Assessment of Repolarization Based on Body Surface Measurements

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Abstract

Activation recovery interval (ARI) has been recently introduced for assessment of repolarization on the cardiac surface. Due to the inhomogeneous conducting effect of the torso we apply statistical tools (first and second moments) for interpreting ARI on the body surface. Variance analysis (Tukey's and Scheffe's test) was accomplished using data of 418 patients. The pathological groups were found to be significantly different from normal. The pair-wise classifications of normal with arrhythmia, CAD and infarcts, yielded 93.2%, 79.2% and 72.3% true negative rate, respectively, with sensitivity of 94.3% and specificity of 80.9 %.

Using the variance of ARI, we achieved the best result in separation of normal and arrhythmia groups, supporting the hypothesis that enhanced ARI variance is a risk factor for VA vulnerability.

1. Introduction

Ventricular arrhythmia (VA) leading to sudden cardiac death is still one of the leading causes of death. Experiments, based on the reentry model, proved that local disparity of the ventricular repolarization might induce this type of arrhythmia. Therefore the clinical importance of non-invasive assessment of repolarization is well established. QT interval (QTI) is the wide spread non-invasive tool for characterization of repolarization and as such an index for VA prone state. Unfortunately, recent canine and torso tank experiments, as well as model studies proved that QTI is not sensitive for local shortening in the setting of global process, and varies with activation sequence [1-3]. The uncertainty in measuring QTI means further difficulty. Our aim is to provide non-invasive method for assessing the repolarization disparity more accurately than QTI measurements are capable.

Due to the problems associated with applying QTI, activation recovery interval (ARI) has been introduced for measuring the repolarization on the epicardial surface (Figure 1). ARI is defined as the time interval from the activation time, the time of intrinsic deflection of the QRS (time of minimum dV/dT) to the recovery time, the time of maximum upstroke velocity near the peak of the T wave (time of maximum dV/dT) [4].

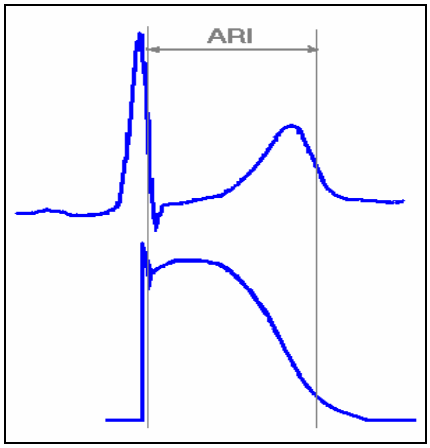

Figure 1. Activation recovery interval on a precordial lead, and in myocardial cell.

2. Data and methods

For interpreting the utility of ARI on the body surface we used data measured with the Lux type 32 leads limited lead system (Figure 2.). By means of an interpolation technique 192 leads body surface potential maps (BSPM) can be produced from the raw data [5]. The records were time normalized: 150 time instants for QRS and 150 for the ST-T segment.

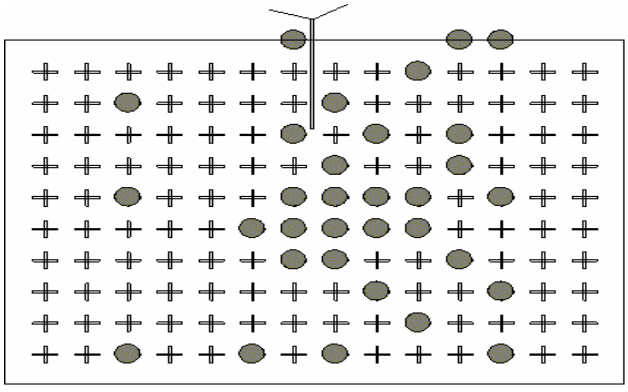

Figure 2. Arrangement of Lux 32 lead electrodes on the body surface (dots). Vertical line represents the sternum; crosses show the interpolated 192 lead electrode positions.

The ARI values of 418 subject were calculated, and the restored values were stored. Although the interpolation error is negligible this time we used the ARI parameters coming from the measured 32 leads. In consequence of the inherent nature, only one single precordial lead was used to calculate QTI.

For this comparison study we used four patient groups. These are 231 individuals under age of 40 without any known previous cardiac event (NORMAL). The other three pathological groups were patients with arrhythmic episodes (ARR: 24), patients with myocardial infraction (MI: 128, anterior, inferior and posterior locations), patients with Coronary Artery disease (CAD: 35). Altogether, among the analyzed group there were 278 male and 140 female, 252 under age of 40, and 166 above.

For each individual the mean ARI was estimated by averaging the 32 lead ARI values. Subsequently, the average for the different subgroups and the standard deviations (SD) were derived from the estimated mean values. The data of negative T wave leads were ignored.

We executed test for separation of the groups by means of variance analysis (ANOVA). Tukey's HSD and Scheffe's test were used for post-hoc comparison. These tests are used to determine the significant differences between group means in analysis of variance settings; furthermore Tukey's test is more conservative.

Subsequently, stepwise linear discriminant analysis (SLDA), both forward and backward, was used for separation. Discriminant function analysis is a useful tool to separate two or more naturally occurring groups and for the predictive classification of cases with a better chance accuracy.

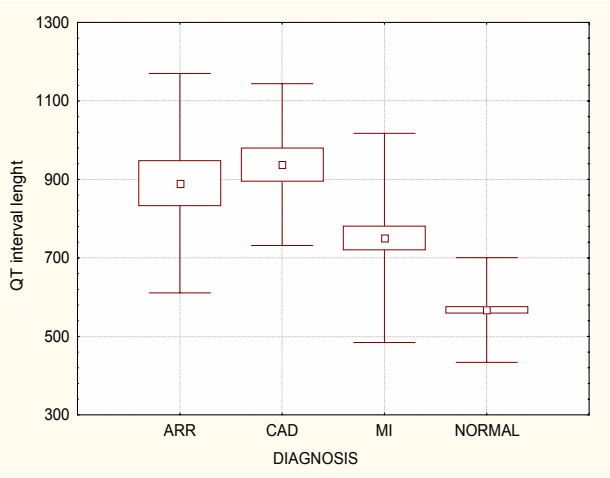

Figure 3. Box and Whisker diagram of means of QT length in subgroups. Means: NORMAL: 621 ms, MI: 751 ms, ARR: 891 ms, CAD: 938 ms. (Dots are representing the mean values, the boxes representing the error due to the limited number of sample, and the lines show the standard deviation values)

3. Results

In line with our expectation QTI has significantly different values for age (627ms under the age of 40, 817 ms above age of 40), sex (Male: 707ms, Female: 597ms). QTI is capable to separate NORMAL vs. pathologic groups ($p < 0.05$) but show large overlapping within the different pathologic groups (see Figure 3.).

Involving mean ARI and the SD of the 32 leads as new parameters we found significantly smaller SD in case of NORMAL group comparing the pathological ones (ARR: 31.7 CAD: 29.7 MI: 27.1 NORMAL: 23.5) as Figure 4 shows it. The range (i.e. the values between the largest and the smallest average ARI within a patient group) in NORMAL is the broadest, while the ARR subgroup has the lowest average. Among the pathological groups only the NORMAL vs. ARR can be separated significantly by Sheffe's test. The other pathological subgroups can be differentiate from the NORMAL significantly, applying the mean SD of ARI.

When SDs and the range of the ARI in NORMAL is analyzed we have to take into account that this group consist of subjects under the age of 40. Therefore both the range and SDs are necessarily higher in case of a more inhomogeneous population, that is the overlapping rate will be higher and the significance level lower.

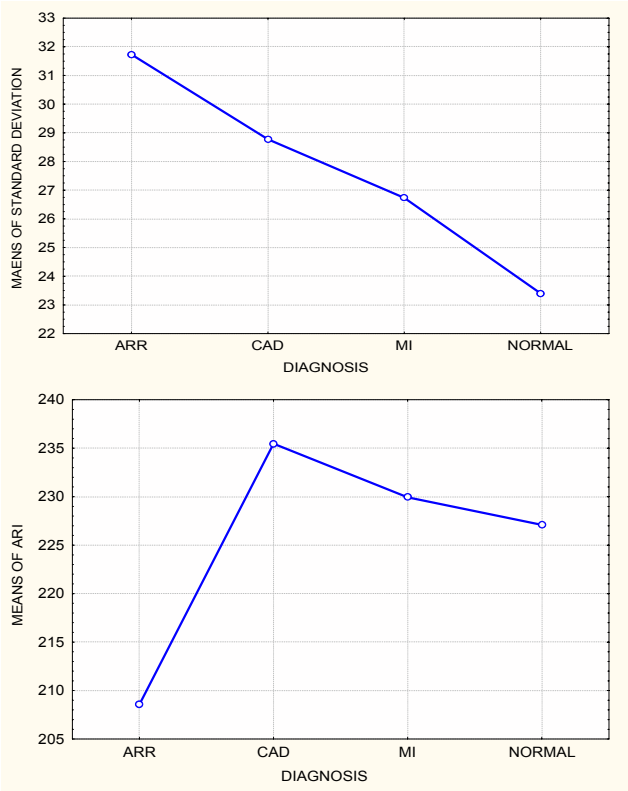

Figure 4. Mean values of standard deviation (above) and average (below) for ARI 32 leads parameters. Units are in ms.

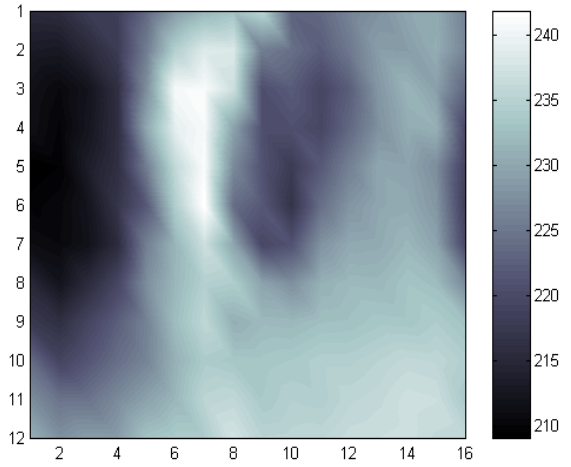

Figure 5. Distribution of ARI mean in normal subjects. Lighter areas show the higher ARI values. Units are in ms. (Electrode arrangement see Figure 2.)

The spatial distribution of the ARI values varies in case of different subgroups, however the highest mean ARI values can be measured on the upper right chest surface and the lowest on the back as it is demonstrated in Figure 5. We found the highest standard deviation in ARR subgroup close to the location of the precordial leads of standard 12 lead ECG.

For accomplishment of the SLDA we used all 32 lead ARI parameters. For the first study only ARI parameters were used, than the ARI values were complemented with the QTI value. The probabilities were set to equal since the large number of NORMAL might lead to misclassifications. Table 1a, 1b, and 1.c. illustrate the correct classification ratios where the "Percent correct" classification ratio means sensitivity (1st column) and specificity (2nd column), respectively (in case of comparison with a normal group). "Total" denotes the true negative rate.

Table 1a, 1.b, and 1.c. Bi-group classification results for ARI of 32 leads (top), for QT interval length (middle) and ARI for 32 leads supplemented with QTI (bottom). (NA: sample size is too small)

Compared subgroups (ARI 32)	Percent correct	Percent correct	Total
ARR vs. NORMAL	81.0	94.3	93.2
CAD vs. NORMAL	54.5	82.7	79.2
MI vs. NORMAL	63.8	76.8	72.3
ARR vs. MI	76.2	86.0	84.5
CAD vs. MI	60.6	71.8	69.3
ARR vs. CAD	90.9	85.3	87.5

Compared subgroups (QTI length)	Percent correct	Percent correct	Total
ARR vs. NORMAL	75.0	82.3	81.6
CAD vs. NORMAL	87.0	83.1	83.5
MI vs. NORMAL	59.3	77.1	72.4
ARR vs. MI	45.8	56.8	54.3
CAD vs. MI	73.9	56.8	60.6
ARR vs. CAD	NA.	NA.	NA.

Compared subgroups (ARI 32 + QTI)	Percent correct	Percent correct	Total
ARR vs. NORMAL	81.0	96.5	95.2
CAD vs. NORMAL	81.8	91.8	90.9
MI vs. NORMAL	76.9	83.8	82.1
ARR vs. MI	95.0	91.1	91.9
CAD vs. MI	72.7	85.1	82.3
ARR vs. CAD	95.4	64.7	76.8

Our test demonstrates that better separation results can be achieved by means of ARI comparing QTI. For example the pair-wise separation of ARR and NORMAL subgroups yielded to sensitivity (Se) of 81% and specificity (Sp) of 94.3%. While for QTI Se was only 75% and Sp was 82.3% that is more than 10% less than in the SDLA with ARI 32 leads parameter values.

The result for the 4 group SLDA for the ARR, CAD, MI, NORMAL consecutively: 76.2%, 68.2%, 50.7%, 80.8%, (total: 73.2%) while without QTI: only 71.4%, 50.0%, 49.6%, 60.9% (total: 57.3%).

4. Conclusion

The study supports the assumption that ARI is a robust parameter for assessment of repolarization. While QTI varied with sex and age, ARI was invariant to these effects. QTI was found a useful tool to indicate the occurrence of cardiac disorders (selected for this study), but the parameter is not able to distinguish the different diagnosis, especially identifying arrhythmia prone state. On contrary, ARI is more characteristically an index for repolarization disturbances but this parameter is not able to classify generally the normal and various heart problems. Using the variance and the spatial distribution of ARI originated from body surface measurements we can confirm that it provides additional information to assessment of local repolarization disparity. Altogether, we gained the best results when both ARI and QTI were used in case for identifying arrhythmia groups.

Our investigations provide evidence for the utility of ARI but limitations like small sample size of pathological groups, uncertainty in interpretation of recovery times on body surface implies the necessity of further analysis to find robust statistical parameters for a better assessment VA prone state.

Acknowledgements

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