How good is QT dispersion as an index of the inhomogeneity of repolarization in in-situ porcine hearts?

Leonard S. Gettes, Takeo Kaneko, Connie Engle, and The Experimental Cardiology Group

Abstract:
QT interval dispersion has been used to estimate ventricular repolarization inhomogeneities. We induced regional lengthening and shortening of ventricular repolarization in the in-situ of porcine heart. Repolarization inhomogeneities were determined by monitoring dispersion in activation recovery intervals from epicardial electrograms. QT dispersion was determined from these electrograms and from unipolar electrograms recorded from the anterior chest wall. Regional hypothermia lengthened activation recovery intervals and increased their dispersion. It increased epicardial QT dispersion, but not body surface QT dispersion. Regional hyperthermia and pinacidil/ischemia shortened ARIs and increased ARI but not QT dispersion. Thus, in our experience, an increase in repolarization in inhomogeneity was not reflected by changes in QT dispersion on the body surface.

The purpose of this work was to determine the usefulness of QT dispersion as an index of the heterogeneity of repolarization.

Methods: We studied the in-situ hearts of pigs weighing 25-38 kg and anesthetized with pentatinol and alpha-chlorolose. A shunt from the carotid artery to the left anterior descending coronary artery routed through a roller pump was installed to permit regional action potential duration lengthening or shortening and thereby cause inhomogeneities in repolarization. Action potential duration in the shunted zone was lengthened by lowering temperature of the shunted blood from 36 to 27 degrees centigrade. Action potential duration in the shunted region was shortened by raising the temperature of the shunted blood to 41 degrees centigrade and by inducing no flow ischemia after first infusing 25 μM pinacidil.

Two sets of experiments were performed using the same protocol. In four experiments, we placed a sock containing 64 evenly distributed unipolar electrodes over the epicardial surface of the heart. In three experiments, we closed the chest after introducing the shunt without placing the sock over the epicardium and then placed 36 unipolar electrodes evenly distributed over the anterior and lateral chest wall.

Action potential duration was assessed by determining activation recovery intervals from the unipolar electrograms.1, 2
The inhomogeneity of repolarization was assessed by determining the mean change and dispersion of action potential recovery intervals induced by the various interventions and compared to the mean values and dispersion of QT intervals recorded from the same electrograms. Dispersion was calculated as the difference between the longest and shortest values. For the sock experiments, we required that paired data from a minimum of 20 electrodes be acceptable for analysis before and after each of the 3 interventions. For the chest experiments, we required paired data from at least 10 electrodes. Statistical significance was determined by the paired T-test.

**Results:** Figure 1 shows examples of the changes in the unipolar electrograms recorded by the sock electrode within the shunted zone and outside the shunted zone. The dots identify the onset of the QRS, the maximum negative dV/dt of the QRS complex, the maximum positive dV/dt of the T wave, and the end of the T wave respectively. The dotted outside lines show the changes in QT interval and the solid lines, the changes in activation recovery intervals induced by the various interventions. Within the shunted regions, the interventions induced greater change in the activation recovery interval than in the QT interval. Outside the shunted zone, the interventions induced only slight changes in both.

Hypothermia caused an increase in mean ARI in all experiments while hyperthermia and pinacidil ischemia caused a decrease in mean ARI in each. The ARI dispersion was increased in 3 of the 4 experiments by hypothermia and in each of the experiments by hyperthermia and pinacidil/ischemia.

Pinacidil/ischemia shortened the mean QT interval of the epicardial electrograms. Hyperthermia caused no significant change. Hypothermia, which caused regional lengthening of action potential duration, increased QT dispersion of the epicardial electrograms. In contrast, the interventions, which caused regional shortening of action potential duration, i.e. hyperthermia and pinacidil/ischemia, caused neither a consistent nor a significant change in epicardial QT dispersion.

The changes in the mean values of both ARI and QT induced by hypothermia, hyperthermia, and pinacidil/ischemia were similar to those recorded on the epicardial surface. However, the increase in QT dispersion noted with hypothermia on the epicardial surface, was not present on the body surface. Indeed, our results suggest that hypothermia tended to shorten QT dispersion on the body surface. Hyperthermia and pinacidil/ischemia failed to cause significant changes in the dispersion of either ARI or QT interval on the body surface.

**Discussion:** An increase in the inhomogeneity of the repolarization is known to facilitate the development of reentry. For this reason, the ability to monitor repolarization in homogeneity caries with it the promise of identifying patients at high risk for potentially life threatening arrhythmias and possibly for initiating prophylactic therapies. Dispersion of the QT interval on the routine 12 lead body surface EKG has been suggested by some to be a marker of repolarization in homogeneity and in some situations, an increase in QT dispersion has been shown to correlate with development of ventricular arrhythmias. However, in other situations, the correlation has been poor and some have argued that QT dispersion as measured on a 12 lead body surface EKG may not reflect the inhomogeneity of ventricular repolarization.

Inhomogeneities in action potential duration have been demonstrated under control conditions by a
variety of methods including measurement to refractory period and recordings of transmembrane or monophasic action potentials and measurement of activation recovery intervals. However, to our knowledge, there are no studies which correlate directly measured changes in the inhomogeneity of repolarization to changes in QT dispersion on either the epicardial or body surface.

In these experiments, we assessed the inhomogeneity of repolarization by determining the dispersion of activation recovery intervals obtained from multiple epicardial unipolar electrograms and compared these results to QT dispersion measured on both the epicardial surface of the heart and on the chest wall. We increased the inhomogeneity of repolarization by lengthening and shortening action potential duration in a discrete region of the left ventricular wall. This was accomplished by altering the temperature of the blood perfusing that region and by inducing no-flow ischemia following pinacidil infusion, an intervention known to cause profound shortening of the duration of the transmembrane action potential and in of the activation recovery interval. These interventions resulted in an increase in the mean value and the dispersion of the activation recovery intervals recorded from the epicardial surface, thereby confirming the ability of the interventions to increase the inhomogeneity of repolarization. QT dispersion of the epicardial electrograms also increased when the inhomogeneity of repolarization was increased by hypothermia, the intervention which caused the regional shortening of repolarization (hyperthermia and pinacidil/ischemia). This result is consistent with the fact that the end of the T wave reflects the last cells to be repolarized. Thus interventions which lengthen some action potential durations would be expected to influence QT dispersion while those which shorten some action potential durations would not. QT dispersion of the unipolar signals recorded from the body surface was not increased by regional hypothermia. Nor was it altered by hyperthermia or pinacidil/ischemia. These results indicate that inhomogeneously lengthened action potentials have the potential to increase QT dispersion.

However, in these experiments, QT dispersion on the body surface did not monitor the increase in the inhomogeneity of repolarization even when these inhomogeneities were caused by lengthening action potential duration in close proximity to the overlying chest leads. This result lends support to the theoretical considerations which argue against the ability of QT dispersion on the body surface to reflect inhomogeneities in repolarization.

References: