Classification of Patients With and Without Syncope by Means of QT Analysis in Hypertrophic Cardiomyopathy: Preliminary Results

F Marciano, S Cuomo*, ML Mignaux, M Boccalatte*, S Betocchi*

Institute of Cybernetics, CNR, *Division of Cardiology, A Cardarelli Hospital, *Institute of Cardiology, Federico II University, Naples Italy

Abstract

In patients with hypertrophic cardiomyopathy a history of syncope is associated with increased risk of sudden death, an important role in its pathophysiology being presumably played by an arrhythmic mechanism. Aim of the present study was to find out whether several ventricular repolarization parameters are useful to discriminate patients with and without syncope.

The Holter recordings of three groups of subjects (HCM with syncope, HCM without syncope and normal) were analyzed and three sets of variables were measured: six spectral, six QT/RR slope, twelve QT time parameters.

All three sets were submitted to tests (e.g. discriminant analysis) in order to verify the differences among groups. Finally classification of single subjects was carried out.

1. Introduction

Hypertrophic cardiomyopathy (HCM) has a genetic origin [1]. Its main characteristic is the presence of left ventricular hypertrophy, when no other cause can justify the increase of cardiac mass [2].

Several studies have pointed out that a history of syncope may be associated with increased risk of sudden death (SD) in subjects with HCM [3,4]. The identification of subjects at high risk of SD, even in cases where there is not yet clear evidence of syncope, represents an important objective.

An arrhythmic mechanism presumably plays a role in the pathophysiology of SD [5]; however, identifying the presence of an arrhythmic substrate in a specific patient remains an unanswered key issue. Abnormalities in ventricular repolarization may be implicated in the development of these arrhythmias. Indeed, abnormal QT and QTc interval prolongation and increased QT dispersion have been described in patients with HCM [6,7]. However, it has been recently reported that QTc and QT dispersion on the 12-lead electrocardiogram are not reliably useful for predicting sudden death in HCM [8]. In addition to differences in ventricular repolarization, abnormalities in autonomic function have been also reported in HCM [9]. Unfortunately, also heart rate variability analysis is not useful in the assessment of risk in HCM [9]. It is possible that combining ventricular repolarization and autonomic function analysis might improve risk stratification in HCM. Aim of the present study is to find out whether among several re-polarisation parameters, measured from 24h Holter recordings, some can be identified as useful in order to discriminate and classify HCM patients with and without syncope.

2. Methods

The study population consisted of 35 subjects belonging to three groups, whose mean age per group is reported in parenthesis: 1) 8 HCM patients with an history of one or more episodes of syncope (39±14), 2) 13 HCM patients without previous syncope (38±11), 3) 14 normal subjects (35±13).

HCM diagnosis was made according to current criteria including the evidence of left ventricular hypertrophy on 2-dimensional echocardiograms in absence of other cardiac or systemic diseases. Both HCM diagnosis and subsequent Holter recordings from three ECG derivations were done at a special outpatient clinic dedicated to HCM at the Institute of Cardiology, Federico II University of Naples. They were analyzed with a homemade system, whose characteristics were previously reported [10]. Also the automatic interactive algorithm for QRST analysis was described before [11]. Out of a large number of time and frequency QT measured variables only some were chosen on the basis of preliminary selective statistical tests. The retained variables were grouped into three sets a, b, c.

a) six spectral domain parameters of QT variability: total power (0-0.35 Hz) in the 24 h and during sleep, ultra low (0-0.0033Hz) in the 24 h, very low (0.0033-0.04Hz) and low (0.04-0.15Hz) and high (0.15-0.35Hz) during sleep.

b) QTc values and QT/RR slopes measured during 24h, awake and sleep periods.

c) 12 time domain parameters of QT variability: average values of QTc (1), M and S variables, defined in fig 1, over 24h, awake and sleep periods, minimum value of M, maximum values of S and QTc over 24h.
of the variables and the average vector \( \mathbf{m}(k) \), the centroid of group \( k (k=1,3) \). \( C_k^{-1} \) is the inverse of the covariance matrix for group \( k \) (see Appendix). In the Euclidean distance the covariance matrix is replaced by the identity matrix. A new case is classified as belonging to the group which is closest.

One subject out of the total available of the three groups was selected in turn as candidate to classification (round robin procedure). The remaining subjects were then utilized to evaluate Mahalanobis and Euclidean distances.

![Figure 2](https://via.placeholder.com/150)

**Figure 2** The 12 variables of the third set are reported in a star plot representation with each ray corresponding to a variable.

## 3. Results

<table>
<thead>
<tr>
<th>Set of variables</th>
<th>Actual Group</th>
<th>Centroid co-ordin.</th>
<th>Predicted results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>a</td>
<td>1</td>
<td>1.5 , 0.52</td>
<td>62.5</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.41, 0.95</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>-1.5, -0.24</td>
<td>0.0</td>
</tr>
<tr>
<td>b</td>
<td>1</td>
<td>1.4, 0.13</td>
<td>75.0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>-0.2, 0.48</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>-0.98, 0.2</td>
<td>10.0</td>
</tr>
<tr>
<td>c</td>
<td>1</td>
<td>3.6, -0.72</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>-0.74, 2.2</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>3.6, -0.72</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table 1 Discriminant test results
4. Conclusions

From the results obtained it looks as if there exists a clear separation among the three groups of HCM with syncpe, HCM without syncpe and normal. It would be interesting at this point to verify how are classified HCM patients who incurred sudden death whose preceding Holter recordings are available. As clearly stated in the title, the work presented should be considered a preliminary study on the possibilities of supplying further evidence in order to identify HCM patients at risk of sudden death. It is an evaluation of a methodology based on Holter recordings and we must stress how important in this case is to dispose of good quality recordings, particularly as the QT signal is concerned. The number of available patients in our study was drastically reduced by the number of Holter recordings discarded for totally or partially QT missing or for poor QT morphology.

Appendix

The average vectors \( \overline{m}(k) \) and covariance matrices \( C(k) \), (one per group of subjects, \( k = 1,3 \)) are:

\[
\overline{m}(k) = \left( \frac{1}{n(k)} \sum_{i=1}^{n(k)} m(k,i) \right) \quad C(k) = \frac{1}{n(k) - 1} \sum_{i=1}^{n(k)} (m(k,i) - \overline{m}(k))(m(k,i) - \overline{m}(k))^T
\]

\( i = 1, \ldots, n(k) \) is the number of subjects per group

\( j = 1,2,3 \) is the number of variables, \( x(k,i,j) \) is the value of variable \( j \), per subject \( i \), per group \( k \)

\[C(k) = \begin{bmatrix}
    e(k,1,1) & e(k,1,2) & \cdots & e(k,1,12) \\
    e(k,2,1) & e(k,2,2) & \cdots & e(k,2,12) \\
    \vdots & \vdots & \ddots & \vdots \\
    e(k,12,1) & e(k,12,2) & \cdots & e(k,12,12)
\end{bmatrix}
\]

the elements of the matrices are given by:

\[e(k,l,j) = \frac{1}{n(k) - 1} \sum_{i=1}^{n(k)} x(k,i,j) \cdot y(k,i,l)\]

\( l = 1,2 \) is a second index for the number of variables.

and \( y(k,i,j) = x(k,i,j) - m(k,j) \)

where \( m(k,j) \) is an element of vector \( m(k) \).

References


Address for correspondence.
Fortunato Marciaro
Istituto di Cibernetica del CNR
Via Campi Flegrei 34
80078 Pozzuoli
Napoli, Italy
formar@biocib.cibn.cnr.it