T-wave Morphology and Arrhythmic Events in Patients with Dilated Cardiomyopathy

JP Couderc, W Zareba, X Xia, M Andrew, AJ Moss

University of Rochester Medical Center, University of Rochester, NY

Abstract

Atypical T wave morphology on scalar ECG may reflect abnormalities of the ventricular repolarization process but the link between these abnormalities and the occurrence of arrhythmic events is unclear. In this study, we investigated whether the occurrence of ventricular tachycardia (VT) in patients with dilated cardiomyopathy (DCM) have specific T wave morphology that may characterize their increased risk for cardiac death (CD). From 24-hour Holter ECG recordings, T-wave morphology and symmetry were quantified in the three orthogonal leads using T-wave area based measurements in addition to conventional QT interval measurements. We compared the T wave characteristics (duration and morphology) between patients according to their cardiac history (VT or CD).

Our results did not evidence significant differences in QT durations between patients with and without a history of VT at any heart rate but revealed a prolongation of the terminal portion of the T-wave at high heart rate in patients with VT (91±21 vs. 102±20 ms, p=0.03 for RR between 600-700 ms). Analysis of T wave morphology may play a role in the identification of patients with dilated cardiomyopathy at higher risk for arrhythmic events.

1. Introduction

Dilated cardiomyopathy is the most common type of cardiomyopathy and represents a large subset of congestive heart failure cases (CHF). In the US, the incidence of CHF is 400,000 cases per year and this disease afflicts 2-3 million people in the US. The role of non-invasive electrocardiographic parameters in the identification of DCM patient with an increased risk of arrhythmic events may help identifying patient who benefits the most from appropriate therapy. In this study, we report preliminary results on the investigation of information from the morphology of the T-wave.

Dynamic features of the repolarization such as beat-to-beat alternans and variability [1;2] have been investigated in patients with DCM. They are non-invasive quantifiers designed to identify potential myocardial vulnerability to VT/VF and sudden cardiac death. Other parameters focusing on repolarization morphology may evidence the presence of myocardial substrate and thus may have prognostic value. A limited number of human and animal studies revealed the presence of information in abnormal T wave morphology complementary to QT prolongation[3;4] Other studies, investigating the effect of drugs modifying ionic current (mainly potassium, Ikr), and triggering torsades de pointes, have evidenced changes in T wave morphology prior to QT prolongation[5;6;7].

In this study, we hypothesise that down-regulation of potassium current in patients with dilated cardiomyopathy [8] may be more pronounced in patients with VT and CD than in patients without VT/CD. This would be reflected by specific repolarization patterns that could characterize patients with a higher risk for TV and CD.

2. Methods

The study relies on a population of 43 DCM patients from the Intercity Digital Electrocardiogram Alliance (IDEAL) database.

2.1. ECG data and repolarization measures

Twenty-four hour digital ECGs were acquired using the SpaceLab-Burdick digital Holter recorder (SpaceLab-Burdick, Inc., Deerfield, WI). The digital ECGs had 200 Hz sampling frequency and 16-bit amplitude resolution.

Automatic QT interval measurements were performed using our software for the Comprehensive Analysis of the repolarization Signal (COMPAS, University of Rochester, NY) that includes repolarization measurements such as QT and QT apex intervals as well as T wave area-based parameters. These repolarization measurements are averaged value obtained from measurements computed on a set of 6 median beats. Each

0276–6547/03 $17.00 © 2003 IEEE

Computers in Cardiology 2003;30:149–152.

median beat is based on 11 consecutives stable normal beats (heart rate variation less or equal to 10%).

The end of the T Wave was identified using the intersection between a slope fitting the descending slope of the T wave and the iso-electric line. The apex of the T wave was located at the highest point of a parabola fitting the maximum amplitude of the T wave (in absolute value). Morphology is quantified using T wave area-based parameters. They measure the time needed to reach a certain percentage of the maximum value of the normalized cumulated area under the T wave. Figure 1 shows the method used for locating the end of the T wave and computing area-based parameters [9]. The so-called QTa50% is the distance between the onset of QRS and Ta 50% (see Figure 1). The beginning of the QRS complex was identified in all leads and the earliest one was used for the measure of the QT intervals in all leads.

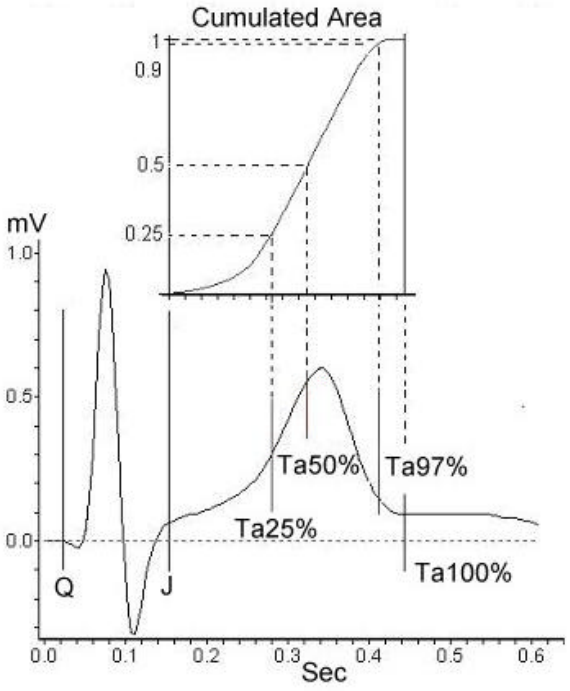

Figure 1. Description of the method used to quantify the morphological features of the T wave. Time between beginning of the QRS complex and Ta 25%, 50% and 97% define QTa25%, QTa50% and QTa97%.

Additional parameters quantifying 1) the terminal portion of the T-wave: QTp-e=QToffset-QTapex and 2) the T wave asymmetry (index of repolarization asymmetry, IRA) defined as IRA=QTapex-QTA50%. The repolarization measurements were filtered and ranked according to heart rate (HR). Only measurements preceded by stable heart rate were included in the analysis (3 minutes prior to analyzed period) insuring the removal of QT adaptation periods. The HR ranges considered were RR = 400 to 1300 by steps and range of 100 ms.

3. Results

The study population included 43 patients who were followed for 2 years. Nine subjects had sudden cardiac death (8 males, 1 female). Nine subjects had documented sustained ventricular tachycardia (VT). Only one patient had both documented VT before dying from CD (1 male). Ages were no significantly different neither between patients with and without VT (56.9±12.1 yrs and 58.3±10.8 yrs, p=0.6), nor between patients who did or did not had a CD (57.0±11.5 yrs and 61.8±9.7 yrs, p=0.3).

RR values in the RR ranges equal to 400-500 and 1200-1300 ms were infrequent. Thus, we limited our study to 500 to 1200 msec heart rate ranges.

Table 1. VT group is compared to no VT and CD group to no CD. Results on repolarization measurements in the four groups (no VT, VT, no CD and CD). These values are obtained for a specific heart rate range (RR=600-700 ms). QT apex, QT offset do not show differences between groups. The stars mark the values significantly different *p=0.06, **p=0.03, ***p=0.04. All parameters are expressed in ms. N is the number of patients in each group. Values for the CD/no CD groups are from lead X whereas they are from lead Z in VT, no VT groups.

	No VT	**VT**	**No CD**	**CD**
N	33	9	25	9
RR	658±16	667±15	663±13	658±18
QT apex	266±27	261±26	278±38	287±29
QT offset	353±23	360±40	367±40	344±38
IRA	**14±9**	**19±13***	15±27	33±13
QTp-e	**91±21**	**102±20 ****	**89±22**	**76±32 *****

Table 1 describes the values (median ± standard deviations) of the repolarization parameters in the four groups for measurements done at specific heart rate: RR between 600 and 700 ms. QT intervals are not significantly different between groups for all heart rate ranges. Significant differences were found with increased QTp-e value and IRA values in patients with VT in comparison to patients without VT (Table 1, 2-last row, bold values) whereas in the group without and without CD, QTp-e was significantly decreased in patients who died of CD. These differences were evidenced at high heart rate (see Figure 2) and vanished when the heart rate decreases. Figure 2 provides the median values for QTp-e in the four populations for all the heart rate ranges.

4. Discussion

Whether an abnormal morphology of the T wave from the

scalar surface ECGs can have a prominent role in the risk stratification of DCM patients with an increased risk for ventricular arrhythmias and cardiac death remains to be elucidated.

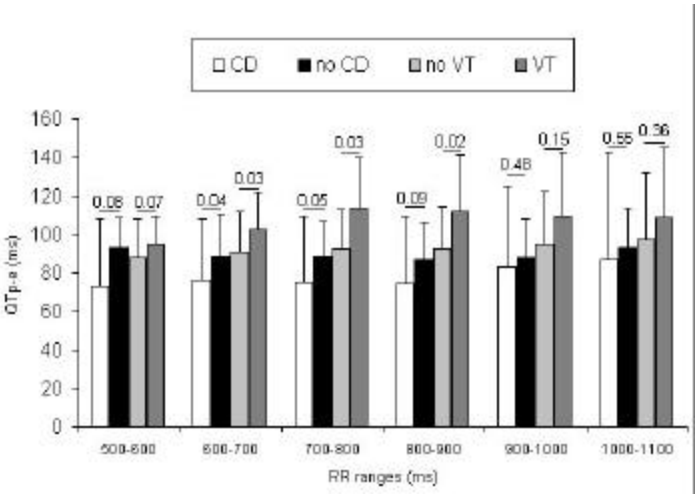

Figure 2. Averaged values for QTp-e intervals in each study group according to heart rate ranges. The main effects are shown to be significant at high heart rate whereas at low heart rate (RR ranging from 900 to 1100 ms) the differences between groups vanish. Values at the top of bars are p values based on non-parametric test (Kruskal-Wallis).

According to our results and in the examples of Figure 3, the morphology of repolarization in each group have the following common features naming 1) a prolongation of the QTp-e intervals in patients with history of VT vs. no VT and 2) a reduction of this interval in patients who died of CD in comparison to those who did not died.

After visual inspection of repolarization morphology in patients who died from CD, the unexpected significant reduction in QTp-e interval was related to classic electrophysiologic patterns of left ventricular hypertrophy (see Figure 3, bottom panel). This observation emphasizes the need for considering the presence of hypertrophy as a confounding factor in the analysis of repolarization morphology.

Our study population consists in patients in who Holter ECGs were recorded under different antiarrhythmic treatments. We did not find significant differences between patients with and without beta-blockers however a significant increase in QTp-e values in patients with antiarrhythmic has been found that might have a relevant effect on our result. QTp-e was equal to 91±11 ms vs. 105±39 ms (p=0.04) in patients without and with antiarrhythmic treatment, respectively and for the same heart rate range than in Table 1. Six out of 9 patients were taken antiarrhythmic drugs when their ECGs were recorded.

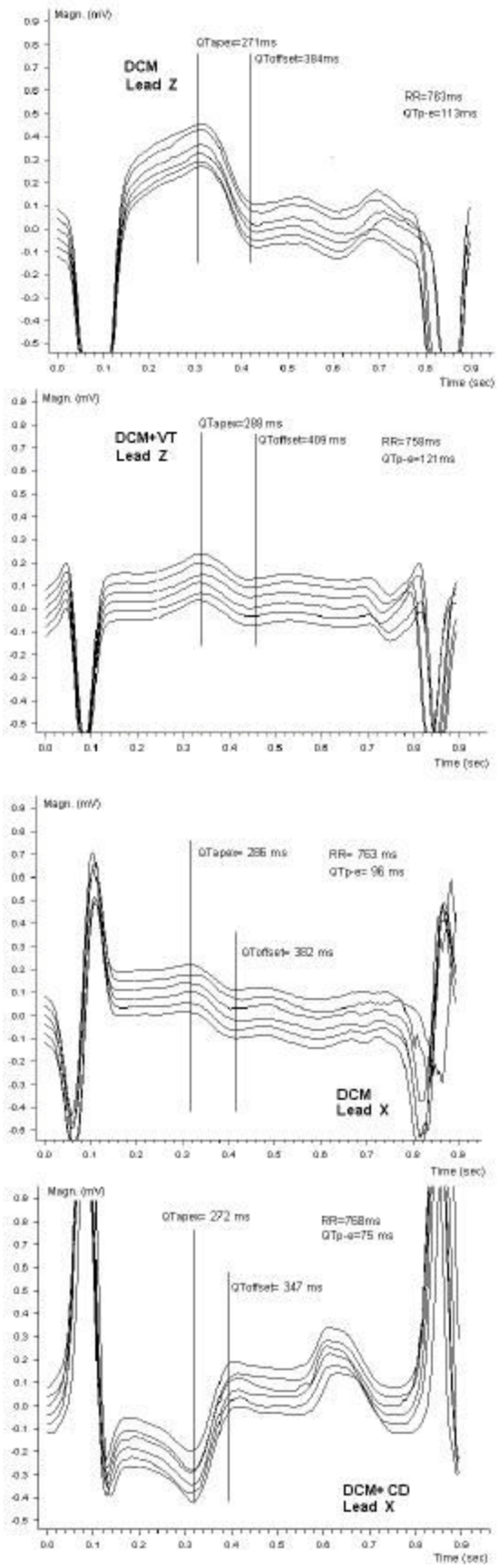

Figure 3. This figure includes examples of ECG tracings for DCM patients with and without VT (lead Y), and DCM patients with and without CD (lead X). These examples describe the different shapes of T wave and morphological features revealed by our quantification in these DCM groups. The shorter QTp-e interval is explained by an inverted T wave pattern usually found in patients with left ventricular hypertrophy.

Thus, our conclusion can only state that prolongation of QTp-e interval is more pronounced in these patients. The reason for this prolongation still remains to be elucidated. None of the patients who died of CD had beta-blockers, 2 out of 9 patients had antiarrhytmic treatment.

The QT interval is slightly prolonged in DCM patient in comparison to healthy subjects (from previous unpublished data) revealing their increased propensity to ventricular arrhythmias and cardiac death. Our study shows that there are morphological repolarization features specific to the study groups. The current work on drug-mediated repolarization abnormalities and arrhythmias evidence that abnormalities of potassium current blockade, triggering ventricular arrhythmias including torsade de pointes is associated with both prolongation of terminal portion of T wave [10]. These morphological changes may reflect increased transmural dispersion responsible for an increased propensity to ventricular events. Being able to quantify transmural dispersion from the surface ECG may help the risk stratification of DCM patients. Our study is detecting abnormalities that could be explained by such hypothesis but additional investigation including larger population would be required to confirm it.

References

[1] Atiga, W. L., Calkins, H., Lawrence, J. H., Tomaselli, G. F., Smith, J. M., and Berger, R. D., "Beat-to-beat repolarization lability identifies patients at risk for sudden cardiac death," *J.Cardiovasc.Electrophysiol.*, vol. 9, no. 9, pp. 899-908, Sept.1998.

[2] Berger, R. D., Kasper, E. K., Baughman, K. L., Marban, E., Calkins, H., and Tomaselli, G. F., "Beat-to-beat QT interval variability: novel evidence for repolarization lability in ischemic and nonischemic dilated cardiomyopathy," *Circulation*, vol. 96, no. 5, pp. 1557-1565, Sept.1997.

[3] Padrini, R., Butrous, G., Camm, A. J., and Malik, M., "Algebraic decomposition of the TU wave morphology patterns," *Pacing Clin.Electrophysiol.*, vol. 18, no. 12 Pt 1, pp. 2209-2215, Dec.1995.

[4] Riccio, M. L., Moise, S., Otani, N. F., Belina, J. C., Gelzer, A. R. M., and Gilmour, R. F., "Vector quantification of T wave abnormalities associated with a predisposition to ventricular arrhythmias and sudden cardiac death," *Annals Non-invas.Electrocardiol.*, vol. 3, no. 1, pp. 46-53, 2003.

[5] Couderc, J. P., Zareba, W., and Moss A.J. Drug-Induced Changes of Ventricular Repolarization: New Incentives for Quantifying T Wave Morphology. Malmivuo, J. and Kauppinen, P. 5[1], 167-170. 2003. International Journal of Bioelectromagnetism.

[6] Couderc, J. P., Zareba, W., Chen, W., Francom, S., Moss, A. J., Sarapa, N., and Morganroth, J. T-wave morphology changes identifies drug-induced repolarization abnormalities. Pacing & Clinical Electrophysiology 26[2, Part II], S19. 2003.

[7] Couderc, J. P., Zareba, W., Moss A.J., Sarapa, N., Morganroth, J., and Darpo, B. Identification of Sotalol-induced Changes in Repolarization Using T-wave Area-based Repolarization Duration Parameters. J.Electrocardiol. 2003.

[8] Koumi, S., Backer, C. L., and Arentzen, C. E., "Characterization of inwardly rectifying K+ channel in human cardiac myocytes. Alterations in channel behavior in myocytes isolated from patients with idiopathic dilated cardiomyopathy," *Circulation*, vol. 92, no. 2, pp. 164-174, July1995.

[9] Couderc, J. P., Zareba, W., Moss A.J., Sarapa, N., Morganroth, J., and Darpo, B. Identification of Sotalol-induced Changes in Repolarization Using T-wave Area-based Repolarization Duration Parameters. J.Electrocardiol. 2003.

[10] Emori, T. and Antzelevitch, C., "Cellular basis for complex T waves and arrhythmic activity following combined I(Kr) and I(Ks) block," *J.Cardiovasc.Electrophysiol.*, vol. 12, no. 12, pp. 1369-1378, Dec.2001.

Address for correspondence.

Jean-Philippe Couderc, PhD, MBA
University of Rochester Medical Center
601 Elmwood Av. , box 653
Rochester, NY 14642
Jean-philippe.couderc@heart.rochester.edu