Reproducibility of T-Wave Morphology Assessment in Patients with Hypertrophic Cardiomyopathy and in Healthy Subjects

Y Gang, K Hnatkova, X Guo, V Batchvarov, B Acar, WJ McKenna, M Malik

Department of Cardiological Sciences, St. George's Hospital Medical School, London, UK

Abstract

This study examined the reproducibility of T-wave morphology assessment in 54 patients with hypertrophic cardiomyopathy (HC) and 70 healthy subjects (HS). Studied indices included: the total cosine R-to-T (TCRT), T-wave morphology dispersion (TMD) and normalized T-wave loop area (TLA). The reproducibility was assessed by coefficient of variance (CV) and ratio of individual range to total range of the measurements (RA).

In supine position, significantly smaller measurements of TCRT while significantly greater TMD and decreased TLA were found in HC compared to HS ($p<0.01$). RA and CV were low in both HS and HC. There was no significant difference in RA or CV between HC and HS. In standing, the same pattern in T wave morphology measurements was found. All measurements tended to be more variable in standing position.

Computerized measurements of T-wave morphology are highly reproducible and may provide a reliable assessment of repolarization abnormalities.

1. Introduction

It has been well recognized that abnormalities in ventricular repolarization are associated with the genesis of ventricular tachyarrhythmias. Conventional QT interval measurement has been commonly used as a simple non-invasive method to assess ventricular repolarization but it is associated with a major difficulty in the accurate localization of the end of the T-wave (1,2). In the recent years, QT dispersion became a popular technique for the evaluation of the variations in ventricular repolarization. However, the concept of QT dispersion has recently been questioned (3-5) and its reproducibility is so poor that could not be used as a reliable risk stratifier.

To explore the new area of non-invasive evaluation of abnormalities of ventricular repolarization, techniques for T-wave morphology assessment were introduced (6,7). While the usefulness of T-wave morphology assessment in risk stratification has been investigated (8), the reproducibility of this assessment warrants a further study.

This study was designed to evaluate the reproducibility of three T-wave morphology measurements in healthy subjects and in patients with hypertrophic cardiomyopathy. The effect of posture on the reproducibility was also evaluated.

2. Methods

2.1. Study populations

This study consisted of 54 patients with hypertrophic cardiomyopathy (HC; aged 39±15 years, 33 men) and 70 healthy volunteers (HS; aged 38±10 years, 35 men).

The diagnosis of HC was based on the World Healthy Organization criteria (9). All healthy volunteers had a normal physical examination and a normal resting ECG.

2.2. ECG recordings

Ten consecutive standard 12-lead ECG recordings were taken in a supine position and 10 consecutive ECGs in a standing position from each patient when they attended our clinic for initial evaluation or follow up. From each patient, the serial ECGs were recorded one immediately after another without changing the electrode attachment. Patients were required to maintain an undisturbed position during the whole recording period. After the 10 recordings in supine position, patients were asked to stand up and recording was reinitiated as soon as the noise caused by postural change disappeared. Data acquisition of each ECG took about 30 seconds. To obtain the 20 ECGs, including the handling of the electrocardiograph and data storage, approximately 15 minutes were required to complete the whole recording session. The ECG recordings from healthy subjects were taken in the exactly same manner.

All ECGs were recorded using a commercially available digital electrocardiograph (MAC VU, GE Medical Systems, WI, USA) with a sampling rate of 500 Hz. All raw data were stored in floppy disks and downloaded to a personal computer for further analysis.

2.3. T-wave morphology analysis

Analysis of the digital ECG recordings was performed in a fully automatic manner with a custom-developed

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software (7). The analytical system was implemented on a standard personal computer and while it was previously developed using Matlab Version 5.2.0 (The MathWorks Inc., 1998), a recent version has been written in C++.

The analytical program performs a singular value decomposition of the ECG signal into a minimum dimensional space. Based on the decomposition, several descriptors are calculated of spatial and temporal variations of T-wave morphology and repolarization wavefront direction (7). Three T-wave morphology indices were calculated and analyzed for the purposes of this study.

2.4. T-wave morphology indices

The following T-wave morphology indices were studied: the total cosine R-to-T (TCRT), T-wave morphology dispersion (TMD) and normalized T-wave loop area (TLA).

TCRT measures the vector deviation between the depolarization and repolarization waves by calculating cosine values between the 3-dimensional R- and T-wave loop vectors within the optimized decomposition space. Negative values correspond to large differences in the orientation of the depolarization and repolarization loops. While the mathematical definition is different, the concept is similar to that of the vectorial angle of ventricular gradient.

TMD expresses the dissimilarities between the T-wave shapes in individual leads, based on the differences between reconstruction vectors of individual ECG leads created from the 3-dimensional T-wave loop. It is calculated as the average of angles between all possible pairs of reconstruction vectors.

TLA describes the shape and irregularity of the T-wave loop by expressing its area as a fraction of the rectangle that encompassed the loop.

2.5. Statistical analysis

The intra-subject reproducibility was assessed separately for the recordings in supine and standing positions by coefficient of variance and ratio of individual range to total range of the measurements (ratio of the ranges).

For each 10 consecutive ECG recordings, the coefficient of variance was calculated as: (standard deviation/mean) × 100%; and ratio of the ranges was calculated as: (maximum – minimum measurements of an individual)/(maximum – minimum measurements of all subjects) × 100%.

Comparison of measurements and reproducibility between groups or between positions was performed using unpaired or paired Student's *t* test as appropriated.

Data were presented as mean ± standard error. A p value of < 0.05 was considered statistically significant.

3. Results

3.1. T-wave morphology measurements

In supine position, the measurements of TCRT in HC were significantly smaller compared to HS. Significantly greater TMD was found in HC compared with HS. There was significantly decreased TLA in HC than in HS (Table 1).

In standing position, the same patter of differences was found between HC and HS. Comparing the measurements in standing with those in supine position, TCRT significantly increased in HC and HS ($p<0.05$) and TMD did not differ. TLA decreased significantly in standing in both HC and HS ($p<0.05$) (Table 1).

3.2. Reproducibility of the T-wave morphology measurements

In supine position, the reproducibility in HC was comparable to that in HS (p=ns). Similarly, no difference was observed either in the ratio of the ranges or in the coefficient of variance regarding TMD between HC and HS. There was no difference in the ratio of the ranges and coefficient of variance between HC and HS (Table 2).

In standing ECGs, there was an obvious trend to all measurements being less reproducible compared with supine ECGs (Table 2).

3.3. Numerical results

Table 1. ECG measurements in relation to posture in patients with hypertrophic cardiomyopathy and in healthy subjects.

Indices	Group	Measurement
TCRT1	HC	-0.047±0.089*‡
	HS	0.511±0.035‡
TMD1	HC	29.5±3.34*
	HS	11.4±0.60
TLA1	HC	0.533±0.023*‡
	HS	0.634±0.013‡
TCRT2	HC	-0.266±0.075*
	HS	0.273±0.049
TMD2	HC	27.5±3.2*
	HS	12.4±1.0
TLA2	HC	0.462±0.024†
	HS	0.532±0.016

1=supine, 2=standing. *p≤0.01; †p<0.05 for comparison between HC and HS; ‡p<0.05 for comparison between supine and standing ECGs. HC=patients with hypertrophic cardiomyopathy; HS=healthy subjects; TCRT=the total cosine R-to-T; TMD=T-wave morphology dispersion; TLA=normalized T-wave loop area.

Table 2. Reproducibility of ECG measurements in relation to posture in patients with hypertrophic cardiomyopathy and in healthy subjects.

Indices	Group	RA (%)	CV (%)
TCRT1	HC	6±1	2±7
	HS	8±1‡	8±2
TMD1	HC	7±1	10±1‡
	HS	8±1‡	7±1‡
TLA1	HC	21±2‡	12±1‡
	HS	19±2‡	8±1‡
TCRT2	HC	9±1	31±34
	HS	13±2	58±40
TMD2	HC	10±2†	15±2
	HS	15±2	18±2
TLA2	HC	34±3	24±3
	HS	37±3	19±2

CV=coefficient of variance; RA=the ratio of individual range to total range of the measurements. See Table 1 for other abbreviations.

4. Discussion

4.1. T-wave morphology

Abnormalities of ventricular repolarization play a critical role in arrhythmogenesis, and have been commonly recognized as markers of cardiac electrical instability. Although in clinical practice, QT interval is the most frequently used ECG parameter for assessing ventricular repolarization, the major difficulty in conventional QT-based method for assessment of ventricular repolarization is the accurate localization of the end of the T-wave (1,2). In contrast, the major advantage of T-wave morphology assessment is its independence of the location of T end (7,8,10).

Malfatto et al. (11) evaluated the diagnostic and prognostic value of morphologic abnormalities of the T wave (mainly notched or biphasic T waves) in 53 patients affected by the idiopathic long QT syndrome. Their study provided evidence that the morphologic analysis of T wave abnormalities may contribute to the diagnosis of the long QT syndrome and the identification of patients at higher risk for syncope or cardiac arrest. In that study, however, T-wave morphology abnormalities were only visually identified which would not be suitable for risk stratification of a larger population. Furthermore, morphologic alterations such as notches can be only qualitatively described but not objectively quantified. In 1997, Priori and co-workers reported their study of quantification of the T-wave morphology abnormalities in 36 patients with long QT syndrome (6). They performed principal component analysis of the T wave from 24-hour 12-lead Holter recordings. They suggested that principal component analysis applied to 12-lead Holter recording adequately quantified the complexity of ventricular repolarization which suggests that they may become a useful noninvasive diagnostic tool in patients with long QT syndrome. Although the principal component analysis of the T wave provided a gross measure of the morphological complexity of the T wave it is not a quantitative measure of the heterogeneity of the T-wave morphologies among the 12 ECG leads. In 1999, Acar et al. proposed a series of T-wave morphology descriptors, which offered new measures of ventricular repolarization abnormalities by evaluating the spatial and temporal variations in T-wave morphologies and the relationship between the depolarization and repolarization patterns (7). A recently published prospective study in 280 post myocardial infarction patients has demonstrated that some of the novel T-wave morphology descriptors from 12-lead ECGs permit accurate risk stratification (8). In particular, in the same patient population, conventional variables of ventricular repolarization dispersion had failed to discriminate patients with arrhythmic events from those events free survivors (12). In the present study, all three measurements distinguish HC from HS at a very significant level.

4.2. Reproducibility of Twave morphology

For a potential risk predictor to be useful, the measurements need to be reproducible. The reproducibility of QT dispersion has been evaluated by a number of early studies. The reported values of inter-observer (and/or intra-observer) relative errors varied widely from 13% to 42% (2,13-16). Hence, in addition to the conceptual problems, there is a general consensus that the reproducibility of QT dispersion is poor.

In comparison with the reproducibility of QT dispersion, this study demonstrated that the reproducibility of the T-wave morphology measurements is substantially better, particularly in supine position, which is the standard position for routine ECG recording and for the conventional QT dispersion assessment. Because of the fully automatic processing method, the reproducibility of these measurements for any given ECG is 100%, and the intra-subject variability would subsequently be much lower than that for QT dispersion measurements obtained manually.

4.3. Comparison of the reproducibility in relation to positions

Ventricular repolarization is a dynamic process so it should be assessed not only under static conditions. With the rapid development in electronic technology, 12-lead Holter monitoring has been introduced into the research area. It was showed that postural changes and autonomic status had an effect on the QT dispersion measurements

and reproducibility (17), and on the T-wave morphology assessment (18,19). This study showed that there were differences in the reproducibility between ECGs in supine and standing positions. These findings confirmed those from previous studies implying that autonomic effects on ventricular repolarization were detectable using this new technique. Caution should be taken when comparing or interpreting measures of ventricular repolarization abnormalities obtained in various positions under different autonomic status.

4.4. Study implications

Our data demonstrate that computerized measurements of T-wave morphology are highly reproducible. Consequently, compared to QT dispersion, the evaluation of T-wave morphology may provide a more reliable assessment of repolarization abnormalities. Because of the differences noted, further studies are warranted to investigate whether this technology will play a role in risk stratification of patients with HC.

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Address for correspondence.

Y Gang
Department of Cardiological Sciences
St. George's Hospital Medical School
Cranmer Terrace
London SW17 0RE, UK
y.gang@sghms.ac.uk