Postextrasystolic QT and Q (T+U) prolongation on Holter Monitoring: new markers of increased arrhythmic risk in patients without long QT syndrome?

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Abstract

Post-extrasystolic repolarization changes in the T-wave and particularly U- wave have been recognized as adverse prognostic signs[1]. Prior studies have incompletely assessed the changes in duration of cardiac repolarization, i.e. changes in the length of the QT interval. The conclusion has been that the length of the post-extrasystolic QT interval has little prognostic value[2]. In our current study, we will assess new markers of arrhythmic risk: the change of the QT interval from baseline averaged QT on Holter monitoring. The study entails the review of Holter records of two groups of patients, those with known arrythmias and those without arrhythmic disease to determine possible prognostic markers. There are no apparent practical or ethical problems related to the performance of this study.

A. Study Purpose and Rationale

Ventricular arrythmias like ventricular fibrillation and tachycardias are lethal entities. The current available diagnostic techniques for a patient presenting with these arrythmias, without a known syndrome such as a Long QT syndromes, may involve invasive procedures such as an EP study. Occasionally these patients undergo non-invasive monitoring such as Holter monitoring of their heart rhythm for a period of 48 hours or longer. Various prognostic markers have been studies in recent years including the changes that occur in repolarization waves (T or U) after ectopic beats. These changes correspond to the electrophysiologic phenomena of delayed after depolarizations. Prior studies have failed to systematically evaluate the change in the duration of the QT interval as an additional marker.

B. Study Design and statistical Analysis

We will analyze the Holter record of three patient groups referred to our electrophysiology clinic. Our control group will be patients with multiple PVC's (premature ventricular contractions) but no organic heart disease or sustained ventricular arrythmias. The second group will be patients with prior Holter records who have been referred for EP study secondary to out-of-hospital ventricular fibrillation or ventricular tachycardias not related to myocardial infarction or long QT syndrome. The third group will be patients with known long QT syndromes.

Using prior reports studying the effect of extrasystole on repolarization and QT dispersion, we estimated the expected difference in the change in QT interval between the two groups. With an alpha of .05 and power of .80, we calculated the need for at least 20 patients in each arm of the study[4,5]. As no prior study in the past has identified the mean and standard deviation for this parameter, recent animal studies and cardiac cellular studies were used to estimate the possible effect to be studied[3,4]. The unpaired t-test will be used to evaluate the difference between the two groups. Student t-test with Bonferroni correction for multiple comparisons will be used to compare the difference between groups. The multivariate analysis will account for age, sex, CAD, LVEF, beta-blocker use, PR interval, QRS, QTc baseline, and QT dispersion. Sensitivity, specificity, and likelihood ratio will be calculated for each univariate predictor. Statistical significance being defined as p value < 0.05.

C. Study Procedure

The study entails the systemic review of Holters dating back to years prior to 2002. The QT corrected as determined by the Holter recording will be used as the averaged baseline measurement. QT intervals after extrasystolic events, i.e. PVC or APC, will be recorded under visual magnification with calipers. The QT interval will be defined as the interval from the Q to the return to the TQ baseline. If there is a U wave, the QT is defined as the trough between the peak of the T-wave and the peak of the U-wave. In addition, the Q (T+U) will be measured as the interval from the Q-wave to the return to the TQ baseline. Of the post-extrasystolic events measured, the value with the largest interval change per patient will be used for final analysis. In addition, other parameters to be measured include, QT dispersion, post-extrasystolic QT dispersion, QRS duration, PR interval. Two investigators blinded to the patient information will measure the above parameters.

D. Study Subjects

Subjects are patients who were referred to Holter lab prior to the year of 2002. Patients will be recruited from a cohort of patients older than 18 years of age. The patients from the VT/VF group may have been referred to the EP labs for invasive studies. Results of Holters from these patients prior to the index event will be reviewed. Control subject will be patients referred for Holter monitoring who have had no events 2 years following Holter recordings, i.e. syncope, death from unknown cause, documented symptomatic ventricular arrythmia. The inclusion criteria of the study are that the index arrythmia was hemodynamically significant, it occurred in the absence of metabolic abnormalities or drug treatments that lead to QT prolongation, including class I and III antiarrythmics. The Holter tracing that will be evaluated must have been recorded in the absence of the above confounding factors. Other exclusion criteria include having a basic rhythm other than sinus rhythm or mitral prolapse because of the association with congenital long QT syndrome for groups one and two.

E. Study Drugs-

N/A

F. Medical Devices-

N/A

G. Study Questionnaires-

N/A

H. Recruitment of Subject-

N/A

I. Confidentiality of Study Data

Patient records will be coded to keep confidential the study data and identity of study subjects.

J. Potential Conflicts of Interest-

N/A

K. Location of the Study

The study will be conducted at CPMC. The data is collected in the Holter records archives.

L. Potential Risks

There is no risk imposed from our study.

M. Potential Benefits

There is no direct benefit to the subjects whose records are being reviewed.

N. Alternative Therapies-

N/A

O. Compensation to Subjects-

N/A

P. Costs to Subjects-

N/A

Q. Minors as research Subjects-

N/A

R. Radiation or Radioactive Substances-

N/A

S. References

1. Jackman et al. The Long QT syndromes: A Critical Review, New Clinical Observations and Unifying Hypothesis. *Cardiovascular Dis*. 1988 21:115-172.
2. Postextrasystolic U wave augmentation, a new marker of Increased Arrythmic Risk Viskin et al. JACC. 1996. 28:1746-52.
3. Effect of Premature Beats on Repolarization of Postextrasystolic beats. Burgess et al. Circulation . 1995; 92: 1969-80.
4. QT dispersion in sinus beats and ventricular extrasystole in normal hearts. Day et al. *British Heart Journal*. 1992. 67: 29-41.
5. Adjusting QT interval for Heart Rate. Sagie et al. *AJC. 1992. 70:797-801.*