

Role of Epicardial QT Intervals in the Assessment of Ventricular Repolarisation Dispersion

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Abstract. The role of cardiac surface QT intervals (QTI) in assessing ventricular repolarisation dispersion was investigated in 10 pentobarbital-anesthetized, open-chest sheep. Activation-recovery interval (ARI) and QTI were measured from multiple ECGs acquired from left ventricular epicardium, before and after procainamide administration (15 mg/min i.v. for 20 min). Procainamide therapy resulted in a significant prolongation in ARI and corrected QT interval (cQTI). A correlation between QTI, cQTI and ARI was found in only one animal ($r = 0.78$ and 0.79 respectively, $p = 0.01$) before procainamide therapy. No correlation was found between pooled QTI and ARI dispersion from the 10 animals at baseline or after procainamide administration ($p > 0.05$). There was a moderate correlation between pooled cQTI and ARI dispersion ($r = 0.69$, $p = 0.02$) before procainamide therapy. In conclusion, epicardial QTI have no significant correlation with the duration of ventricular repolarisation. Epicardial QTI dispersion is not a useful index of repolarisation heterogeneity.

Key words: QT interval — Activation-recovery interval — Ventricular repolarisation — Cardiac electrophysiology

Introduction

The maximum difference between QT intervals (QTI) on a standard 12-lead body surface ECG, or QTI dispersion, has been used to predict heterogeneity of ventricular repolarisation and risk of fatal ventricular arrhythmias in patients with cardiac disorders, particularly myocardial ischemia or infarction (Mirvis 1985; Higham et al. 1995; Kautzner and Malik 1997; Suzuki et al. 1998). This application is based on the assumption that QTI represent the length of ventricular repolarisation, whereas QTI dispersion reflects repolarization dispersion of the heart. Although some studies have found that body surface QTI dispersion is related to the dispersion of monophasic action potential duration directly measured from the heart (Zabel et al. 1995, 1998), many recent animal experiments have indicated the otherwise (Macleod et al. 1996; Lux et al. 1998; Tomassoni et al. 1998; Fuller et al.

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2000). Studies in our laboratory have also found that body surface QTI dispersion often underestimates the spatial dispersion of ventricular repolarization measured from the epicardium (Wang 2000).

Whether QTI dispersion directly measured from the heart surface has a better correlation with repolarisation heterogeneity than body surface QTI dispersion remains unknown. In isolated canine hearts, neither body surface nor epicardial QTI dispersion provides adequate estimates of recovery time dispersion (Fuller et al. 2000). The primary purpose of the present study was to assess the role of epicardial QTIs in predicting the spatial dispersion of ventricular repolarisation in an intact animal heart.

Materials and Methods

Animal preparations

This study was approved by the Animal Ethics Care Committee of our institution. The surgical preparation of this animal model has been previously reported (Wang 1999, 2000; Li et al. 2001). Briefly, 10 sheep (23–32 kg body weight) were anesthetized with sodium pentobarbital (30 mg/kg, i.v., maintenance dose 2 mg/min). They were intubated and artificially ventilated with room air at a ventilation rate of 15–18 strokes/min. A left thoracotomy was performed from the 4th intercostal space and the heart was suspended in a pericardial cradle. The left ventricular pressure and surface ECG leads II, III and aVF were continuously monitored during the experiments.

Epicardial ECG acquisition and analysis

Under sinus rhythm, data were acquired simultaneously from 64 epicardial sites with an electrode sock attached to the left and right ventricular epicardium. After baseline data acquisition, procainamide (15 mg/min i.v.) was administered for 20 min in each animal to induce prolongation of ventricular repolarisation.

For simplicity reason, only ECGs acquired from the left ventricular epicardium were selected for analysis. Activation-recovery interval (ARI) was measured from unipolar ECGs. We have previously reported the methodology of ARI measurement from unipolar epicardial ECG (Wang 1999; Wang 2000; Li et al. 2001). In brief, the time difference between the most rapid decrease in voltage in the QRS complex (dV/dt_{\min}) (activation time) and the most rapid increase (dV/dt_{\max}) near the peak of the *T* wave (repolarisation time) was defined as ARI (Fig. 1). ARI was found to reflect the duration of action potential of cardiac myocytes (Millar et al. 1985; Haws and Lux 1990).

After the completion of ARI measurement, bipolar ECGs were computed by subtracting the signals of two adjacent unipolar ECGs acquired from the left ventricular epicardium. The measurement of QTI was performed automatically by a computing program. QTIs were measured from these bipolar ECGs, from the onset of QRS complex to the end of *T* wave (Fig. 1). The end of the *T* wave was

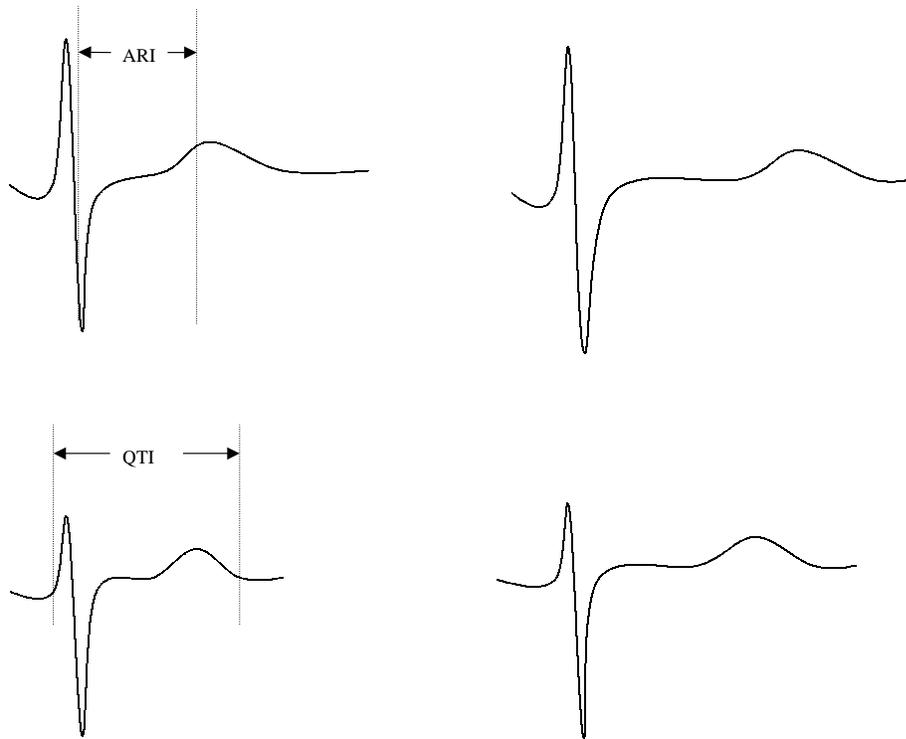


Figure 1. ARI (upper panel) and QTI (lower panel) interval before (left panel) and after (right panel) intravenous infusion of procainamide.

defined as the crossing point between the downstroke of the *T* wave and the baseline. Corrected QTI (cQTI) was calculated by using Bazett's formula in order to analyse pooled QTIs from all animals and to avoid the influence of heart rate on the interval.

The average ARI value from the two adjacent unipolar ECGs, from which a bipolar ECG was constructed for QTI analysis, was used as reference duration of local ventricular repolarisation. The average ARI was also used for correlation studies with QTIs.

In each animal, the spatial dispersion of QTI, cQTI or ARI was defined as the difference between the maximum and the minimum values from multiple epicardial sites.

Statistics

Data were expressed as means \pm S.D. The average QTI, cQTI and ARI were determined in each animal. The values of these parameters and their spatial dispersion were pooled in the 10 animals. Comparisons of QTI, cQTI and ARI and their

dispersion were performed by an ANOVA test. A regression analysis was used to assess the correlation between QTI, cQTI and ARI, and the correlation between the dispersion of these parameters. $p < 0.05$ was considered to be statistically significant.

Results

Epicardial QTI, cQTI and ARI

Bipolar ECG was obtained from an average of 18 ± 3 epicardial sites. The average values of QTI, cQTI and ARI in the 10 animals were shown in Fig. 2. Procainamide infusion prolonged QTI, cQTI and ARI, but the increase in QTIs was not statistically significant ($p = 0.07$, Fig. 2).

Correlation between QTI, cQTI and ARI

The correlation coefficients between QTI, cQTI and ARI in the 10 animals were shown in Table 1. No significant correlation was found in 9 of the 10 animals before or after procainamide infusion. In animal No. 8, however, there was a significant correlation between QTI, cQTI and ARI before procainamide administration ($p = 0.01$, Table 1).

Dispersions of QTI, cQTI and ARI

The pooled QTI, cQTI and ARI dispersion in the 10 animals before and after procainamide administration were shown in Fig. 3. At baseline, cQTI dispersion was greater than QTI and ARI dispersion although this was not statistically significant

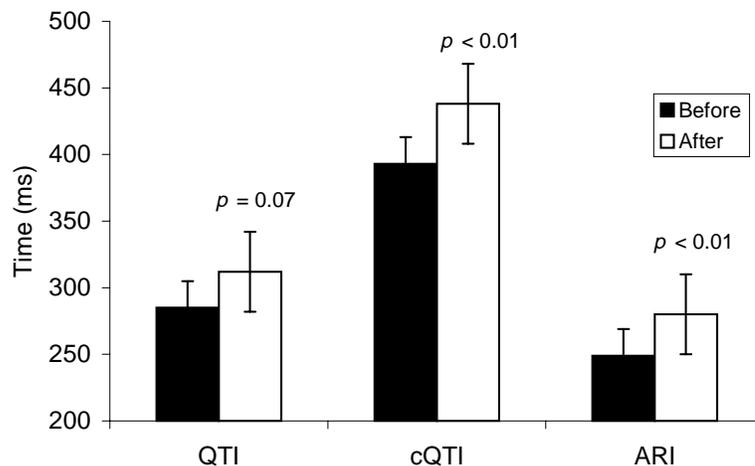


Figure 2. Increase in QTI, cQTI and ARI after intravenous infusion of procainamide.

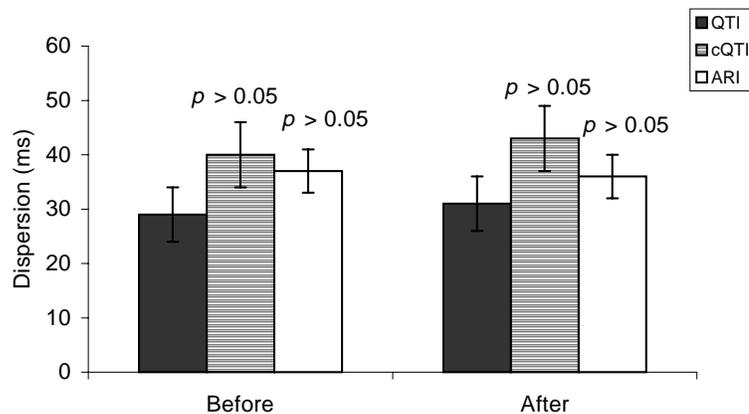
Table 1. Correlation coefficients between QTI, cQTI and ARI before and after procainamide administration

Animal No.	Before procainamide		After procainamide	
	QTI <i>vs</i> ARI	cQTI <i>vs</i> ARI	QTI <i>vs</i> ARI	cQTI <i>vs</i> ARI
1	0.53	0.43	0.17	0.20
2	0.34	0.19	0.34	0.50
3	0.17	0.17	0.29	0.28
4	0.30	0.31	0.11	0.31
5	0.18	0.19	0.29	0.29
6	0.46	0.40	0.46	0.40
7	0.43	0.40	0.37	0.26
8	0.79*	0.78*	0.37	0.26
9	0.23	0.25	0.06	0.09
10	0.39	0.42	0.35	0.29

* $p = 0.01$

($p > 0.05$). Procainamide administration did not result in any significant change in the pooled QTI, cQTI or ARI dispersion (Fig. 3, $p > 0.05$).

cQTI dispersion before procainamide administration correlates moderately well with ARI (Fig. 4). However, QTI dispersion before and after procainamide treatment, and cQTI dispersion after procainamide therapy had no correlation with ARI dispersion, with a correlation coefficient of 0.48, 0.18 and 0.19, respectively ($p > 0.05$).

**Figure 3.** Spatial dispersion of QTI, cQTI and ARI before and after intravenous infusion of procainamide.

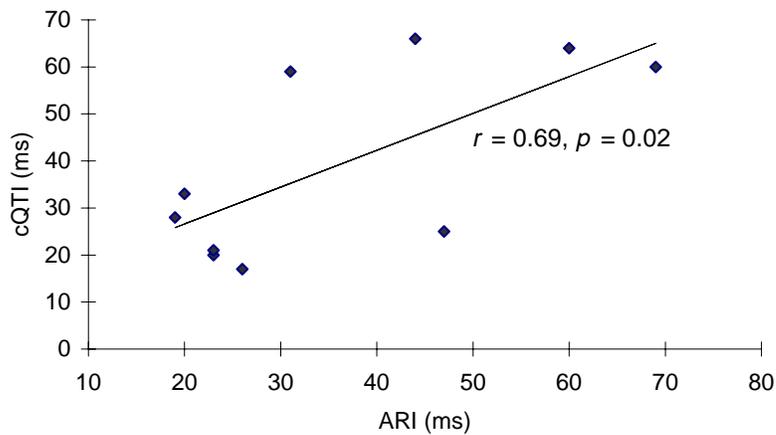


Figure 4. Correlation between cQTI and ARI dispersion in the 10 animals.

Discussions

QTI dispersion from body surface ECG

Although QTI dispersion from a 12-lead ECG has been used as a clinical index of arrhythmia risk in a number of cardiac disorders, the definitive relationships between the two have not been adequately investigated. Earlier studies in the isolated rabbit heart showed a moderate correlation between body surface QTI dispersion and the dispersion of epicardial action potential duration, or recovery time, with a correlation coefficient of 0.58 and 0.64, respectively (Zabel et al. 1995). In isolated canine heart, there was no correlation between body surface QTI and epicardial ARI dispersion (Macleod et al. 1996). In the intact sheep heart, body surface QTI dispersion is less than epicardial ARI dispersion in value, and is not correlated to the later (Wang 2000). These results indicate that the electrophysiological significance of body surface QTI dispersion and its value in clinical risk assessments of cardiac arrhythmias require further evaluation.

Characteristics of epicardial QTIs

Unlike a body surface QTI, the precise physiological meaning of an epicardial QTI is not fully understood. It perhaps represents the recovery time of the local myocardium. Epicardial ARI, however, is a measure of local action potential duration or refractory period (Millar et al. 1985; Haws and Lux 1990). Our study shows that an epicardial QTI is longer than an epicardial ARI in a normal heart (Fig. 2). This is also the case in a heart with acute myocardial ischemia (Wang 1999). Although an epicardial QTI can be prolonged by procainamide, the extent of prolongation is less than ARI from the nearby epicardial site (Fig. 2), suggesting that epicardial QTIs are less sensitive than ARIs in reflecting changes in local repolarization

duration. In addition, an epicardial QTI is insensitive in detecting the shortening of regional repolarisation duration in isolated canine heart (Lux et al. 1998). As with a previous study in isolated heart (Lux et al. 1998), the present whole animal experiment has failed to show any significant correlation between epicardial QTIs and ARI.

Role of epicardial QTIs in assessing ventricular repolarisation dispersion

Similar to body surface QTI dispersion, epicardial QTI dispersion does not seem to reflect the dispersion in repolarization duration. In isolated canine heart, QTI dispersion does not adequately show the actual changes in local repolarisation heterogeneity (Lux et al. 1998; Fuller et al. 2000). In the present whole animal study, only cQTI dispersion before procainamide administration was found to correlate with ARI dispersion, whereas QTI dispersion at baseline or after procainamide therapy are not associated with ARI dispersion of the same epicardial sites.

The poor correlation between epicardial QTI dispersion and ARI dispersion is not fully understood. In a recent study, different projections of a common *T*-wave vector were found to be responsible for the body surface QTI dispersion (Kors et al. 1999). However, the variation in *T*-wave projection is unlikely the cause of the poor correlation between epicardial QTI and ARI dispersion, because the *T*-waves were derived from local bipolar ECGs with minimal vector projection involved.

Summary

Repolarisation dispersion plays an important role in arrhythmogenesis in a number of cardiac disorders, particularly in acute or chronic myocardial ischemia. Accurate assessment of repolarisation dispersion and timely prediction of the risk of cardiac arrhythmias have significant clinical implications. Our whole animal study has revealed that epicardial QTIs have no correlation with ARIs and QTI dispersion does not reflect ARI dispersion. These results indicate that epicardial QTIs from local bipoles are not a useful measure of repolarisation dispersion.

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