Postextrasystolic T Wave Change to Stratify Risk of Pump Failure Death in Patients with Chronic Heart Failure

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Abstract

The postextrasystolic T wave change (PEST) is an electrocardiographic phenomenon in which the morphology of the normal T wave is altered for a short time after a ventricular ectopic beat (VEB). It has been observed in patients with other cardiac pathologies but it has not been proposed as a risk index for cardiac death. Since PEST seems to be potentiated in patients with depression of myocardial contractility, we hypothesize that PEST could be used to predict pump failure death (PFD) in patients with chronic heart failure (CHF). For the purpose of quantifying PEST, the parameters morphological change onset (MCO) and morphological change slope (MCS) were introduced. MCO describes an initial morphological change of the T wave after a VEB, while MCS is responsible for the description of the restitution to its original shape.

537 records from the MUSIC study were separated according to their cause of death and comparisons against the others (including survivors) were carried out. In addition, receiver operating characteristic (ROC) curves were used to determine the optimal separating thresholds for MCO and MCS that maximized the sum of sensitivity and specificity for PFD risk prediction. The results showed that no significant differences could be established and the proposed parameters do not seem to be related to any kind of cardiac death. In future, other forms of PEST quantification together with more databases can be used to definitely conclude that PEST has no predictive power.

1. Introduction

The postextrasystolic T wave change (PEST) is an electrocardiographic alteration of the normal T wave morphology after a ventricular ectopic beat (VEB). The morphological variation can be given by changes in amplitude, width or symmetry [1]. The modified postectopic T wave returns to its original shape within one or two beats. Although PEST has been observed in the past in patients with cardiac pathologies such as coronary artery disease or left ventricular dysfunction [2], it has not been proven to be useful for the identification of those patients. However, in a previous study [3], PEST was shown to be related to postextrasystolic contractile potentiation and it was found to be more notorious in the presence of depression of myocardial contractility.

PEST-based risk assessment could complement the predictability achieved by the heart rate turbulence (HRT), which is a phenomenon that reflects short time variations in heart rate after a VEB. HRT has been proven to be a strong risk stratifier for death from any cause, cardiac death and fatal and nonfatal cardiac arrest in patients with different cardiac diseases [4]. The HRT parameters deliver a positive predictive value and sensitivity of approximately 30% for both fatal and nonfatal cardiac arrest, which is crucial in the treatment of cardiac patients and facilitates the choice of implanting devices such as cardioverters.

In this work, we hypothesize that PEST could be used as a non-invasive risk index for PFD and assess the predictive value of two ECG-derived markers specially design to quantify the initial morphological T wave change (MCO) and its restitution to its original morphology (MCS) in a

 ISSN: 2325-887X DOI:10.22489/CinC.2016.011-402

population with chronic heart failure (CHF).

2. Materials

The MUSIC (MUerte Súbita en Insuficiencia Cardiaca) study is a prospective, multicenter, longitudinal study that was created to evaluate risk indexes in ambulatory patients with symptomatic CHF [5]. Originally, 992 patients labeled with New York Heart Association (NYHA) classes II and III participated in the MUSIC study. They were prospectively followed up for a median of 44 months (range 28-51). However, for this paper, only patients having sinus rhythm, and for whom PEST parameters could be calculated, were considered. Thus, the original cohort was reduced to 537 patients from which 59 (11.0 %) died of pump failure, 44 (8.2 %) were victims of SCD, 24 (4.5 %) died of other causes and the rest survived the study. The class cardiac death (CD) was introduced and defined as SCD and PFD together and the class total mortality (TM) was defined for all causes of death together. During Holter monitoring no medications were withdrawn. A summary of the clinical characteristics of the patients considered for this work can be found in table 2.

The 24 hour Holter ECG acquired for each patient consist of two or three Frank's leads obtained through linear transformation from original 12 lead recordings. The sampling rate of the ECG signals is 200 Hz. The annotation of the QRS complexes together with its classification were also given in the database.

3. Methods

3.1. Signal preprocessing

A clean T wave morphology is necessary for a correct quantification of PEST. Thus, we filtered the ECG signal to the frequency band of the T wave. For this purpose, baseline wander was suppressed using a concatenation of two median filters, high frequency perturbations and muscle noise were removed using a low pass filter while power line hum was eliminated with a notch filter. T waves with low signal quality were also removed. For this purpose, a T wave template was created for every patient and its spectral properties were compared to the spectrum of each T wave in the signal. Waves having considerably different spectral properties (and thus a lower signal-to-noise ratio) were removed from the analysis.

3.2. T wave detection

The T wave was detected using the stationary wavelet transform (SWT) [6]. The detection algorithm starts with the cancellation of the QRS complex (already given in the database) and P wave in the filtered ECG. The resulting signal is decomposed using the reverse biorthogonal 3.3 wavelet up to level 4. The largest detail coefficient of the transformed signal that is detected after the QRS complex is set as T wave maximum. This procedure is performed in each of the ECG leads. Synchronization of detected waves among the three channels is also carried out. This facilitates the correction of wrong detected T waves.

3.3. Quantification of postextrasystolic T wave change

The algorithm for quantification of PEST starts by finding all VEB in the signal that satisfy the rules imposed for HRT [4]. For PEST, as for HRT, five beats prior to the VEB and another 15 afterwards (denoted with $n = -5, ..., 15$) are used for the analysis. We refer to this interval as the vicinity of the VEB. Second, a local T wave template in each channel is created as the mean T wave among the first four T waves. Then, a linear combination of the ECG leads is performed to create a virtual channel with maximal T wave amplitude. For this purpose, a T wave loop is created from the templates, and the ECG is projected onto the direction of the maximal loop magnitude. Maximizing T wave amplitude reduces other artifacts and increases the chances of observing PEST. The similarity between the template and each T wave in the vicinity of the VEB is measured using the $l\_operator$. For two signals $x(t)$ and $y(t)$, the $l\_operator$ is defined in the following manner:

$$l\_operator\{x(t), y(t)\} = 1 - \frac{E\{(x(t) - y(t))^2\}}{E\{x(t)^2\} + E\{y(t)^2\}}$$

where $E\{\cdot\}$ denotes the expected value operator. The $l\_operator$ is a distance-based similarity measure that delivers values in the interval $[-1, +1]$. It can be used to quantify any kind of morphological changes and is equal to +1 only when the two signals are exactly the same. A series of $l\_operator$ values is calculated when comparing the T wave template ($Template(t)$) to each T wave ($T_n(t)$) in the vicinity of the VEB:

$$lop(n) = l\_operator\{Template(t), T_n(t)\}$$

A second signal quality assessment is carried out at this point. T waves that should not be affected by the VEB ($n = [-5, ..., -2] \cup n = [3, ..., 15]$) are required to have a high $lop(n)$ value of at least 0.96. If any of the mentioned T waves does not fulfill this criterion, the whole series is discarded. Finally, the median $l\_operator$ series among all VEB fulfilling the requirements is used for the actual quantification of PEST. Two parameters, MCO and MCS, were defined to measure PEST as follows:

$$\begin{aligned} MCO &= \left(lop(1) - \frac{1}{4} \sum_{n=-5}^{-2} lop(n) \right) \cdot 1000\ [‰] \\ MCS &= \frac{lop(2) - lop(1)}{RR(2)} \cdot 1000\ [‰/s] \end{aligned}$$

MCO describes an initial morphological change of the T wave after the VEB, while MCS is responsible for the description of the restitution to its original morphology. An example of how the quantification of PEST is carried out for a patient in the MUSIC database can be seen in figure 1. A preliminary formulation of the quantification algorithm was presented in [1].

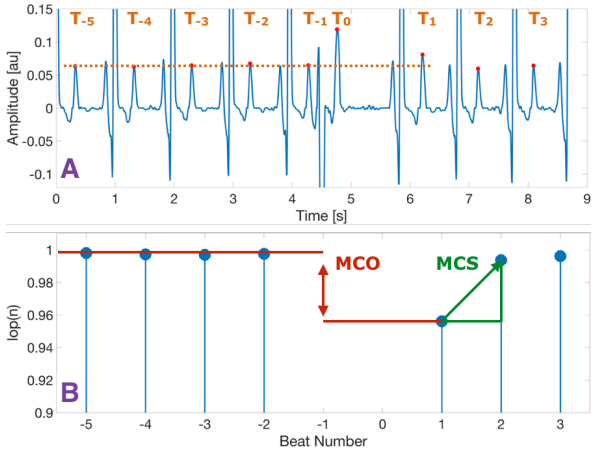

Figure 1. Quantification of PEST. A: First T wave after VEB has larger amplitude. B: Definition of MCO and MCS from the median $l\_operator$ series.

3.4. Statistical analysis

In order to address the question if MCO and MCS can be used for risk assessment, a series of statistical tests were carried out. First, the patients in the data set were separated according to its cause of death and comparisons of each cause against the others (including survivors) were carried out using the two-tailed Wilcoxon-Mann-Whitney test.

Secondly, the complete study population was divided into MCO+ and MCO-, and MCS+ and MCS- according to the risk of suffering from PFD. In order to find the optimal separating thresholds, a receiver operating characteristic (ROC) curve was created for each parameter. Figure 2 shows the ROC curves.

The results of the statistical analysis are presented in table 2. The data are given as median±interquartile range (med±iqr) for continuous variables and as number and percentage for categorical variables. For the univariate comparison of the continuous and categorical data, a two-tailed Wilcoxon-Mann-Whitney and a Fisher's exact test were performed respectively.

The SPSS software was used for all statistical analyses and the significance level was defined for $p<0.05$.

4. Results

First, no significant differences could be established between the distributions of MCO and MCS for the classes in the study.

Secondly, in the analysis with respect to PFD, a med±iqr of -6.97±13.66 and 6.38±15.22 were calculated among the study population for MCO [‰] and MCS [$‰/s$] respectively. In addition, an area under the curve (AUC) of 0.546 and 1-0.452=0.548 were found for MCO and MCS respectively. The optimal cutoff values that maximized the sum of sensitivity and specificity were MCO=-7.0 ‰ and MCS=6.733 $‰/s$. From the total 537 patients, 265 were included in the group MCO- while 272 were in MCO+. Regarding MCS, 280 patients were categorized as MCS- and 257 as MCS+.

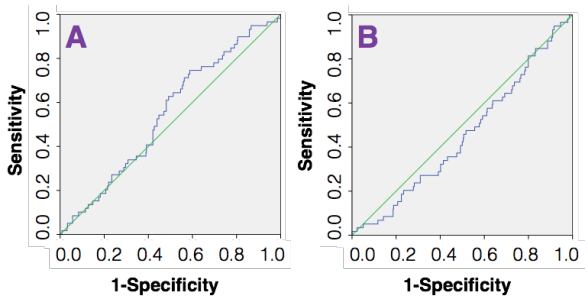

Figure 2. A: ROC curve for MCO with respect to PFD. B: ROC curve for MCS with respect to PFD.

In table 2, the clinical variables were compared for each of the two groups MCO+ and MCO- just as MCS+ and MCS-. Differences were significant for QRS $>$ 120 ms in both parameters and for the average heart rate in MCS.

5. Discussion

The results presented in this study show that the PEST parameters do not seem to be related to any kind of cardiac death. The comparisons from table 1 demonstrated that the classes defined in this study do not come from different populations when analyzed with respect to MCO or MCS. In addition, the further statistical analysis for PFD using the ROC curve and dividing the population into two groups was not significant either. These results seem to be in accordance with the findings from earlier studies, where PEST was not significant for the identification of coronary artery disease or left ventricular dysfunction [2]. According to [3], PEST appears to be a normal phenomenon present in all patients manifesting more or less equally independent of their cardiac disease.

However, the Fisher's exact test performed for PFD with respect to groups MCO- and MCO+ (shown in table 2) delivered an error probability of p=0.054 which is not far from the significance level. This could mean that the algorithm used to quantify PEST is already pointing in the right direction but still needs to be improved. The usage of only one morphological feature, the $l\_operator$, to quantify PEST is probably not enough to consistently describe all possible morphological T wave changes.

Table 1. med±iqr for MCO and MCS of each cause of death. The error probability (p value) for the comparisons among classes is also given.

	MCO [‰]			MCS [‰/s]		
	cause of death med±iqr	others med±iqr	p-value	cause of death med±iqr	others med±iqr	p-value
SCD - other	-8.22±11.74	-6.79±14.06	0.614	7.10±12.29	6.36±15.49	0.757
PFD - other	-5.74±8.23	-7.18±53.85	0.245	4.58±11.68	6.61±15.37	0.227
CD - other	-5.98±10.85	-7.14±14.50	0.567	6.20±11.34	6.57±15.43	0.456
TM - other	-6.69±12.05	-7.00±14.27	0.917	6.29±13.68	6.48±15.40	0.631

Table 2. Summary of clinical characteristics of patients.

	Overall population (N=537)	MCO- (N=265)	MCO+ (N=272)	p-value	MCS- (N=280)	MCS+ (N=257)	p-value
Age (y)	64±17	64±19	65±15	0.133	65±15	63.5±19	0.148
Gender (men)	389 (72.4%)	187 (70.6%)	202 (74.3%)	0.385	210 (75%)	179(69.6%)	0.177
NYHA class III	101 (18.8%)	54 (20.4%)	47 (17.3%)	0.378	45 (16.1%)	56 (21.8%)	0.098
LVEF $< 35\%$	308 (57.4%)	143 (54.0%)	165 (60.7%)	0.138	171 (61.1%)	137 (53.3%)	0.081
Diabetes	213 (39.7%)	106 (40.0%)	107 (39.3%)	0.930	106 (37.9%)	107 (41.6%)	0.379
Beta-Blockers	367 (68.3%)	179 (67.5%)	188 (69.1%)	0.711	196 (70.0%)	171 (66.5%)	0.404
Amiodarone	47 (8.8%)	23 (8.7%)	24 (8.8%)	1.000	26 (9.3%)	21 (8.3%)	0.760
ARB or ACE inhibitors	103 (19.2%)	46 (17.4%)	57 (21.0%)	0.324	60 (21.4%)	43 (16.7%)	0.188
Average heart rate (bpm)	71±17	71±17	71±15	0.863	70±15	72±17	**0.014**
Maximum heart rate (bpm)	113±23	114±23	113 ± 21	0.448	113 ± 22	115±25	0.056
Heart rate range (bpm)	64±19	65±21	62±18	0.078	62±18	66±22	0.057
QRS > 120 ms	225 (41.9%)	81 (30.6%)	144 (52.9%)	**0.000**	143 (51.1%)	82 (31.9%)	**0.000**
Nonsustained VT and more than 240 VPB in 24h	145 (27.0%)	66 (24.9%)	79 (29.0%)	0.287	82 (29.3%)	63 (24.5%)	0.243
PFD	59 (11.0%)	22 (8.3%)	37 (13.6%)	0.054	37 (13.2%)	22 (8.6%)	0.098

Data are presented as absolute frequencies and percentages and as med ± iqr.
NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; ACE = angiotensin-converting enzyme;
ARB = angiotensin receptor blocker; VT = ventricular tachycardia; VPB = ventricular premature beat;
MCO+ = morphological change onset positive group; MCO- = morphological change onset negative group;
MCS+ = morphological change slope positive group; MCS- = morphological change slope negative group.
Significant differences between MCO- and MCO+ just as MCS- and MCS+ are indicated in bold.

Finally, even though we filtered the ECG to highlight the frequency band of the T wave, it is plausible that the remaining noise and other artifacts, still impede a clean PEST analysis.

6. Conclusion and Outlook

In this paper, we showed that the proposed PEST parameters, MCS and MCO, do not seem to be related to any kind of cardiac death. Furthermore, the division of the PEST parameter into subgroups did not show predicting power for PFD either. In order to definitely prove that PEST cannot be used for risk assessment, other parameters such as T wave amplitude, width or symmetry can be utilized to design a more elaborated quantification of PEST. In addition, other databases with higher signal quality would lead to a cleaner estimation of PEST parameter and should be considered also.

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