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Evaluation of acute ischemia in pre-procedure ECG predicts myocardial salvage after primary PCI in STEMI patients with symptoms >12 hours ☆

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Abstract

Background: Primary percutaneous coronary intervention (pPCI) is recommended in patients with ST Elevation Myocardial Infarction (STEMI) and symptom duration <12 hours. However, a considerable amount of myocardium might still be salvaged in STEMI patients with symptom durations >12 hours (late-presenters). The Anderson-Wilkin's score (AW-score) estimates the acuteness of myocardial ischemia from the electrocardiogram (ECG) in STEMI patients. We hypothesized that the AW-score is superior to symptom duration in identifying substantial salvage potential in late-presenters.

Methods: The AW-score (range 1–4) was obtained from the pre-pPCI ECG in 55 late-presenters and symptoms 12–72 hours. Myocardial perfusion imaging was performed to assess area at risk before pPCI and after 30 days to assess myocardial salvage index (MSI). We correlated both the AW-score and pain-to-balloon with MSI and determined the salvage potential (MSI) according to AW-score ≥3 (acute ischemia) and AW-score <3 (late ischemia).

Results: Late-presenters had median MSI 53% (inter quartile range (IQR) 27–89). The AW-score strongly correlated with MSI ($\beta = 0.60$, $R^2 = 0.36$, $p < 0.0001$), while pain-to-balloon time did not ($\beta = -0.21$, $R^2 = 0.04$, $p = 0.14$). Patients with AW-score ≥3 (n = 16) compared to those with AW-score <3 (n = 27) had significant larger MSI (82.7% vs 41.5%, p = 0.014). MSI > median was observed in 79% in patients with AW-score ≥3 vs 32% in patients with AW-score <3 (adjusted OR 6.74 [95% CI 1.35–33.69], p = 0.02).

Conclusion: AW-score was strongly associated with myocardial salvage while pain-to-balloon time was not. STEMI patients with symptom duration between 12 –72 hours and AW-score ≥3 achieved substantial salvage after pPCI.

Keywords: Prehospital ECG; Ischemia; STEMI; Late presentation

Introduction

Reperfusion of the occluded coronary artery either by fibrinolytic therapy or primary percutaneous coronary intervention (pPCI) within 12 hours of symptom onset in patients with ST-segment elevation myocardial infarction (STEMI) is associated with increased myocardial salvage, preserved left ventricular function and improved survival [1,2]. As the benefits of early reperfusion therapy after 12 hours from symptom onset, is insignificant or may be even harmful [3–7], the American and European Societies of Cardiology guidelines recommend pPCI in STEMI patients with symptom duration within 12 hours [1,2], but are more cautious about the potential value of reperfusion therapy in patients with symptom duration of more than 12 hours (late-presenters). However, the progression of myocardial necrosis has great inter-individual variation and depends on

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the vulnerability of the myocardium to ischemia, which in turn is related to the amount of coronary arterial collateral blood flow and metabolic pre-conditioning [8,9]. Moreover, patient self-reported time of symptom onset is often unprecise and affected by silent angina pectoris or pre-infarction angina pectoris, which pre-conditions the ischemic myocardium leading to cardioprotection [10].

Late-presenters represent 8.5–40% of all STEMI patients [11]. Several findings suggest that reperfusion therapy may be beneficial even in patients who present late after symptom onset [12,13]. In addition, previous studies have not only demonstrated that pPCI is superior to fibrinolysis, but also that the time window of efficacy for pPCI may be wider than that for fibrinolysis [14–16]. However, accurate clinical identification of late-presenters with the potential of myocardial salvage has not been clinically possible. The Anderson-Wilkins acuteness score (AW-score), which quantifies the acuteness of myocardial ischemia from the electrocardiogram (ECG), has been shown to be superior to treatment delay (time from pain-to-balloon) in predicting final infarct size (FIS), salvage and mortality in patients with symptom duration within 12 hours [17–19]. We aimed to evaluate the associations of symptom duration and AW-score with myocardial salvage index (MSI) after pPCI in STEMI patients with symptoms for 12–72 hours (late-presenters). We hypothesized that the AW-score is superior to symptom duration in identifying late-presenters with substantial salvage potential when treated with pPCI.

Methods

The present study is a sub-study from a prospective study that was designed to evaluate whether the 12 hours symptom limit in performing pPCI constituted a relevant cut-off point beyond which myocardial salvage could no longer be obtained [12]. The study evaluated the impact of pain-to-balloon on myocardial perfusion imaging (MPI) of left ventricular (LV) outcome after pPCI for STEMI patients with symptom durations 0–12 hours vs STEMI patients with symptom durations 12–72 hours (late-presenters). No correlation was found between pain-to-balloon and MPI assessed LV outcomes in the overall population [12]. In brief, 396 STEMI patients with pain-to-balloon time interval (0–72 hours) (among those 55 late-presenters) treated with pPCI in Skejby University Hospital, Aarhus, Denmark, from 1 May 2005 to 26 April 2007 were included in the study. The study complied with the Declaration of Helsinki and was approved by the local ethics committee. All patients provided written informed consent [12]. The 55 late-presenters were considered for the inclusion in the present study. The design, inclusion and exclusion criteria have previously been reported in detail [12]. Pain-to-balloon time was defined as time from onset of symptoms to first balloon inflation during pPCI.

ECG analysis

The Anderson-Wilkins score (AW-score) uses quantitative 12-lead ECG criteria to estimate acuteness of the ischemia in STEMI patients. The AW-score, which assesses changes in ST-T segments, T-waves and Q-waves, was obtained from the digital pre-pPCI (prehospital or admission) ECGs. ST elevation ≥ 0.10 mV was considered significant in leads I, aVL and all of the precordial leads while ST elevation ≥ 0.05 mV was considered significant in leads II, III and aVF. The T-wave and Q-wave morphology criteria are previously described [20]. All digital ECGs were measured electronically (using CODE-STAT-Reviewer version 9.0 Software, Physio-Control, Inc.). Each lead was designated an acuteness phase (1A, 1B, 2A or 2B) based on the presence or absence of a tall T-wave or an abnormal Q-wave; phase 1A, tall T-wave and no abnormal Q-wave; phase 1B, positive T-wave and no abnormal Q-wave; phase 2A, tall T-wave and an abnormal Q-wave; phase 2B, positive or initial >50% positive T-wave and an abnormal Q-wave [21]. In addition, leads with ST elevation, negative T-wave and Q-wave were designated phase 2B (n = 9 ECGs). Leads with ST elevation, negative T-wave and no Q-wave were excluded (n = 4 ECGs). ECGs without ST elevation were also excluded (n = 8). Thus 43 ECGs were eligible for AW-score. AW-score ranges from 1 (late ischemia/least acute) to 4 (early ischemia/most acute) and was calculated from the formula:

$$AW\ \ score = \frac{4(\#\ \ leads\ \ 1A) + 3(\#\ \ leads\ \ 1B) + 2(\#\ \ leads\ \ 2A) + 1(\#\ \ leads\ \ 2B)}{\sum \#\ \ leads\ \ with\ \ 1A, 1B, 2A, 2B}.$$

Myocardial perfusion imaging

MPI was performed at inclusion in order to measure the non-perfused myocardial area at risk (AAR) before pPCI. MPI was repeated 30 days after pPCI to assess final myocardial infarct size (FIS), myocardial salvage index (MSI), LV ejection fraction (LVEF) and LV end-diastolic and end-systolic volumes (EDV and ESV). An i.v. bolus of 99mTc-Sestamibi 700 + 70 MBq was used as tracer for single photon emission computed tomography (SPECT) both at inclusion and at follow-up. AAR was assessed by injection of 99mTc-Sestamibi before pPCI and subsequent SPECT imaging within 8 hours. Although SPECT was performed after pPCI, the measured AAR reflects the myocardial perfusion defect before pPCI because 99mTc-Sestamibi does not redistribute once bound to viable myocardium [22]. SPECT at 30 days was gated for assessment of LVEF. MSI was calculated as the ratio (AAR–FIS)/AAR, i.e. the proportion of salvaged AAR. LVEF was calculated as (EDV–ESV)/EDV. SPECT was performed using a dual-headed rotating gamma camera (Forte, ADAC, Milpitas, CA, USA) with a high-resolution, parallel-holed collimator. Two experienced readers of nuclear cardiology studies analyzed data independently and were blinded to pain-to-balloon interval. Images were analyzed with the commercially available automatic quantitative programs QPS and QGS (Cedars-Sinai Medical Center) [12].