QRS slopes for ischemia monitoring in PCI recordings

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Abstract—**In clinical practice ST elevation is used in the ECG to detect myocardial infarction. Additional information from the depolarization phase (QRS complex) can improve diagnosis and risk stratification of the patient. In this paper we present a study of the upward ($\mathcal{I}_{US}$) and downward ($\mathcal{I}_{DS}$) slopes of the QRS complex as an alternative for detecting and quantifying ischemia induced depolarization changes. From ECG recordings both in a resting state (control recordings) and during PCI-induced transmural ischemia, we develop a method for quantification of $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ that incorporates dynamic ECG normalization so as to improve sensitivity in the detection of ischemia induced changes. We show that $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ present high stability at resting state, thus providing a stable reference for ischemia characterization. In PCI recordings we show that $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ present maximum relative factors of change of 6.01 and 9.31, respectively, with respect to their own variability at control. We also show that the timing for the occurrence of significant changes in $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ varies with lead, ranging from 30 s to 2 min after initiation of coronary occlusion. We conclude that QRS slopes offer a robust tool for evaluating depolarization changes during myocardial ischemia.**

Keywords—**PCI, depolarization, QRS slopes, ischemia.**

I. Introduction

Prolonged percutaneous coronary intervention (PCI) provides an excellent human model to investigate the electrophysiological changes during the initial minutes of transmural ischemia [1], [2]. Several studies have reported potentially reversible changes in the depolarization phase in addition to ST-T changes during acute myocardial infarction in both animals and humans. These include changes in QRS amplitudes [3], QRS duration [4] and "distorsion of the end of the QRS complex" [5] in the standard electrocardiogram (ECG). The latter, in addition to relating to more severe ischemia, also correlates to worse clinical outcome in a large cohort. Changes in high frequency QRS components of the high-resolution signal-averaged ECG have been reported as well [1]. These methods have, however, not been implemented clinically. Among various limitations, one is the difficulty of correctly delineating the end of the QRS complex with simultaneous pronounced ST elevation. In a recent study, Pueyo et al. proposed a more reliable method for characterizing changes in the QRS complex during ischemia, considering both amplitude and duration changes by determining the upslope and downslope of the QRS complex during PCI [6]. In that work, the variability of the QRS slopes in a control recording was used as a reference for quantification of the ischemia induced changes. However, the stability of this reference was not further explored by means of the normal or intra-individual variation within or between different recordings, nor was an analysis performed to properly characterize factors that affect the measurement of the QRS slopes.

The objectives of the present study are to: 1) Evaluate the normal variation of the QRS slopes at resting state (control recordings) in a larger population, with the purpose of determining reliable limits of significant QRS slope changes due to an ischemic pathophysiological process. 2) Test the performance of this improved method in tracking QRS slope changes along the dynamic ECG recordings during PCI-induced ischemia. 3) Determine the timing of significant changes during PCI.

II. Materials and Methods

A. Data

The total study population consists of 151 patients, 73 of whom were admitted to the Department of Clinical Physiology at Lund University Hospital, Sweden for exercise testing (STRESS dataset). The other 78 patients were admitted to the Charleston Area Medical Center in WV, USA for elective PCI (STAFF III dataset) [1], [3]. Only control recordings at rest were used in the STRESS population, whereas both control recordings and PCI recordings were used in the STAFF III subset of patients (see below).

All ECGs were recorded using the same equipment by Siemens-Elema AB (Solna, Sweden). Nine standard leads (V1-V6, I, II, and III) were recorded and digitized at a sampling rate of 1 kHz with amplitude resolution of 0.6 μV. The augmented leads aVR, aVL, and aVF were calculated from the limb leads to generate the standard 12-lead ECG.

Control recordings: For all 151 patients, two control recordings, continuously acquired at rest for 5 minutes each in a supine position prior to any procedure (stress test/PCI), were used. The electrodes were located at the same position

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in the two recordings, either by keeping the electrode or by marking their position.

PCI recording: In the subset of the 78 patients from the STAFF III, the ECG acquired during the PCI, starting and ending at balloon inflation and deflation, respectively, was additionally used. The mean inflation duration was 4 min and 26 s. The occlusion sites of the PCI procedures were: LAD in 26 patients, RCA in 35 and LCX in 17.

B. Preprocessing

All signals involved in the study are preprocessed as follows: (1) QRS detection, (2) normal beats selection according to [7], (3) baseline drift attenuation via cubic spline interpolation, and (4) delineation using a wavelet-based technique [8].

C. QRS slopes analysis

To quantify the ischemic QRS changes we first compute, for each beat of each lead, the following two indices:

- $\mathcal{I}_{\text{US}}$: the upward slope of the QRS complex.
- $\mathcal{I}_{\text{DS}}$: the downward slope of the QRS complex.

These indices, proposed and computed as described in detail in [6], represent the slope values that result from fitting two lines to the 8-ms segments of the QRS complex centered at the points with maximum and minimum slope, respectively, within the QRS. The upward slope is measured between the Q and R waves, and the downward slope between the R and S waves.

To quantify the ability of a certain index $\mathcal{I}$ ($\mathcal{I}_{\text{US}}$ or $\mathcal{I}_{\text{DS}}$) to track ischemic changes, we introduce the parameter $\mathcal{R}_{\mathcal{I}}$ [2]. At each time t during the PCI, the parameter $\mathcal{R}_{\mathcal{I}}$ is defined as the ratio between the absolute change observed in the index $\mathcal{I}$ from oclussion start until time t, denoted by $\Delta_{\mathcal{I}}(t)$, and the normal fluctuations of $\mathcal{I}$ at rest, measured by the standard deviation (SD) $\sigma^{\mathcal{I}}$ of the index $\mathcal{I}$ during the control recording preceding the PCI.

D. Normalization procedure

The use of the parameter $\mathcal{R}_{\mathcal{I}}$, aimed at providing an estimate of the extent of ischemia induced changes in $\mathcal{I}$ that are additional to those observed at rest, heavily relies on the way normal fluctuations $\sigma^{\mathcal{I}}$ at rest are evaluated. When large physiological variations occur in the ECG signal at rest, the potential value of $\mathcal{R}_{\mathcal{I}}$ as a marker of ischemia is highly reduced because of the increase of $\sigma^{\mathcal{I}}$ at the denominator in $\mathcal{R}_{\mathcal{I}}$. This occurs when respiration or other low frequency modulation on the ECG affects the QRS complex amplitude and so the slope estimates. To compensate for this, an ECG signal normalization procedure is proposed in the present study. In brief, the normalization considers a running window of 15-ms duration centered around each processed beat $b_i(n)$, with i denoting beat index, and n beat sample. The median of the R wave amplitudes corresponding to the N beats within the window is computed: $R_{m_i} = \text{median}\{R_{i-N/2}, ..., R_{i+N/2}\}$, and the normalized beat $\hat{b}_i(n)$ is defined as $\hat{b}_i(n) = \frac{R_{m_i}}{R_i} b_i(n)$. The normalization is applied to both control and PCI recordings.

E. Intra-individual variability of QRS slopes variations

To assess the intra-individual variability of QRS slopes variations, we measure $\mathcal{I}_{\text{US}}$ and $\mathcal{I}_{\text{DS}}$ on the normalized beats of the two control recordings. The SD of $\mathcal{I}$ ($\mathcal{I}_{\text{US}}$ or $\mathcal{I}_{\text{DS}}$), denoted by $\sigma^{\mathcal{I}}_{l,k}(j)$, is computed for each patient $j = 1, ..., J$, and lead $l = 1, ..., 12$, in each of the two control recordings ($k = 1, 2$). The difference between the SDs of the two control recordings is quantified: $d^{\mathcal{I}}_l(j) = \sigma^{\mathcal{I}}_{l,1}(j) - \sigma^{\mathcal{I}}_{l,2}(j)$.

A statistical test (1-sample t-test) is applied to the difference $d^{\mathcal{I}}_l(j)$ evaluated for the whole set of patients, and each lead l and index $\mathcal{I} = \mathcal{I}_{\text{US}}$ or $\mathcal{I}_{\text{DS}}$, with the purpose of contrasting the following hypothesis:

- H_0: the intra-individual change is different from zero.
- H_1: the intra-individual change is null.

F. Inter-individual variability of QRS slopes variations

To assess the inter-individual variability of QRS slopes variations, the mean of the two SDs $\sigma^{\mathcal{I}}_{l,k}(j)$, $k = 1, 2$, is computed for each patient j, lead l, and index $\mathcal{I}$: $\sigma^{\mathcal{I}}_l(j)$ = $\frac{1}{2}\{\sigma^{\mathcal{I}}_{l,1}(j)$ + $\sigma^{\mathcal{I}}_{l,2}(j)\}$. Then the SD of $\sigma^{\mathcal{I}}_l(j)$ over patients is quantified, and denoted by $s^{\mathcal{I},\updownarrow}_l$. Additionally, the SD of the $\sigma^{\mathcal{I}}_{l,k}(j)$, $k = 1, 2$, for each patient j is also computed and denoted by $s^{\mathcal{I},\leftrightarrow}_l(j)$ = $\frac{1}{\sqrt{2}}|\sigma^{\mathcal{I}}_{l,1}(j) - \sigma^{\mathcal{I}}_{l,2}(j)|$ = $\frac{1}{\sqrt{2}}\left|d^{\mathcal{I}}_l(j)\right|$.

A statistical test (1-sample t-test) is applied to compare the intra-individual variability, $s^{\mathcal{I},\leftrightarrow}_l(j)$, $j = 1, ..., J$, with the inter-individual SD of the whole population, $s^{\mathcal{I},\updownarrow}_l$.

G. Changes in QRS slopes during ischemia

Determination of significant changes in the QRS slopes due to the induced ischemia during PCI, and identification of their timing, is performed in this study by applying a statistical test of the type described in section II-E. In this case, differences are computed between the mean, $\mathcal{I}_{ref}$, of the analyzed index $\mathcal{I}$ ($\mathcal{I}_{\text{US}}$ or $\mathcal{I}_{\text{DS}}$) during the first five seconds of the PCI recording (taken as a reference) and the current values of $\mathcal{I}$ in the PCI recording, $\mathcal{I}_{\text{PCI}}(t)$, evaluated at time instants t taken in increments of 3 s from the onset of occlusion ($t = 0$) at each lead l.

III. Results

A. Intra-individual variability of QRS slopes variations

Figure 1 presents the QRS slope values measured in the two control recordings and the PCI recording of a particular

patient of the STAFF III population. As can be observed from the comparison of the two control recordings (left and middle columns), both the upward and downward QRS slopes show high stability. More importantly, their degree of variation in the two control recordings is very similar.

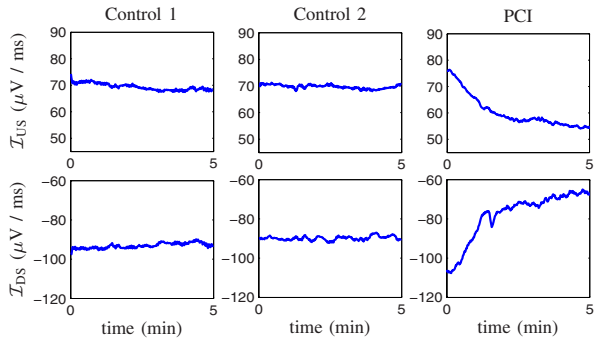

Fig. 1 QRS slopes evaluated on normalized ECGs of a patient from the STAFF III dataset. Top: $\mathcal{I}_{US}$, and bottom: $\mathcal{I}_{DS}$, in control and PCI recordings.

An example of the effect of the normalization technique described in section II-D is presented in Fig. 2, which shows sequences of $\mathcal{I}_{DS}$ values measured before and after application of the ECG normalization. It is clear from the figure that normalization cancels the low frequency oscillations, most likely generated by respiration, that affect the slope measurements through modulation of the QRS amplitude. As a consequence, the variability observed in $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ in any recording at rest becomes substantially lower after applying the normalization procedure, thus making those measurements suitable for assessing ischemia induced changes through evaluation of the relative ratio $\mathcal{R}_{\mathcal{I}}$.

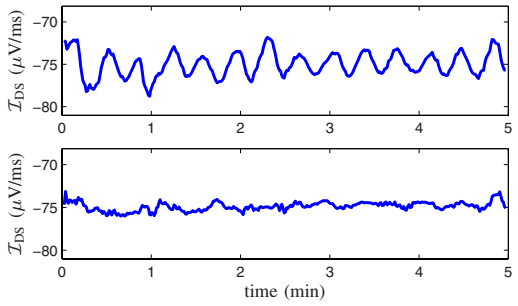

Fig. 2 $\mathcal{I}_{DS}$ values measured in a control recording of a patient from the STAFF III dataset before (top) and after (bottom) applying ECG normalization.

The high intra-individual stability of the QRS slopes variations is confirmed by the results of the statistical test described in section II-E. In all leads, except for V3, I, -aVR and II, the p-value of the test is < 0.05 and the hypothesis H_1 of the intra-individual QRS slope change being negligible is accepted. In leads V3, I, -aVR and II, despite showing a $p > 0.05$, differences between the two control recordings are very close to 0. To illustrate that, Fig. 3 presents averaged results for the differences $d_l^{\mathcal{I}}(j)$ between the SDs of $\mathcal{I}$ ($\mathcal{I}_{US}$ or $\mathcal{I}_{DS}$) in the two control recordings.

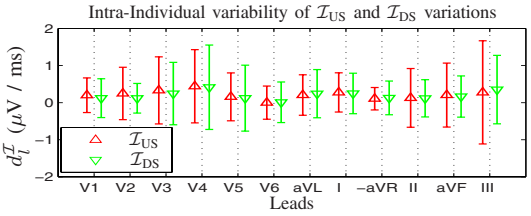

Fig. 3 Mean $\pm$ SD over patients of the difference $d_l^{\mathcal{I}}(j)$ between the SDs of $\mathcal{I}$ ($\mathcal{I}_{US}$ or $\mathcal{I}_{DS}$) in two control recordings.

B. Inter-individual variability of QRS slopes variations

The inter-individual variability of the QRS slopes variations is also investigated in the present study. A representation of how the SDs of $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$ at resting state vary within the whole population is presented in Fig. 4.

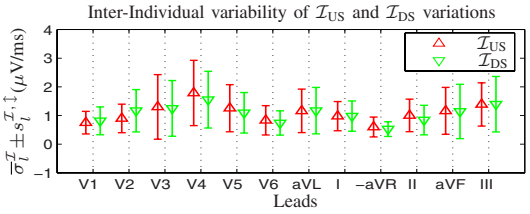

Fig. 4 Mean $\pm$ SD over patients of the variations $\sigma_l^{\mathcal{I}}(j)$ for $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$.

The statistical test explained in section II-F confirms that in all the leads, the differences between the intra-individual variations $s_l^{\mathcal{I},\leftrightarrow}(j)$ and the SD $s_l^{\mathcal{I},\updownarrow}$ of the whole dataset are highly signicant ($p < 0.05$), being always $s_l^{\mathcal{I},\updownarrow} > \overline{s}_l^{\mathcal{I},\leftrightarrow}$.

C. Dynamic changes of QRS slopes during ischemia

Relative changes of the QRS slopes measured during PCI, and averaged over patients, are found to reach maximum values in leads V3 and V5. In lead V3, the maximum factors of change of $\mathcal{I}_{DS}$ and $\mathcal{I}_{US}$, quantified by the parameter $\mathcal{R}_{\mathcal{I}}$, are found to be 9.31 and 5.11, respectively. In lead V5, the maximum factors of change are 8.06 and 6.01. This means that QRS slopes are very sensitive to the ischemia induced changes, and their values during PCI change by at least a factor of five (in leads V3 and V5) with respect to their normal variations during control.

The amount of relative change, $\mathcal{R}_{\mathcal{I}}$, averaged for all patients and leads is found to increase by 27.3% when the ECG normalization described in section II-D is applied prior to measuring $\mathcal{I}_{US}$ and $\mathcal{I}_{DS}$.

D. Timing of significant QRS slope change during PCI

Figure 5 shows examples of the time course during PCI of the p-values computed for the statistical test described

in section II-G. A p-value < 0.05 implies that significant changes in the QRS slopes occur due to the induced ischemia. In leads V4 and V5 significant changes in $\mathcal{I}_{\text{US}}$ and $\mathcal{I}_{\text{DS}}$ are found to occur between 1 and 2 min after initiation of the coronary occlusion. In lead V3 significant changes are already seen at around 30 sec. In leads V3 and V4 significant changes occur in $\mathcal{I}_{\text{DS}}$ earlier than in $\mathcal{I}_{\text{US}}$. This performance is representative of most of the other leads. Notice that, as time progresses, there is a decline in the number of patients under occlusion and, consequently, the p-values shown in Fig. 5 are computed for a different number of patients at each time instant.

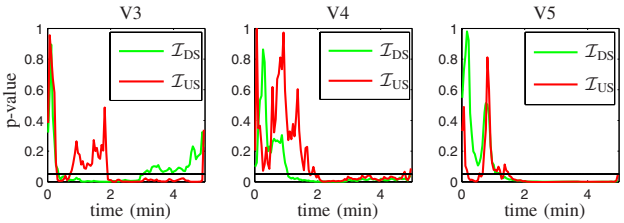

Fig. 5 Significance of changes in $\mathcal{I}_{\text{US}}$ and $\mathcal{I}_{\text{DS}}$ along time during PCI as evaluated by the p-value of the statistical test described in section II-G. The threshold for significance, $p = 0.05$, is shown in black solid line.

IV. Discussion

In this study we measure the slopes of the QRS complex and assess their performance for detection and quantification of ischemia induced changes in patients undergoing PCI. QRS slopes were first introduced in [6] as a method for characterizing ECG alterations due to myocardial ischemia. In the present work we propose an improvement for the quantification of QRS slope changes, with the purpose of providing more sensitive and reliable estimates of the occurrence of significant changes in the ECG caused by ischemia. Our proposal is to dynamically normalize the QRS signal amplitude so as to avoid low and very low frequency oscillations (due to respiration and very low frequency of uncertain origin) that directly influence variability of the estimated slopes. Results obtained after applying normalization provide measurements of relative QRS slope changes, $\mathcal{R}_{\mathcal{I}}$, during PCI that are 27.3% larger than those measured without normalization. The reason for that improvement can be found in the fact that the SD of the QRS slopes in normalized control recordings is substantially reduced, thus leading to an increase in the relative ratio $\mathcal{R}_{\mathcal{I}}$ during PCI.

Analysis of the intra-individual slope variability in different control recordings showed that the slopes present high stability for each patient, thus providing reliable reference for the evaluation of ischemic changes in the QRS complex. On the other hand, the inter-individual variability was significantly larger, thereby supporting the proposal of having a patient dependent normalization of the $\mathcal{R}_{\mathcal{I}}$ index, $\mathcal{R}_{\mathcal{I}} = \Delta_{\mathcal{I}}/\sigma^{\mathcal{I}}$, provided the reference $\sigma^{\mathcal{I}}$ used in the proposed method is taken from the same patient so as to be able to assess ischemia variations.

Significant changes in QRS slopes during PCI-induced ischemia are found to occur around 30 s after initiation of the artery occlusion in some of the analyzed leads and up to 2 min in other leads. The $\mathcal{I}_{\text{DS}}$ index shows earlier reaction to the induced changes than $\mathcal{I}_{\text{US}}$ in most leads.

V. Conclusion

The performance of the QRS slopes as indices for assessing ischemia induced changes in ECG ventricular depolarization is investigated in this study. We show that QRS slopes and their variations at resting state present high intra-individual stability, thus being suitable for characterizing changes due to ischemia in PCI recordings. Temporal analysis during PCI shows that significant changes in QRS slopes occur between 30 s and 2 min after initiation of the coronary occlusion, depending on the analyzed lead. Changes in the downward slope usually occur earlier than in the upward slope.

VI. Acknowledgments

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