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Effect of pre-test probability on diagnostic and prognostic performance of high-sensitivity cardiac troponin for acute myocardial infarction

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Background: There is concern that high-sensitivity cardiac troponin (hs-cTn) may have low diagnostic accuracy in patients with low pre-test probability.

Purpose: To investigate the diagnostic and prognostic performance of hs-cTnT and hs-cTnI among patients presenting with acute chest discomfort and low pre-test probability for an acute coronary syndrome (ACS) to the emergency department (ED).

Methods: We prospectively enrolled patients presenting with acute chest discomfort to the ED. Pre-test probability was quantified using two complementary methods. First, patients were stratified into three groups according to their pre-test probability for an ACS as assessed by the treating ED-physician using a visual analogue scale (VAS): ≤10%, 11–79%, 80%, reviewing all information available at 90 minutes. Second, to generate an alternative classification, bootstrap analysis was used. We 10,000 times randomly sampled 100 AMI cases and 1900 non-AMI cases to an incidence of AMI of 5%. hs-cTnT- and hs-cTnI-concentrations were determined in a blinded fashion at presentation and serially thereafter. Two independent cardiologists adjudicated the final diagnosis.

Results: Among 3,828 patients eligible for analysis, 1,189 patients had low (≤10%) pre-test probability for ACS. The incidence of AMI increased from 1.3% to 12.2% and 54.8% in patients with low, intermediate and high pre-test probability, respectively. The positive predictive value (PPV) value of hs-cTnT/I was low in patients with low pre-test probability and increased with the incidence of AMI, while the diagnostic accuracy of hs-cTn-I for AMI as quantified by the area under the curve (AUC) and specificity were very high and comparable among all three strata (e.g. AUC hs-cTnI 0.96 (95% CI 0.94–0.97); 0.87 (95% CI 0.85–0.89), and 0.89 (95% CI 0.87–0.92), respectively (Figure 1). Findings were validated using bootstrap analysis to define low pre-test probability for AMI. Similarly, higher hs-cTnT/I levels independently predicted all-cause mortality within two years (e.g. hs-cTnT hazard ratio 1.39, 95% CI 1.27–1.52) irrespective of ACS pre-test probability.

Conclusions: Diagnostic and prognostic accuracy and utility of hs-cTnT/I remain high in patients with acute chest discomfort and low pre-test probability.

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Direct comparison of the ESC 0/3h-algorithm with four very early rule-out strategies for acute myocardial infarction using high-sensitivity cardiac troponin I

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Background: The current guidelines of the European Society of Cardiology (ESC) recommend a 0/3h-algorithm for rule-out of acute myocardial infarction (AMI). Besides that, four very early rule-out strategies for AMI using high-sensitivity cardiac troponin I (hs-cTnI) have been identified recently. It remains unclear which strategy is most attractive for clinical application.

Purpose: To directly compare the performance of the ESC 0/3h-algorithm with four very early rule-out strategies for AMI in one large multicentre cohort.

Methods: We prospectively enrolled unselected patients presenting to the emergency department (ED) with symptoms suggestive of AMI. The final diagnosis was adjudicated by two independent cardiologists. hs-cTnI levels were measured at presentation and after 1h and 3h in a blinded fashion. We directly compared the ESC 0/3h-algorithm with all four hs-cTnI-based rule-out strategies: limit of detection (LOD, hs-cTnI <2ng/L), single cut-off (hs-cTnI <5ng/L), 1h-algorithm (hs-cTnI <5ng/L), 1h-change <2ng/L), and the 0/1h-algorithm recommended in the ESC guideline combining LOD and 1h-algorithm. Efficacy was defined as the percentage of patients ruled-out for AMI and safety was quantified by the resulting sensitivity, negative predictive value (NPV) and long-term survival.

Results: The performance of the algorithms is shown in Figure 1. Among 1044 enrolled patients, AMI was the final diagnosis in 144 (14%) patients. The ESC 0/3h-algorithm ruled-out 665 patients (64%) with a sensitivity of 92.4% (95% CI, 85.7–96.1%) and NPV of 98.4% (95% CI, 97.1–99.2%). In comparison, the LOD approach ruled-out 147 patients (14%) with a sensitivity of 100% (95% CI, 97.5–
100%) and NPV of 100% (97.5–100%), the single cut-off 556 patients (53%) with a sensitivity of 97.9% (95% CI, 94.0–99.6%) and NPV of 99.5% (96.4–99.9%), the 1-hour algorithm 529 patients (51%) with a sensitivity of 99.3% (95% CI, 96.2–100%) and NPV of 99.8% (99.0–100%), and the 0.1-hour algorithm 529 patients (51%) with sensitivity of 99.9% (99.0–100%) and NPV of 99.8% (98.9–100%). Two-year survival was 95% with the ESC 0/3h-algorithm, 100% with LOF, and 97.4% with the other three early rule-out strategies (p < 0.01 compared to LOD).

Conclusions: While the ESC 0/3h algorithm has a higher efficacy, its safety as quantified by the resulting sensitivity and NPV for rule-out of AMI and long-term survival is significantly lower as compared to the four very early rule-out strategies.

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Positive troponin values above the 99th percentile strongly predict adverse outcomes in patients with acute chest pain in whom acute coronary syndrome was ruled out

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Background: Current data indicate, that high-sensitivity troponin levels above the 99th percentile in patients presenting with chest pain are indicative for future cardiac events, even when acute coronary syndrome (ACS) was ruled out.

Methods: BACC is a prospective study comprising 1,661 consecutive patients presenting to the emergency department of a large tertiary care center with suspected ACS since 2013. Main outcome measures were death, non-fatal AMI, or coronary revascularization.

Results: Within the BACC study, 279 patients with at least one positive troponin T (Roche Diagnostics, 99th percentile 14 ng/L) value were discharged as non-ACS. Out of these, 40 subjects (14.3%) suffered an endpoint during 12 months of follow-up. Within the StenoCardia study 144 subjects had at least on positive troponin I value (Abbott Diagnostics, 99th percentile 26.2 ng/L), and were finally discharged as non-ACS. Out of these, 18 subjects (12.5%) suffered an endpoint during 6 months of follow-up. The vast majority of these non-ACS patients were discharged without specific preventive therapy (anti-platelet or anti-coag.).

Conclusions: Troponin levels above the 99th percentile, in patients presenting with chest pain in whom ACS was ruled out, seem to mirror subclinical myocardial ischemia. There seems an unmet need and huge potential to reduce mortality and morbidity in these patients.

The results of the studies paved the way for the large controlled clinical trial “GRAYZONE”: 3,000 troponin positive patients presenting at emergency room with acute chest pain, in whom an ACS was ruled out, will be assigned randomly to Aspirin and/or Atorvastatin versus placebo (2x2 factorial design).

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The highest predictive value of neuron-specific enolase for clinical outcomes in cardiac arrest survivors is on day 3 and day 4 after collapse: results from a prospective study

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Background: Despite marked advances in intensive cardiologic care, current options for outcome prediction in cardiac arrest survivors remain significantly limited.

Purpose: The aim of our study was, therefore, to compare the day-specific predictive values of neuron-specific enolase (NSE) in cardiac arrest survivors treated with endovascular hypothermia.

Methods: Eligible patients were out-of-hospital cardiac arrest survivors treated with endovascular hypothermia (30°C for 24 h). Blood samples for NSE levels measurement were drawn on days 1, 2, 3 and 4 after hospital admission. Thirty-day neurological outcomes according to the Cerebral Performance Category (CPC) scale and 12-month mortality were evaluated as clinical end points.

Results: A total of 153 cardiac arrest survivors (mean age 64.2 years) were enrolled in the present study. The NSE levels were significantly lower in the CPC 1–2 group in comparison with the CPC 3–5 group at each time point (P < 0.05). Using ROC analysis, optimal cut-off values of NSE for prediction of CPC 1–2 score on specific days were determined as: day 1: 20.4 mcg/mL (sensitivity 62.1%; specificity 63.3%; P < 0.002); day 2: 29.0 mcg/mL (94.4%; 72.5%; P < 0.001); and day 3: 20.7 mcg/mL (86.7%; 94.4%; P < 0.001). The highest predictive value, however, was observed on day 4: 19.4 mcg/mL (91.0%; 93.5%; P < 0.001); NSE value >50.2 mcg/mL at day 4 was associated with poor outcome with 100% specificity and 73% sensitivity. Moreover, NSE levels measured on all individual days also predicted 12-month mortality (P < 0.001); the highest predictive value for death was observed on day 3: 18.1 mcg/mL (85.3%; 72.0%; P < 0.001). Significant association with prognosis was found also for changes in NSE at different time points.

An NSE level on day 4 > 20.0 mcg/mL, together with a change > 0.0 mcg/mL from day 3 to day 4, predicted poor outcome (CPC 3–5) with 100% specificity and 73% sensitivity.

Conclusions: Results of the present study suggest that NSE estimation is a useful tool for prediction of neurological outcome(s) and long-term mortality in out-of-hospital cardiac arrest survivors treated with endovascular hypothermia. The highest predictive values for NSE were observed on day 4 and day 3 after cardiac arrest. Using the NSE values from these days poor prognosis can be predicted with 100% specificity and reasonable sensitivity.

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Prophylactic pulmonary vein isolation during ishthmus ablation for atrial flutter: three-year outcomes of the prevent AF I study

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Background: The PREVENT AF I study demonstrated that prophylactic pulmonary vein isolation (PVI) in patients with typical atrial flutter (AFL) resulted in substantial reduction of new onset atrial fibrillation (AF) during 1-year follow-up as assessed by continuous implantable loop recorder (ILR).

Objective: To assess the 3-year outcome in AF prevention by prophylactic PVI in patients with only typical AFL.

Methods: Fifty patients with documented AFL were randomized to either cavo-tricuspid isthmus (CTI) ablation alone (n=25) or CTI with concomitant PVI (PVI+CTI; n=25). All patients received an ILR with regular follow-up for 3 years following initial ablation. The primary endpoint of the study was the occurrence of any atrial tachyarrhythmia including AF or AFL after ablation with the monthly burden exceeding 0.5% on the ILR.

Results: At the end of 3 years, 80% of the patients in CTI only group vs 52% of the patients in PVI+CTI group developed AF/AFL recurrences [hazard ratio (HR) 2.40; 95% confidence interval (CI) 1.18–4.86, P = 0.015] (see Figure). More patients in the CTI only group underwent redo ablation compared to PVI+CTI group, 32% vs 8%, respectively (p = 0.037). The three-year AF burden also favored the combined ablation group compared to the CTI ablation only group: 6.2% vs 16.8% (p = 0.038). In CTI only group, 12 (48%) patients were hospitalized during follow-up compared to 4 (16%) in PVI+CTI group (p = 0.032). Two patients in CTI only group developed stroke with no clinical adverse events in PVI+CTI group.

Conclusions: Prophylactic PVI in patients with only typical AFL resulted in a significant reduction of new onset AF and burden during long-term follow-up as assessed by continuous ILR, with consequent reduction in hospitalizations and need to perform repeat ablation for AF.

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Location and coupling interval of ectopic beats have key roles in the onset of atrial fibrillation from the pulmonary veins

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Background: Ectopic beats originating from the pulmonary vein (PV) trigger atrial fibrillation (AF). We analyzed factors that determine the onset of AF regarding electrophysiologic properties of the PVS.

Methods: We performed pacing studies in the PVs (single extra stimulus) from ring type or basket type multiple electrodes in patients undergoing AF ablation (n=81) and observed onset of AF. Inducibility of AF, conduction properties and effective refractory period (ERP) in the PVs were analyzed.

Results: A single extra stimulus in the left superior PV (LSPV) could induce AF in 19 patients (31.1%), which mimicked spontaneous onset of AF. The onset of