals and with Bazett-corrected QT intervals. Subgroup analyses were performed *post hoc* for gender, beta-blocker treatment, and vessel status (disease or non-diseased). Analyses were performed with SAS Version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

The baseline characteristics of the patient population included in this analysis are outlined in Table 1. The consecutively chosen patients were 64 ± 10 years old, 112 patients were men. Baseline characteristics did not significantly differ between patients of the three groups, except for the gender distribution with 64% men for LAD, 78% for LCX, and 88% for RCA measurements ($P = 0.013$). Overall, 55 of the measurements were performed in angiographically normal vessels, among those, 33 patients had no CAD at all, whereas 22 had minor but non-significant stenoses ($>70\%$ diameter stenosis by visual assessment or fractional flow reserve >0.75) or a previously implanted patent stent in another coronary artery. No patient in our cohort had an LVEDP > 27 mmHg. This level is regarded critical for accurate CFI measurements.²⁵ None of the patients had LV wall motion abnormalities at rest in the region supplied by the index vessel. All patients with measurement in the RCA or the LCX had a right dominance.

QT interval during vessel occlusion

Framingham correction performed best regarding minimizing QTc correlation with heart rate ($R^2 = 0.0005$, $P = 0.78$). Thus, all following analyses are based on QTc based on the Framingham formula.

Mean QTc interval for patients during occlusion of the LAD increased from 422 ± 33 to 439 ± 36 ms ($P < 0.001$), whereas that during LCX occlusions increased from 414 ± 32 to 427 ± 27 ms ($P < 0.001$). QTc was not influenced by RCA occlusion (417 ± 35 and 415 ± 34 ms, respectively; $P = 0.86$; Figure 1).

Correlation between QT time change and collateral function

Linear regression analysis showed an inverse relation between CFI and QTc prolongation during occlusion of the LCA ($R^2 = 0.122$, $P = 0.0002$; Figure 2), but no such correlation during occlusion of the RCA ($R^2 = 0.009$; $P = 0.744$; Figure 3).

A multivariate linear regression analysis to adjust for potential confounding factors showed CFI to be independently related to QTc change (Difference A) in the LCA (regression coefficient = -17.2 , $P = 0.0021$, $R^2 = 0.09$). No correlation was observed between CFI and QTc prolongation in the RCA ($P = 0.74$).

Heart rate during vessel occlusion

Heart rate before, during, and after the 1 min occlusion changed differently between LCA and RCA: whereas the LAD and LCX showed an average increase of $1.1 (\pm 5.1)$ b.p.m., heart rate tended to decrease in the RCA by $1.4 (\pm 7.4)$ b.p.m. (P for interaction of timepoint and vessel site = 0.048 ; Figure 4).

Subgroup analyses

The results were mostly consistent among subgroups. In the RCA, no prolongation of QTc was found for any of the stratified analyses (female or male; individuals with or without beta-blocker

Table 1 Baseline characteristics

	LAD (n = 66)	LCX (n = 41)	RCA (n = 43)	P-value
Clinical characteristics				
Age	62 ± 10	64 ± 11	64 ± 11	0.625
Men	42 (64)	32 (78)	38 (88)	0.013
BP mean	95 ± 16	92 ± 18	89 ± 14	0.125
Heart rate	69 ± 11	71 ± 8	70 ± 10	0.522
LVEF (%)	58 ± 10	60 ± 11	61 ± 9.0	0.352
% Diameter stenosis	63 ± 21	66 ± 20	67 ± 23	0.778
Non-stenosed vessels	24 (36)	13 (32)	16 (37)	0.863
Measurement prox/mid/dist	36 (55)	23 (56)	26 (60)	0.961
Potassium (mmol/L)	3.9 ± 0.6	4.1 ± 0.4	4.0 ± 0.3	0.287
Collateral flow index	0.165 ± 0.105	0.171 ± 0.086	0.170 ± 0.082	0.928
Cardiovascular risk factors				
Diabetes	7 (11)	10 (24)	4 (9)	0.095
Hypertension	36 (55)	28 (68)	27 (73)	0.347
Smoker	16 (24)	9 (21)	7 (16)	0.608
Cholesterol (mmol/L)	5.0 ± 1.1	5.1 ± 1.0	5.0 ± 1.1	0.777
Medication				
Ca antagonists	8 (12.1)	4 (10)	4 (9.5)	0.897
Beta-blockers	42 (64)	22 (54)	23 (55)	0.508
Nitrates	8 (12)	4 (10)	3 (7)	0.702
ASS	48 (73)	28 (68)	36 (84)	0.237
Statins	35 (53)	20 (49)	29 (67)	0.184
ACE-inhibitors/AT2 antagonists	15 (23)	12 (29)	13 (30)	0.623
Diuretics	18 (27)	11 (27)	7 (16)	0.373

For categorical variables, numbers are presented as absolute numbers and percentages. ASS, acetylsalicylate; AT2, angiotensin II receptor; BP, blood pressure; Ca, calcium; CFI, collateral flow index; dist, distal vessel segment; LAD, left coronary artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; mid, mid-segment; prox, proximal segment. RCA, right coronary artery. Mean values ± SD.

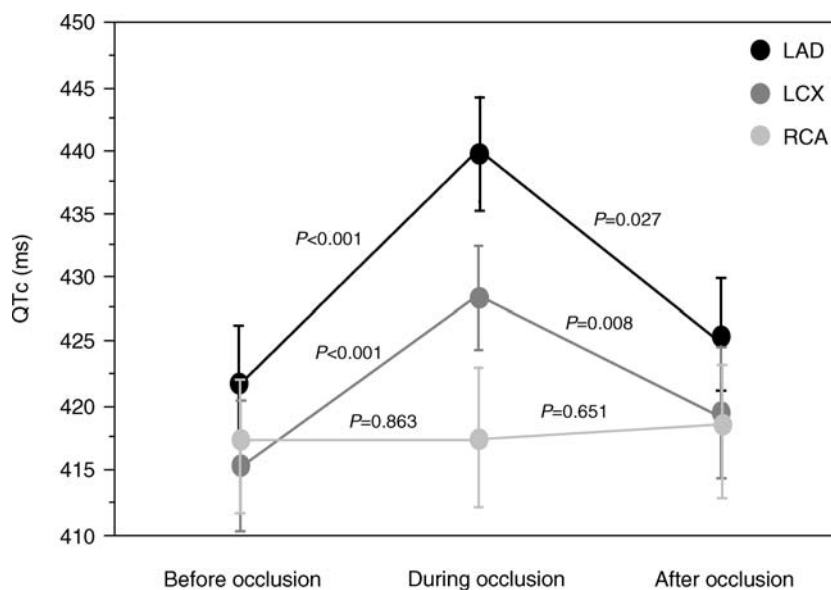


Figure 1 QTc time (ms, mean ± standard error, SE) before, during, and after a 1 min balloon occlusion of the left anterior descending (LAD), the left circumflex (LCX), or the right coronary artery (RCA). QTc: corrected QT time.

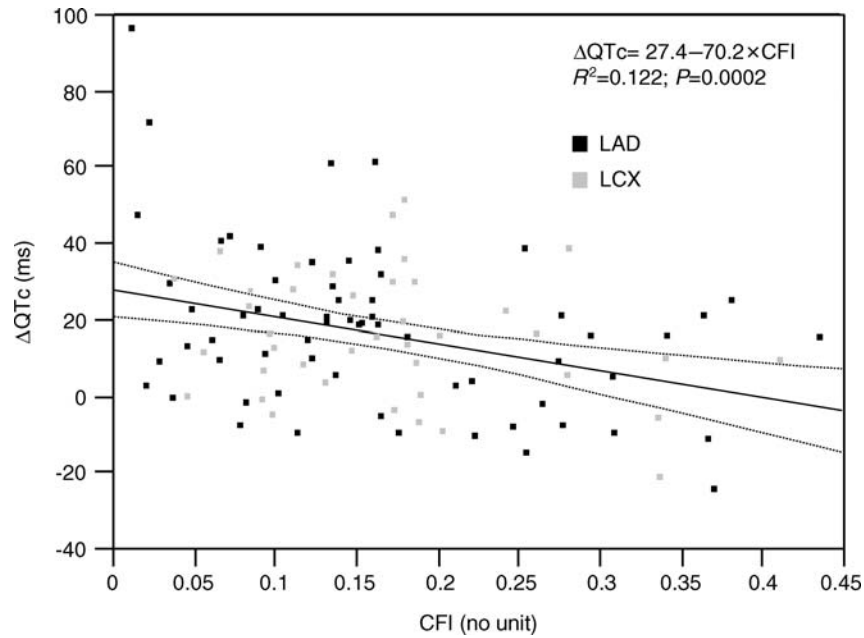


Figure 2 Linear regression plot of collateral function (CFI) and QTc change during a 1 min vessel occlusion of the left coronary artery (LCA; left anterior descending artery, LAD, black symbols; left circumflex coronary artery, LCX, grey symbols). CFI, collateral flow index; ΔQTc , QTc difference between QTc during vessel occlusion and QTc at baseline (=Difference A) (ms). The regression line is given for both LAD and LCX.

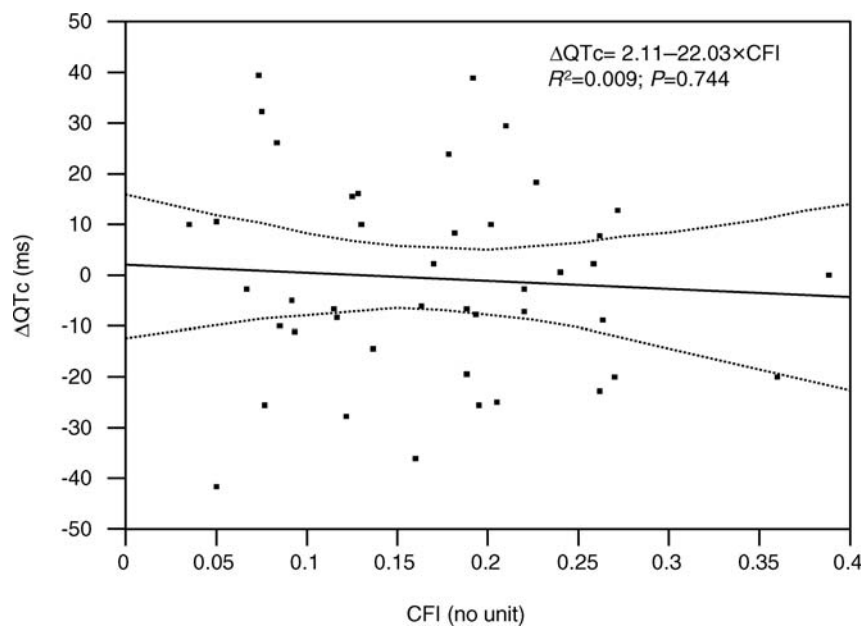


Figure 3 Linear regression plot of collateral function (CFI) and QTc change during a 1 min vessel occlusion of the right coronary artery (RCA). CFI, collateral flow index; ΔQTc , QTc difference between QTc during vessel occlusion and QTc at baseline (=Difference A) (ms).

treatment, stenosed, or non-stenosed vessels) (see Supplementary material online, *Table S1*). Correspondingly, no association between QTc change during vessel occlusion and CFI was found either (see Supplementary material online, *Table S2*).

For the LCA, results were consistent among subgroups with the exception of QTc changes for the LCX in female patients (QTc interval increase during vessel occlusion was not statistically significant, $P = 0.089$). The QTc increase in the LCA during vessel

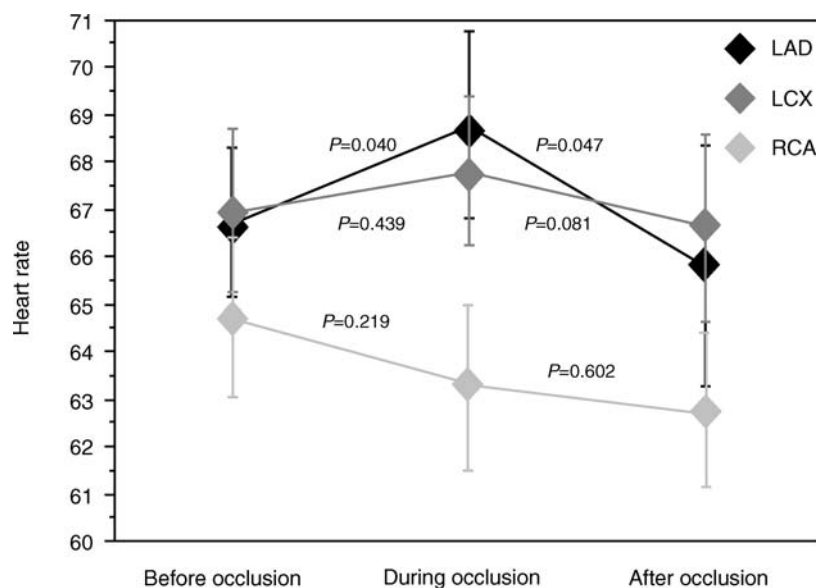


Figure 4 Heart rate (HR, mean \pm standard error, SE) before, during, and after a 1 min vessel occlusion of the left anterior descending (LAD), the left circumflex (LCX), or the right coronary artery (RCA).

occlusion was negatively correlated with CFI in all subgroups (see Supplementary material online, Table S2).

Discussion

According to our knowledge, this is the first study demonstrating that the human collateral circulation prevents QT prolongation during a brief coronary occlusion, indicating its protective mechanism against electrical instability. This is the case in the LCA but not in the RCA territory. In the latter, QTc prolongation is prevented by a different anti-ischaemic mechanism, i.e. reduction of heart rate.

QT prolongation during ischaemia

Our data are in line with the previous work showing that acute myocardial ischaemia is associated with changes in cardiac electrophysiological properties. Kurz *et al.*²⁶ found that ischaemia induced a significant slowing of electrical restitution. Other groups also described electrophysiological changes during early ischaemia in humans, with prolongation of action potential duration.²⁷ Most recently, Kenigsberg *et al.*⁷ have found a relevant QT interval prolongation in a clinical setting of balloon occlusion during coronary revascularization. However, occlusion time was not standardized and rather variable (40 ± 19 s).

As an interesting finding, LCA occlusion showed a different reaction when compared with RCA occlusion. A partly similar phenomenon has been described in patients with acute myocardial infarction by Kobusiak-Prokopowicz *et al.*²⁸ After thrombolytic reperfusion, QT and QTc intervals decreased in anterior wall myocardial infarction, but QT and QTc stayed unchanged after reperfusion in inferior wall infarction. In comparison to our setting, patients in this study have been stratified by infarct location and not by coronary vessels. Different susceptibility to ischaemia of

LCA and RCA has also been described by de Marchi *et al.*¹⁶ ST-elevation, normalized to QRS amplitude to correct for area at risk, was enhanced in LCA compared with RCA during controlled vessel occlusion.

Kenigsberg *et al.* did not describe this phenomenon of regional disparity. However, their study size was rather small ($n = 74$), stratified analyses by vessel therefore probably limited. In 23% of their patients, QT did not increase during ischaemia. The authors did not mention whether there was an RCA or LCA predominance in this 'non-reactive' sub-group. Furthermore, occlusion time was variable and may not always have been sufficient to induce measurable functional changes in ischaemic myocardium. In comparison, our study was based on a standardized 1 min occlusion protocol.

Reasons for the different findings in LCA and RCA remain speculative. The fact that heart rate slightly decreased during early RCA ischaemia, while it tended to increase in LCA indicates that the autonomous nervous system may play a role. Despite the very low absolute change in HR, we wanted to exclude a purely artificial finding due to a potential HR (over)adjustment of QT intervals: we performed the analyses also with uncorrected QT time which decreased the differences between LCA and RCA but still showed significant differences (data not shown). The autonomous nervous system may either influence repolarization via reduced myocardial oxygen consumption or it may directly alter electrical repolarization.²⁹ In addition, de Marchi *et al.*¹⁶ found the curvature radius of the anterior wall to be higher compared with the inferior wall, possibly leading to higher regional left ventricular wall stress leading to augmented myocardial oxygen consumption.

QT time and collateral circulation

The only previous study addressing the relation between QT interval and coronary collaterals in humans was performed by

Tandogan *et al.*³⁰ They assessed the relation between coronary collateral circulation and QT dispersion (QTd). However, QT intervals were not measured during vessel occlusion. QT dispersion describes the inter-lead variability of QT intervals in a 12-lead ECG. The authors found an increased QTd in patients with well-developed collaterals, whereby correction by Bazett formula erased most of the differences. QT dispersion has been related to worse prognosis in clinical settings and previous work revealed an increase of QTd during ischaemia.^{31,32} Therefore, the finding of Tandogan *et al.* appears at variance with our study. Furthermore, several methodological issues of Tandogan's study have to be considered. Apart from a limited study size ($n = 100$), the major problem was the crude assessment of coronary collaterals. The authors relied on a visual assessment of coronary angiographies with regard to spontaneously visible and not to recruitable collaterals during occlusion, an imprecise method that is rather observer dependant and correlates poorly with gold standard quantitative measures.³³

Clinical relevance of QT time and QT variation

QT prolongation and QT variation seem to be important independent predictors of sudden cardiac death (SCD). Even small absolute differences are related to worse outcome (mean QTc was found 17 ms longer in the cases of SCD compared with control group; $P < 0.0001$).^{8,14} Heterogeneity in conduction time and recovery period represent a dangerous ground for malign re-entry arrhythmia.²⁶ QT prolongation during abrupt vessel occlusion occurs in ischaemic myocardium, whereas it stays unchanged in adjacent non-ischaemic tissue, the fact of which defines the dangerous regional electrical heterogeneity.²⁶

Limitations

Even though there is strong evidence that QT prolongation is associated with worse outcome independent of underlying reasons, it remains unclear whether this is also valid for prolongation provoked by vessel occlusion as in the present study. Whether the QT prolongation during vessel occlusion in patients with poor collateralization directly translates into higher risk for malign arrhythmia is probable but unproven and unprovable in humans for ethical reasons.

The demonstrated inverse relationship in the LCA territory between collateral function and QTc prolongation is statistically highly significant. However, residual variation is considerable. Despite our control for co-factors in a multivariate analysis, the number of included variables was limited. Non-cardiac medication, genetic polymorphisms, etc. have not been determined but may play an important role.³⁴

Moreover, selection of measurement location (LCA or RCA) was not random. For patients with relevant CAD, the measurement was performed at the site of the tightest stenosis. Potential confounding due to other (e.g. genetic) reasons related to stenosis location as well as QT variability is unlikely but cannot be precluded.

Determination of QT changes from surface ECG does not allow region-specific measurements but rather reflects 'global' changes. Local QT changes in ischaemic myocardium may therefore be underestimated.

Moreover, our study could be confounded by an effect of ischaemic preconditioning. As shown previously, stenosis severity decreases ventricular ectopic activity during acute coronary balloon occlusion,³⁵ which could be an effect of preconditioning leading to electrical stability. Stenosis severity also correlates with CFI.³⁶ To exclude stenosis severity as a confounder in our study, we included diameter stenosis as a covariable in the multivariate model. Furthermore, we performed a univariate regression analysis between stenosis severity and QTc prolongation during vessel occlusion; no correlation was observed ($R^2 = 0.002$; $P = 0.59$, data not shown). Therefore, such confounding is unlikely. Conversely, we hypothesize that the above-mentioned finding of Airaksinen *et al.* could partly derive from better collateralization in patients with pronounced coronary stenosis and is consistent with our data.

Concentration of electrolytes such as magnesium and calcium were not measured routinely; they may influence baseline QT intervals and QT interval changes during ischaemia. However, each patient served as his or her own control for measurements before, during, and after vessel occlusion and thus, electrolyte concentrations were the same. On the other hand, we cannot exclude random imbalances in magnesium or calcium levels between patients with measurements in the RCA, the LCX, or in the LAD. If considerable imbalances were present, this would represent a potential confounding factor with regard to the differential QT interval changes during vessel occlusion.

The results of the subgroup analyses (see Supplementary material online, *Tables S1 and S2*) should be interpreted with caution. The subgroups were not pre-defined and no corrections for multiple testing were applied. The precision of parameter estimates for these subgroup analyses is reduced due to limited statistical power, even more so for small subsets such as female individuals and non-diseased coronary vessels.

Conclusion

Myocardial ischaemia leads to QT prolongation during a controlled 1 min occlusion of the LCA but not the RCA. This QT prolongation during early ischaemia in the LCA is reduced in the presence of a well-developed coronary collateral circulation, indicating a protective mechanism of collaterals against cardiac death. Owing to this early protective effect, our attempts to promote coronary collaterals should rather start before than after development of severe ischaemia.

Supplementary material

Supplementary Material is available at *European Heart Journal* online.

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Conflict of interest: none declared.

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