Analysis of T-wave Amplitude Adaptation to Heart Rate Using RR-binning of Long-Term ECG Recordings

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Abstract

The prognosis of patients with coronary artery disease at the early stage of the disease is a challenge of modern cardiology. There is an urgent need to risk stratify these patients. Holter technology is a cheap and cost effective tool to evaluate electrical abnormalities in the heart. We propose to investigate T-amplitude adaptation to heart rate (HR) using RR-binning. We used daytime recordings from healthy subjects and subjects with acute myocardial infarction (AMI) from the Telemetric and Holter ECG Warehouse. The AMI subjects were divided into two groups based on location of their infarction (group A: anterior or anterior lateral, group B: inferior or inferior lateral). Both AMI groups had acute and stable phase recordings. Population-based T-adaptation to HR was observed for healthy subjects (R^2 = 0.92) but was less pronounced for AMI subjects: Group A- R^2_{acute} = 0.56 and R^2_{stable} = 0.00, and Group B- R^2_{acute} = 0.57 and R^2_{stable} = 0.33.

1. Introduction

We propose a novel representation technique for ECG recordings based on the RR-binning principle to investigate the relationship between T-amplitude and heart rate (HR). Couderc et al. [1] have reported an impaired relationship between HR and T-amplitude in patients with the congenital long QT syndrome (type 2) and in healthy subjects exposed to the class III antiarrhythmic d,l-sotalol. Graff et al. [2] have further demonstrated that a consistent effect of the torsadogenic drug d,l-sotalol, is the development of flat T-waves which are similar in appearance to the flat T-waves observed in the congenital type 2 long QT syndrome. These observations linked down-regulation of the rapid components of the repolarizing potassium current (I_{Kr}) of the myocardial cells to profound effects on the ampliutude of the T-wave. Huang et al. [3] studied the down-regulation of potassium after infarction in an animal model and demonstrated that K+ channel down-regulation occurs early and may be dissociated from the slower time course of myocardial remodeling. Based on this observation, we hypothesize that subjects with acute myocardial infarction (AMI) may present down-regulation of ventricular cells that could be reflected on Holter ECGs by an impaired adaptation of the T-amplitude to HR changes.

The RR-binning was initially proposed by Badilini et al. [4]. RR-binning has been used as a tool to group cardiac beats into bins of similar HR from which the QT interval could be measured independently from HR [4]. This technique provides an average cardiac beat which is representative of the ECG patterns for a given limited range of HRs (RR-bin) by filtering out the unstable beats (instability being based on HR variability).

We designed a method based on this concept to analyse ECGs from subjects with AMI and we compared our results to the ones obtained from Holter ECGs from healthy subjects.

2. Methods

2.1. Study populations

Two datasets with 24-hour Holter recordings were used from the Telemetric Holter ECG Warehouse (THEW) of the Center for Quantitative Electrocardiography and Cardiac Safety at University of Rochester Medical Center (Rochester, NY, USA) [5]. The healthy database (E-HOL-03-201-003) included of 154 subjects (37 $\pm$15 yrs), 79 males (37 $\pm$14 yrs) and 75 females (37 $\pm$16 yrs).

The AMI database (E-HOL-03-160-001) was divided into two groups based on infarct location. Subjects with transient ST depressions were excluded. Group A consists of subjects with a myocardial infarct with anterior or anterior lateral location, and includes 25 subjects (57 $\pm$16 yrs), 18 males (51 $\pm$13 yrs) and 7 females (71 $\pm$16 yrs). Myocardial infarct locations for group B were inferior or inferior lateral. Group B includes 28 subjects (56 $\pm$13 yrs), 22 males (55 $\pm$12 yrs) and 6 (62 $\pm$15 yrs). The two groups contained recordings for both the acute and stable phase

of the myocardial infarct. Further clinical characteristics of these populations can be found on the THEW project website (`http://www.thew-project.org`).

2.2. ECG preprocessing

The ECG recordings were digitally recorded at 200 Hz. The ECGs were filtered using a fifth order IIR forward-backwards bandpass filter with a lower cutoff frequency of 0.5 Hz and a higher cutoff frequency of 35 Hz to remove the effects of baseline wander and muscle noise. The lead configuration used in these two datasets (Healthy and AMI) was similar and included 3 pseudo-orthogonal leads (X, Y and Z). In this study we only used lead X. All ECGs were recorded with the same Holter equipment and exported from the THEW file server in ISHNE format for both the raw ECG signals and the corresponding cardiac beat annotation.

2.3. Rpeak detection and beat selection

The Holter recordings from the THEW provided location of the center of gravity (COG) of the QRS complexes. In this study, we used the Rpeak as a reference for the detection of the onset and the end of cardiac beats. The location of the COG was used as an aid to detect these fiducial points. Using a 150 ms search window centered on COG, the largest maxima in the window was defined as Rpeak.

Non-sinus cardiac beats were identified using the annotation information from the THEW, and these beats were excluded from the analysis. Furthermore, RR intervals and cardiac beats prior and after the non-sinus cardiac beats were excluded.

The cardiac beats associated with HRs below 60 BPM or above 100 BPM were discarded from our analysis in order to have a sufficient number of beats to compute a representative cardiac beat for a given HR.

Finally, only cardiac beats from the diurnal period were included in order to consider similar autonomic regulation of the heart. The diurnal period was defined between 7:00 am and 11:00 pm.

2.4. RR-bin and ECG profile definitions

The width of each bin was defined as 1/fs, where fs is the sampling frequency of the ECG signal. Bins with less than 20 cardiac beats were considered not representative.

The cardiac beats associated with a given RR bin (previous RR interval was used) were aligned using the Rpeak. Then for each collection of beats in a bin we calculated a "median beat". The "median beat" was computed from the median values of the amplitude of all synchronized samples across beats in a given RR-bin. We used the median instead of the mean to ensure a better estimate in case of the presence of noisy beats or undetected artifacts.

Subject profiles were used to calculate population profiles. For the subject-based profiles, "median beats" were calculated for all RR-bins. For the population-based profiles, the "median beats" from subjects belonging to the same study population, and having the same previous RR interval were grouped and normalized using the amplitude of the Rpeak. For each population-based RR-bin, the reported "median beat" was calculated by synchronizing the subject-specific median beats on the Rpeak.

2.5. Detection of Tpeak

To detect the location of Tpeak in the profiles, we used a wavelet-based technique [6]. This delineation method was applied on the "median beats" in all bins to get the amplitude of Tpeak for that specific RR-bin.

2.6. Implementation

Filtering and beat extraction were implemented in C++ using BOOST libraries. All graphs of the profiles and statistics were done using MATLAB 7.9.0 (Mathworks Inc, Natick, MA, USA).

3. Results

3.1. Healthy population profile

The profile for the healthy population is shown in Figure 1. For this population-based profile, there was an R^2 = 0.92 between T-amplitude and the RR interval.

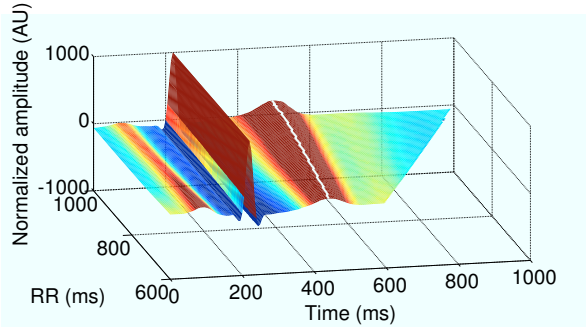
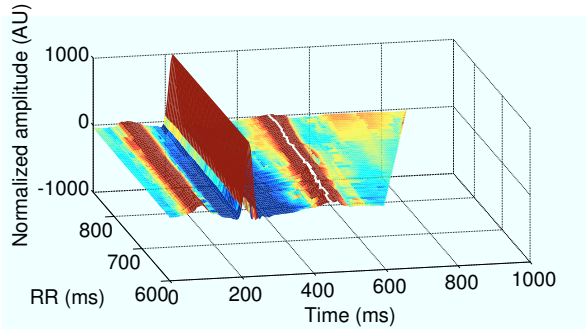
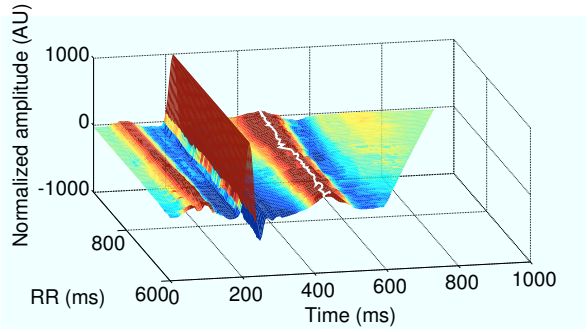


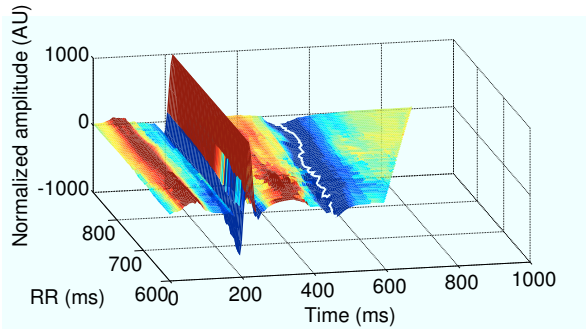
Figure 1: Waterfall plot in 3D (time, amplitude and RR values) of the population-based profile for healthy subjects. The line across T-waves marks the automatically detected T-wave peaks. The slope for T-amplitude versus RR interval was: $0.29\,\mathrm{ms}^{-1}$ (95 % CI: $0.27\,\mathrm{ms}^{-1}$ to $0.31\,\mathrm{ms}^{-1}$), $p < 0.01$.



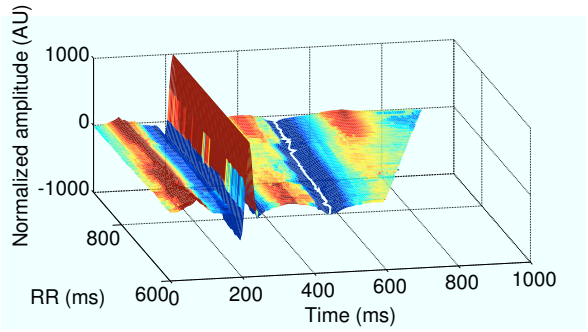
(a) Group A, Acute: The slope for T-amplitude versus RR interval was: $0.29\,\mathrm{ms}^{-1}$ (95 % CI: $0.23\,\mathrm{ms}^{-1}$ to $0.36\,\mathrm{ms}^{-1}$), $p < 0.01$.



(b) Group A, Stable: The slope for T-amplitude versus RR interval was: $0.20\,\mathrm{ms}^{-1}$ (95 % CI: $0.23\,\mathrm{ms}^{-1}$ to $0.36\,\mathrm{ms}^{-1}$), $p < 0.01$.



(c) Group B, Acute: The slope for T-amplitude versus RR interval was: $-0.36\,\mathrm{ms}^{-1}$ (95 % CI: $-0.44\,\mathrm{ms}^{-1}$ to $-0.27\,\mathrm{ms}^{-1}$), $p < 0.01$.



(d) Group B, Stable: The slope for T-amplitude versus RR interval was: $-0.02\,\mathrm{ms}^{-1}$ (95 % CI: $-0.08\,\mathrm{ms}^{-1}$ to $0.05\,\mathrm{ms}^{-1}$), $p = 0.62$.

Figure 2: Waterfalls plot in 3D (time, amplitude and RR values) for the acute and stable phases of AMI subjects. The line across T-waves marks the automatically detected T-wave peaks.

Table 1: The slopes for the T-amplitude and RR relationship and R^2 for subject specific profiles.

Population	Slope (95 % CI) (μV/ms)	R^2
Healthy	0.43 (0.42 to 0.43)†	0.85
AMI Group A		
Acute	0.06 (0.05 to 0.07) †	0.00
Stable	-0.11 (-0.13 to -0.09) †	0.34
AMI Group B		
Acute	-0.07 (-0.10 to -0.03) †	0.05
Stable	-0.04 (-0.06 to -0.02) †	0.00

† The p-value of the slope was significant ($p < 0.01$)

3.2. AMI population profiles

The relationship between T-amplitude and the RR interval for group A of the AMI population was: R^2_{acute} = 0.56 and R^2_{stable} = 0.00, figure 2a and 2b. For group B, the relationship between T-amplitude and the RR interval was: R^2_{acute} = 0.57 and R^2_{stable} = 0.33, figure 2c and 2d.

3.3. Slopes

The slopes for the T-amplitude and RR relationship of the population-based profiles are shown under the respective waterfall plots in figures 1 and 2. The slopes and the R^2 values of the subject specific profiles are listed in Table 1. There is agreement in direction and magnitude between subject and population specific profiles for the healthy population, but this agreement was less pronounced for the AMI populations.

4. Discussion and conclusions

In this work we proposed a method based on RR-binning that provides a graphical representation of cardiac beats across HRs using Holter recordings. We used this method to assess the relationship between HR and T-amplitude. We condensed the massive amount of information available in diurnal ECG recordings after preprocessing the signal and detecting a set of fiducial points. With the proposed method we assessed the T-amplitude dependency on HR. For healthy subjects we identified a HR dependency of the T-amplitude as previously reported [1, 7].

Such HR dependency of T-amplitude was less pronounced in the group of AMI patients regardless of the topography of their myocardial infarction. These results suggest that the regulation of the ventricular repolarization process is impaired. The reason for this abnormality remains unclear, yet one could speculate that the down-regulation of potassium current described by Huang et al. [3] in animals at early and late stage of the MI could applied to the human heart. Then, impairment of T-amplitude adaptation to HR could represent a new dynamic marker of increased risk for life-threatening arrhythmias. One would also note that there might be other mechanisms regulating myocardial ischemia and that the HR modulation of T-amplitude, may also depend on location of the infarction. Further studies are needed to investigate this relationship.

The agreement in slope between the subject and population based profiles for the healthy group, indicates that the population-based profile is representitative of the individual subjects. This agreement was not found for the AMI populations and one could speculate that this discrepancy holds diagnostic information.

The proposed method was limited to analysis of the T-amplitude and the HR. It is noteworthy that the technique could be applied to investigate other aspects of the ECG signal across HRs. One clinical example would be to evidence ST changes during exercise, or to identify HR dependent block in patients with conduction abnormalities.

Acknowledgements

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