# Comparison of Six Decision Aid Rules For Diagnosis of Acute Myocardial Infarction In Elderly Patients Presenting To The Emergency Department With Acute Chest Pain

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# Abstract

**Background:** Using decision aid rules for diagnosis of acute myocardial infarction (AMI) is not common practice in our region. Elderly patients are often neglected in clinical trials, and the proper diagnostics of acute myocardial infarction in this group remains problematic. The objective of this study was to evaluate the accuracy and effectiveness of different strategies for the diagnosis of AMI in the elderly in real-life clinical practice.

**Methods:** In a retrospective single-center study, we included patients older than 70 years presenting to the emergency department with chest pain as a dominant symptom. The performance of six decision aid rules (T-MACS, HEART, EDACS, TIMI, GRACE, and ADAPT) and solo troponin T strategy for diagnosing acute myocardial infarction was evaluated by calculating sensitivity, specificity, odds ratios, negative and positive predictive values.

**Results:** A total of 250 patients, with a mean age of 78.5 years, were enrolled. Forty-eight patients (19.2%) had an acute myocardial infarction in a 30 day follow-up period. The sensitivity for ruling-out AMI was 100% for T-MACS, HEART, and ADAPT; 97.9% for EDACS, 93.8% for TIMI, and 81.3% for GRACE and solo TnT strategy. For ruling-in AMI, the specificity was 97.5% for T-MACS, 95% for TIMI, 83.2% for HEART, 81.7% for GRACE, and 46% for ADAPT. C-statistics were 0.52 for T-MACS, 0.51 for ADAPT, 0.47 for EDACS and GRACE, 0.46 for HEART and TIMI, and 0.33 for solo TnT strategy.

**Conclusion:** T-MACS decision aid had the best performance with 100% sensitivity and 100% negative predictive value for rule-out AMI; 97.5% specificity and 64.3% positive predictive value for rule-in AMI. Other evaluated protocols were less accurate. Risk stratification of patients with suspected acute coronary syndrome based on decision aid rules can be used in real-life practice, even in the population of the elderly.


# Introduction

Chest pain is a common reason for the visit to the emergency department. A broad spectrum of underlying causes can be masked in this symptom. A misdiagnosis of such diseases as acute myocardial infarction (AMI), pulmonary embolism, or acute aortic dissection could lead to severe life harm or even death. We must often use a full spectrum of current examination possibilities, starting with the patient's history, rapid assessment of symptoms and non-specific physical findings, electrocardiography, cardiac imaging, and biochemical analysis.

Current guidelines for the management of acute coronary syndromes recommend serial troponin testing [1]. The introduction of high-sensitive troponin assays resulted in the higher sensitivity of this approach - we could earlier detect a minimal myocardial injury. However, we must not forget that even a slight myocardial injury can be caused by many non-coronary cardiac states, non-cardiac, or even physiological conditions. This strategy contributes to higher costs, staff over-occupancy, and prolonged stay at emergency departments, leading to adverse patient outcomes such as increased morbidity and mortality [2].

Older patients frequently have atypical symptoms, which prolongs the time to correct diagnosis and proper treatment. Visual and auditory impairment and cognitive deterioration contribute to delayed arrival to the emergency department and even misinterpretation of symptoms by the patient himself. Patients at high age, in many cases, have more associated diseases, which independently increase the risk for coronary events. Comorbidities, associated states, medication, and their interactions may also affect electrocardiographical findings and troponin levels. For example, repolarization changes in left ventricle hypertrophy or digoxin use; or multifactorial mild elevation of cardiac troponins in chronic kidney disease.

Many protocols were tested to make the diagnostic process efficient. This study evaluates six decision aid rules: T-MACS, HEART, EDACS, TIMI, GRACE, and ADAPT; and a strategy of the decision based only on a single troponin T value with a cut-off at 95th percentile upper reference limit (solo TnT strategy). These six risk stratification scores were validated in large multicentre trials and had shown great sensitivity and negative predictive value, especially in the ability to rule-out acute myocardial infarction. Using these decision aids is not common in our region, so we decided to evaluate their accuracy and effectiveness in everyday clinical practice. We chose the selected population of the elderly because they are often neglected in clinical trials, and the proper diagnostics of acute myocardial infarction in this group remains the challenge.

# Methods

Study design and participants

The study was performed at a single center - University Hospital in Hradec Králové, which serves as a regional hospital for a district of around 160 thousand inhabitants. We enrolled patients examined in the emergency department of our hospital for one year (from January 1 to December 31, 2016). The ethical committee of University Hospital approved the study. The trial was conducted following the principles of the Declaration of Helsinki. The inclusion criteria were chest pain as a dominant symptom, age above 70 years, twelve lead electrocardiogram (ECG) recorded, and at least one blood sample for high sensitive troponin T (hs-TnT) analyzed. We excluded patients with apparent ST-segment elevations on the ECG (these were recommended for acute coronary angiography) and those unable to follow up.

Data collection

Demographic data, chest pain characteristics, ECG findings, past medical history, and hs-TnT concentrations for every patient were gathered from the hospital information system retrospectively. They were used to calculate T-MACS, HEART, EDACS, TIMI, GRACE, and ADAPT scores.

Laboratory analysis

Upon arrival to the emergency department, the blood sample was taken from a peripheral vein and immediately sent to the local laboratory for analysis. We analyzed blood samples for the concentration of high sensitivity troponin T (hs-TnT) with the assay Elecsys from Roche Diagnostics (99th percentile upper reference limit of 14ng/L for men and women, coefficient of variation < 10% at 13 ng/L).

Decision aid rules

Each of these chosen aids uses different clinical, electrocardiographical, or biochemical variables. According to the predicted probability of acute myocardial infarction calculated by the test score, patients can be divided into different risk groups. Original decision aid rule authors proposed managing the patient at the emergency department following the calculated risk. For example, safe discharge from the emergency department for low-risk groups, admission to the ward and invasive approach for high-risk groups, and additional examination such as serial troponin testing or stress/ imaging tests for moderate-risk groups [3]. Table 1 shows the summary of the selected decision aids.

**Troponin-only Manchester Acute Coronary Syndrom Score Decision Aid Rule (T-MACS)** operates with six dichotomous variables and one single hs-TnT concentration (measured at the time of arrival to the emergency department) [4]. Patients could be divided into four groups according to their probability of acute coronary syndrome or 30-days major adverse cardiac events (MACE) - very low-risk, low, medium, or high risk. This protocol can essentially exclude MACE in the very low-risk patients (rule-out diagnostics) and predicts MACE in high-risk patients (rule-in diagnostics) with high probability [5].

**HEART** is the acronym for History, ECG, Age, Risk factors, and Troponin concentration. This model predicts the 6-week risk of MACE. Low-risk patients (score 0–3) should be discharged from emergency, moderate risk patients (score 4–6) are recommended for further examination during a hospital stay, and patients with high risk (score above 6) could undergo early invasive coronary angiography [6].

**Emergency Department Assessment of Chest Pain Score (EDACS)** identifies chest pain patients with a low risk for major cardiac events in 30 days. Risk stratification is based on age, sex, coronary artery disease risk factors, and symptoms and signs of myocardial ischemia. In the initial evaluation, troponin testing is not required. However, patients who do not meet the low-risk criteria should be ruled out for acute myocardial infarction with usual chest pain protocols with serial troponin testing [7, 8]. Only low-risk patients (score < 16) without ischemic changes on ECG and with negative troponins are safe for early discharge.

**GRACE (Global Registry of Acute Coronary Events)** is an extensive multicentre international database [9]. Formerly, the GRACE score was studied to estimate in-hospital mortality of patients with the confirmed acute coronary syndrome and is still recommended in current ESC guidelines for the management of acute coronary syndrome without ST-segment elevations [1]. In this study, we hypothesized about its predictive value in a general population of chest pain patients. We used an improved version of GRACE 2.0, which involves eight variables (age, pulse, systolic blood pressure, ECG ischemia, abnormal cardiac enzymes, creatinine value, cardiac arrest at admission, and Killip class) [10, 11].

**TIMI (Thrombolysis in Myocardial Infarction) risk score for unstable angina/ non-ST elevation myocardial infarction** is one of the first widely implemented chest pain decision rules. Seven variables - age 65 years or older, at least three risk factors for coronary artery disease, prior coronary stenosis of 50% or more, ST-segment deviation on the electrocardiogram at presentation, at least two anginal events in last 24 hours, use of aspirin, and elevated serum cardiac markers - were identified from huge international database using multivariate logistic regression. The score predicts a percentual risk of 14-days MACE (all-cause mortality, myocardial revascularization, or myocardial infarction) [12]. Patients with a score of 0 and 1 point are at low risk of adverse outcomes. High-risk score patients (6 and 7 points) require aggressive pharmacological treatment and an early invasive approach.

**Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms (ADAPT)** evaluates electrocardiogram, 0-hour and 2-hour troponin value, and TIMI score. Initially, this protocol was created to identify patients at low risk for 30 days MACE, suitable for rapid discharge from the emergency department [13]. A combination of normal troponin, normal ECG and TIMI score of zero represents the low-risk population; abnormal troponin or abnormal ECG constitutes a high-risk group.

**Solo Troponin T (TnT) strategy**

we hypothesized about the accuracy of strategy using only one variable - single high-sensitivity Troponin T (hs-TnT) concentration with the cut-off value at the 99th percentile upper reference limit for used assay (14ng/L for men and women) for determination. Patients with hs-TnT value below 15ng/L were identified as low-risk, others as high-risk.

**Table 1 Summary of chosen decision aids - evaluated variables, clinical outcomes in original trials, risk stratification, and value of age for prediction of ACS/ MACE**

| Protocol | T-MACS | HEART | EDACS | TIMI | GRACE | ADAPT |
|---|---|---|---|---|---|---|
| **Variables** | ECG ischemia | History | Age | Age ≥ 65 | Age | Abnormal troponin at 0 or 2 hours |
| | Crescendo angina | ECG | Sex | ≥ 3 risk factors for CAD | Heart Rate | Ischemic changes on ECG |
| | Pain radiating to shoulder | Age | Known CAD or ≥ 3 risk factors for CAD | Know CAD | Systolic Blood Pressure | Age ≥ 65 |
| | Pain associated with vomiting | Risk factors | Diaphoresis | ASA use | Creatinine | ≥ 3 risk factors for CAD |
| | Sweating observed | Initial Troponin | Pain radiating to arm, shoulder, neck, or jaw | Severe angina | Cardiac Arrest at Admission | Know CAD |
| | Hypotension | | Pain worsened with inspiration | ECG ischemic changes | ST-segment deviation | ASA use |
| | Initial Troponin | | Pain reproduced by palpation | Positive cardiac marker | Abnormal cardiac enzymes | Severe angina |
| | | | | | Killip class | |
| **Outcomes** | 30 days ACS or MACE[a] | 6 weeks MACE[a] | 30 days MACE[b] | 14 days MACE[a] | 6 months death | 30 days MACE[b] |
| **Risk stratification** | Very low risk (0-1%) | Low risk (score 0-3) | Low risk (score <16) | Low risk (score 0-1) | Low risk ( < 109 pts) | Low risk (normal TnT, normal ECG and TIMI 0) |
| | Low risk (2-4%) | Moderate risk (score 4-6) | Not-low risk (score ≥ 16) | Moderate risk (score 2-5) | Medium risk (109-140 pts) | Intermediate (normal TnT, normal ECG, and TIMI 1) |
| | Moderate risk (5-94%) | High risk (score >6) | | High risk (score 6-7) | High risk (> 140 pts) | High (abnormal TnT or abnormal ECG, any TIMI) |
| | High risk (>94%) | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Value of age on total score** | none * | age ≥ 65 = 2 pts | 70 years = 12 pts<br>71-75 years = 14 pts<br>76-80 years = 16 pts<br>81-85 years = 18 pts<br>≥86years = 20pts | age ≥ 65 counts = 1 pt | 70-79 years= 73pts<br>>79years = 91pts | age ≥ 65 counts for TIMI score ≥1 |
| **Maximum score** | 100% | 10 pts | 38 pts | 7 pts | 340 pts | NA |

ACS - acute coronary syndrome; AIM - acute myocardial infarction; ASA - acetylsalicylic acid; CAD - coronary artery disease; ECG - electrocardiogram; MACE - major adverse cardiac event; MACE[a] - a composite of acute myocardial infarction, myocardial revascularization, and all-cause death (applicable for T-MACS, HEART, and TIMI); MACE[b] - a composite of acute myocardial infarction, myocardial revascularization, cardiac death, cardiogenic shock, cardiac arrest, ventricular arrhythmia and high-grade atrioventricular block (applicable for EDACS and ADAPT); NA - not applicable; * age is not involved in the calculation.

Outcomes

As in most of the original trials of decision aid rules mentioned above, we followed patients for one month. The primary endpoint was an occurrence of acute myocardial infarction (AMI) and major adverse cardiac events (MACE). MACE includes composite of AMI, myocardial revascularization, and all-cause mortality. The diagnosis of AMI was made out according to the current guidelines [1, 14].

### Statistical analysis

Categorical data were presented as proportions and percentages, continuous data as median and interquartile range. Selected patient characteristics between the groups of patients with and without AMI were compared, the continuous data were tested with the Mann-Whitney U test and categorical data with the Pearson's Chi-square test for independence. The diagnostic accuracy of decision aid rules was evaluated by calculating sensitivity, specificity, odds ratios, negative and positive predictive values with respected 95% confidence intervals and constructing the receiver operator characteristics (ROC) curves. Sensitivities and specificities of decision aids were compared using McNemar`s test. Statistical analysis was performed using M.S. Office Excel (Microsoft, Redmont, Washington, USA) and open-source software SOFA Statistics v1.4.6 (Paton-Simpson & Associates Ltd).

## Results

A total of 250 patients were enrolled. The median age was 78 years (70–94 years), and 50% were males. Acute myocardial infarction in 30 days follow-up period occurred in 48 patients (19.2%), myocardial revascularization (PCI/CABG) in 28 patients (11.2%), MACE - major adverse cardiac event (combination of AMI, death, and revascularization) in 55 patients (22%), and four patients died (1.6%). Table 2 demonstrates the baseline characteristics of the included participants.

Table 2
**Baseline characteristics of included patients**.

| **Baseline characteristics** | |
|---|---|
| Total - n | 250 |
| Age - median (IQR) | 78 (73–84) |
| Men - n (%) | 126 (50.4%) |
| *Personal history* | |
| Coronary artery disease - n (%) | 106 (42.4%) |
| Peripheral artery disease - n (%) | 23 (9.2%) |
| TIA/ stroke - n (%) | 25 (10.0%) |
| Dyslipidaemia - n (%) | 146 (58.4%) |
| Hypertension - n (%) | 209 (83.6%) |
| Diabetes mellitus - n (%) | 73 (29.2%) |
| Current smoking - n (%) | 73 (29.2%) |
| *Chest pain characteristics* | |
| Typical angina - n (%) | 97 (38.8%) |
| Propagation do arm - n (%) | 40 (16.0%) |
| Relief after nitrates - n (%) | 62 (24.8%) |
| Nausea/ vomitting - n (%) | 24 (9.6%) |
| Sweating observed - n (%) | 23 (9.2%) |
| Produced by palpation - n (%) | 49 (19.6%) |
| Worsened with inspiration - n (%) | 26 (10.4%) |
| *ECG and biochemical findings* | |
| No new ischemic ECG changes - n (%) | 183 (73.2%) |
| hs-TnT at arrival ng/L - median (IQR) | 16 (10–25) |
| creatinine μmol/L - median (IQR) | 93 (80–112) |

*CABG - coronary artery bypass graft surgery; CKD-EPI eGFR - Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate equation; ECG - electrocardiogram; hs-TnT - high-sensitive Troponin T concentration; IQR - interquartile range; New ischemic ECG changes - new or presumably new horizontal or descending ST-segment depression ≥ 0.5mm or T wave inversion in at least two adjacent leads; PCI - percutaneous coronary intervention.*

| Baseline characteristics | |
|---|---|
| CKD-EPI eGFR ml/min/1.73m$^{2-}$median (IQR) | 59.4 (46.2–70.2) |
| *Decision aids average score for the whole population* | |
| T-MACS - median (IQR) | 6% (3-26.8%) |
| HEART - median (IQR) | 5 (4–7) |
| EDACS - median (IQR) | 20 (16–23) |
| TIMI - median (IQR) | 3 (2–4) |
| GRACE - median (IQR) | 116 (102–136) |
| *Others* | |
| Hospitalizations - n (%) | 99 (39.6%) |
| Coronary angiography performed - n (%) | 39 (15.6%) |
| Revascularization – CABG/PCI (n, %) | 28 (11.2%) |
| Acute myocardial infarction - n (%) | 48 (19.2%) |
| Deaths - n (%) | 4 (1.6%) |
| Major adverse cardiac events - n (%) | 55 (22.0%) |

*CABG - coronary artery bypass graft surgery; CKD-EPI eGFR - Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate equation; ECG - electrocardiogram; hs-TnT - high-sensitive Troponin T concentration; IQR - interquartile range; New ischemic ECG changes - new or presumably new horizontal or descending ST-segment depression ≥ 0.5mm or T wave inversion in at least two adjacent leads; PCI - percutaneous coronary intervention.*

The highest prevalence of acute myocardial infarction (64.3% and 49.3%, respectively) was in high-risk groups identified by T-MACS and HEART score. In the low-risk groups pointed by these decision aids, there was no acute myocardial infarction (AMI). The proportion of patients with AMI in each risk group for the selected decision aid rule is in table 3.

Table 3
**Risk stratification** - total number and proportion of patients with acute myocardial infarction in each risk group for evaluated decision aid rules and solo TnT strategy.

| **T-MACS** | **total, n** | **%** | **AMI, n** | **%** |
|---|---|---|---|---|
| Very Low | 11 | 4.4% | 0 | 0.0% |
| Low | 95 | 38.0% | 3 | 3.2% |
| Moderate | 130 | 52.0% | 36 | 27.7% |
| High | 14 | 5.6% | 9 | 64.3% |
| **HEART** | total, n | % | AMI, n | % |
| Low | 35 | 14.0% | 0 | 0.0% |
| Moderate | 148 | 59.2% | 15 | 10.1% |
| High | 67 | 26.8% | 33 | 49.3% |
| **EDACS** | total, n | % | AMI, n | % |
| Low risk | 54 | 21.6% | 1 | 1.9% |
| Not-low risk | 196 | 78.4% | 47 | 24.0% |
| **TIMI** | total, n | % | AMI, n | % |
| Low | 49 | 19.6% | 3 | 6.1% |
| Moderate | 183 | 73.2% | 37 | 20.2% |
| High | 18 | 7.2% | 8 | 44.4% |
| **GRACE** | total, n | % | AMI, n | % |
| Low | 99 | 39.6% | 9 | 9.1% |
| Moderate | 94 | 37.6% | 19 | 20.2% |
| High | 57 | 22.8% | 20 | 35.1% |
| **ADAPT** | total, n | % | AMI, n | % |
| Low | 0 | 0.0% | 0 | 0.0% |
| Intermediate | 96 | 38.4% | 3 | 3.1% |
| High | 154 | 61.6% | 45 | 29.2% |
| **Solo TnT strategy** | total, n | % | AMI, n | % |
| TnT < 15ng/L | 113 | 45.2% | 9 | 8.0% |
| TnT ≥ 15ng/L | 137 | 54.8% | 39 | 28.5% |

We found a significant difference in the incidence of peripheral arterial disease, active smoking, typical angina, and hs-TnT concentration at arrival in patients with AMI compared to those without AMI. Worsening of pain by respiration, pain produced by palpation, and the absence of new ischemic changes on ECG seem to be protective factors. Analysis of risk factors possibly contributing to the occurrence of AIM shows Table 4.

Table 4
Comparison between patients with and without AMI during the follow-up period

| | **With AMI** | **Without AMI** | **p-value** |
|---|---|---|---|
| Total - n | 48 | 202 | |
| Age - median (IQR) | 81 (73-85.8) | 77 (73–83) | 0.101 |
| Male sex - n (%) | 35 (72.9%) | 89 (44.1%) | **< 0.001** |
| CAD - n (%) | 22 (45.8%) | 84 (41.6%) | 0.592 |
| PAD - n (%) | 8 (16.7%) | 15 (7.4%) | **0.046** |
| Stroke - n (%) | 5 (10.4%) | 20 (9.9%) | 0.915 |
| Dyslipidemia - n (%) | 23 (47.9%) | 123 (60.9%) | 0.101 |
| Hypertension - n (%) | 40 (83.3%) | 169 (83.7%) | 0.956 |
| Diabetes mellitus - n (%) | 19 (39.6%) | 54 (26.7%) | 0.078 |
| Current smoker - n (%) | 21 (43.8%) | 52 (25.7%) | **0.014** |
| Typical angina - n (%) | 39 (81.3%) | 58 (28.7%) | **< 0.001** |
| Propagation do arm - n (%) | 8 (16.7%) | 32 (15.8%) | 0.889 |
| Relief after nitrates - n (%) | 24 (50.0%) | 38 (18.8%) | **< 0.001** |
| Nausea/ vomitting - (%) | 9 (18.8%) | 15 (7.4%) | **0.017** |
| Sweating observed - n (%) | 6 (12.5%) | 17 (8.4%) | 0.379 |
| Pain produced by palpation - n (%) | 2 (4.2%) | 47 (23.3%) | **0.003** |
| Pain worsened with inspiration - n (%) | 1 (2.1%) | 25 (12.4%) | **0.036** |
| ECG without ischemia - n (%) | 23 (47.9%) | 160 (79.2%) | **< 0.001** |
| hs-TnT at time 0 ng/L - median (IQR) | 26.5 (16.3–61.8) | 14 (10–22) | **< 0.001** |
| hs-TnT at time 1 ng/L - median (IQR) | 59 (27–120) | 20 (14–30) | **< 0.001** |
| Creatinine µmol/L - median (IQR) | 92,5 (81-106.3) | 93 (78–114) | 0.961 |
| T-MACS % - median (IQR) | 34 (13–90) | 4 (2–16) | **< 0.001** |
| HEART score - median (IQR) | 7 (6–8) | 5 (4–6) | **< 0.001** |

*AMI - acute myocardial infarction; CAD - coronary artery disease; CAG - coronary angiography; ECG without ischemia - no new or presumably new horizontal or descending ST-segment depression ≥ 0.5mm or T wave inversion in at least two adjacent leads; hs-TnT at time 0 - concentration of high-sensitivity troponin T in ng/L in arrival; hs-TnT at time 1 - concentration of high-sensitivity troponin T in ng/L after 3,6, or 12 hours after initial evaluation (available only in 150 patients); PAD - peripheral arterial disease.*

| | With AMI | Without AMI | p-value |
|---|---|---|---|
| EDACS score - median (IQR) | 22 (20–25) | 19 (14–22) | **< 0.001** |
| TIMI score - median (IQR) | 4 (2–5) | 3 (2–4) | **0.002** |
| GRACE score - median (IQR) | 132 (116-148.5) | 111.5 (100-130.3) | **< 0.001** |
| ADAPT high risk - n (%) | 45 (93.8%) | 109 (54.0%) | **< 0.001** |
| Hospitalizations - n (%) | 46 (95.8%) | 53 (26.2%) | **< 0.001** |
| CAG performed - n (%) | 27 (56.3%) | 12 (5.9%) | **< 0.001** |

*AMI - acute myocardial infarction; CAD - coronary artery disease; CAG - coronary angiography; ECG without ischemia - no new or presumably new horizontal or descending ST-segment depression ≥ 0.5mm or T wave inversion in at least two adjacent leads; hs-TnT at time 0 - concentration of high-sensitivity troponin T in ng/L in arrival; hs-TnT at time 1 - concentration of high-sensitivity troponin T in ng/L after 3,6, or 12 hours after initial evaluation (available only in 150 patients); PAD - peripheral arterial disease.*

The diagnostic accuracy of each protocol is represented in table 5. Separately, we rated competence to rule out AMI by comparing low-risk and non-low risk groups identified by each decision aid model. T-MACS, HEART, and ADAPT had the highest sensitivity, however, with very poor specificity. On the other hand, we measured the ability to rule in AMI by comparing high-risk groups and non-high-risk groups. HEART and ADAPT protocol showed the highest sensitivity with decent specificity. EDACS decision aid and solo TnT strategy were reviewed only in the rule-out part because of their dichotomous character (low-risk and not low-risk; below and above upper reference limit, respectively). Head-to-head comparison of sensitivity and specificity of decision protocols in the rule-out and rule-in diagnostics of AMI are presented in table 6.

**Table 5 Diagnostic accuracy of decision aid rules in rule-out and rule-in diagnostics of acute myocardial infarction.**

| Rule-Out | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Accuracy | LR + | LR - | OR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| T-MACS | 100.0% (100-100%) | 5.4% (2.3-8.6%) | 20.1% (15.0-25.2%) | 100.0% (100-100%) | 23.6% | 1.1 | 0.0 | NA |
| HEART | 100.0% (100-100%) | 17.3% (12.1-22.6%) | 22.3% (16.8-27.9%) | 100.0% (100-100%) | 33.2% | 1.2 | 0.0 | NA |
| EDACS | 97.9% (93.9-100.0%) | 26.2% (20.2-32.3%) | 24.0% (18.0-30.0%) | 98.1% (94.6-100.0%) | 40.0% | 1.3 | 0.1 | 16.7 (2.3-124.2) |
| TIMI | 93.8% (86.9-100.0%) | 22.8% (17.0-28.6%) | 22.4% (16.6-28.2%) | 93.9% (87.2-100.0%) | 36.4% | 1.2 | 0.3 | 4.4 (1.3-14.9) |
| GRACE | 81.3% (70.2-92.3%) | 44.6% (37.7-51.4%) | 25.8% (18.9-32.8%) | 90.9% (85.3-96.6%) | 51.6% | 1.5 | 0.4 | 3.5 (1.6-7.6) |
| ADAPT | 100.0% (100-100%) | 0.0% | 19.2% (14.3-24.1%) | NA | 19.2% | 1.0 | NA | NA |
| Solo TnT | 81.3% (70.2-92.3%) | 51.5% (44.6-58.4%) | 28.5% (20.9-36.0%) | 92.0% (87.0-97.0%) | 57.2% | 1.7 | 0.4 | 4.6 (2.1-10.0) |
| **Rule-In** | **Sensitivity (95% CI)** | **Specificity (95% CI)** | **PPV (95% CI)** | **NPV (95% CI)** | **Accuracy** | **LR +** | **LR -** | **OR (95% CI)** |
| T-MACS | 18.8% (7.7-29.8%) | 97.5% (95.4-99.7%) | 64.3% (39.2-89.4%) | 83.5% (78.7-88.2%) | 82.4% | 7.6 | 0.8 | 9.1 (2.9-28.6) |
| HEART | 68.8% (55.6-81.9%) | 83.2% (78.0-88.3%) | 49.3% (37.3-61.2%) | 91.8% (87.8-95.8%) | 80.4% | 4.1 | 0.4 | 10.9 (5.3-22.2) |
| TIMI | 16.7% (6.1-27.2%) | 95.0% (92.1-98.0%) | 44.4% (21.5-67.4%) | 82.8% (77.9-87.6%) | 80.0% | 3.4 | 0.9 | 3.8 (1.4-10.3) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GRACE | 41.7% (27.7-55.6%) | 81.7% (76.4-87.0%) | 35.1% (22.7-47.5%) | 85.5% (80.5-90.5%) | 74.0% | 2.3 | 0.7 | 3.2 (1.6-6.3) |
| ADAPT | 93.8% (86.9-100.0%) | 46.0% (39.2-52.9%) | 29.2% (22.0-36.4%) | 96.9% (93.4-100.0%) | 55.2% | 1.7 | 0.1 | 12.8 (3.9-42.5) |

CI - 95% confidence interval; LR + positive likelihood ratio; LR - negative likelihood ratio; NA - not applicable (because of division by zero); NPV - negative predictive value; OR - odds ratio; PPV - positive predictive value.

Table 6
Comparison of sensitivities and specificities of decision aid rules.

| Rule Out AMI | Protocol 1 sensitivity | Protocol 2 sensitivity | p-value | Protocol 1 specificity | Protocol 2 specificity | p-value |
|---|---|---|---|---|---|---|
| T-MACS vs. HEART | 100.0% | 100.0% | NS | 5.4% | 17.3% | < .001 |
| T-MACS vs. EDACS | 100.0% | 97.9% | NS | 5.4% | 26.2% | < .001 |
| T-MACS vs. TIMI | 100.0% | 93.8% | NS | 5.4% | 22.8% | < .001 |
| T-MACS vs. GRACE | 100.0% | 81.3% | NS | 5.4% | 44.6% | NS |
| T-MACS vs. ADAPT | 100.0% | 100.0% | NS | 5.4% | 0.0% | NS |
| T-MACS vs. solo TnT | 100.0% | 81.3% | NS | 5.4% | 51.5% | < .001 |
| HEART vs. EDACS | 100.0% | 97.9% | NS | 17.3% | 26.2% | 0.016 |
| HEART vs. TIMI | 100.0% | 93.8% | NS | 17.3% | 22.8% | 0.046 |
| HEART vs. GRACE | 100.0% | 81.3% | NS | 17.3% | 44.6% | < .001 |
| HEART vs. ADAPT | 100.0% | 100.0% | NS | 17.3% | 0.0% | < .001 |
| HEART vs. solo TnT | 100.0% | 81.3% | NS | 17.3% | 51.5% | < .001 |
| EDACS vs. TIMI | 97.9% | 93.8% | NS | 26.2% | 22.8% | 0.42 |
| EDACS vs. GRACE | 97.9% | 81.3% | NS | 26.2% | 44.6% | < .001 |
| EDACS vs. ADAPT | 97.9% | 100.0% | NS | 26.2% | 0.0% | < .001 |
| EDACS vs. solo TnT | 97.9% | 81.3% | NS | 26.2% | 51.5% | < .001 |
| TIMI vs. GRACE | 93.8% | 81.3% | 0.25 | 22.8% | 44.6% | < .001 |
| TIMI vs. ADAPT | 93.8% | 100.0% | 0.25 | 22.8% | 0.0% | < .001 |

| Rule Out AMI | Protocol 1 sensitivity | Protocol 2 sensitivity | p-value | Protocol 1 specificity | Protocol 2 specificity | p-value |
|---|---|---|---|---|---|---|
| TIMI vs. solo TnT | 93.8% | 81.3% | NS | 22.8% | 51.5% | < .001 |
| GRACE vs. ADAPT | 81.3% | 100.0% | NS | 44.6% | 0.0% | NS |
| GRACE vs. solo TnT | 81.3% | 81.3% | NS | 44.6% | 51.5% | < .001 |
| ADAPT vs. solo TnT | 100.0% | 81.3% | NS | 0.0% | 51.5% | < .001 |
| **Rule In AMI** | Test 1 sensitivity | Test 2 sensitivity | p-value | Test 1 specificity | Test 2 specificity | p-value |
| T-MACS vs. HEART | 18.8% | 68.8% | < .001 | 97.5% | 83.2% | < .001 |
| T-MACS vs. TIMI | 18.8% | 16.7% | NS | 97.5% | 95.0% | NS |
| T-MACS vs. GRACE | 18.8% | 41.7% | NS | 97.5% | 81.7% | < .001 |
| T-MACS vs. ADAPT | 18.8% | 93.8% | < .001 | 97.5% | 46.0% | < .001 |
| HEART vs. TIMI | 68.8% | 16.7% | < .001 | 83.2% | 95.0% | < .001 |
| HEART vs. GRACE | 68.8% | 41.7% | < .001 | 83.2% | 81.7% | < .001 |
| HEART vs. ADAPT | 68.8% | 93.8% | < .001 | 83.2% | 46.0% | < .001 |
| TIMI vs. GRACE | 16.7% | 41.7% | NS | 95.0% | 81.7% | < .001 |
| TIMI vs. ADAPT | 16.7% | 93.8% | < .001 | 95.0% | 46.0% | < .001 |
| GRACE vs. ADAPT | 41.7% | 93.8% | < .001 | 81.7% | 46.0% | < .001 |

The receiver operator characteristics (ROC) and area under the curve (AUC) analysis of chosen diagnostic protocols shows Fig. 1. The areas under the curve (AUC) were comparable for every decision rule. T-MACS had the highest AUC (0.52), and solo TnT strategy had the lowest AUC (0.33).

# Discussion

This single-center study retrospectively evaluated the diagnostic accuracy of six decision aids and the single troponin value strategy in the rule-out and rule-in diagnostics of acute myocardial infarction in everyday practice in the emergency department in a selected population of the elderly. Our results show that these protocols can be used even in the highly selected groups of very old persons with similar results. This population was not evaluated in large trials.

In our study, T-MACS and HEART scores have 100% sensitivity and 100% negative predictive value for ruling out AMI between selected decision aid rules. T-MACS rule also has an excellent performance in rule-in diagnostics for AMI in the high-risk group with 97.5% specificity and 64.3% positive predictive value - the highest from evaluated risk stratification protocols. The HEART score had slightly lower specificity (83.2%, $p\text{-value} < 0.001$ for difference) and identified a lower proportion of AMI patients in the high-risk group compared to T-MACS score (49.3% vs. 64.3%).

The EDACS score had very high sensitivity and negative predictive value for rule-out AMI (97.9% and 98.2%, respectively), missing just one patient with acute myocardial infarction classified in low-risk groups. Because of its dichotomous character (low-risk versus not low-risk), we have not tested its performance in rule-in diagnostics.

In the ability to rule out AMI, GRACE score and solo TnT strategy had the weakest performance with the lowest sensitivity (around 80%) between selected decision aids with specificities around 50% and a negative predictive value of 90.9% and 92%. GRACE also had low specificity and positive predictive value (81.7% and 35.1%, respectively) when used to rule in AMI. Further, the solo TnT strategy was not tested in the rule-in part for the same reasons as the EDACS protocol. We proved that the single parameter decision rule (the solo TnT strategy with a cut-off at the upper reference limit) is just not good enough for the risk stratification of patients with the suspected acute coronary syndrome. It seems that the conjunction of clinical, biochemical, and ECG markers gives better results. However, the GRACE score is the model with the most parameters used than other decision aid rules.

Results of ADAPT protocol are conflicted due to the inability to choose any patients as low risk. Patients over 65 years could be determined just as moderate or high risk because of age restrictions used in this model. Nevertheless, we decided not to exclude this decision aid rule from the study to show the real-life practice.

When looking at the performance in rule-in diagnostics of AMI in high-risk patients, the T-MACS score had the best results with the highest specificity (97.5%) and positive predictive value (64.3%). TIMI also has excellent specificity (95%) but with a lower positive predictive value. In contrast, ADAPT had the highest sensitivity and negative predictive value (almost 94% and 97%, respectively) with the most significant proportion of high-risk patients (63%), however with no low-risk patients - as discussed above.

It is known that age is an independent variable for the incidence of acute myocardial infarction and major adverse cardiovascular events. Age played a crucial role in the risk stratification in ADAPT protocol in this trial. Age higher than 64 years old means non-low risk score. As opposed, in the T-MACS model, age is not even evolved. Moreover, this could be one of the reasons for excellent performance on this protocol In our trial. Age above 70 years old presents 20% of total possible score points acquired in the HEART model, 14% in the TIMI protocol, 21–26% in the GRACE score (for septuagenarians and octogenarians, respectively), and the highest proportion of maximum possible points in the EDACS protocol (31–52% points according to the age).

Some trials evaluated different risk stratification protocols in diagnosing acute myocardial infarction in patients with a suspected acute coronary syndrome without apparent ST-segment elevations. A retrospective study of Sun et al. [15] compared HEART and TIMI risk scores for prediction of MACE (all-cause death, acute myocardial infarction, and urgent revascularization) in 8255 patients with suspected acute coronary syndrome presenting to nine emergency departments between years 1999–2001. They found lower sensitivity and positive predictive value for TIMI and HEART, but higher specificity compared to our results (sensitivity for TIMI 62.8% vs. 93.8%; specificity 63.8% vs. 22.77%; NPV 96.3% vs. 93.9%; PPV 10.2% vs. 22.4%; sensitivity for HEART 85.8% vs. 100%, specificity 51.2% vs. 17.33%; NPV 98.2% vs. 100%; and PPV 10.3% vs. 22.3%).

Compared with the study of Body et al. [6], we found similar results for sensitivities of T-MACS (100% vs. 99.2%) and EDACS (97.9% vs. 96.2%), we had higher sensitivity of HEART (100% vs. 91.8% in Body's trial) and lower sensitivity of TIMI score (93.8% vs. 97.5%). Our C-statistics were much lower, 0.52 vs. 0.96 for T-MACS, 0.46 vs. 0.78 for HEART, and 0.46 vs. 0.69 for TIMI. Unlike our study, Body's trial was prospective, multi-centric, included much more patients (999 pts) but of younger age (mean age 58.1 years), and evaluating just four decision aids (T-MACS, HEART, TIMI, and EDACS) and troponin-only strategy using a value 3ng/L of the high-sensitivity troponin I assay as a cut-off.

Carlton et al. [17] compared five risk scores (TIMI, HEART, GRACE, modified Goldman and Vancouver Chest Pain Rule) and two high sensitivity troponin assays in the ability to rule out myocardial infarction quickly. Almost a thousand patients with a mean age of 58 years were included. Their results were similar to ours: sensitivity for HEART score 98.7% vs. 100% in our trial; for GRACE 92.3% vs. 81.25%; for TIMI 94.9% vs. 93.8%; and 83.5% vs. 81.3% for single hs-TnT value with cut-of at 14ng/L - same as in our trial.

## Study Limitations

The first limitation of this study is its retrospective course. Data were collected from the hospital information system as described by treating physicians who were not using risk stratification protocols. However, the authors of this study personally overviewed all electrocardiograms for signs of ischemia and calculated risk scores.

Secondly, a study was conducted in single-center and included fewer patients than the trials mentioned above. This could lead to a lack of patients in low/very-low risk groups and the low specificity of studied protocols in rule-out AMI in this trial.

Finally, we evaluated a highly selected population of the elderly. Patients with high age have their specific features. It was reflected in higher comorbidity rates, fewer typical symptoms, and electrocardiographical signs of ischemia. However, there are not many global trials evaluating data about this specific group.

## Conclusions

We evaluated decision aid rules for diagnostics of acute myocardial infarction in very old patients in the emergency department with the suspected acute coronary syndrome. T-MACS decision aid had the best performance with 100% sensitivity and 100% negative predictive value for rule-out AMI, 97.5% specificity, and 64.3% positive predictive value for rule-in AMI. The HEART score was excellent in rule-out AMI (100% sensitivity and 100% NPV) but with lower specificity for ruling in AMI (83.2%). Other evaluated protocols and solo TnT strategy were less accurate. ADAPT protocol should be used with cautions for rule-out AMI in very old patients. This study proves that risk stratification of patients with suspected acute coronary syndrome based on decision rule aids can be used in real-life practice, even in the population of the elderly.

## Abbreviations

**ACS** - acute coronary syndrome; **AUC** - area under the curve; **ADAPT** - Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms; **AMI** - acute myocardial infarction; **CABG** - coronary artery bypass graft surgery; **CI** - confidence interval; **EDACS** - Emergency Department Assessment of Chest Pain Score; **ECG** - electrocardiogram; **HEART** - HEART (History, ECG, Age, Risk factors, and Troponin concentration) score; **hs-TnT** - high-sensitive Troponin T; **IQR** - interquartile range; **MACE** - major adverse cardiac events; **NPV** - negative predictive value; **LR+** - positive likelihood ratio; **LR-** negative likelihood ratio; **OR** - odds ratio; **PCI** - percutaneous coronary intervention; **PPV** - positive predictive value; **ROC** - receiver operator characteristics; **TIMI** - Thrombolysis in Myocardial Infarction risk score for unstable angina/ non-ST elevation myocardial infarction; **T-MACS** - Troponin-only Manchester Acute Coronary Syndrom Score Decision Aid Rule; **TnT** - troponin T.

## Declarations

# Ethics approval and consent to participate

This study was approved by the Ethical Committee of University Hospital Hradec Králové. All data were obtained as part of routine clinical practice, so Ethical Committee did not require informed consent. The trial was conducted following the principles of the Declaration of Helsinki.

# Consent for publication

Not applicable.

# Availability of data and materials

The datasets used for this study are available from the corresponding author by request.

# Competing interests

The authors declare no conflict of interest.


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# Authors' contributions

JH and RP invented study conception and design. JH and JD collected and analyzed data. JH, JD and RP interpreted data and critically revised the manuscript. All authors read, edited, and approved the final manuscript.


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# Figures

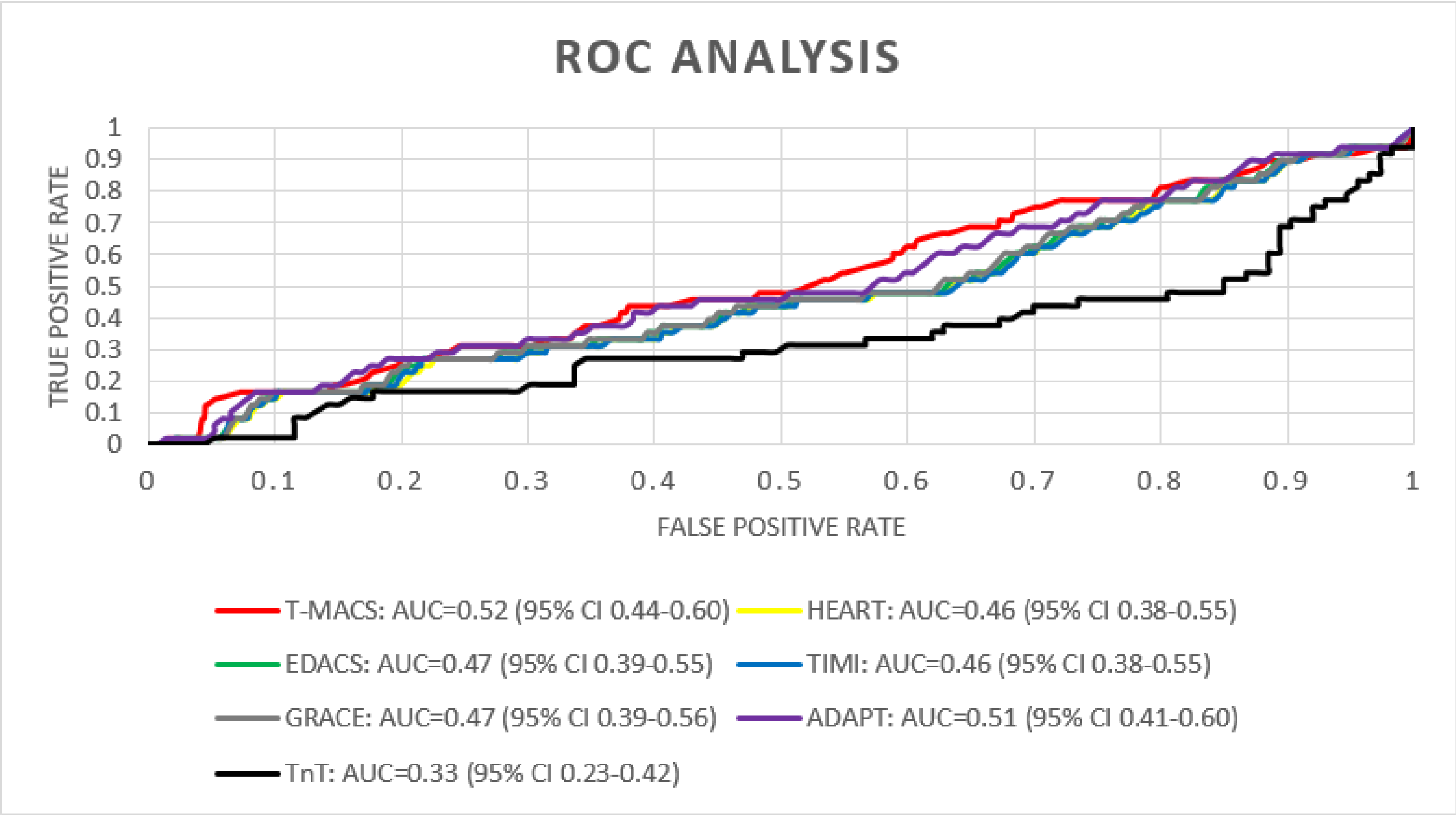


**Figure 1**

Receiver operator characteristics (ROC) analysis of studied decision aid rules for the diagnosis of acute myocardial infarction.