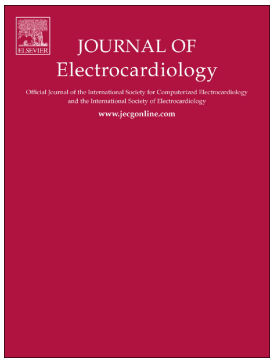

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Accuracy of Intracoronary ECG Parameters for Myocardial Ischemia Detection

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Abstract

Introduction The electrocardiogram (ECG) is a valuable diagnostic tool for the diagnosis of myocardial ischemia during acute coronary syndrome. Aside from the commonly used ST-segment shift indicative of ischemia, several other ECG parameters are pathophysiologically reasonable. Thus, the goal of this study was to assess the accuracy of different ischemia parameters as obtained by the highly susceptible intracoronary ECG (icECG).

Method This was a retrospective observational study in 100 patients with chronic coronary syndrome. From each patient, a non-ischemic as well as ischemic icECG at the end of a one-minute proximal coronary balloon occlusion was available and analysed twice by three different physicians, as well as once together for consensual results. The evaluated parameters were icECG ST-segment shift (mV), ST-integral (mV*sec), T-wave-integral (mV*sec), T-peak (mV), T-peak-to-end time (TPE, msec) and QTc-time (msec).

Results All six icECG parameters showed significant differences between the non-ischemic and the ischemic recording. Using the icECG recording during coronary patency or occlusion as criterion for absent or present myocardial ischemia, ROC-analysis of icECG ST-segment shift showed an area under the curve (AUC) of 0.963±0.029 (p<0.0001). AUC for ST-integral was 0.899±0.044 (p<0.0001), for T-wave integral 0.791±0.059 (p<0.0001), for T-peak 0.811±0.057 (p<0.0001), for TPE 0.667±0.068 (p<0.0001), and for QTc-time 0.770±0.061 (p<0.0001). The best cut-off point for the detection of ischemia by icECG ST-segment shift was 0.365mV (sensitivity 90%, specificity 95%).

Conclusions When tested in a setting with artificially induced absolute myocardial ischemia, icECG ST-segment shift at a threshold of 0.365mV most accurately distinguishes between absent and present ischemia.

Keywords: Intracoronary electrocardiogram, myocardial ischemia, ST-segment shift, ST-integral, T-wave-integral, T-peak, T-peak-to-end time, QTc-time

Introduction

The electrocardiogram (ECG) is a valuable diagnostic tool and essential in the diagnosis of various cardiac pathologies, in particular acute myocardial ischemia. The presence or absence of ECG ST-segment elevation determines subsequent therapeutic management[1].

Historically, acute myocardial ischemia has been thought to cause sequential and stepwise development of ECG-alteration, starting with a tall and upright T-wave, followed by ST-segment elevation and finally QRS-complex alteration. However, intracoronary ECG (icECG) during invasive coronary angiography with its increased susceptibility to ischemia as compared to the standard 12-lead surface ECG[2, 3] has provided evidence for a continuous transition among these steps[4], the fact of which is reasonable as myocardial ischemia affects all energy dependent cellular processes over the entire cardiac cycle involving de- and repolarization alike. Hence, ischemia can be detected and quantified by various ECG parameters. Nevertheless, assessment of the ST-segment shift has dominated in clinical practice so far. ECG ST-segment shift is based on the reduced resting potential of the ischemic myocardial cells, caused by a pathologic ion current across the “injured” cellular membrane with subsequent distortion of the normally isoelectric ST-segment[5]. Of note, not only the shift, i.e., the amplitude of the distortion but also the temporal area of the repolarization abnormality, i.e., ST-segment integral, can serve as a measure of ischemia.

Simultaneously, inadequate energy supply during ischemia causes opening of adenosine triphosphate-potassium channels[6], thus, directly affecting the morphology and duration of the T-wave as electrocardiographic representation of the ventricular repolarization[5]. Accordingly, quantification of voltage (amplitude or area under the T-wave) or temporal (T-wave peak to end interval, TPE) T-wave parameters have been evaluated in various settings[7, 8]. QT interval reflecting both de- and repolarization has been shown to be affected during ischemia[6, 8-10].

So far, comprehensive and side-by-side accuracy testing of these pathophysiologically reasonable ECG parameters during controlled myocardial ischemia has been lacking. Thus,

the goal of this study using icECG was to assess the diagnostic accuracy of the described myocardial ischemia parameters.

Methods

Study design and patients

This was a retrospective observational study in 100 patients with chronic coronary syndrome undergoing coronary angiography due to chest pain and participating in clinical trials[11, 12] of our research group with determination of coronary collateral flow index (CFI), the quantitative measure of coronary collateral function during a brief, artificial coronary occlusion. A detailed description of CFI has been previously published[13]. In brief, CFI is a measure of coronary collateral blood supply obtained during a 1-minute proximal coronary artery balloon occlusion, and is defined as mean coronary occlusive pressure relative to mean aortic pressure, both subtracted by central venous pressure[14]. Hence, in the absence of sufficient collateral blood supply, coronary balloon occlusion induces maximal myocardial ischemia at the end of the occlusion. This allows the direct comparison of icECG-parameters during non-ischemic (i.e. before the occlusion) and controlled ischemic (i.e. at the end of occlusion) conditions. Study endpoints were the six icECG parameters described below. Criteria for retrospective study inclusion were previously conducted measurement of CFI with simultaneous recording of icECG, and written informed consent for further use of the patient's data. Exclusion criteria were prior Q-wave myocardial infarction in the vascular territory undergoing icECG measurement, presence of ECG bundle branch blocks, presence of non-sinus rhythm or paced rhythm as well as sufficient coronary collateral supply (defined as CFI ≥0.217[15]).

All original studies had been approved by the Ethics Committee of the Canton of Bern, Switzerland, and all patients gave written informed consent for further use of their data.

Acquisition of the intracoronary ECG

IcECG was acquired by attaching an alligator clamp to the 0.014-inch pressure monitoring angioplasty guidewire (PressureWire™ X Guidewire, Abbott, Chicago, Illinois, United States) positioned in the distal third of a major coronary artery, and connecting it to a precordial lead. The structure of this guidewire with non-conductive coating allows the generation of an icECG-lead between the Wilson Central Terminal and the conductive pressure sensor of the guidewire located near the tip without the need for additional isolation. IcECG recording was performed at a sampling frequency of 2'000 Hz, and with standard system filtering (corresponding to a bandpassfilter 0.05-100Hz). Of note, the same angioplasty guidewire served as guidance for the balloon catheter used for proximal coronary balloon occlusion.

In a subsequent step, 12 to 15 consecutive cardiac cycles were manually chosen, signal averaged, and, according to the time of recording, labelled as "non-ischemic" or "ischemic", thus, leading to 100 non-ischemic icECGs and 100 ischemic icECGs.

Assessment of the ECG parameters

Quantitative processing of icECG parameters was performed with customized software (written in Matlab, R2017b), presenting each icECG without information on the ischemic state. All icECGs were analysed twice by three different physicians (MRB, PZ and AP) as well as once together for a consensual result. Calculation of the different icECG-parameters was based on the following cornerstones (figure 1):

- Isoelectric line (figure 1, solid red line, manually determined): The reference line for the determination of any shifts. PQ-junction, which is the end of the PR segment, was used in the absence of a relevant atrial repolarization signal (occasionally visible in the icECG) as recommended[16]. In case of unstable PR-segment, TP-segment served as reference.
- Q-point (figure 1, solid black line, manually determined): Start of the QRS-complex
- Junction(J)-point (figure 1, intersection between the two dashed black lines, manually determined): Transition of the QRS-complex to the ST-segment

- Start of T-wave (figure 1, dashed/dotted red line, automatically determined): Point of intersection between the height of J-point (figure 1, vertical dashed black line) and the tangent at the steepest point of T-wave upslope (figure 1, dashed green line).
- Peak of T-wave (figure 1, solid blue line, automatically determined): Automatically determined by the algorithm as maximum between the start and end of T-wave.
- End of T-wave (figure 1, dashed/dotted red line, automatically determined): Point of intersection between isoelectric line (figure 1, solid red line) and the tangent at the steepest point of T-wave downslope (figure 1, dashed green line).

Alternatively, start and end of T-wave was determined manually in case of a noisy signal disturbing tangent calculation.

Using the described cornerstones, the different parameters were defined as follows:

- ST-segment shift: Difference in mV between the isoelectric line and the ST-amplitude at the J-point. In addition, ST-segment shift was assessed 40, 60 and 80msec after the J-point.
- ST-integral: Area under the ST-segment in mV*sec defined as the time integral between the isoelectric line and the entire ST-segment from the J-point to the start of the T-wave.
- T-wave integral: Area under the T-wave in mV*sec defined as the time integral between the isoelectric line and the entire T-wave between the start and the end of the T-wave.
- T-peak: Amplitude of the T-wave in mV.
- T-peak-to-end time: Time in msec between T-peak and the end of the T-wave.
- QTc-time: Defined as QT-interval between Q-point and the end of the T-wave in msec, corrected according to Framingham[17] (QTc = QT + 0.154*(1000-RR)) as previously described[18].

Statistical analysis

The two study groups of non-ischemic and ischemic icECG were based on the time of icECG recording, i.e., before or at the end of the coronary balloon occlusion. Between-group comparison of continuous demographic variables and hemodynamic parameters was performed by a paired student's t-test.

For determining measurement variability, one way analysis of variance (ANOVA), Bland and Altman[19] analysis as well intraclass correlation coefficients (ICC)[20] were calculated. Intra-rater ICC was based on absolute-agreement, two-way mixed-effects model for all individual measurements (i.e. n=1200). Inter-rater ICC was based on an absolute-agreement, two-way random-effects model for the second performance (n=600). Linear regression analysis was performed for calculation of the regression line in the scatter plots for the illustrative presentation of intra-rater as well as inter-rater variability.

Nonparametric receiver operating characteristics (ROC) curve analysis was used for accuracy assessment of detecting myocardial ischemia by the icECG parameters. For reasons of readability, only the parameter with the best performance was presented in case of multiple possibilities (i.e., different time points after the J-point for the determination of ST-segment shift). Optimal cut-off points for each parameter were determined by the Youden-Index. Comparison of the area under the ROC curves was performed using the DeLong-Test.

Statistical significance was defined at a p-level of <0.05. Continuous variables are given as mean ± standard deviation. All analyses were performed using SPSS version 25 (IBM Statistics, Armonk, New York) or MedCalc for Windows, version 19.1 (MedCalc Software, Ostend, Belgium).

Results

Two hundred icECGs from 100 patients were included in the study. From each patient, a non-ischemic as well as an ischemic icECG were analysed. Left anterior descending (LAD) artery served twice as often as the study vessel than the other coronary arteries.

Patient characteristics

Patient characteristics are presented on table 1.

Intra-rater and inter-rater variability

One-way ANOVA factorial analysis did not show significant differences between intra-rater or inter-rater measurements (supplemental table 1). Determination of the ICC showed the lowest variability for T-peak (intra-rater ICC 0.996, inter-rater ICC 0.994), followed by T-wave integral (intra-rater ICC 0.990, inter-rater ICC 0.987), ST-segment shift (intra-rater ICC 0.987, inter-rater ICC 0.979) and ST-integral (intra-rater ICC 0.953, inter-rater ICC 0.949). The highest variability was observed with time measurements. Classified according to Koo et al.[21], extent of variability was excellent for ST-segment shift, ST-integral, T-wave-integral and T-peak, good for QTc-time and moderate for TPE. Please see table 2 for a presentation of the variability analysis, figures 2 and 3 for graphical illustration of the intra-rater respectively inter-rater variability and supplemental figures 1 and 2 for Bland and Altman plots.

Descriptive statistics

Descriptive statistics are presented on table 3 and on figure 4, grouped according to the non-ischemic vs. ischemic state. Overall, all six icECG parameters showed significant differences between the groups, while TPE was not different on a per vessel basis in the LAD, and in the right coronary artery (RCA, table 3). There was a significant gender-difference in all parameters except for QTc-time during ischemia (table 4). Of note, because of the inclusion of seventy-seven patients from a pharmacological stress study with intravenous administration of dobutamine and atropine before CFI measurement, heart rate in the absence of ischemia was significantly lower than during ischemia.

Receiver-operating characteristic curves

Using the time point of icECG recording as allocation reference for absent or present myocardial ischemia, ROC-analysis of icECG ST-segment shift showed an area under the curve (AUC) of 0.963±0.029 (p<0.0001). There was no statistically significant difference between the assessment of the ST-segment shift at vs after the J-point (p = 0.951, p = 0.578, p = 0.226 for 40, 60 and 80ms after the J-point respectively). AUC for ST-integral was 0.899±0.044 (p<0.0001), for T-wave integral 0.791±0.059 (p<0.0001), for T-peak amplitude 0.811±0.057 (p<0.0001), for TPE 0.667±0.068 (p<0.0001), and for QTc-time 0.770±0.061 (p<0.0001, figure 5).

DeLong-Test of the ROC-curves showed a significant difference of AUC for ST-segment shift in comparison to all other parameters (p≤0.0001), as well as a significant difference for ST-integral as compared to the remaining parameters (p≤0.0009). T-wave integral and T-peak showed a significant difference between each other (p=0.029) as well as vs TPE (p≤0.0008 and p≤0.0005, respectively), but not vs QTc-time (p=0.641, respectively p=0.352). There was no significant difference between the AUCs of the time measurements (p=0.076).

Regarding the optimum cut-off of the parameters for ischemia detection, a ST-segment shift of 0.365mV distinguished best between non-ischemic and ischemic ECG, sensitivity 90%, specificity 95%. The best cut-off point for ST-integral was 0.061mV*sec (sensitivity 77%, specificity 88%), for T-integral 0.242mV*sec (sensitivity 53%, specificity 91%), for T-peak 1.834mV (sensitivity 62%, specificity 87%), for TPE 60msec (sensitivity 76%, specificity 57%) and for QTc-time 396msec (sensitivity 84%, specificity 63%). Of note, all parameters but QTc-time increased during ischemia. Thus, the optimum cut-off point for QTc-time is inverse (i.e., ischemia below 396msec).

Discussion

When tested in an experimental setting with systematically induced, complete coronary balloon occlusion, and thus, absolute myocardial ischemia, non-ischemic and ischemic icECG is distinguishable most accurately by icECG ST-segment shift at an ischemia threshold of 0.365mV. Conversely, icECG time measurements are significantly less accurate for ischemia detection.

IcECG ST-segment shift

One hundred years ago, ST-segment shift as an ECG pattern during acute myocardial infarction was first described by Harold Pardee[22]. Since then, ECG ST-segment shift assessment in suspected acute coronary syndrome has become crucial for the subsequent management, and the extent of ST-segment shift (number of leads, amplitude of the shift) reflects the size of myocardial ischemia, and as such, cardiovascular outcome[23]. However as stated by Menown et al.[24], "the definition of significant ST-elevation varies considerably with respect to both the required minimum height of ST-elevation, and the number of leads with ST-elevation". In the same study, myocardial ischemia has been defined as an ECG ST-segment shift of >0.1mV in inferior/lateral leads, or >0.2mV in anteroseptal leads[24]. ECG ST-segment shift is strongly affected by age[25], gender[26] and ethnicity[27], and is highly variable even in healthy individuals without myocardial ischemia[27, 28]. In the latter, elevated J-points reflect earlier onset of repolarization, which is an expression of variations in the ion channels across the myocardium[29]. This affects more often men than women, since testosterone is thought to be the common mechanism accounting for this phenomenon[30]. Additionally, the amplitude of ST-segment shift in the surface ECG is directly affected by lead positioning, habitus and even by the posture of the patient as stated by Birnbaum and Alam[28].

Conversely, icECG is located directly on the epicardium and thus, less affected by noise signals. Furthermore, its configuration with a pseudo-unipolar lead between Wilson Central Point and the pressure sensor ensures site specificity, which cannot be achieved by the 12-lead surface ECG. Consequently in our study, icECG ST-segment shift demonstrated a

narrow distribution around zero in the non-ischemic state, and a distinctive increase during myocardial ischemia (figure 4). Also, the present study protocol with systematically controlled for proximal balloon occlusion, identical ischemia duration, and for exclusion of patients with sufficient collateral supply provides ideal, but clinically realistic conditions for the comprehensive analysis of electrocardiographic behavior during ischemia. Hence, icECG should serve as reference for ischemia threshold determination, followed by adjustment for the 6-fold lower signal amplitude in the surface ECG (unpublished data, comparison between icECG recordings in the LAD and lead V_3 and V_6). Thus, taken into account the optimal icECG ST-segment ischemia detection threshold of 0.365mV measured at the J-point, the optimal cut-off point using the surface ECG should be around 0.06mV. Interestingly, this corresponds well with the recommendation in isolated posterior myocardial infarction (≥0.05mV in posterior chest wall leads V_7-V_9)[1], and is quite close to the abovementioned 0.1mV registered in inferior leads.

Less accurate icECG ischemia parameters

Concerning the other parameters, icECG ST-integral as alternative measure of the same pathophysiologic process as icECG ST-segment shift performed second best (figure 5). The application of this parameter as a measure of myocardial ischemia has been known for decades, and has been explored for the improvement of coronary artery disease diagnosis during exercise test[31, 32]. In addition, assessment of ST- and T-wave integral (ST-T-integral) as well as T-wave amplitude with body surface potential mapping has been shown as sensitive and specific markers of transient myocardial ischemia[32]. However, despite the use of the more sensitive icECG[2, 3], the present study could not reproduce these findings and showed substantially less accuracy of all these parameters when compared to ST-segment shift. Also, ischemia parameters were significantly less pronounced in women than in men (table 4). A possible explanation for this finding is the variable myocardial mass being 25% to 38% bigger in men than in women[33], thus, generating a larger-amplitude ischemic signal.

Concerning time measurements on icECG, they provide less accurate and less reliable results than the other parameters. Interestingly, both TPE and QTc-time haven been shown clinically useful in estimating arrhythmic risk[5], while their behavior during myocardial ischemia remains ambiguous. It has been shown, that TPE as an index for transmural dispersion of repolarization[5] (T-peak marks the end of epicardial repolarization while the end of the T-wave marks the end of repolarization for the entire myocardium[7]) decreases by 14msec after successful percutaneous treatment in patients with ST-elevation myocardial infarction[7]. This finding could be indirectly confirmed in the present study, in which a prolongation of icECG TPE of 10msec during ischemia was documented. The slight difference may be due to the shorter ischemia time in our study. IcECG TPE showed the lowest accuracy for ischemia detection in our study, and in the LAD and RCA even failed to be statistically different during ischemia as compared to the non-ischemic state (table 3).

The effect of temporary acute ischemia on the QTc-time has been widely evaluated with ambiguous results. Meier et al. measured QTc-time from surface ECG leads II, aVL and aVF in 150 patients during a one-minute coronary balloon occlusion and showed a significant increase during occlusion of the LAD and the left circumflex artery (LCX), but not in the RCA[18]. These findings are in line with other measurements of QT-interval from surface ECG during balloon angioplasty[31, 35]. On the other hand, QTc-interval during ischemia assessed by icECG quite consistently revealed a shortening[6, 36] within the range of our results. In the present study, both, QTc-time as well as uncorrected QT-time decreased significantly during ischemia.

Because of the consistent difference between icECG and surface ECG, a systematic difference responsible for the diverging findings is most likely. Possibly, the higher sensitivity of the icECG associated with more frequent recording of ischemia induced U-waves than in the surface ECG is liable for the difference[37]. Thus, considering the recommended measurement at the nadir between T- and U-wave[38], QT-time will be systematically shorter in the presence versus the absence of an U-wave. However, since the U-wave as well as the

behavior of the QT-interval in the surface ECG were not analyzed in this study, the above explanation remains untested. Consequently, further prospective studies with simultaneous recording of icECG and surface ECG would be required to elucidate the actual behavior of the QT-interval during acute ischemia.

Study limitations

The present study results were obtained in a selected population (no arrhythmia or bundle branch blocks) of the same ethnicity, and may be not generally representative. Furthermore, the low percentage of female patients did not allow a separate ROC-analysis for calculation of gender-specific ischemia threshold values of icECG ST-segment shifts.

In addition, retrospective inclusion of seventy-seven patients from a pharmacological stress study with higher heart rate at the time of ischemia directly affected the time-measurements (i.e. TPE and QTc-time) as well as time integrals. However, first, QT-interval was corrected for heart rate and second, a posthoc-analysis of the remaining twenty-three patients revealed similar results.

Clinical implication

Quantitative assessment of myocardial ischemia by icECG should be performed by measuring ST-segment shift at the J-point. An ST-segment shift of 0.365mV distinguished best between non-ischemic and transmural ischemic myocardium. Thus, cut-off values commonly used in the surface ECG (i.e. 0.1-0.2mV) are not applicable in the icECG.

Conclusion

When tested in a setting with artificially induced absolute myocardial ischemia, icECG ST-segment shift at a threshold of 0.365mV most accurately distinguishes between absent and present ischemia.

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None.

Disclosures

None.

Author statement on the contribution for the manuscript JECG-D-20-00242

MRB: conception and design, data analysis, interpretation, visualization, drafting and revising of the manuscript; PZ and AP: data analysis and interpretation, revising of the manuscript; CS: data interpretation, drafting and revising of the manuscript.

Figure 1: Assessment of the icECG parameters. Isoelectric line = solid red line; Q-point = solid black line; J-point = dashed black lines; tangents for the determination of start and end of the T-wave = dotted green lines; start and end of the T-wave = dashed/dotted red lines; T-peak = solid blue line; P- and S-peak = dotted blue lines

Figure 2: Linear regression between test and retest measurements. Solid black lines = regression lines; dashed grey lines = reference lines, i.e. y=x

Figure 3: Linear regression between the raters. The second performance of individual measurements were used for the illustration with the pairing MB-PZ, MB-AP and PZ-AP, resulting in n=600. Solid black lines = regression lines; dashed grey lines = reference lines, i.e. y=x

Figure 4: Frequency distribution of the icECG parameters grouped by the physiologic state. Dark-grey: distribution of the non-ischemic group, light-grey: distribution of the ischemic group. All values are mean±standard deviation

Figure 5: Nonparametric receiver-operating characteristic curve of the icECG parameters using the time point of icECG recording as reference. Of note, all parameters but QTc-time increased during ischemia. Thus, QTc-time is below the reference line (dashed black line)

Table 1: Patient characteristics

	Overall
Number of patients	100
Patient characteristics	
Age (years)	68±11
Female gender (%)	22
Body mass index (kg/m²)	27±4
Angina pectoris before intervention (%)	50
Duration of angina pectoris (months)	11±22
Canadian cardiovascular society class of angina pectoris	1.98±0.92
Diabetes mellitus (%)	25
Arterial hypertension (%)	68
Current smoking (%)	14
Cumulative pack years of cigarettes	42±28
Dyslipidemia (%)	76
Family history for coronary artery disease, CAD (%)	29
Prior myocardial infarction in vessel of interest	10
Medical treatment	
Aspirin (%)	84
Platelet inhibitor (%)	41
Calcium channel-blocker (%)	25
Beta-blocker (%)	49
Nitrate (%)	13
Oral anticoagulation (%)	9
Statin (%)	78

ACE inhibitor or ARB (%)	66
Diuretics (%)	31

Table 2: Intraclass correlation coefficient and Bland and Altman analysis for intra-rater and inter-rater variability

	Intraclass correlation coefficients		Bland and Altman				
	ICC coefficient	**95%CI**	**$Mean_{Diff}$**	**SE of $Mean_{Diff}$**	**95% CI for $Mean_{Diff}$**	**SD_{Diff}**	**95% limits of agreement**
ST-segment shift at J-point (mV)							
Intra-rater analysis	0.987	0.985-0.989	0.0067	0.0065	-0.006-0.019	0.1580	-0.303-0.316
Inter-rater analysis	0.978	0.971-0.983	-0.0446	0.0082	-0.061- -0.029	0.2013	-0.439-0.350
ST-segment integral (mV*sec)							
Intra-rater analysis	0.953	0.945-0.960	0.0023	0.0012	-0.001-0.004	0.0283	-0.054-0.057
Inter-rater analysis	0.949	0.936-0.960	0.0021	0.0012	-0.004-0.000	0.0291	-0.059-0.055
T-wave integral (mV*sec)							
Intra-rater analysis	0.990	0.989-0.992	-0.0006	0.0012	-0.003-0.002	0.0304	-0.060-0.059
Inter-rater analysis	0.987	0.983-0.990	0.0045	0.0014	0.002-0.007	0.0354	-0.065-0.074
T-peak (mV)							
Intra-rater analysis	0.996	0.996-0.997	0.0058	0.0065	-0.007-0.019	0.1597	-0.307-0.319
Inter-rater analysis	0.994	0.993-0.995	0.0050	0.0084	-0.011-0.022	0.2061	-0.399-0.409
T-peak to end-time (msec)							
Intra-rater analysis	0.760	0.724-0.792	-0.2290	0.6735	-1.549-1.091	16.4974	-32.56-32.11
Inter-rater analysis	0.674	0.610-0.733	-1.4881	0.7871	-3.031-0.055	19.2800	-39.28-36.30
QTc-time (msec)							
Intra-rater analysis	0.792	0.760-0.820	-0.6521	1.0199	-2.651-1.347	24.9821	-49.62-48.31
Inter-rater analysis	0.802	0.756-0.842	-4.2105	0.9516	-6.076- -2.345	23.3094	-49.90-41.48

Table 3: Study parameters

	Non-ischemic	**Ischemic**	**p-value**
Overall, n	**100**	**100**	**-**

ST-segment shift at J-point (mV)	-0.011±0.270	1.272±0.998	p<0.001

	Non-ischemic	Ischemic	
ST-segment integral (mV*sec)	0.013±0.047	0.124±0.093	p<0.001
T-wave integral (mV*sec)	0.060±0.133	0.273±0.232	p<0.001
T-peak (mV)	0.493±1.291	2.420±1.929	p<0.001
T-peak to end-time (msec)	63.64±25.79	73.95±19.86	p<0.001
Heart rate	71±13	95±25	p<0.001
QTc-time (msec)*	409.73±39.66	377.74±26.62	p<0.001
Left anterior descending artery, n	**50**	**50**	**-**
ST-segment shift at J-point (mV)	0.006±0.236	1.1[illegible]±0.692	p<0.001
ST-segment integral (mV*sec)	0.037±0.033	0.11[illegible]±0.062	p<0.001
T-wave integral (mV*sec)	0.129±0.105	[illegible].316±0.156	p<0.001
T-peak (mV)	1.074±1.004	2.802±1.117	p<0.001
T-peak to end-time (msec)	69.80±31.2[illegible]	77.22±16.59	p=0.099
Heart rate	72±14	104±22	p<0.001
QTc-time (msec)*	407.73±[illegible]5.17	371.86±19.76	p<0.001
Left circumflex artery, n	**25**	**25**	**-**
ST-segment shift at J-point (mV)	[illegible]041±0.324	2.120±1.278	p<0.001
ST-segment integral (mV*sec)	-0.001±0.056	0.205±0.117	p<0.001
T-wave integral (mV*sec)	0.053±0.128	0.367±0.314	p<0.001
T-peak (mV)	0.575±1.372	3.287±2.689	p<0.001
T-peak to end-time (msec)	55.79±11.86	71.00±18.90	p<0.001
Heart rate	69±12	92±20	p<0.001
QTc-time (msec)*	416.80±35.42	382.80±22.03	p<0.001
Right coronary artery, n	**25**	**25**	**-**
ST-segment shift at J-point (mV)	-0.099±0.244	0.630±0.542	p<0.001
ST-segment integral (mV*sec)	-0.021±0.030	0.069±0.062	p<0.001
T-wave integral (mV*sec)	-0.073±0.078	0.094±0.165	p<0.001
T-peak (mV)	-0.751±0.781	0.790±1.314	p<0.001
T-peak to end-time (msec)	59.16±20.99	70.35±25.75	p=0.065
Heart rate	70±13	83±28	p=0.030
QTc-time (msec)*	406.66±51.38	384.45±38.67	p=0.041

*QTc-time = QT-time corrected according to the Framingham method

Table 4: Study parameters according to gender

	Male	Female	p-value	Male	Female	p-value
Overall, n	**78**	**22**	**-**	**78**	**22**	**-**
ST-segment shift at J-point (mV)	-0.015±0.298	0.000±0.133	p=0.732	1.358±0.110	0.967±0.383	p=0.010
ST-segment integral (mV*sec)	0.014±0.050	0.012±0.033	p=0.901	0.135±0.101	0.086±0.037	p=0.001
T-wave integral (mV*sec)	0.057±0.141	0.068±0.103	p=0.705	0.294±0.249	0.199±0.138	p=0.022
T-peak (mV)	0.455±1.376	0.627±0.941	p=0.503	2.628±2.072	1.682±1.034	p=0.004
T-peak to end-time (msec)	63.33±26.04	64.73±25.43	p=0.824	71.56±18.77	82.41±21.70	p=0.023
Heart rate	70±13	76±14	p=0.062	94±24	102±26	p=0.178
QTc-time (msec)*	407.80±39.99	416.59±38.57	p=0.361	376.39±27.69	382.54±22.31	p=0.341

*QTc-time = QT-time corrected according to the Framingham method

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Supplemental figures

Supplemental figure 1: Bland and Altman plots for intra-rater variability. Difference = measurement 1 minus measurement 2; Solid black lines = mean difference; dashed grey lines = 95% limits of agreement. Y-axis is scaled 1,5-fold minimum respectively maximum value. Please see table 2 for the detailed Bland and Altman analysis

Supplemental figure 2: Bland and Altman plots for inter-rater variability. Difference = rater 1 minus rater 2 with the following pairing: MB-PZ, MB-AP, PZ-AP; Solid black lines = mean difference; dashed grey lines = 95% limits of agreement. Y-axis is scaled 1,5-fold minimum respectively maximum value. Please see table 2 for the detailed Bland and Altman analysis.

Supplemental table 1: ANOVA table of results for intra-rater and inter-rater variability

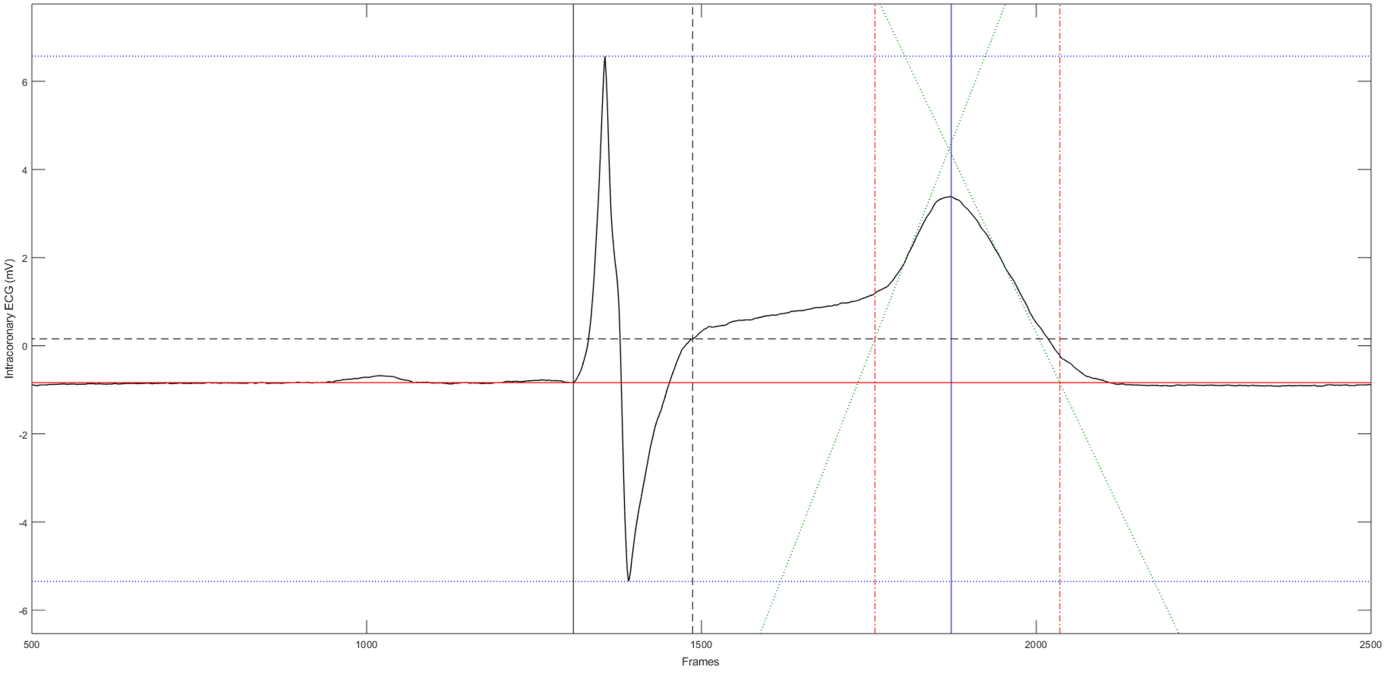
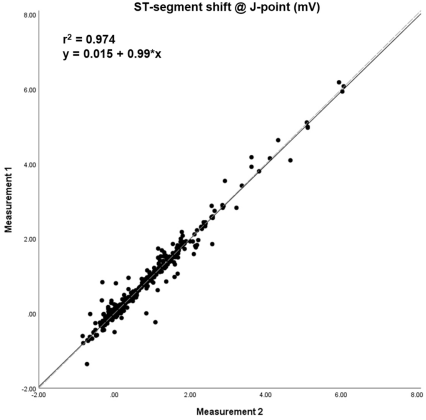
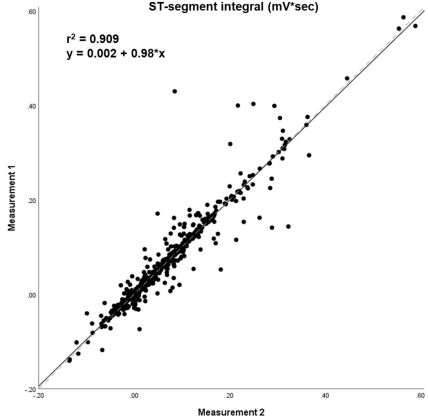
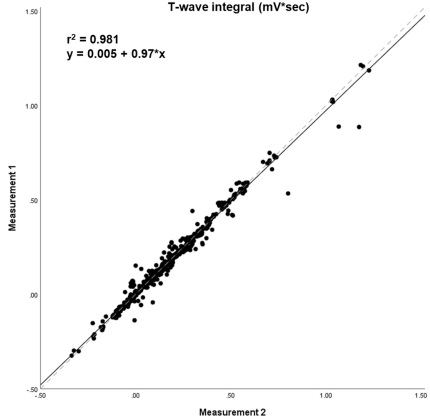
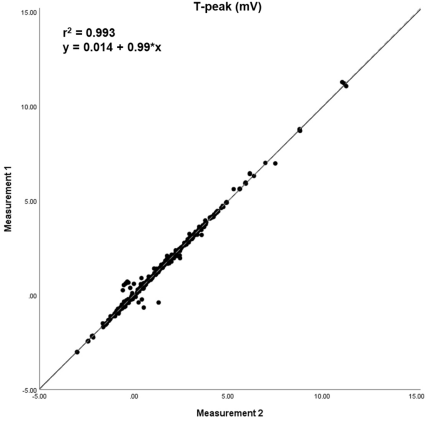

Intracoronary ECG (mV)
6
4
2
0
-2
-4
-6
500
1000
1500
2000
2500
Frames

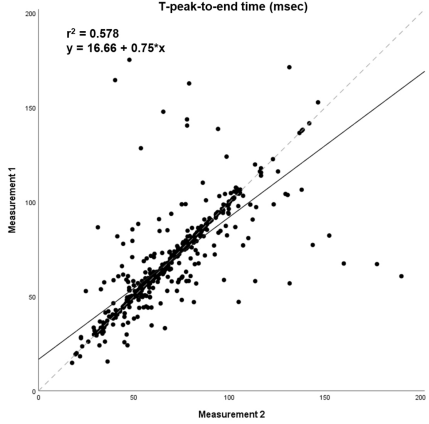
Figure 1











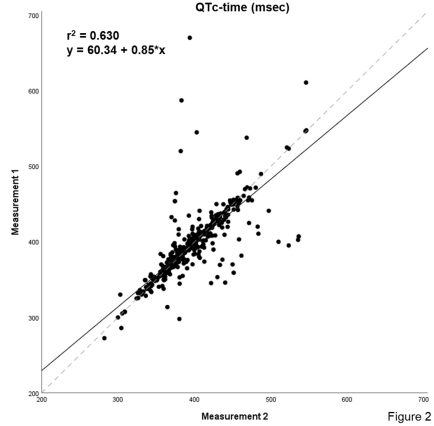
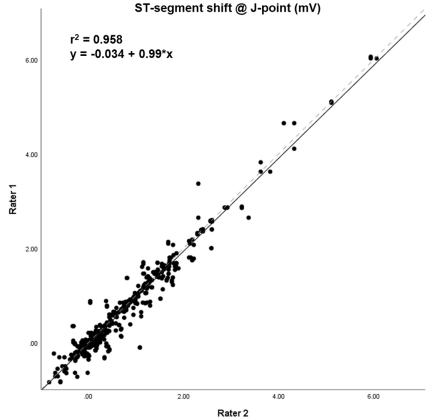
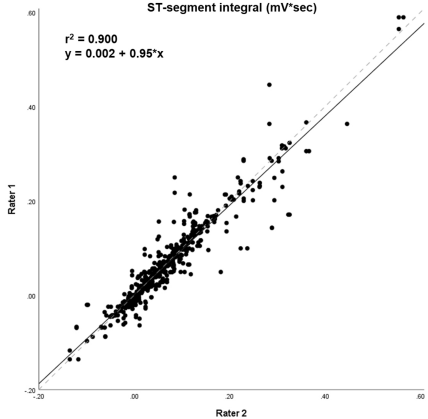
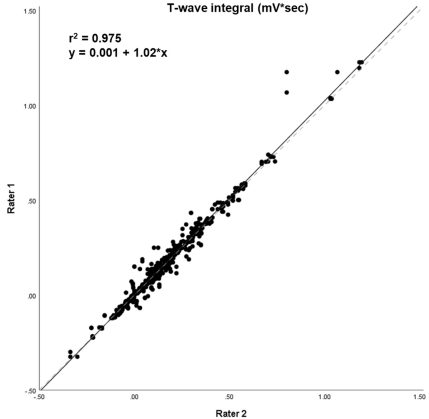


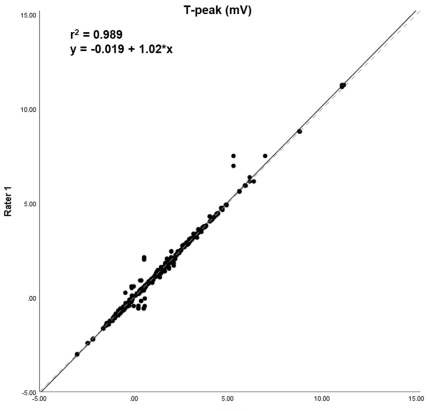
Figure 2

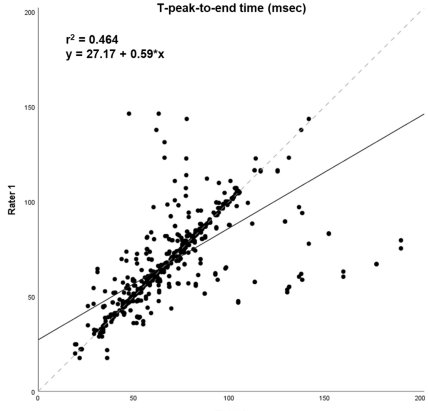
Figure 2











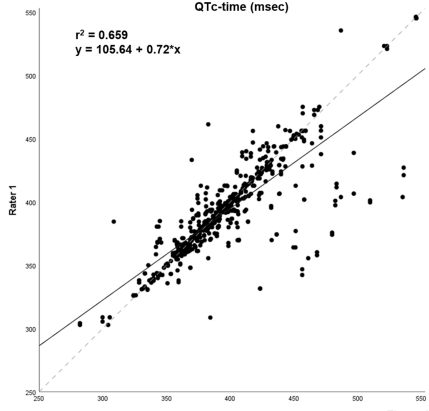
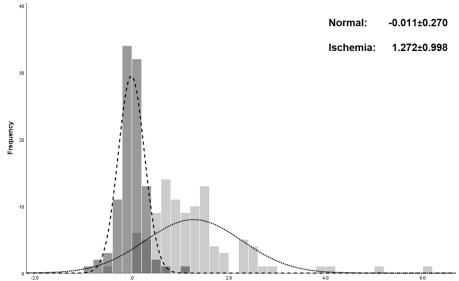
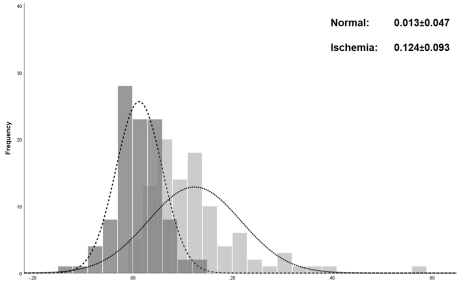
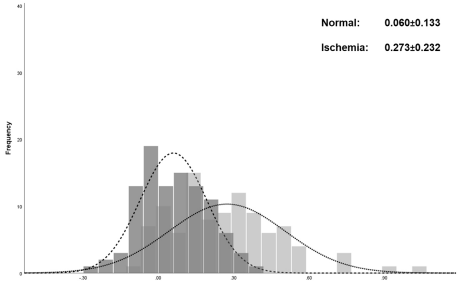


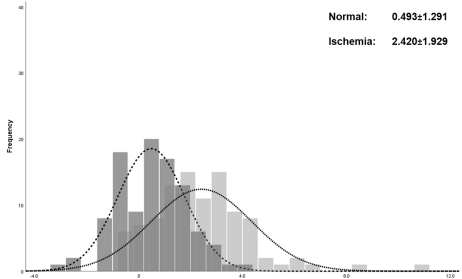
Figure 3

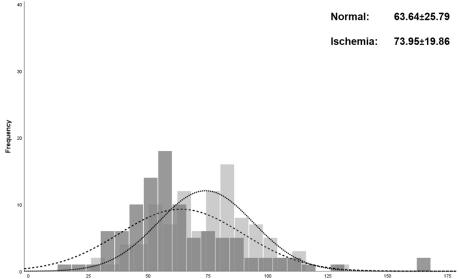
Figure 3











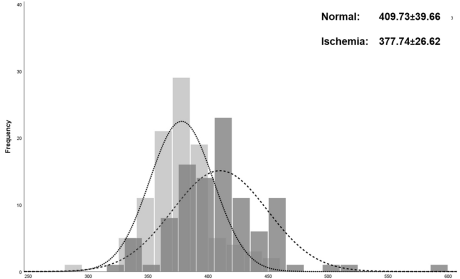


Figure 4

Figure 4

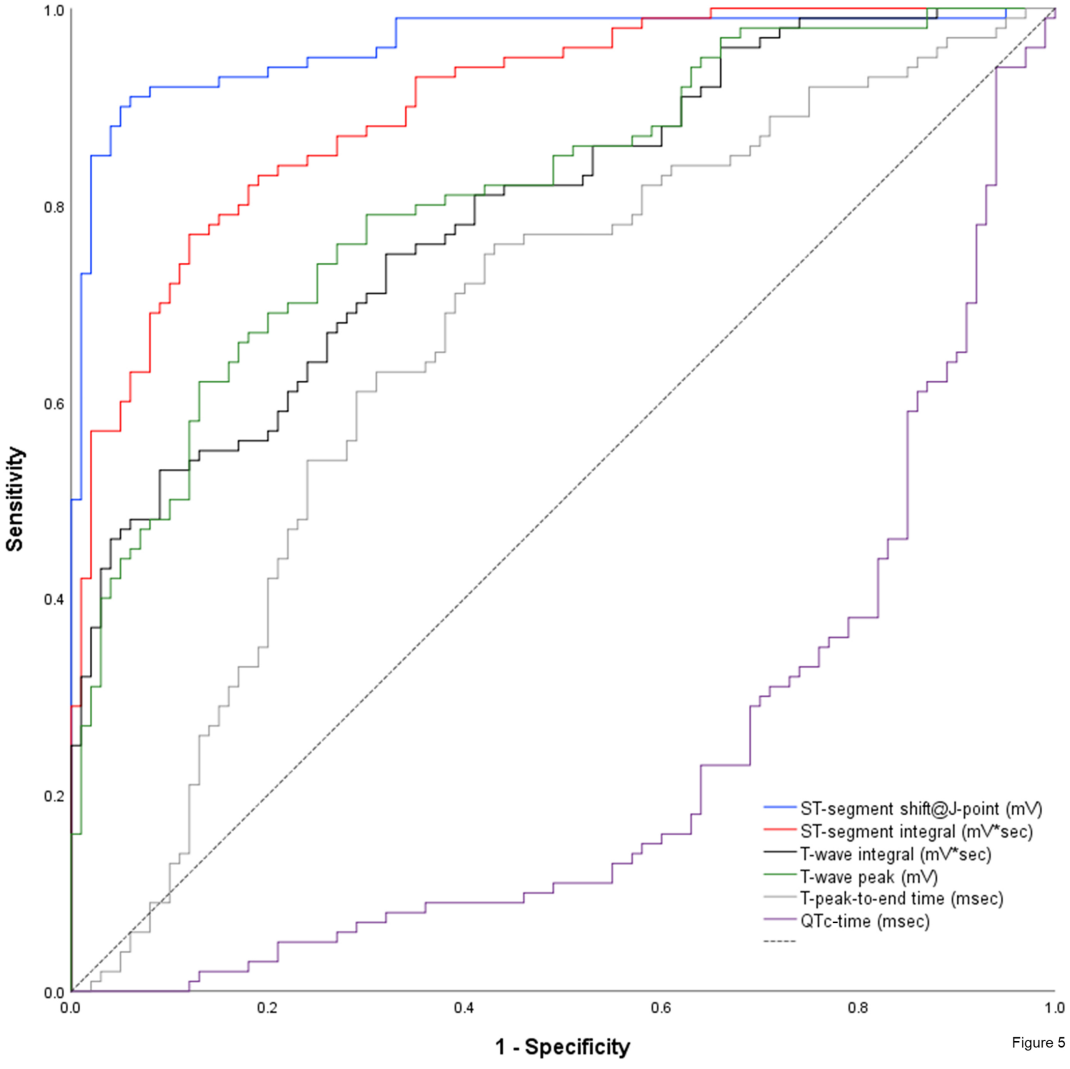


Figure 5

Figure 5