Comparisons of the Spatial QRS-T Angle with Intra-cardiac Markers of Depolarization and Repolarization

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Abstract

The spatial QRS-T angle (QRS-Ta), a non-invasive risk marker for arrhythmia and sudden cardiac death, captures information on the spatiotemporal dynamics of ventricular depolarization and repolarization. QRS-Ta peak is the angle between QRS and T-wave loop maximal amplitudes. We compared QRS-Ta peak with intra-cardiac unipolar electrocardiogram parameters simultaneously recorded in the right ventricle, left ventricle (LV) endocardium and LV epicardium (coronary sinus) in 10 patients with structurally normal hearts. S1S2 restitution protocols were performed by pacing from the LV at intervals decrementing from 1000 ms to the effective refractory period (ERP). Repolarization time (RT), activation time (AT) and activation-recovery interval (ARI), a standard surrogate for local action potential duration, were calculated using standard definitions. Decreasing cycle length (CL) correlated with an increase in QRS-Ta. Two phases were identified 1) A stable QRS-Ta between CLs 1000 to 400ms and 2) a subsequent rapid increase in QRS-Ta with further decrements and a small decrease in QRS-Ta just prior achieving ERP. When plotted against the pacing interval, the QRS-Ta distribution mirrored the repolarisation restitution curve. The QRS-T angle inversely correlated with mean RT (-0.59, -0.81 / -0.34, P=0.023) and mean ARI (-0.72, -0.73 / -0.42, P<0.02).

1. Introduction

The spatial QRS-T angle (QRS-Ta), is a recognised non-invasive risk marker for ventricular arrhythmia, sudden cardiac death and cardiac-related mortality in clinical and general populations [1-3]. The QRS-Ta can be calculated from the 12-lead electrocardiogram (ECG) using standard transformations to produce representative X, Y and Z vector beats [4]. QRS-Ta peak is subsequently measured as the angle between QRS and T-wave loop maximal amplitudes with values between 0° and 180°.

The QRS-Ta captures information on the spatiotemporal dynamics of ventricular depolarization and repolarization [1]. It is hypothesised that a wider QRS-Ta could be due to local variation in action potential duration (APD), conduction velocity and cardiomyocyte morphology [5,6]. A large proportion of our understanding however is based on predominantly theoretical studies and comparison of the QRS-Ta with intra-cardiac electrophysiological measurements in humans, has never been performed.

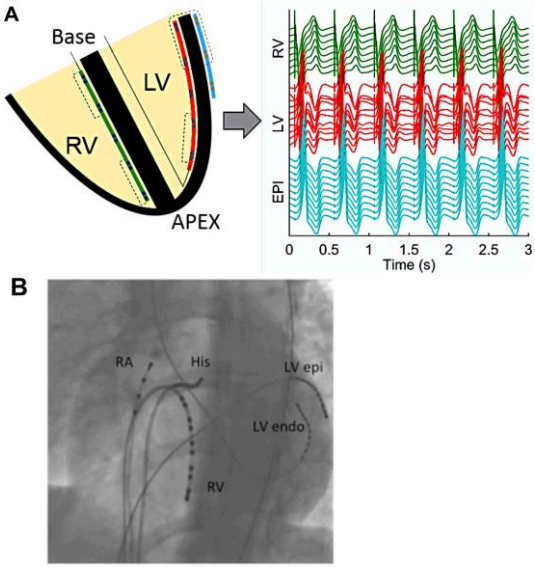

Figure 1. Orientation of catheters for recording
Panel A: Position of catheters in an apicobasal orientation in the left ventricle (LV), right ventricle (RV) and transmural across the lateral base of the LV epicardium (EPI) with corresponding unipolar electrograms. Panel B: Catheter positions checked using fluoroscopy. RA: Right atrium, His: Bundle of His. Reproduced from Srinivasan *et al*.[7]

2. Methods

The study protocol methods and ECG acquisition has previously been described [7,8]. Using 3 decapolar catheters, intra-cardiac unipolar electrocardiograms (UEG) were recorded simultaneously in the right ventricle, left ventricle (LV) endocardium and LV epicardium (coronary sinus) in 10 patients (Figure 1). Each patient had a structurally normal heart and normal 12-lead ECG, and was undergoing an electrophysiology study for the assessment of supraventricular tachycardia. UEGs were recorded at a sampling frequency of 2000 Hz, 0.5 – 500 Hz. Standard S1S2 restitution protocols were conducted by LV pacing at intervals decrementing from 1000ms to the effective refractory period (ERP) [9,10]. In detail, following a train of nine steady-state S1S1 stimuli at 600 ms, an extra stimulus at a shorter coupled pacing interval (S2) was introduced. The S1S2 coupling interval was decremented in 50 ms steps from 1000 ms to 400 ms, then by 20 ms intervals between 380 and 400ms, and thereafter in 5 ms steps until ERP. At ERP an S2 stimulus at 10 ms + ERP was applied followed by further decrementing S2 in steps of 2 ms.

UEG signals from each cardiac location were annotated and included in these analyses. Local activation time was measured at the minimum of the first derivative, min(dV/dt), of the UEG signal within the depolarisation phase. Repolarization time (RT) was measured following a standard and validated definition [11,12], at the maximum of the first derivative, max(dV/dt), of the signal during the T-wave. Activation-recovery interval (ARI), a surrogate for APD [13], was calculated as RT - AT. Dispersion of RT (DRT) was calculated as latest minus earliest RT.

Simultaneous to UEG acquisition, a continuous 12-lead surface ECG was recorded. To calculate the QRS-Ta peak, X, Y and Z vectors were constructed using Kor's transformation matrix [14]. For each S2 beat, maximal amplitudes for QRS and T-wave loops were calculated, and the QRS-Ta peak obtained as the angle between the two vectors (Figure 2). Waveforms were excluded from analysis if an ectopic was present which subsequently encroached on the T-wave of the analysed beat, preventing accurate estimation of the T-wave loop maximal amplitude.

For each individual and paced S2 beat, 3D plots were constructed and the QRS and T-wave loops manually inspected (Figure 2). The QRS-Ta distribution according to pacing interval and UEG derived parameters was plotted for each patient. Intra-patient spearman-rank correlation coefficient was calculated against RT, AT, ARI and DT. Trends were then evaluated and the inter-patient median and inter-quartile range (IQR) calculated. Significant deviation from 0 to evaluate inter-patient relationships, was determined using the Wilcoxon signed-ranks test.

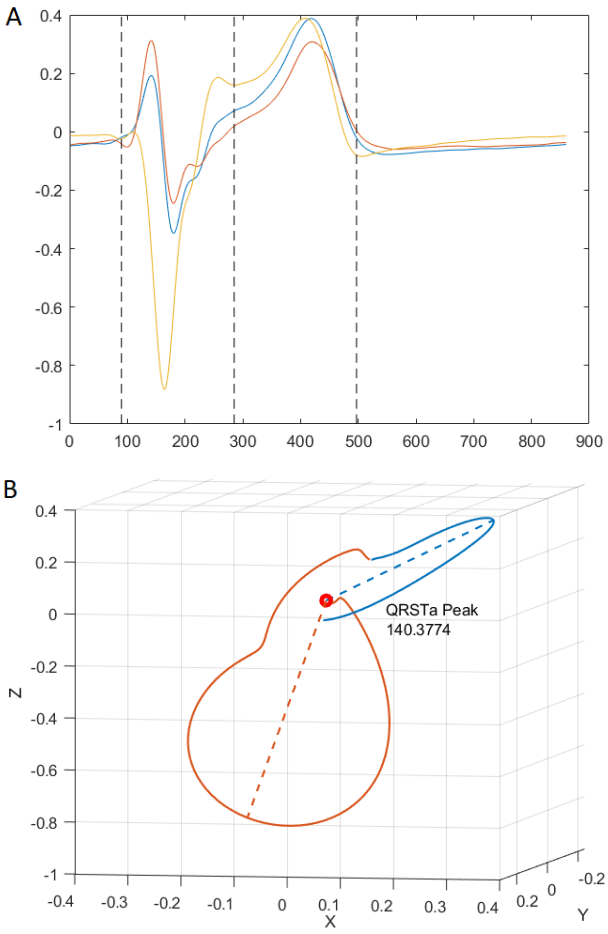

Figure 2. VCG signals and construction of QRS and T wave loops
Panel A. Transformed X, Y and Z leads from surface 12-lead ECG. Panel B. QRS (red) and T-wave (blue) loops. Dotted lines indicate vectors directed towards the maximal amplitude.

3. Results

After manual inspection of rhythms strips and plots, two patients were excluded due to a significant burden ectopy limiting the number of analysable beats.

Results for correlation analyses are shown in Table 1. Across the 8 patients included in analysis, decreasing cycle length (CL) correlated with an increase in QRS-Ta. Two phases however were identified 1) a stable QRS-Ta between CLs 1000 to 400ms (144.06°, 142.63 – 146.87) 2) a subsequent rapid increase in QRS-Ta with further decrements followed by a small decrease just prior achieving ERP (157.72°, 149.57 – 161.56). An example of this can be seen in Figure 3. This pattern was well aligned to AT and when plotted against pacing interval, the QRS-Ta distribution mirrored the repolarisation restitution curve (Figure 3).

Table 1. Inter-patient median and IQR of correlation between QRS-Ta and intra-cardiac parameter.

Parameter	Correlation	IQR	P value
S1-S2 CL	-0.57	-0.74 - -0.42	**0.016**
RT	-0.60	-0.81 - -0.34	**0.016**
ARI	-0.72	-0.73 - -0.41	**0.016**
AT	0.32	0.21 – 0.60	0.125
DRT	0.47	-0.06 – 0.68	0.453

CL: Cycle length, IQR: Interquartile range, P value: Output from sign-rank test

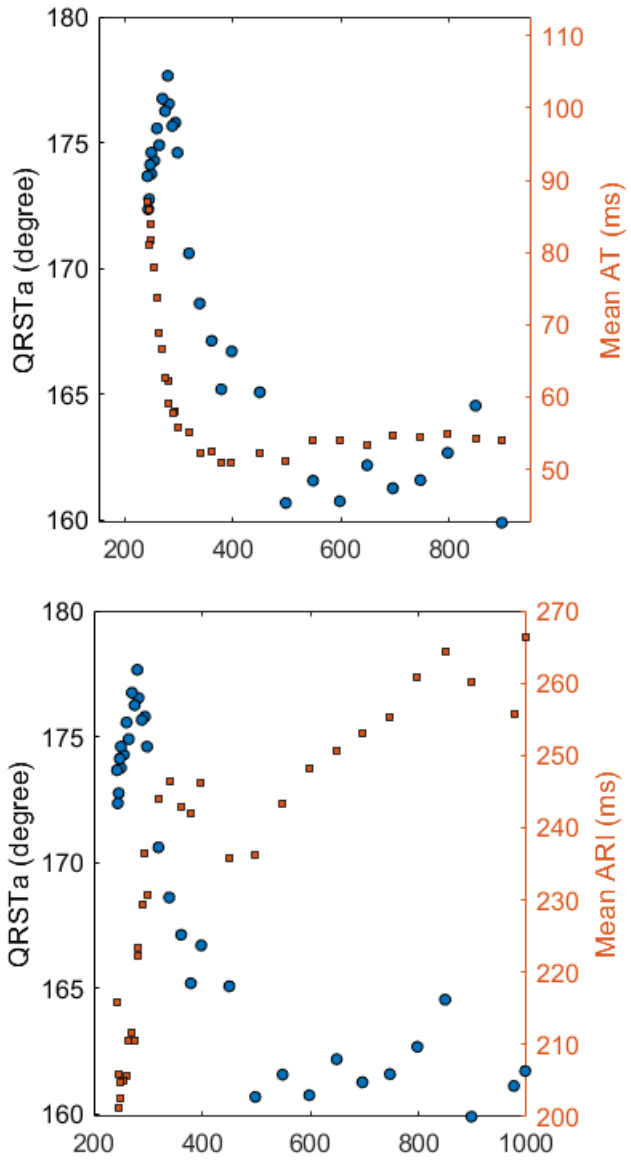

Figure 3. Scatter plot comparing QRS-Ta with intra-cardiac measure
Top plot: X axis: Cycle length (ms), Y axis right: Mean AT, Y axis left: QRS-Ta. Bottom plot: X axis: Cycle length (ms), Y axis right: Mean ARI, Y axis left: QRS-Ta.

There was a negative correlation between QRS-Ta and mean RT and ARI. A positive correlation with AT and DRT was observed however did not reach significance in these analyses (Table 1).

4. Discussion

Ventricular repolarization and its spatio-temporal distribution are primary factors in arrhythmogenesis, but accurate non-invasive markers are still lacking. The QRS-Ta has been proposed as a marker of activation-repolarization heterogeneity, but its formal association with intracardiac markers of activation and repolarization in the in-vivo human heart had yet to be explored. This study compared for the first time the QRS-Ta peak calculated from the surface 12-lead ECG, with intra-cardiac UEG derived parameters of depolarization and repolarization from within the right ventricle, left ventricular endocardium and epicardium. The main results are an inverse association with changes in ARI and RT and an increase in QRS-Ta with decreasing pacing interval.

A spatial ventricular gradient (SVG), a vector representing the degree and direction of myocardial electrical heterogenetiy, is present in all normal hearts, for example representing apico-basal and transmural inhomogeneity of repolarization time [1,6]. The QRS-Ta is thoughts to differ from the SVG in that it captures information on secondary repolarization heterogeneity due to depolarization abnormalities, while the SVG is thought to represent primary heterogeneity of repolarization [1,15,16]. There has however been limited study of both concepts from a mechanistic perspective and experimental validation is still undetermined.

In this preliminary study using ventricular pacing to induce changes in conduction velocity and repolarization and inverse correlation was observed between ARI, a surrogate for action potential duration, and QRS-Ta peak. A similar result was found for RT. There was also a consistently weak positive correlation with AT however this was non-significant. The observation in this limited study of an inverse relationship with ARI and RT suggest a widened QRS-Ta may represent abnormalities of ventricular conduction as opposed to primary repolarization abnormalities.

Strengths and Limitations

This is a small study and therefore it may be underpowered for the assessment of some relationships such as with DRT. It is however the first study of its kind in confirmed structurally normal hearts and a larger study is warranted. Additionally, the relationship between RT and ARI and QRS-Ta in the presence of left ventricular dysfunction, myocardial scar or fibrosis, may differ. Thus the results of this study should be approached cautiously

when applying to individuals with structurally abnormal hearts. Further study is warranted to assess the QRS-Ta as a potential non-invasive marker of dispersion of repolarization [8,17].

Recent evidence suggests the QRS-Ta peak and mean (angle between mean QRS and T-wave amplitudes) may offer complementary information on underlying electrophysiological processes [18]. This study focused on QRS-Ta peak, being the most robust measure for these analyses however additional study of the influence of intra-cardiac parameters on QRS-Ta mean would be of interest.

Conclusion

This study highlights QRS-Ta trends according to pacing interval and an inverse association with changes in APD and RT, which may explain the increased arrhythmic risk in individuals with a wider QRS-Ta.

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