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EVALUATION OF DEPOLARIZATION CHANGES DURING ACUTE MYOCARDIAL ISCHEMIA BY ANALYSIS OF QRS SLOPES

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Running title: QRS slope changes during coronary artery occlusion

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ABSTRACT

Objective: This study evaluates depolarization changes in acute myocardial ischemia by analysis of QRS slopes.

Methods: In 38 patients undergoing elective percutaneous coronary intervention (PCI), changes in upward slope between Q and R waves (US) and downward slope between R and S waves (DS) were analyzed. In leads V1-V3 upward slope of the S-wave (TS) was additionally analyzed. Ischemia was quantified by myocardial scintigraphy. Also conventional QRS and ST measures were determined.

Results: QRS slope changes correlated significantly with ischemia (for DS: r=0.71, p<0.0001 for extent and r=0.73, p<0.0001 for severity). Best corresponding correlation for conventional ECG parameters was sum of R-wave amplitude change (r=0.63, p<0.0001; r=0.60, p<0.0001) and sum of ST-segment elevation (r=0.67, p<0.0001; r=0.73, p<0.0001). Prediction of extent and severity of ischemia increased by 12.2 and 7.1% by adding DS to ST.

Conclusions: DS correlates with ischemia and could have potential value in risk stratification in acute ischemia in addition to ST-T analysis.

Key words: QRS slope, myocardial ischemia, depolarization changes, ST-segment deviation, PCI

INTRODUCTION

Analysis of the standard 12-lead ECG is most valuable in the clinical evaluation of suspect acute myocardial infarction (AMI), both in pre-hospital and in-hospital setting. In addition to ischemia detection, the ECG recorded in the acute phase of myocardial infarction (both "snapshot" ECG as well as ECG retrieved from a monitoring system), can also add further information about prognosis and risk stratification, i.e. possibilities for improved early triage and tailoring of the acute treatment for better outcome. To achieve that, other information within the ECG signal than the conventional ST-T analysis needs to be evaluated. Myocardial ischemia in more severe stages also affects the depolarization phase. Some of these changes are considered to represent already necrotic areas (Q waves), but other, potentially reversible changes in the QRS complex also appear, although they are less well understood and are usually not considered for clinical decision making. Earlier studies on depolarization changes during ischemia due to acute coronary occlusion have considered QRS prolongation (1-5), amplitude changes of the R- and S-waves (4, 6, 7), "distortion" of the terminal part of the QRS complex (8-12) as well as changes in the high-frequency components of the QRS complex (13-15). Prolongation of the QRS complex has been described as a marker of more severe ischemia with slow conduction, both in animal studies and in humans during percutaneous coronary intervention (PCI) and AMI (1, 4-6, 16). Also in a large cohort of ST-elevation myocardial infarction (STEMI) patients, Wong et al reported an independent, positive relationship between QRS duration on admission ECG and 30-day mortality for anterior infarct location (2, 3). Prolongation of the QRS duration is,

however, difficult to determine correctly, since ST elevation commonly obscures the delineation between the end of the depolarization and beginning of the repolarization.

In the Sclarovsky-Birnbaum ischemia grading system distortion of the terminal part of the depolarization, in addition to pronounced ST elevation (grade 3 ischemia), has in several studies been found to be a sign of more severe myocardial ischemia and predict larger infarct size, lesser degree of ST-segment resolution, impaired microvascular patency and worse clinical outcome after revascularization by either thrombolysis or primary PCI (8-11). These changes have been reported to be stronger predictors of clinical outcome than ST measures alone. This ischemia grading system or any other method of assessing depolarization changes, have not, however, been implemented in clinical practice. To facilitate clinical implementation, a more robust and clinically feasible method of QRS complex analysis is needed, as well as better understanding of the pathophysiological bases of the depolarization changes.

In 2008, Pueyo et al proposed a method for evaluation of depolarization changes by analyzing the slopes of the QRS complex: upward slope between Q and R waves (US) and downward slope between R and S waves (DS) (17). During coronary artery occlusion by PCI, the QRS slopes became considerably less steep than in the control situation, in particular for the DS, as a combined result of both changes of the QRS amplitude and duration. This analysis method has now been developed further and has become more robust, showing very low intra-individual variation in a control situation (18). We have furthermore introduced calculation of the most terminal slope for leads with an S wave (TS). In the same ischemia model (during elective PCI), but in a larger study population, we showed that changes of the DS among the 12 standard ECG leads are generally more pronounced than US changes regardless of

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coronary vessel occluded, and that this measure performs equally to TS (in applicable leads V1-V3 during anterior ischemia) (18). Left anterior descending artery (LAD) occlusions showed larger changes of the slopes than did right coronary artery (RCA) and left circumflex (LCX) occlusions. In previous studies changes of the QRS slopes have not been correlated to the actual amount of ischemia, or compared to other conventional ECG indices of ischemia.

Myocardial perfusion scintigraphy (MPS) is a reliable method of detecting and quantifying myocardial ischemia induced by elective PCI (19, 20). The general objective of this study was to further evaluate QRS slope changes during ischemia induced by elective PCI of LAD, RCA and LCX, quantified by MPS. Specific aims were to test:

1. If the amount of QRS slope changes correlates to the extent and severity of ischemia as determined by MPS, and compare the correlation to that of conventional depolarization parameters (R-wave amplitude change and QRS prolongation).

2. If QRS slope changes add information to conventional ST-elevation analysis in the correlation to the extent and severity of ischemia.

3. If the slope changes hold spatial information regarding coronary occlusion site.

METHODS

Study population

A total of 38 consecutive patients (age 63±12 (33-80), 25 (66%) men) admitted to the Charleston Area Medical Center, WV, USA for prolonged elective PCI (occlusion time 4.9±0.9 (2.4-7.3) min) due to stable angina pectoris, were considered for this study.

The distribution of coronary artery occluded was: LAD 8, LCX 9 and RCA 21. The study was approved by the local Investigational Review Board and informed consent was obtained from each patient prior to enrolment. The inclusion criteria were: No evidence of an acute or recent myocardial infarction, intraventricular conduction delay with QRS duration ≥120 msec (including RBBB and LBBB), pacemaker rhythm, low voltage, atrial fibrillation/flutter, any ventricular rhythm at inclusion or during the PCI procedure and appropriate signal quality. Balloon inflation was maintained for ≥ 5 minutes whenever clinically feasible. For all 38 patients myocardial scintigraphic imaging was additionally performed during the PCI and as a control the following day to provide a means of quantifying the ischemia.

ECG Acquisition

With the patient resting in the supine position in the cath lab, a continuous 12-lead ECG recording was performed, starting prior to the PCI procedure and acquired continuously during the PCI to approximately 4 minutes after balloon deflation. The part of the recording corresponding to the period of occlusion was extracted for off-line analysis. For the limb leads Mason-Likar electrode configuration was used to minimize the noise level (21). The precordial leads V1-V6 were obtained using the standard electrode placements. The signals were digitized at a sampling rate of 1 kHz, with an amplitude resolution of 0.6 µV. If more than one balloon inflation was performed during the procedure, only the first one was considered, in order to avoid possible bias due to either ischemia-induced collateral recruitment and preconditioning within the area of a previous inflation or persistent ischemia in the myocardium.

Preprocessing and normalization

The ECG for each patient was preprocessed by QRS detection, normal beat selection, baseline drift attenuation via cubic spline interpolation and wave delineation using a wavelet-based technique, as previously described (17, 18). To reduce and compensate for low frequency noise such as respiration modulations of the depolarization phase, a normalization procedure was applied to all the ECG signals prior to the evaluation of the indices (18).

QRS slope analysis

Three QRS slopes were determined in each beat:

1. US: The upward slope of the R wave
2. DS: The downward slope of the R wave
3. TS: The upward, terminal slope of the S wave (only in leads V1-V3).

The different slopes are shown in Figure 1a. The successive steps of slope analysis are as follows (18). Initially, time locations for Q, R and S wave peaks were determined by delineation and denoted by n_Q, n_R and n_S. Beats for which no R wave peak was present were rejected from the analysis. If the delineator determined an R wave peak, but could not determine a Q- or S-wave peak, a second search was undertaken. A Q wave - and S wave peak were identified as corresponding to the lowest signal amplitude in the time window of 2 ms after QRS onset to 2 ms prior to the R wave peak, and 2 ms after R wave peak to 2 ms before the QRS offset, respectively. The time instants for the maximum absolute derivative of the slopes between the Q and R wave peaks and between the R and S wave peaks, n_U and n_D, respectively, were determined. Then a line was fitted in the least squares sense to the ECG signal, in a window of 8 ms centered around the time of each of the

maximum absolute derivatives n_U and n_D, so as to generate a slope for that particular sequence of the QRS complex. Only in leads V1-V3 with a typical S wave peak below baseline a third slope was measured by fitting a line to the ECG signal in a window centered around the maximal derivative n_T of the ECG between the S-wave peak n_S and the end of the QRS complex n_{OFF}. Leads other than V1-V3 with measurable TS in some patients have not been considered due to the low statistical value derived from the measurement. For beats where the 8-ms window centered at points n_U, n_D and n_T was not fully present inside its corresponding limits [n_Q, n_R], [n_R, n_S] and [n_S, n_{OFF}], respectively, the associated slope measurement was rejected. In those cases where the S wave disappeared during ischemia evolution in the involved leads (V1-V3), the TS slope measurement was not evaluated for the successive beats after that time instant. One example of the evolution of the US, DS and TS changes is shown in Figure 1b, as well as representative beats at the beginning and end of the PCI procedure, respectively.

Calculation of the QRS slope changes during PCI

To quantify the total amount of change of the QRS slopes due to the ischemia at the end of the PCI procedure, the change (labeled ΔUS_{PCI} and ΔDS_{PCI}) were computed for each of the 12 leads, for each patient. First the dynamic QRS slope measures for all beats involved from the onset of the occlusion (t = 0) and until the end, t = t_{PCI} were blockwise averaged in subsets of 8 beats. Then, a line was fitted over these averaged values in a least square sense. Subsequently, the change $\Delta\alpha_{PCI}$ (α = US or DS) was defined as the product of the slope ℓ of the resulting fitted line and the total duration t_{PCI} of the PCI process, and denoted by $\Delta\alpha_{PCI} = \ell \cdot t_{PCI}$(17). This fitting strategy was used to reduce the effect of possible outlier measurements on $\Delta\alpha_{PCI}$. A

graphic representation of this strategy is shown in Figure 2. Among all 12 leads the maximal positive delta of the DS deflection (positive change- DS slope getting less steep) and maximal negative change of the US deflection (negative change- US slope getting less steep) was determined for each patient. The sum of all positive delta change of the DS deflection and negative change of the US deflection was calculated as to quantify the changes.

R-wave amplitude- and QRS duration analysis

R- and S wave amplitudes were automatically measured using the PR interval as the isoelectric level. Delta changes of the R- and S-wave amplitudes (ΔRa_{PCI} and ΔSa_{PCI}) were determined in the same way as that used for the QRS slopes in each lead at the end of the PCI recording. The QRS duration was determined by taking a global measurement from the standard 12 leads. In each beat the earliest QRS onset and the latest QRS offset among the 12 leads were selected as the beginning and end, respectively, of the depolarization phase taken as the longest temporal projection for the electrical activity of the depolarization. In addition, a multilead detection rule was applied to reduce the risk of misestimation for example due to large simultaneous ST-segment deviation or noise (22). In brief, with this multilead detection rule, the earliest mark of the QRS onset and the latest mark of the QRS end, respectively, in any of the 12 leads were accepted only if they did not differ from the three closest corresponding marks in other leads by more than 6 and 10 ms, respectively, for each beat. The automatically determined QRS onset and end were also manually validated, with no disagreement about the delineations between the two methods. Finally, the delta of the QRS duration $\Delta QRSD_{PCI}$ was determined using the same methodology applied for the above indices.

ST segment analysis

ST segment measurements were made automatically in each lead at the ST-J point, using the PR interval as the isoelectric level. Absolute ST deviation ΔST_{PCI} at the end of the PCI recording relative to the ST level at rest was determined for each lead. In addition, the maximal ST elevation and sum of ST elevation (positive values for ΔST_{PCI}) among all leads at the end of the PCI recording were determined for each patient.

Acquisition of radionuclide images

Approximately 30 mCi (1100 MBq) of sestamibi was injected intravenously in each patient after confirmation of total coronary artery occlusion by the balloon. The scintigraphic imaging carried out by a single-head rotating gamma camera (Elscint, Haifa, Israel) was obtained within 3 hours after completion of the PCI procedure. The acquisitions were made with a high-resolution collimator in a 64x64 matrix, 6.9 mm pixel size, using 30 projections (25s/projection) over 180° (from 45° right anterior oblique to 45° left posterior oblique). Using filtered backprojection with a Butterworth filter transverse sections were reconstructed, without attenuation correction. Short axis sections were reconstructed for further analysis (23).

For the control study another injection of ~ 30 mCi (1110 MBq) ^{99m}Tc-sestamibi was administered and imaging was performed 2-3 hours later with the same gamma

camera and acquisition protocol as for the PCI study. All patients were clinically stable between the two examinations.

Evaluation of radionuclide images

The Cedars-Sinai and Emory quantitative analysis program (CEqual, ADAC Laboratories, Milpitas, California) (24, 25) was used for making volume-weighted bull´s eye plots from the short-axis slices. Any loss of perfusion during the PCI study compared to the control study was determined by an automatic procedure by comparing the bull´s eye plot of the 2 studies for each patient (23), and expressed as both extent and severity of the myocardial ischemia, as described earlier (14). Reduction of perfusion by 25% or more was used as the threshold for indicating significantly hypoperfused myocardium (23). This area in the bull´s eye plot was delineated as an "extent map", representing all added slices (or volume) of the left ventricular (LV) myocardium, expressed as a percentage of the LV and defining the extent of ischemia. The total pixel count difference (or local perfusion loss) between the control and occlusion study within this delineated hypoperfused area in the "extent map" was the severity and expressed as a percentage of the total pixel count in the control situation within the same area (23). The extent and severity of the ischemia were calculated for each patient. All the scintigraphic data analysis was performed at the Department of Clinical Physiology, Lund University, Sweden, blinded to the ECG data.

Statistical Methods

Results are presented as mean± one standard deviation. Due to the small number of patients in the study, nonparametric tests were used. Spearman rank correlation coefficient (r) was used for correlation analysis. Mann-Whitney U test was used for comparison between groups. Multiple linear regression analysis was used to evaluate additional value of different QRS changes to ST changes in predicting the amount of ischemia. All these variables were considered continuous. All statistical tests were two-sided and significance was defined as $p < 0.05$. The statistical analysis was performed by SPSS, version 15.0 for Windows.

RESULTS

Myocardial scintigraphy

The extent and severity of the ischemia produced by the coronary occlusion by PCI, as estimated by myocardial scintigraphy, are presented in Table 1 for all patients and subgroups based on occluded artery. Among all patients the extent varied between 0 and 65% of the left ventricle (mean 20±17%) and the severity between 26 and 63% (mean 38±8%).

QRS slopes (US, DS and TS)

In Figure 3 the mean±SD of the QRS slope changes for LAD (anterior leads) and RCA occlusions (inferior leads) are shown, respectively. The change of US and DS was statistically different in leads V2-V4 and in II, aVF and III for the two separate ischemia locations, whereas the difference between DS and TS change in the LAD group was non-significant. The amount of slope change was greater in the LAD group than in the RCA group in general. In Figure 4 the changes of DS during the

PCI are shown among all 12 leads for patients with LAD, LCX and RCA occlusions, respectively. The spatial distribution of DS change was most evident for anterior and inferior ischemia with most marked changes in leads V2 to V5 and leads II, aVF and III, respectively. In the LCX group the most pronounced changes were noted in leads V5 and aVL. Due to the present finding of TS being less or equally affected by the ischemia compared to DS, as in our previous study with a larger population (18), and the variable presence of S-waves in most leads except from V1-V3, only US and DS were considered in the following correlation analysis.

Correlation between depolarization changes and ischemia

R-wave downslope (DS) change

DS changes at the end of the PCI were found to be positive in 299 (66%) of the total analyzed leads by 14.8 ± 18.2 (0.1-124.9) µV/ms, and negative in 157 (34%) leads by 8.6 ± 11.2 (0-58.8) µV/ms. The quantitative distribution among the patients of the maximum positive DS change in any lead, sum of all positive DS change as well as sum of all DS change regardless of direction, respectively, are presented in Table 2a. Additionally the correlation between the different quantifications of DS change and the extent and severity of ischemia is shown. For all DS measures there were significant correlations to the amount of ischemia, with the highest Spearman rank correlation coefficient found for sum of positive DS change among all 12 leads (r=0.71 p<0.0001 for extent and r=0.73, p<0.0001 for severity).

R-wave upslope (US) change

At the end of the PCI the US showed a negative mean change by 7.6 ± 10.2 (0-94.2) µV/ms in 301 (66%) leads, whereas 155 leads (34%) presented a positive change by 7.8 ± 13.1 (0-94) µV/ms. In Table 2b the correlation between corresponding

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quantifications of US change and amount of ischemia are presented as well as the distribution of the different patient specific US measures. A comparison between US change and DS change with respect to correlation to ischemia is presented in Figure 5, where the DS change shows the strongest correlation.

R- wave amplitude change

The R wave amplitude at the end of the PCI decreased in 284 (62%) leads by 115.3±128.7 (0.7-851.9) µV and increased by 120.5 ± 158.8 (0.2-866.3) µV in 172 (38%) of the total analyzed leads. In Table 2c the Spearman rank correlation coefficients are presented regarding the correlation between R-wave amplitude changes (sum of all R-wave increase and decrease and sum of all R-wave changes among the leads, respectively) and the measures of ischemia. All correlations were significant, with the sum of total R-wave amplitude change among all leads showing the highest correlation coefficient (r=0.63 p<0.0001 and r=0.60 p<0.0001 for extent and severity, respectively). In the same panel also the distribution of the R-wave measures among the subjects is displayed.

QRS duration change

At the end of the PCI 24 patients (63%) showed a prolongation of the QRS duration, whereas 14 patients (37%) showed a decrease as displayed in Table 2d. For both subgroups the correlation between delta QRS duration change and the amount of ischemia was very weak and non-significant.

ST-segment analysis

The maximal ST elevation in any lead and the summed ST elevation among all 12 leads are presented in Table 3, with the largest changes in the LAD group followed

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by the LCX and RCA group, respectively. The correlation between maximal ST elevation and extent and severity of ischemia was r=0.73, p<0.0001 for both ischemia measures. The corresponding correlation for summed ST elevation was r=0.67, p<0.0001 and r=0.73, p<0.0001 for extent and severity, respectively.

Association between QRS slope and ST segment changes

The correlation between QRS slope changes (US and DS) and ST-segment change considering both maximum ST elevation and sum of ST elevation is presented in Figure 6. The correlation between DS change and max/sum ST elevation was stronger than that of US (r=0.75 and r=0.69, respectively for DS, compared to r=0.44 and r=0.61 for US), all highly significant.

Regression analysis

To evaluate if depolarization changes provide information to predict the extent and severity of the ischemia in addition to the conventional ST elevation analysis, a multiple linear regression analysis was performed. The results are displayed in Table 4, where US and DS provided the largest increase above and beyond that of the ST segment. Regarding the extent of ischemia, the portion of the dependent variable explained by the independent variables, R^2, increased by 12.9% after adding US and by 12.2% after adding DS. A combination of the two increased the prediction of extent by 14.5%. The corresponding values for the severity of ischemia were 4.0%, 7.1% and 7.1%, respectively. The additive effect of R-wave amplitude change was lower.

DISCUSSION

The main finding in our study was that changes in the downward slope of the R wave (DS) significantly correlate to both the extent and severity of ischemia. The correlation coefficient was higher than that between conventional QRS parameters and ischemia, and similar to that of ST elevation. Sum of positive DS change among all leads showed higher correlation coefficients than other QRS slope quantifications. DS change correlated to simultaneous ST elevation but also gave separate, additive predictive information about the amount of ischemia beyond that provided by conventional ST-segment changes alone.

The severity of ischemia and hence risk of fast development of irreversible myocardial necrosis due to a sudden, total coronary occlusion, depends on a number of local factors such as the presence of collaterals and ability of the myocardium to adapt to anaerobic metabolism (pre-conditioning). Fast development of new acute treatment regimens for STEMI (more aggressive anti-platelet therapy and especially invasive strategies with primary PCI) have improved clinical outcome. It has, however, also resulted in a higher number of referrals to more remotely located PCI centers as well as early, often pre-hospital ECG-based triage. Using as much information as possible from the index standard 12-lead ECG is essential for early ischemia detection, risk stratification based on ischemia severity assessment as well as prediction of outcome.

In addition to ST-T changes caused by the injury current, more severe ischemia affects the myocytes and conduction system, thus slowing down the conduction and affecting the depolarization phase of the ECG. Localized conduction delay may lead to the loss of cancellation effects from opposite electrical forces, changing the QRS-

wave amplitudes and slightly increasing the QRS duration. Depolarization changes are more challenging than ST-T changes to measure and quantify.

In this study we apply a new robust method to evaluate changes of the slopes in the QRS complex in a well defined situation of ischemia due to coronary occlusion. We have previously shown DS to be more sensitive to ischemia than the US in a larger patient population (18) using the same ischemia model. In addition, we found that the upslope of the S wave (TS) in leads V1-V3 showed equal information to the DS. Although the DS in different leads represents different timing during the depolarization phase, we here show its dynamic change as a sum of all leads to correlate to the amount of ischemia and also display lead specific, spatial information with respect to coronary occlusion site.

In the Sclarovsky-Birnbaum ischemia grading system, loss of antero-septal S-waves during anterior STEMI, and changes in the R-wave amplitude/ST-J point ratio in inferior STEMI, respectively, indicate more severe ischemia, less salvage, worse microvascular flow, failure of ST-segment resolution and worse prognosis (8, 10, 11). In a canine model of ischemia, QRS prolongation was a sign of less myocardial protection and more severe ischemia (5).

The QRS slope changes and especially changes in the downward slope of the R wave (DS) evaluated in the present study, represent variations in the R- and S-wave amplitudes, as well as changes in the total depolarization duration. The slope measurement is not affected by simultaneous ST elevation and J-point drift, making it stable to calculate. In this study there was a correlation between the ST elevation and the sum of DS change, however not high enough implying they are due to exactly the same pathogenesis, but instead suggesting DS to be influenced by reduced conduction due to the ischemia. By regression analysis we also found the DS change

to add another 12 and 7%, respectively for predicting the extent and severity of ischemia quantified by myocardial scintigraphy, although this is observed after just 5 minutes of ischemia. It could be hypothesized that longer ischemia duration would produce even more pronounced depolarization changes in addition to ST changes. Therefore it is plausible to suggest that depolarization analysis presented by DS change could add relevant information about the severity of ischemia in addition to the conventional ST-T analysis.

Limitations

The study population is small, and therefore the statistical finding must be interpreted with this in mind. This human model of about 5 minutes of controlled ischemia by PCI with myocardial scintigraphy as gold standard is unique. Nevertheless, it just represents the first few minutes of ischemia and the method should also be applied to situations with longer periods of ischemia, where even more severe grades of ischemia could be expected, possibly affecting the QRS complex more. This method is applied on continuous ECG recordings with calculations of dynamic changes, and is suitable for sequential ECGs recorded in a monitoring situation rather than a "snap-shot" ECG without known baseline values.

Conclusion

QRS slope analysis allows quantification of depolarization changes during ischemia. R-wave downslope (DS) demonstrate dynamic changes during coronary artery occlusion, that correlate to the extent and severity of the ischemia assessed by myocardial scintigraphy. Furthermore, it provides information beyond that given by conventional ST-segment analysis, suggesting its potential value in risk stratification of patients with acute coronary syndrome.

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Legends to Figures

Figure 1

a. Beat example showing the delineation marks used to evaluate the QRS slopes. n_{ON} = QRS onset; n_Q, n_R and n_S = time locations for the Q, R and S wave peaks, respectively; n_U= maximum derivative between n_Q and n_R; n_D = maximum derivative between n_R and n_S; n_T = maximum absolute derivative between n_S and n_{OFF} ; n_{OFF}= QRS offset.

b. Temporal evolution of the US, DS and TS for a particular ECG recording during the PCI procedure. Initial and final beat of the recording are additionally plotted to show how they link to the corresponding slope measurements.

US= upward slope of the R wave ; DS= downward slope of the R wave; TS= upward slope of the S wave

Figure 2. Representation of the strategy by which a line is fitted to the averaged DS values during the PCI procedure in a least square sense to reduce the effect of possible outlier measurements on the DS change computation.

DS= downward slope of the R wave

Figure 3. Mean±SD of the QRS slope changes for LAD (leads V1-V6) and RCA occlusions (leads II, aVF and III). TS changes are shown only for leads V1-V3 in the LAD group.

US= upward slope of the R wave ; DS= downward slope of the R wave; TS= upward slope of the S wave

Figure 4. Spatial distribution of DS changes among the 12 leads for the LAD, LCX and RCA subgroups, respectively.

DS= downward slope of the R wave.

Figure 5. Correlation between QRS slope changes (US and DS) and amount of ischemia (extent and severity). DS- dashed line.

US= upward slope of the R wave ; DS= downward slope of the R wave; LV= left ventricle.

**Figure 6.** Correlation between QRS slope changes (US and DS) and ST elevation. DS- dashed line.
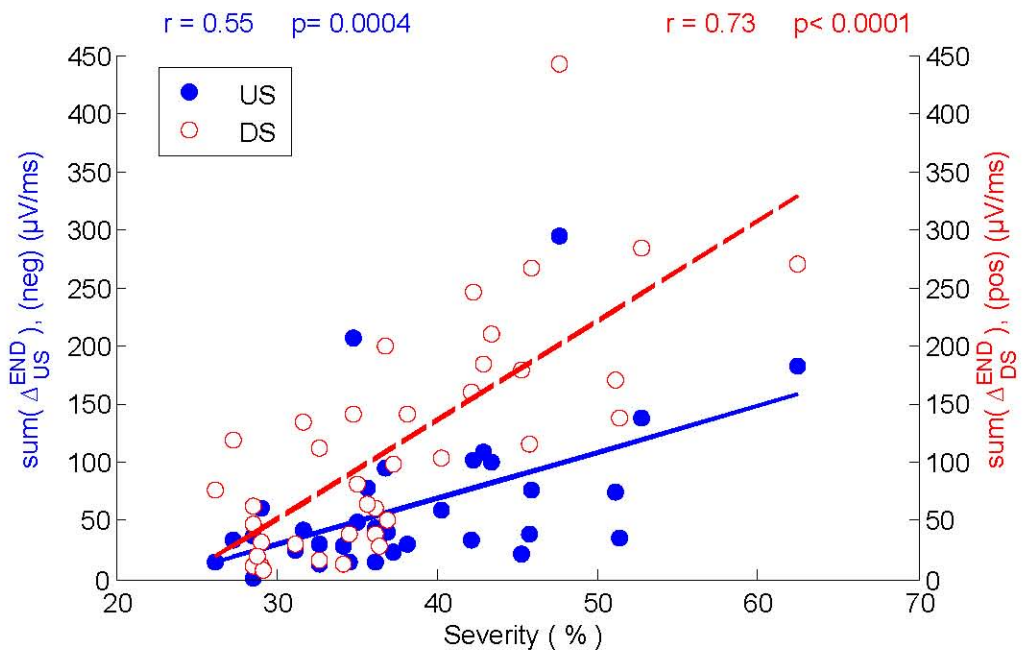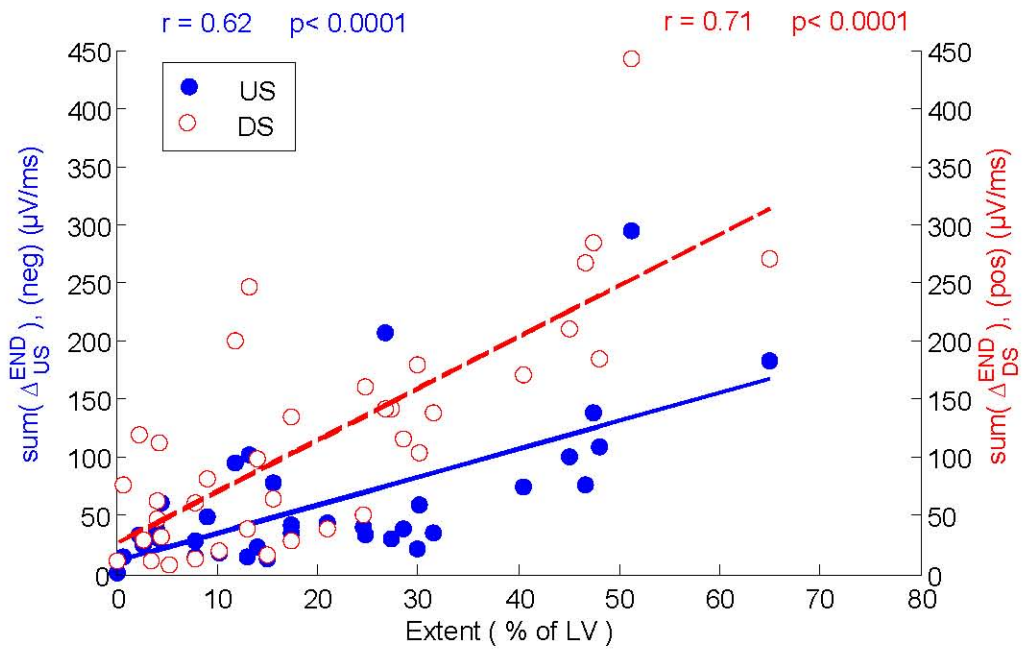
US= upward slope of the R wave; DS= downward slope of the R wave; sum US (neg)= sum of negative US change in all leads at the end of PCI; sum DS (pos)= sum of positive DS change in all leads at the end of PCI; sum ST el = sum of ST elevation in all leads at the end of PCI; max ST el= maximal ST elevation in any lead at the end of PCI .

a)

b)

ℓ : slope of the fitted line

$\Delta DS_{PCI} = \ell \cdot t_{PCI}$
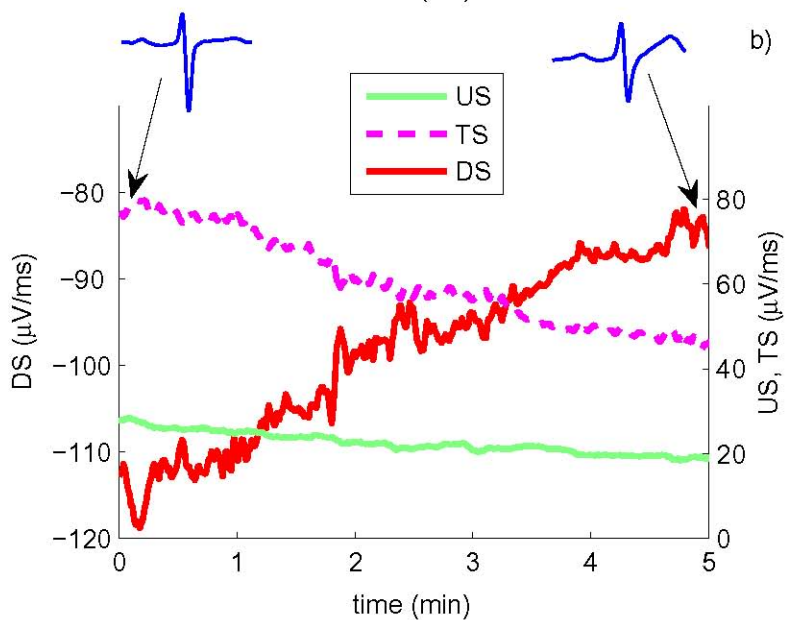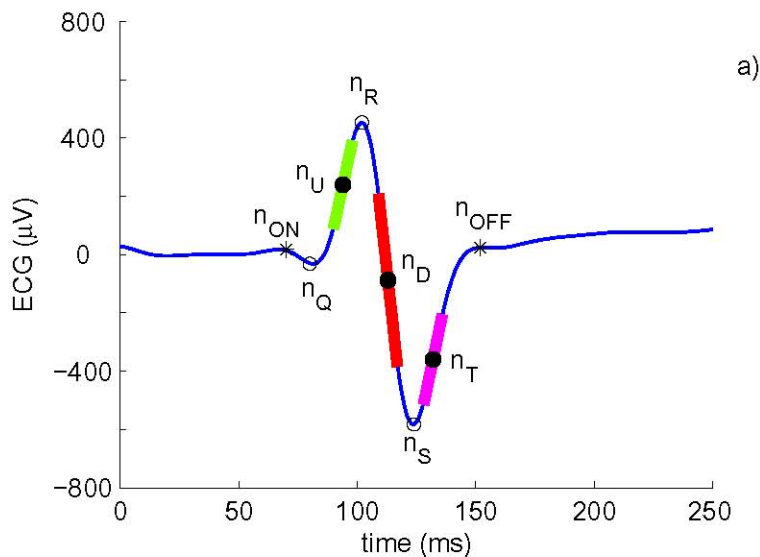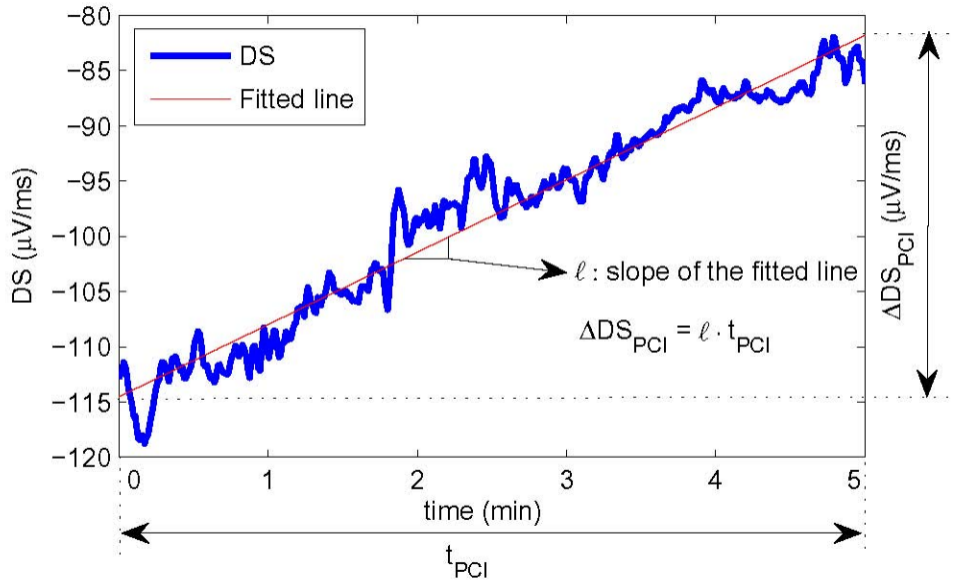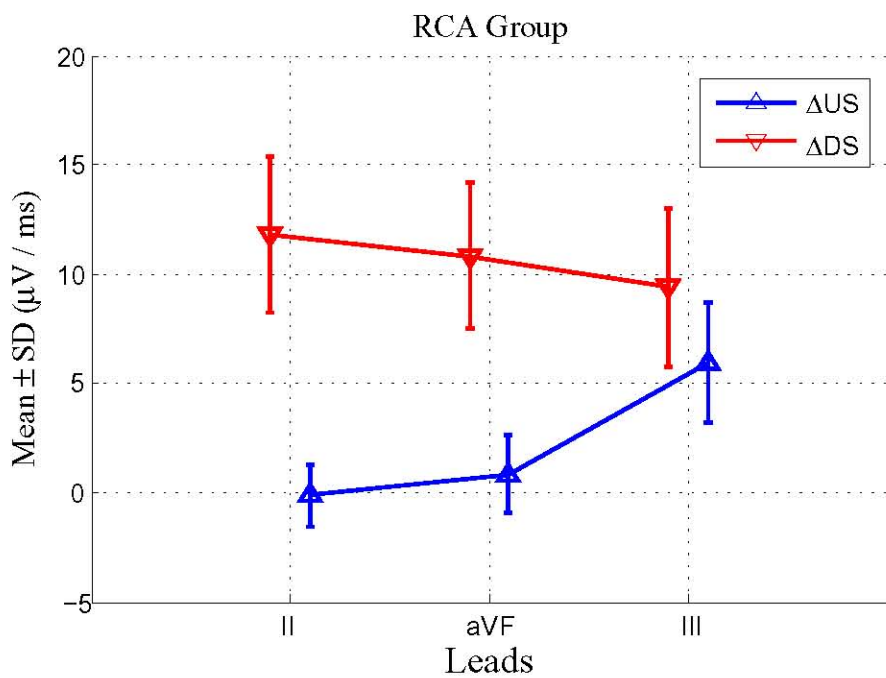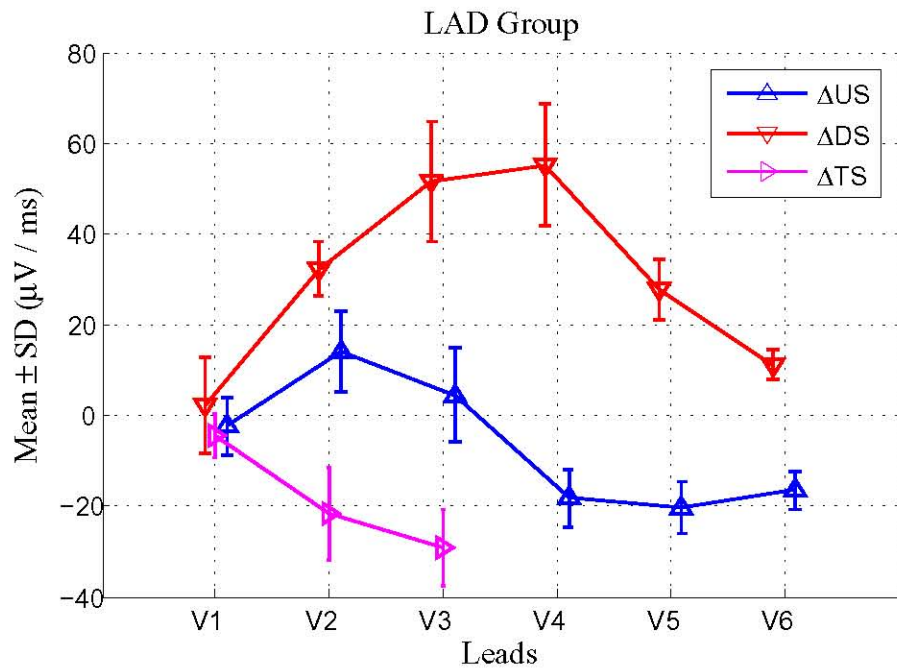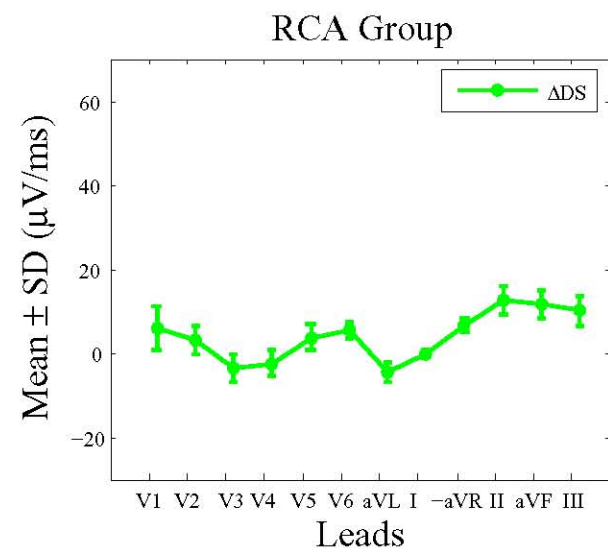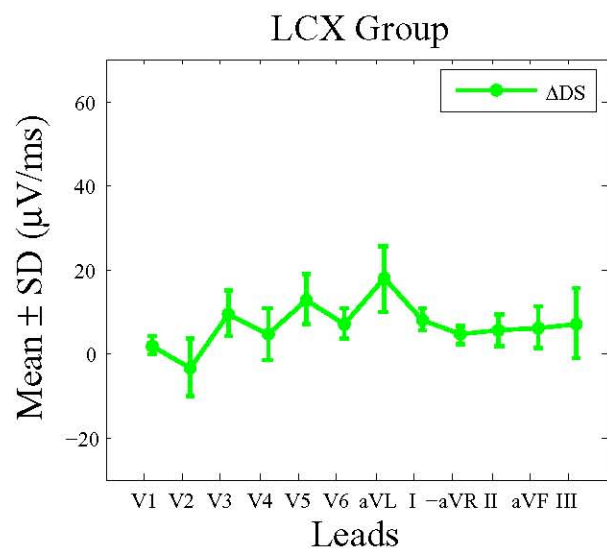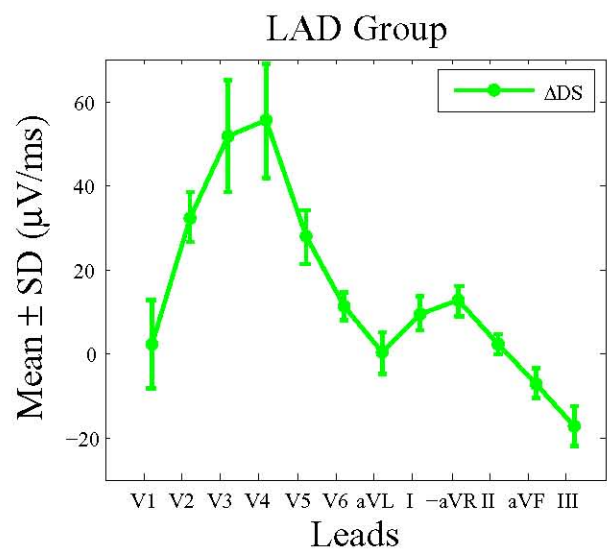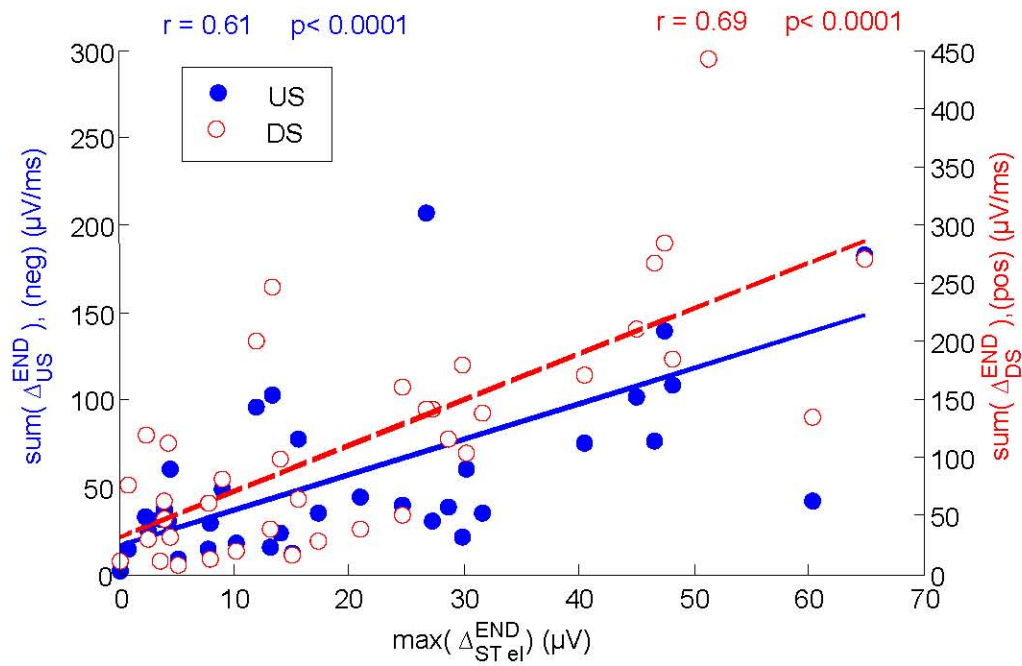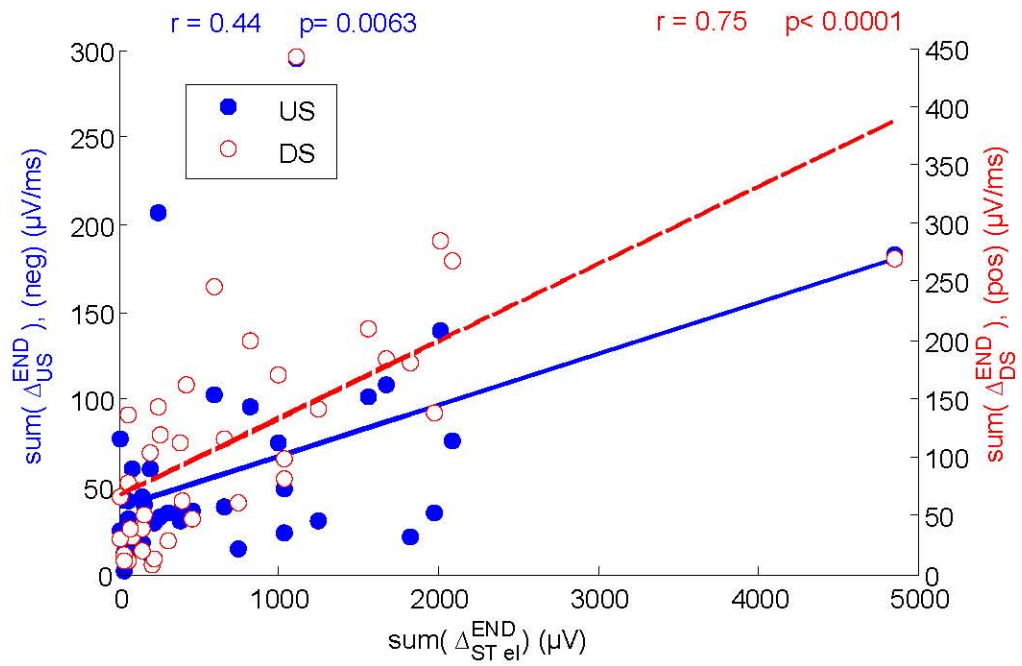
Table 1. Myocardial ischemia during PCI expressed as extent and severity in the total study population and subgroups based on coronary artery occluded. LV = left ventricle

Coronary artery occluded	Extent (% of LV) Mean±SD (range)	Severity (%) Mean±SD (range)
Total (n=38)	20±17 (0-65)	38±8 (26-63)
LAD (n=8)	43±15 (15-65)	47±9 (33-63)
LCX (n=9)	19±14 (4-45)	35±5 (29-43)
RCA (n=21)	12±10 (0.1-32)	35±7 (26-51)

Table 2. Quantitative distribution of the depolarization changes A.) DS change, B.) US change, C.) R wave amplitude change and D.) QRS duration change, as well as their correlation to ischemia (Spearman rank correlation). DS= downward slope of the R wave; US= upward slope of the R wave; Ra= R wave amplitude; LV = left ventricle

QRS parameter	Mean±SD (range)	Extent (% of LV) (r p)		Severity (%) (r p)	
A.) ΔDS (μV/ms)					
Max pos DS change	35±28 (3-125)	0.60	<0.0001	0.58	0.0001
Sum pos DS change	116±97 (8-125)	0.71	<0.0001	0.73	<0.0001
Sum tot DS change	154±114 (17-552)	0.62	<0.0001	0.62	<0.0001
B.) ΔUS (μV/ms)					
Max neg US change	15±13 (0.9-54)	0.50	0.0015	0.47	0.0032
Sum neg US change	60±60 (1-295)	0.62	<0.0001	0.55	0.0004
Sum total US change	92±74 (16-319)	0.39	0.0155	0.33	0.0390
C.) ΔR-wave (μV)					
Sum Ra increase	701±862 (39-3291)	0.41	0.0110	0.46	0.0040
Sum Ra decrease	871±811 (79-3668)	0.52	0.0010	0.45	0.0040
Sum tot Ra change	1574±1377 (190-6291)	0.63	<0.0001	0.60	<0.0001
D.) ΔQRS (ms)					
QRS widening (n=24)	8.4±6.6 (0-23)	0.17	NS	0.30	NS
QRS narrowing (n=14)	4.0±5.0 (0.3-17.1)	0.39	NS	0.28	NS

Table 3. Delta changes of ST-J from t=0 to the end of the PCI expressed as the maximum ST elevation in any of the 12 leads and the sum of ST-elevation among all leads (μV).

ECG parameter	LAD	RCA	LCX
Max ST elevation (μV)	567$\pm$ 459(25-1384)	150$\pm$ 133(0-486)	214$\pm$ 239(18-727)
Sum ST elevation (μV)	1622 $\pm$1514(36-4858)	520$\pm$ 561(0-1979)	552$\pm$ 540(52-1557)

Table 4. Multiple regression analysis. Prediction of extent and severity of ischemia by adding Δ of QRS slope (US and/or DS in μV/ms) or ΔR wave amplitude changes (μV) to Δ sum of ST elevation (mV).
US= upward slope of the R wave; DS= downward slope of the R wave; Ra= R wave amplitude; Ra sum neg/pos= Sum of the decrease/increase of Ra among all leads; Ra sum tot = Sum of all changes in Ra among all leads; LV= left ventricle; arrow, increase of the explanation of the dependent variable by the added independent variable/s

Predictor variables	Dependent variable					
	Extent of ischemia (% of LV)			Severity of ischemia (% of LV)		
	R^2	p		R^2	p	
ST	0.593	<0.0001		0.665	<0.0001	
ST, US	0.722	<0.0001	↑ 12.9 %	0.705	<0.0001	↑ 4.0 %
ST, DS	0.715	<0.0001	↑ 12.2 %	0.736	<0.0001	↑ 7.1 %
ST, DS, US	0.738	<0.0001	↑ 14.5 %	0.736	<0.0001	↑ 7.1 %
ST, Ra sum neg	0.688	<0.0001	↑ 9.5 %	0.693	<0.0001	↑ 2.8 %
ST, Ra sum pos	0.593	<0.0001	↑ 0.0 %	0.669	<0.0001	↑ 0.4 %
ST, Ra sum tot	0.644	<0.0001	↑ 5.1 %	0.673	<0.0001	↑ 0.8 %