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Automatic electrocardiographic algorithm for assessing severity of ischemia in ST-segment elevation myocardial infarction

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ABSTRACT

Background: Terminal QRS distortion on the electrocardiogram (ECG) is a sign of severe ischemia in patients with STEMI and can be quantified by the Sclarovsky-Birnbaum Severity of Ischemia. Due to score complexity, it has not been applied in clinical practice. Automatic scoring of digitally recorded ECGs could facilitate clinical application. We aimed to develop an automatic algorithm for the severity of ischemia.

Methods: Development set: 50 STEMI ECGs were manually (Manual-score) and automatically (Auto-score) scored by our designed algorithm. The agreement between Manual- and Auto-score was assessed by kappa statistics. Test set: ECGs from 199 STEMI patients were assigned a severity grade (severe or non-severe ischemia) by the Auto-score. Infarct size estimated by median peak Troponin T (TnT) and Creatinine Kinase Myocardial Band (CKMB) was tested between the groups.

Results: The agreement between Manual- and Auto-score was 0.83 ((95% CI 0.55–1.00), $p < 0.0001$), sensitivity 75% and specificity 100%, PPV 100% and NPV 94.6%. In the test set 152 (76%) patients were male, mean age 61 ± 12 years. The Auto-score designated severe ischemia in 42 (21%) and non-severe ischemia in 157 (79%) patients. Patients with ECG signs of severe vs. non-severe ischemia had significantly higher levels of biomarkers of infarct size. In multiple linear regression, ECG sign of severe ischemia was an independent predictor for higher TnT and CKMB levels.

Conclusion: The automatic ECG algorithm for severity of ischemia in STEMI performs adequately for clinical use. Severe ischemia obtained by the Auto-score was associated with biomarker estimated larger infarct size.

1. Background

In patients with ST-segment elevation myocardial infarction (STEMI), rapid reperfusion of the acutely occluded coronary artery, either by primary percutaneous coronary intervention (pPCI) or thrombolytic therapy, is of major importance to both myocardial salvage, risk of subsequent heart failure and survival [1–3]. The progression rate of myocardial necrosis varies between individuals and depends on the severity of myocardial ischemia, which is partly associated with the amount of coronary arterial collateral flow and metabolic preconditioning [4,5]. Although current guidelines do not consider the severity of ischemia in patients for triage purposes [3], rapid reperfusion therapy might be even more essential in the group of patients with severe ischemia. An ECG ischemia severity score has been developed ("Sclarovsky-Birnbaum grades of ischemia") (as one proposed biomarker method to estimate the severity of ischemia) and can be measured from the standard 12 lead electrocardiogram (ECG) [6–9]. This score provides a semi-quantitative estimate for distortion of the terminal portion of the QRS-complex as a sign of severe ischemia and predicts worse outcome and prognosis [6,9,10]. Although the validity of this severity score has been demonstrated by independent researchers [6,8,9,11,12], and the score might be a reliable tool for pre-hospital risk stratification and choice of treatment in STEMI patients [13,14], the hitherto required manual calculation is time-consuming and thus unpractical in the acute setting of STEMI. The purpose of this study was to develop an automated algorithm for the severity of ischemia

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(Auto-score) from ECGs in STEMI patients and test the association of the Auto-score with myocardial infarct size estimated by peak Troponin T (TnT) and peak Creatinine Kinase Myocardial Band (CKMB). Myocardial infarct size was hypothesized to be significantly higher in patients with severe ischemia compared to those with non-severe ischemia obtained by the Auto-score.

2. Methods

The study was divided in two parts; a development part with a learning dataset (n = 50) and assessment part with a testing dataset with the main study population (n = 1175).

2.1. Development

For the learning and development of the automatic algorithm, a total of 50 randomly chosen pre-hospital (printed and digital) 12-lead ECGs (obtained in the ambulances) from STEMI patients treated with pPCI were used. Each printed ECG (25 mm/s, 0.05–150 Hz, 10 mm/mV) was manually scored according to the severity score by two independent experts (MMS and MS) blinded to the results from the automated algorithm. The scores were then reviewed and discussed for each ECG and an adjudicated manual score (Manual-score) was determined between MMS and MS. In cases, where there were substantial disagreements, a 3rd expert (YB), blinded to all information reviewed the ECGs, assigning each ECG a final Manual-score (severe or non-severe ischemia) which was implemented in the Manual-Score. This dataset was used to set the detection and recognition rules for the automatic algorithm. Pre-hospital digital ECGs from the same 50 printed ECGs were then automatically processed using the developed automatic algorithm of severity score (Auto-score). The agreement between the Manual-score vs Auto-score was assessed in the training set.

2.2. Assessment

Consecutive STEMI patients treated with pPCI in Rigshospitalet, Copenhagen, Denmark, between March 1, 2014 and December 31, 2014 (n = 1175) were identified in the main study. All identifiable and available digital standard 12-lead ECGs (Pre-PCI ECG) obtained and saved electronically in the cath-lab before pPCI were collected retrospectively. Patients without Pre-PCI ECG or with unidentifiable Pre-PCI ECG were excluded (n = 791). In total, we identified 384 patients who were examined with coronary angiography during the study period and had an ECG digitally recorded in the cath-lab. Of these, 42 patients had missing clinical and biomarker data and 143 ECGs were not eligible for the severity score either due to lack of ST-segment elevation (n = 116) or other factors (7 bundle brunch block, 1 Wolf-Parkinson-White pattern, 7 negative T-waves, 12 noisy ECG). Hence, 199 patients were eligible for the analysis. For all patients included, baseline, demographics, clinical and procedural data were retrieved from an electronic patient record (Web-PATS) database dedicated to interventional cardiology, prospectively registering all patients undergoing procedures. All Pre-PCI ECGs were designated a severity score (severe or non-severe ischemia) by the Auto-score. Troponin T (TnT) (high sensitive troponin T, Roche diagnostics, Mannheim, Germany) and Creatinine Kinase Myocardial Band (CKMB) during the first 72 h from the time of primary admission were registered. Peak TnT and CKMB were than used as marker for infarct size. Finally, the estimated infarct size was compared for patients with severe and non-severe ischemia.

2.3. ECG measurement

2.3.1. The ECG severity score

Sclarovsky-Birnbaum grades of ischemia are based on the presence or absence of distortion of the terminal portion of the QRS complex in leads with ST-segment elevation [10]. Distortion of the terminal QRS complex is defined as: 1: Absence of an S-wave in ≥2 adjacent leads that usually have a terminal S configuration (leads V1 to V3); or 2: In all other leads, ST-J point amplitude ≥50% of the R-wave amplitude measured from the TP baseline in ≥2 adjacent leads. For the manual score ST-segment deviation was measured manually to the nearest 0.5 mm at the J-point in 11 of the 12 ECG leads, excluding aVR, by using the TP-segment as the isoelectric line. Alternatively, the PR-segment was used if the TP-segment was not distinct. In addition, leads with ST-segment elevation and negative T-waves were excluded in manual and automatic score. Detailed criteria of the Sclarovsky-Birnbaum grades of ischemia are described elsewhere [15].

2.3.2. ECG signal processing and noise reduction

For the Auto-score CODE-STAT software (CODE-STAT-Reviewer version 9.0 Software, Physio-Control, Inc., Minneapolis, MN, USA), 12SL measurements were used directly from digital 12-lead ECG XML source files output from the LIFEPAK® 15 (Physio-Control, Inc., Minneapolis, MN, USA) recording system, thus enabling near real-time analysis. LIFEPAK 15 records ECGs at sample rate of 500 Hz, bandwidth of 0.05 to 150 Hz and amplitude resolution of 4.88 μV. The 12SL algorithm locates fiducial points on a median beat which is formed from dominant beats in the 10 s ECG, which results in a cleaner and most noise-free ECG [16–18]. QRS-onset and offset are determined by simultaneous analysis of slopes in all 12 leads. First, Q-onset is demarcated, then Q-offset. QRS-onset is defined as the earliest deflection in any lead. QRS-offset is defined as the latest deflection in any lead [19]. After QRS onsets and offsets have been demarcated in the median complex, the waves for each complex are identified. This is done in all 12 leads by finding points at which the ECG crosses the baseline. Waves defined by crossing points that exceed 160 μV·ms are significant and 12SL will label the wave (for example the S-wave) as a separate wave. For ST-measurements, the median beat is shifted so that the voltage at Q-onset is zero by definition. ST levels can then be measured with respect to the voltage at this point or the TP baseline. The threshold for digital ST-segment elevation was changed from 0.1 mV to 0.085 mV to more closely reflect visual impression of manual coding of ST-segment elevation due to line thickness on a printed ECG. The algorithm was applied to the same 11 of the 12 ECG leads as the manual scoring (excluding aVR). Detailed criteria of the Sclarovsky-Birnbaum grades of ischemia are described elsewhere [15]. We defined severe ischemia in the presence of QRS distortion in ≥2 contiguous leads and non-severe ischemia in the absence of QRS distortion. Severity of ischemia was considered in each lead with ST elevation ≥0.10 mV.

3. Statistical analysis

Categorical variables are reported as numbers (percentages) and continuous variables as median (25th–75th quartiles) or mean ± SD. The reliability between the Manual-score and the Auto-score was assessed by kappa statistics. The Kappa coefficient with corresponding 95% confidence intervals (CI) was used to measure the agreements between Manual-score and Auto-score in severe vs non-severe ischemia in the development part. IBM SPSS Bootstrapping (number of samples = 1000) was used for obtaining a 95% CI. The reading of the Kappa coefficient was according to the following usually recognized scale: 0.00–0.10 – virtually none; 0.11–0.40 – slight; 0.41–0.60 – fair; 0.61–0.80 – moderate; 0.81–1.0 – substantial [20].

Assessment: Baseline clinical and biomarker data were analyzed according to patients with severe vs. non-severe ischemia. Pearson's χ^2 test was used for the comparison of categorical variables. Continuous variables within the groups were compared using Student's t-test or Wilcoxon matched pairs test, as appropriate. Variables not normally distributed (treatment delay (time from pain to reperfusion), system delay (time from first medical contact to reperfusion), CKMB and TnT) were log transformed in the analysis models, as appropriate.

Multivariable linear regression analyses were used for testing the association between the Auto-score and infarct size. The model was adjusted for age, gender, diabetes mellitus, hypertension, hypercholesteremia, current smoking, anterior infarct location, TIMI flow 0–1 before pPCI, treatment delay, system delay and severe vs non-severe ischemia. Separate models were performed considering only non-overlapping intervals of time to reperfusion: model 1 considered system delay and model 2 considered treatment delay.

Exploratory multivariable binary logistic regression analysis was performed to evaluate risk of infarct size larger than 1st quartiles of TnT and CKMB levels in patients with severe ischemia, compared to those with non-severe ischemia.

All statistical tests were two-sided and the level of statistical significance was defined as $p < 0.05$. All analyses were performed using SPSS statistical software (SPSS version 22.0, SPSS Inc., Chicago, IL).

4. Results

4.1. Development part - reliability analysis

Severe ischemia was coded in 8 (18.6%) and 6 (14.0%) ECGs by manual-score and auto-score, respectively. Sensitivity and specificity for severe ischemia obtained by the auto-score were 75% and 100%, respectively. Positive and negative predictive values were 100% and 94.6%, respectively. The agreement between the Manual-score and Auto-score for severe ischemia and non-severe ischemia was 0.83 ((95% CI 0.54–1.00), $p < 0.0001$).

4.2. Assessment part

The study population had a mean age 61 years (SD ± 12) and 152 (76%) were males. Median treatment delay was 174 min (IQR 123–255) and system delay 87 min (72–102). Median peak of TnT and CKMB were 4860 (1940–8790) ng/L and 228 (85–321) μg/L, respectively. Severe