Assessing sensitivity and specificity of the Manchester Triage System in the evaluation of acute coronary syndrome in adult patients in emergency care: a systematic review

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EXECUTIVE SUMMARY

Background: Triage is the first assessment and sorting process used to prioritize patients arriving in the emergency department (ED). As a triage tool, the Manchester Triage System (MTS) must have a high sensitivity to minimize the occurrence of under-triage, but must not compromise specificity to avoid the occurrence of overtriage. Sensitivity and specificity of the MTS can be calculated using the frequency of appropriately assigned clinical priority levels for patients presenting to the ED. However, although there are well established criteria for the prioritization of patients with suspected acute coronary syndrome (ACS), several studies have reported difficulties when evaluating patients with this condition.

Objective: The objective of this review was to synthesize the best available evidence on assessing the sensitivity and specificity of the MTS for screening high-level priority adult patients presenting to the ED with ACS.

Method: The current review considered studies that evaluated the use of the MTS in the risk classification of adult patients in the ED. In this review, studies that investigated the priority level, as established by the MTS to screen patients under suspicion of ACS or the sensitivity and specificity of the MTS, for screening patients before the medical diagnosis of ACS were included. This review included both experimental and epidemiological study designs.

Results: The results were presented in a narrative synthesis. Six studies were appraised by the independent reviewers. All appraised studies enrolled a consecutive or random sample of patients and presented an overall moderate methodological quality, and all of them were included in this review. A total of 54,176 participants were included in the six studies. All studies were retrospective. Studies included in this review varied in content and data reporting. Only two studies reported sensitivity and specificity values or all the necessary data to calculate sensitivity and specificity. The remaining four studies presented either a sensitivity analysis or the number of true positives and false negatives. However, these four studies were conducted considering only data from patients diagnosed with ACS. Sensitivity values were relatively uniform among the studies: 0.70–0.80. A specificity of 0.59 was reported in the study including only patients with non-traumatic chest pain. On the other hand, in the study that included patients with any complaint, the specificity of MTS to screen patients with ACS was 0.97.

Conclusion: The current review demonstrates that the MTS has a moderate sensitivity to evaluate patients with ACS. This may compromise time to treatment in the ED, an important variable in the prognosis of ACS. Atypical presentation of ACS, or high specificity, may also explain the moderate sensitivity demonstrated in this review. However, because minimal data were available, it was not possible to confirm this hypothesis.

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It is difficult to determine the acceptable level of sensitivity or specificity to ensure that a certain triage system is safe.

Keywords Accuracy; acute coronary syndrome; emergency department; Manchester Triage System; sensitivity and specificity

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Summary of findings

Question: Should MTS be used to diagnose adequate prioritization in ACS suspicion in adults in ED?

Sensitivity	0.70 to 0.80		Prevalences	0.58%	9.4%						
Specificity	0.59 to 0.97										

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease quality of evidence					Effect per 100 patients tested		Test accuracy QoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Pre-test probability of 0.58%	Pre-test probability of 9.4%	
True positives (Patients prioritized by MTS and with diagnosis of ACS)	6 studies[10,11,20,29-31] 1291 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious	not serious	none	0 to 0	7 to 8	⊕⊕⊕◯ MODERATE
False negatives (Patients not prioritized by MTS and with diagnosed of ACS)								1 to 1	1 to 2	
True negatives (Patients not prioritized by MTS and without diagnosis of ACS)	2 studies[11,31] 52943 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	59 to 96	53 to 88	⊕⊕◯◯ LOW
False positives (Patients prioritized by MTS and without diagnosis of ACS)								3 to 40	3 to 38	

a. Methodological limitations across studies, particularly in terms of blinding
b. Differences between study population

Background

Triage is the first assessment and sorting process used to prioritize patients arriving in the emergency department (ED) to suitably handle patient flow. Prioritizing patients is necessary due to the considerable demand for emergency care, frequent ED overcrowding and limited available resources.[1,2] The prioritization of medical care is based on the severity of each patient, based on the concept that what is urgent is not always serious and that what is serious is not always urgent.[3]

Using inadequate or poor quality triage protocols for risk classification may have unintended consequences, including ''undertriage'' (i.e. considering the patient's priority level lower than it should be) or ''overtriage'' (i.e. considering the patient's priority level higher than it is).[4] In practice, both under-triage and over-triage represent a risk to patient safety because the classification of the patient with a priority level higher than necessary results in demand that slows the care of those patients who present with a real risk.[5] On the other hand, classification of the patient to a less-severe level than necessary can result in a waiting time for medical evaluation that is longer than what would be considered safe. In addition, because administrative decisions and quality improvement efforts are tied to triage profiles in the EDs, triage decisions need to be consistent and robust.[2] Worldwide, various triage systems with different characteristics are used in the EDs. The most used triage systems are the Australasian Triage Scale,[6] the Canadian Triage and Acuity Scale (CTAS),[7] the Manchester Triage System (MTS)[8] and the Emergency Severity Index (ESI).[9]

Manchester Triage System sensitivity and specificity

The MTS was created in the United Kingdom between 1994 and 1997 by the Manchester Triage Group. The MTS sets a time limit for attending to

Table 1: Manchester Triage System priority levels and maximum response times for medical attention

Number	Clinical priority	Color	Maximum response time (min)
1	Immediate	Red	0
2	Very urgent	Orange	10
3	Urgent	Yellow	60
4	Standard	Green	120
5	Non-urgent	Blue	240

Table adapted from Emergency Triage: Manchester Triage Group, 2014.[8]

each patient without risking the patient's health (Table 1).[8] One of the main principles of the MTS is that the higher the perceived risk to the patient's health, the shorter the waiting time for medical attention must be.[10] The MTS in clinical practice revolves around the concept of a presenting complaint – the chief sign or symptom identified by the patient. A list of 55 flowcharts associated with various complaints is available, and the clinical practitioner must choose one of them to screen the patient.[8] In each flowchart, there are discriminators that, when selected, will determine the clinical priority of the patient (Table 1).

The MTS is widely used in European countries, some Asian countries and, recently, in Brazil. The accuracy, effectiveness, validity, reliability, sensitivity and specificity of this system have been the subject of several studies.[1,11,12] However, evaluation of the MTS is not straightforward given that many variables, such as the setting, skills of the healthcare professional and population characteristics (including the types of disease and disease severity) can interfere with accuracy. Nonetheless, the sensitivity and specificity of a test are important to evaluate its performance.[13] Highly sensitive tests should be used at the beginning of the diagnostic process when a negative result may rule out some possible diagnoses.[14] As a triage test, the MTS must have a high sensitivity to minimize the occurrence of under-triage, but must not compromise specificity to avoid the occurrence of overtriage. Sensitivity and specificity of the MTS can be calculated using the frequency of appropriately assigned clinical priority levels for patients presenting to the ED.

Acute coronary syndrome triage

Many countries, irrespective of economic status, are faced with the burden of cardiovascular diseases, including ischemic heart diseases[15] such as acute coronary syndrome (ACS). Ischemic heart disease is the single greatest cause of mortality and loss of disability-adjusted life-years worldwide, especially in low- and middle-income countries.[16] According to the guideline from the American Heart Association, every patient who presents with symptoms of chest discomfort suggestive of ischemia must receive medical attention within 10 minutes.[17] However, the MTS does not use a specific flowchart for evaluating patients with suspected ACS because the MTS is based on signs and symptoms presented by the patient and not on medical diagnosis. Therefore, to adequately classify patients with such symptoms when they reach an ED, the healthcare professional applying the MTS must establish priority levels of ''red'' or ''orange'' (Table 1), regardless of the flowchart used in the evaluation. Thus, the triage of patients presenting to the ED who will eventually receive a diagnosis of ACS may follow various flowcharts according to the patient's main complaint. Therefore, the MTS should consider the presentation of both typical and atypical symptoms to efficiently screen patients with ACS. In addition, a reliable triage system should be able to detect critically ill patients to avoid complications while these patients await medical care.[18] However, although there are well established criteria for the prioritization of patients with suspected ACS, several studies have reported difficulties when evaluating patients with these conditions.[11,19,20] Thus, to assess the performance of the MTS, it is necessary to compare it to a standard procedure. As the diagnosis of ACS is clinical, using the medical diagnosis of ACS as the comparison for the MTS is the best way to evaluate the performance of the MTS.

Primary studies have addressed this issue from different perspectives[10,19-21] including evaluating the sensitivity of the MTS used by nurses to identify high-risk cardiac chest pain,[19] evaluating the MTS performance for patients with typical presentation of acute myocardial infarction (AMI)[10] or ACS,[11] and evaluating the effect of the MTS on time to first medical assessment and on time to hospital admission for patients with ACS.[20] Furthermore, a similar systematic review evaluated the efficacy of the MTS for different groups of patients (adults and children with or without specific clinical conditions) and included studies that evaluated the MTS in relation to various outcomes including validity, specificity and sensitivity.[22] However, the present review included only primary studies that investigated the performance of the MTS for a specific subpopulation – patients with ACS. Moreover, the previously published review did not critically appraise the primary studies included in the review.[22] Thus, our systematic review, which synthesizes the available evidence regarding the sensitivity and specificity of the MTS for classifying patients who will eventually be diagnosed with ACS, will contribute to improving the performance of the system. The objectives, inclusion criteria and analytical methods for this review have been specified in an *a priori* published protocol.[23]

Objectives

The objective of this review was to synthesize the best available evidence assessing the sensitivity and specificity of the MTS for screening high-level priority adult patients presenting to the ED with ACS.

Inclusion criteria

Types of participants

The current review considered studies that included adult patients (aged >18 years) who sought emergency care for any complaint and whose MTS evaluation was conducted under suspicion of ACS. Studies involving children (aged ≤18 years) were excluded because ACS generally affects the adult population, and the incidence is highly related to risk factors such as age, sex, smoking, hypertension and diabetes.[24,25]

Index test

The current review considered studies that evaluated the use of the MTS (without modifications) by nurses or doctors in the risk classification of patients, aiming at the correct prioritization of patients with ACS.

Reference test

The reference test used was the clinical diagnosis of ACS performed by the doctor, since the medical diagnosis of ACS in clinical practice is performed considering not only one test, but a clinical evaluation that includes factors such as clinical history, physical examination, ECG findings and troponin dosage.

Diagnosis of interest

The diagnosis of interest considered was the correct priority established by the MTS for patients with ACS.

The current review considered studies that included the following data:

- The priority level, as established by the MTS to screen patients under suspicion of ACS.
- The sensitivity or specificity of the MTS for screening patients before the medical diagnosis of ACS.

In this review, the MTS was considered a test; the test was deemed ''positive'' when the classification of patients was ''red'' or ''orange''. The sensitivity of the MTS was determined by assessing the MTS classification in diagnosed cases of ACS (true positives [TPs] and false negatives [FNs]), while the specificity of the MTS was determined by assessing the MTS classification in cases without an ACS diagnosis (true negatives [TNs] and false positives [FPs]).

Types of studies

The current review included both experimental and epidemiological study designs, including randomized controlled trials, quasi-experimental studies, before-and-after studies, prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies.[26]

Search strategy

The search strategy aimed to find both published and unpublished studies. A three-step search strategy

was utilized in this review. An initial limited search of MEDLINE and CINAHL was undertaken, followed by an analysis of the words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms was then undertaken across all included databases. Third, the reference list of all identified reports and articles was searched for additional studies. Studies published after 1994 (the year when the MTS was created)[8] in all languages were considered for inclusion in this review.

The databases searched included MEDLINE, CINAHL, Web of Science, Embase, Scopus, LILACS, Bandolier, Clinical Evidence, Science Direct, IBECS, ProQuest Dissertation and Theses and the Cochrane Central Register of Control Trials. The search for unpublished studies was conducted in Google Scholar, Banco de Teses – CAPES and Digital Dissertations. The search strategy is detailed in Appendix I. The initial keywords used were ACS, myocardial infarction, triage system, severity index, Manchester Triage System, sensitivity and specificity.

Assessment of methodological quality

Papers selected for retrieval were assessed for methodological validity by two independent reviewers prior to inclusion in the review using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Diagnostic Test Accuracy Studies.[23] Any disagreements between reviewers were resolved through discussion. Although we planned to include both randomized and non-randomized studies in this review,[23] when the critical appraisal of the studies was conducted, the reviewers decided to include only studies that had been conducted specifically with randomized or consecutive samples. This decision was made to avoid bias related to sample selection, which usually leads to overestimation of test accuracy.[13] Thus, for a study to be included in this review, the first question of the critical appraisal tool (Was a consecutive or random sample of patients enrolled?) had to be fulfilled (i.e. score a ''yes''). Furthermore, question 5 of the critical appraisal (If a threshold was used, was it pre-specified?) was considered not applicable because the MTS is a closed protocol and, therefore, does not permit changes to the threshold. The methodological quality of the included studies in this review was established using nine questions from the JBI appraisal tool. The number of positive answers determined the quality of the study (0–4: low quality, 5–7: moderate quality and 8–9: high quality). Only moderate- or high-quality studies were included.

Data extraction

Data were extracted from papers included in the review using the JBI standardized data extraction tool for accuracy of diagnostic test studies.[23] In addition to sensitivity and specificity data, the sample size; participant demographic characteristics; setting; geographic location; study methodology; main aims; main results and the number of TPs, FNs, FPs and TNs were extracted from the papers.

Data synthesis

The TP, FP, TN and FN values were extracted directly from the papers, while sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios (LR+ and LR−, respectively) and 95% confidence intervals (CIs) were calculated from the extracted data.[13,14] Data are displayed using a forest plot and tables summarizing the characteristics and findings of the studies. Review Manager (RevMan) Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014[27] was used for the statistical analysis. Results of this review are presented as a narrative synthesis as well as in tables and graphs to show important primary data and derived values.

Results

Study inclusion

Using the search strategy detailed in Appendix I, 16 potentially relevant records were identified and assessed for eligibility. Ten studies were excluded from the review after full-text retrieval (eight did not meet the inclusion criteria, and two were conference abstracts with full texts published under different titles that were already among the included studies). Finally, six studies were selected and included in the systematic review narrative synthesis after critical appraisal conducted by the reviewers. The PRISMA flowchart[28] (Figure 1) details the study selection and inclusion process.

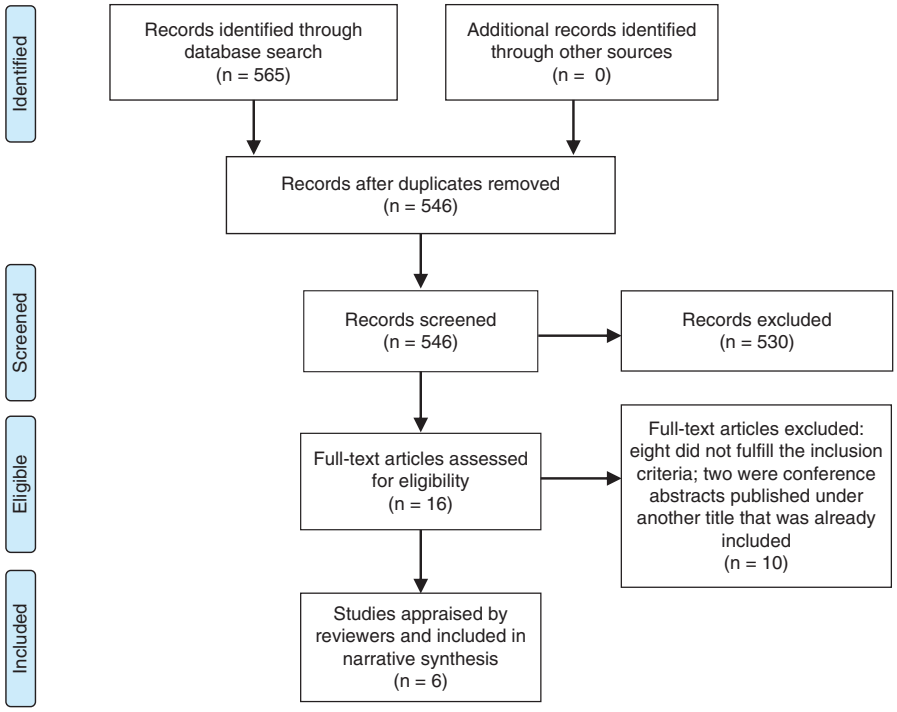


Figure 1: Flowchart of the study selection and inclusion process[26]

Methodological quality of the included studies

The six studies[10,11,20,29-31] were appraised by the independent reviewers. All appraised studies enrolled a consecutive or random sample of patients (Table 2, Q1) and presented an overall moderate methodological quality. Results of the methodological quality evaluation are presented in Table 2.

Table 2: Assessment of methodological quality of the included studies using the JBI critical appraisal checklist for diagnostic test accuracy studies[13]

Study		Critical appraisal										
		Y (yes); N (no); U (unclear); NA (not applicable)										Total "Yes"
Reference	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	
Trigo *et al.*[29]	2008	Y	Y	Y	U	NA	Y	U	Y	Y	Y	7
Matias *et al.*[20]	2008	Y	Y	N	U	NA	Y	U	Y	Y	Y	6
Pinto *et al.*[11]	2010	Y	Y	Y	U	NA	Y	U	U	Y	Y	6
Providência *et al.*[10]	2010	Y	Y	N	U	NA	Y	U	Y	Y	Y	6
Gouvêa *et al.*[30]	2015	Y	Y	Y	U	NA	Y	U	Y	Y	U	6
Leite *et al.*[31]	2015	Y	Y	Y	U	NA	Y	U	U	Y	Y	6

Questions in the critical appraisal tool[13]: Q1 – Was a consecutive or random sample of patients enrolled? Q2 – Was a case-control design avoided? Q3 – Did the study avoid inappropriate exclusion? Q4 – Were the index test results interpreted without knowledge of the results of the reference standard? Q5 – If the threshold was used, was it pre-specified? Q6 – Is the reference standard likely correctly classify the target condition? Q7 – Were the reference standard results interpreted without knowledge of the results of the index test? Q8 – Was there an appropriate interval between the index test and the reference standard? Q9 – Did all patients receive the same reference standard? Q10 – Were all patients included in the analysis?

Issues about blinding were not reported in any study (Table 2 – Q4 and Q7). Two studies made inappropriate exclusions. In both cases, patients admitted to the ED transported by a "medical emergency and resuscitation vehicle" were excluded from the study.[10,20] These patients probably presented with evident high severity; hence, exclusion may have resulted in under-estimation of the performance of the MTS.

Description of studies

A total of 54,176 participants were included in the six studies. All studies were retrospective and were conducted from consecutive samples. Five studies were conducted in hospitals in Portugal[10,11,20,29,31] and one in Brazil.[30] The included studies were conducted in different settings with different characteristics; in all studies, the MTS was applied by nurses. Age, sex, comorbidities, symptoms, medical diagnosis, the MTS flowchart used, the final MTS classification, outcomes and waiting times were analyzed by all studies. Various analyses were conducted from these data. One study that included patients <18 years[11] was included in this review. This deviation from the protocol[23] was accepted because the proportion of the participants aged between 13 and 20 years was small (8.9%; $n = 4741$), and the study included a large sample size (53,039 participants) (Table 3).

Table 3: Data extracted from the included studies

Reference	Setting	Study design	Population	Outcome measures/analysis	Results
Trigo *et al.*[29]	Coronary care unit (Faro Hospital)	Retrospective, analytical cross-sectional study with a consecutive sample	Sample size: $N = 278$ Age: 68 ± 14 years Gender: male = 65.7%; female = 34.3% Inclusion criteria: patients with STEMI admitted to the coronary care unit through the ED	Outcome measures: Clinical variables (risk factors, cardiovascular history and chest pain) Prehospital delay In-hospital delay Percentage of patients who underwent reperfusion therapy MTS classification Analysis: Comparison of categorical variables between group A (triaged as red or orange) and group B (triaged as yellow, green or blue)	There were no significant differences in demographic variables between the groups The majority ($n = 220$, 79%) of patients were classified as red or orange, while 58 (21%) were classified as yellow, green or blue MTS classification influenced the in-hospital delay (Group A median: 1 h 19 min vs Group B median: 2 h 10 min; $P = 0.004$) MTS classification influenced the door-to-balloon time. Median in Group A ($n = 91$) was 1 h 26 min, significantly shorter than in Group B ($n = 24$), in which it was 2 h 15 min ($P = 0.017$)
Matias *et al.*[20]	Cardiology department (Reynaldo dos Santos Hospital)	Retrospective, analytical cross-sectional study with a consecutive sample	Sample size: $N = 103$ Age: 64.3 ± 1.2 years Gender: Male = 66%; Female = 44% Inclusion criteria: patients admitted to the cardiology department with ACS	Outcome measures: Type of ACS MTS classification Time between arrival in ED and triage Time between triage and first medical assessment Time to admission ACS presentation (typical or atypical) Analysis: Relationship between MTS classification and time to first medical assessment, type of ACS and ACS presentation (typical or atypical)	Most patients admitted with ACS were screened as red (0.9%), orange (62.3%) or yellow (17%). Nevertheless, a significant proportion of patients were classified as low-level priority (11%). The MTS was associated with the time to first medical assessment but not with the time to admission Clinical presentation was associated with MTS classification (patients with typical presentation were evaluated and admitted quickly)

Table 3. (*Continued*)

Reference	Setting	Study design	Population	Outcome measures/analysis	Results
Pinto *et al.*[11]	Emergency department (São João Hospital)	Retrospective, analytical cross-sectional study with a pseudo-randomized sample	Sample size: *N* = 53,039 Age: 30.9% over 60 years Gender: male = 47.7%; female = 52.3% Inclusion criteria: patients ≥13 years admitted to the ED with any symptom	Outcome measures: Sensitivity and specificity of the MTS for patients with ACS MTS classification ACS presentation (typical or atypical) Positive and negative predictive values LR+ and LR− Analysis: Sensitivity of MTS for patients with ACS (overall and stratified by gender, age, type of ACS, month of the year and time of arrival to the ED) Comparison of the sensitivity in assigning a high priority between groups	The MTS had a high sensitivity (87.3%) for the triage of patients with ACS. The combinations of flowcharts and discriminators suggestive of ACS have high specificity and moderate sensitivity The sensitivity of the MTS for patients with ACS varied according to the symptoms present The LR+ of combinations of flowcharts and discriminators suggestive of ACS was 28.3, while that of other combinations was 0.26
Providência *et al.*[10]	ED (Coimbra's Hospital Center)	Retrospective, analytical cross-sectional study with a consecutive sample	Sample size: *N* = 332 Age: 69.0 ± 13.6 years Gender: male = 65.1%; female = 34.9% Inclusion criteria: patients with AMI admitted to the ED	Outcome measures: Demographic characteristics indicating risk for AMI MTS classification Several AMI parameters Number of days in hospital Intra-hospital mortality Time to first observation Analysis: MTS performance in the subgroups according to MTS priority and selected variables Correlation between the MTS priority and mortality as well as time to first observation	Younger patients and patients with STEMI seemed to be protected by the MTS Triage was performed applying the chest pain flowchart in 72% of patients with AMI. A majority (76.5%) of patients with AMI were classified into an adequate priority level Time to first observation was reduced in patients with a typical AMI presentation and patients aged ≥70 years
Gouvêa *et al.*[30]	ED (a cardiology hospital in Joinville)	Retrospective, analytical cross-sectional study with a consecutive sample	Sample size: *N* = 191 Age: 59.1 ± 11.92 years Gender: male = 65%; female = 35% Inclusion criteria: patients ≥18 years admitted to the ED with ACS	Outcome measures: Health history Symptoms on admission Type of ACS MTS classification Clinical outcomes Time to medical care Time to admission Time to ECG Length of stay Analysis: Correlation between the MTS priority and selected variables	The MTS correctly classified 83.8% of patients with ACS Waiting times exceeded the recommended times All patients who died during the hospital stay ($n = 7$) were classified as red or orange
Leite *et al.*[31]	ED (a tertiary hospital)	Retrospective cohort study with a consecutive sample	Sample size: *N* = 233 Age: 58 ± 19 years Gender: male = 55.4%; female = 44.6% Inclusion criteria: patients admitted to the ED with non-traumatic chest pain	Outcome measures: Demographic characteristics indicating risk for AMI Mortality HEART score All-cause mortality, AMI and unscheduled revascularization in a 6-week follow-up period Analysis: Correlation between MTS classification in chest pain patients and ACS diagnosis Multivariate analysis to establish ACS-predictive factors	According to the MTS, chest pain patients with a red or orange priority had a higher incidence of ACS (16.5 vs. 3.8%, $P = 0.006$) The HEART score seems to be a useful tool for risk stratification in acute chest pain patients

ACS, acute coronary syndrome; AMI, acute myocardial infarction; ECG, electrocardiogram; ED, emergency department; HEART, specific score whose acronym stands for the parameters evaluated to determine the score (history: ECG: age: risk factors and troponin); LR−, negative likelihood ratio; LR+, positive likelihood ratio; MTS, Manchester Triage System; STEMI, ST elevation myocardial infarction.

Studies included in this review varied in content and data reporting. Only two[11,31] reported sensitivity and specificity values or all the necessary data to calculate sensitivity and specificity. The remaining four studies presented either a sensitivity analysis or the number of TPs and FNs.[10,20,29,30] However, these four studies were conducted considering only data from patients diagnosed with ACS; therefore, FP and TN values were not computed, and it was not possible to calculate specificity. A large difference in specificity was found between the two studies reporting sensitivity and specificity data[11,31] (Figure 2). This difference is directly related to the different inclusion criteria used in these studies.[32] While one study included participants with any complaint,[11] the other included only patients with non-traumatic chest pain.[31] The different characteristics among the participants in the two studies cited reflect an important inter-study variation.[33] The data extracted from the studies (setting, main results, participants characteristics and main results) are presented in Table 3.

Sensitivity and specificity

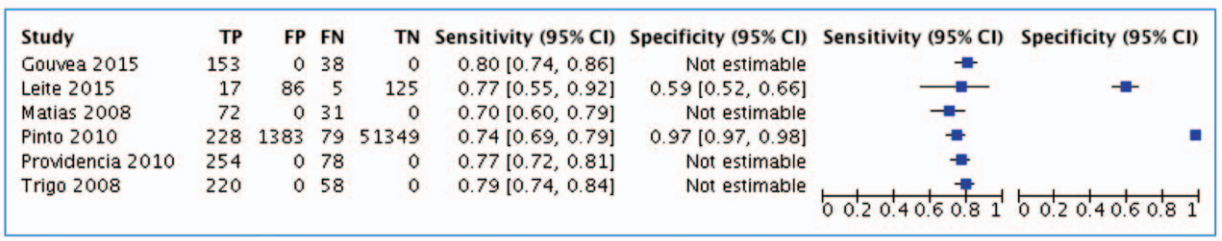
Calculated sensitivity and specificity values of the MTS for evaluating patients with ACS are shown in Figure 2. Sensitivity values were relatively uniform among the studies (0.70–0.80; Figure 2). However, only half of the studies had a CI lower limit that was higher than 0.70,[10,29,30] and only one had a CI upper limit greater than 0.90.[31] However, this study also had a very large CI, reducing its weight.

These results suggest that 70–80% of cases of ACS were evaluated as red (emergency) or orange (very urgent). Consequently, 20–30% of patients with ACS were evaluated and assigned less-than-adequate severity levels, compromising the safety of patients waiting for medical care in the ED. In addition, the two studies including patients screened by the MTS who did not have ACS found very different specificity values. A specificity of 0.59 was reported in the study including only patients with non-traumatic chest pain,[31] indicating that 59% of patients without ACS were evaluated as yellow (urgent), green (standard) or blue (non-urgent). On the other hand, in the study that included patients with any complaint, the specificity of MTS to screen patients with ACS was 0.97,[11] indicating that 97% of patients without ACS were correctly screened.

Predictive values and likelihood ratios

Considering the characteristics and application of the MTS, it was important to analyze its predictive values and examine the proportion of patients correctly triaged.[32] Thus, predictive values and LRs were calculated for all studies that reported the necessary data (i.e. TPs, FPs, TNs and FNs)[11,31] (Table 4). The negative predictive value represents the proportion of individuals screened as yellow, green or blue (negative triage) who really did not have ACS. This value was 0.96[31] in one study and 0.99 in another study,[11] meaning that 96–99% of patients were correctly screened as patients without ACS. These data show that the MTS was a safe protocol for evaluating patients with ACS, given that the proportion of patients classified as yellow, green or blue presenting without ACS was high. The positive predictive values were 0.14[11] and 0.16,[31] showing that 14–16% of patients who had a positive screening (red or orange) actually had ACS.

The LRs represent how much more likely a subject with ACS is to have a positive test result compared to a subject without ACS;[34] in other words, it



FN: false negative; FP: false positive; TN: true negative; TP: true positive. The zero value on the graph indicates the absence of data on the primary study.

Figure 2: Paired forest plot of the MTS sensitivity and specificity values among patients with ACS in the ED

Table 4: TPs, FNs, FPs, TNs and accuracy data calculated from the data provided in included studies

Reference	Participants	TP	FN	FP	TN	Sensitivity (95% CI)	Specificity (95% CI)	Prevalence	LR+ (95% CI)	LR− (95% CI)	PPV (95% CI)	NPV (95% CI)
Trigo *et al.*[29]	278	220	58	–	–	0.79 (0.74–0.84)	–	–	–	–	–	–
Matias *et al.*[20]	103	72	31	–	–	0.70 (0.60–0.79)	–	–	–	–	–	–
Pinto *et al.*[11]	53,039	228	79	1383	51,349	0.74 (0.69–0.79)	0.97 (0.97–0.98)	0.58%	28.31 (26.03–30.79)	0.26 (0.22–0.32)	0.14 (0.12–0.16)	0.99 (0.99–0.99)
Providência *et al.*[10]	332	254	78	–	–	0.76 (0.72–0.81)	–	–	–	–	–	–
Gouvêa *et al.*[30]	191	153	38	–	–	0.80 (0.74–0.86)	–	–	–	–	–	–
Leite *et al.*[31]	233	17	5	86	125	0.77 (0.55–0.92)	0.59 (0.52–0.66)	9.4%	1.89 (1.43–2.50)	0.38 (0.18–0.83)	0.16 (0.10–0.25)	0.96 (0.91–0.98)

CI, confidence interval; FN, false negative; FP, false positive; LR−, negative likelihood ratio; LR+, positive likelihood ratio; NPV negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

represents the probability of a particular result in someone with ACS and the probability of the same result in someone without ACS.[13] In the study by Pinto *et al.*[11] (population with any complaint), the LR+ was 28.31 (95% CI, 26.03–30.79). On the other hand, in the study by Leite *et al.*[31] (only patients with non-traumatic chest pain), the LR+ was 1.89 (95% CI, 1.43–2.50). The LR− values of the two studies that evaluated the specificity were 0.26[11] and 0.38[31] (Table 4).

Discussion

The sensitivity data for the MTS reported in this review are congruent with other triage systems with five priority levels. For example, a previous study showed that the ESI had a sensitivity of 75% for patients with any medical diagnosis using the two higher priority levels (and an average of 68% using all priority levels).[35] On the other hand, one Swedish study, conducted with fictional cases based on real scenarios, reported that the sensitivity of the CTAS was 57.7% for patients with any complaint for all priority levels,[36] indicating that the MTS showed better sensitivity values than the CTAS. However, comparisons between the performance of the MTS and other triage systems for screening patients with ACS were not possible in the present analysis because of a lack of studies evaluating other triage systems.

The specificity values reported in the studies included in this review were 0.59 and 0.97,[11,31] meaning that 59–97% of patients who were screened as yellow, green or blue did not, in fact, have ACS. However, it is necessary to be cautious when interpreting the specificity values presented in the forest plot (Figure 2), since only two studies[11,31] reported specificity data or data that permitted the calculation of the specificity. Of these two studies, one[31] was conducted with a much smaller sample and presented lower specificity values than the other,[11] which had a larger sample and a very small CI (95% CI, 0.97–0.98). The difference in sensitivity estimates may be explained by differences in the populations of these studies. A study by Leite *et al.*[31] (i.e. with lower specificity values) investigated only patients admitted to the ED with non-traumatic chest pain, while the study by Pinto *et al.*[11] included patients with any symptom. The MTS feature is not geared only for the evaluation of patients with suspected ACS; therefore, the classification of patients with any complaint will also include patients with symptoms obviously unrelated to ACS, increasing the specificity of MTS for the evaluation of patients with ACS compared with the evaluation of patients whose main complaint is chest pain. Hence, to interpret these results, it is important consider that it is difficult to distinguish patients without ACS among those with chest pain, especially considering that chest pain is a symptom typically reported by patients with ACS. The population differences may also explain the contrast in the calculated prevalence of ACS in these studies[11,31] (Table 4). The specificity among groups with no special conditions has also been investigated.[37] For example, Storm-Versloot *et al.*[37] found that the specificity values for the ESI were 100% and 95% for the two higher priority levels, respectively. In addition, another study reported 100 and 97% specificity for the two higher priority levels, respectively, using the ESI with an average specificity of 91% (95% CI, 88–94%) for all priority levels.[35]

Therefore, these values may also be useful for comparing and evaluating the performance of the MTS in discriminating patients who have ACS from those who do not. Ideally, the performance of a test must have high sensitivity and high specificity; however, these variables are inter-dependent, meaning that it is possible to increase sensitivity by reducing specificity and vice versa. A triage test is expected to have high sensitivity values.[14,34] However, this review showed that the MTS did not meet this criterion; it had a high specificity and a moderate sensitivity when evaluating patients with ACS from general ED population. This may compromise the main purpose of the triage test, which is to detect the most severe patients and thus prioritize the medical care of these patients. These results are supported by a previous systematic review investigating the validity and the reliability of the MTS,[1] which concluded that the MTS might be unsafe because of the high rate of under-triage. In particular, the study showed that the MTS had a low sensitivity for screening high-priority levels.[1]

However, to establish the safety of MTS in the evaluation of patients with ACS, it should also consider the predictive values, particularly the NPV, reported as 0.96 and 0.99 in the studies included in this review.[10,31] These values suggest that MTS is a safe protocol for evaluating patients with ACS, given the high proportion of patients classified as lower severity (yellow, green or blue) who did not have ACS. Furthermore, one study that included only patients with the diagnosis of AMI found that the mortality rate using the MTS was 35.7% in the standard category, 15.9% in the urgent, 10.3% in the very urgent and 54.5% in the immediate category.[10] These results suggest that the mortality might be related to the severity and also with under-triage.

Limitations of the review

The current study has some limitations, one being the fact that we included one study with patients <18 years despite the pre-established protocol[23] stating otherwise. Furthermore, using a medical diagnosis (i.e. ACS) as the index test to compare the MTS performance is not ideal because this test is also imprecise.[38,39] However, no other gold standard is available for comparison.[35,40] The heterogeneity observed between the populations of the two studies with specificity data[11,31] as well as the lack of specificity data in the remaining four studies[10,20,29,30] made it impractical to conduct a meta-analysis or construct a receiver operating characteristic curve to assess the balance between the sensitivity and specificity of the MTS for evaluating patients with ACS. Furthermore, conducting a meta-analysis could not produce a consistent pooled estimate.[33]

Implications for practice and research

The results of the present review should be considered when using the MTS in an ED given its moderate sensitivity for screening patients with ACS. Ways to improve the performance of MTS, particularly its sensitivity, should be discussed and evaluated. For example, changing the chest pain flowchart,[11] implementing institutional protocols (electrocardiogram or laboratory tests, such as troponin)[41] and investigating information related to cardiovascular disease risk factors during triage may improve patient and professional safety. Although other triage systems have not shown satisfactory results with severely ill patients,[1] implementation of the MTS in cardiology hospitals, hospitals where patients with chest pain may present, needs to be carefully evaluated.

JBI grades of recommendation

Because this is a systematic review based on evidence of low and moderate quality (see the ''Summary of findings'' section) and does not seem to consider the preferences of the patients, the grade of recommendation for the use of MTS in the evaluation of adult patients from the perspective of the diagnosis of ACS is weak.

JBI grade of recommendation: Grade B.

Assessing confidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessing confidence in the quality of evidence was used for this review, and the results were presented in a summary of findings (see the ''Summary of findings'' section) created using GRADEPro.[42]

Conclusion

Because of the limited number of studies examining only patients with ACS, there was limited data on TN and FP values. Thus, it was not possible to assess the specificity of the MTS or establish its accuracy. However, this review demonstrates that the MTS has

a moderate sensitivity to evaluate patients with ACS. This may compromise time to treatment in the ED, an important variable in the prognosis of ACS, and thus patient safety.[17] Atypical presentation of ACS, or high specificity, may also explain the moderate sensitivity demonstrated in this review. However, because of minimal data it is not possible to confirm this hypothesis. It is difficult to determine the acceptable level of sensitivity or specificity to ensure that a certain triage system is safe. For example, to reach a high sensitivity, the specificity may be very low, and, although this does not impair patient safety, it may strain resources.[37] Therefore, ways to improve the sensitivity of the MTS for ACS patients, such as changes to protocols or application of the MTS, should be discussed. It is also noteworthy that ACS, an important reason for ED presentation due to its frequency and potential severity, may not be detected as expected, despite widespread use of a triage protocol.

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Appendix I: Search strategy

PubMed (pubmed.gov), searched on January 28, 2016

((((((((((((''acute coronary syndrome''[MeSH Terms] OR ''acute coronary syndrome$''[Title/Abstract]) OR ''myocardial infarction''[MeSH Terms]) OR ''myocardial infarction$''[Title/Abstract]) OR ''cardiovascular stroke$''[Title/Abstract]) OR ''myocardial infarct$''[Title/Abstract]) OR ''infarct$, myocardial''[All Fields]) OR ''chest pain''[MeSH Terms]) OR ''chest pain''[Title/Abstract]) OR ''pain, chest''[Title/Abstract]) OR ''angina pectoris''[MeSH Terms]) OR ''angina pectoris''[Title/Abstract]) OR ''stenocardia$''[Title/Abstract]) OR ''angor pectoris''[Title/Abstract]) OR ''heart attack''[Title/Abstract]) AND ((''manchester triage''[Title/Abstract] OR ''manchester protocol''[Title/Abstract]) OR ''manchester triage system''[Title/Abstract])

CINAHL (ebscohost.com), searched on January 28, 2016

((MH ''acute coronary syndrome'' OR TI ''acute coronary syndrome$'' OR AB ''acute coronary syndrome$'' OR MH ''myocardial infarction'' OR TI ''myocardial infarction$'' OR AB ''myocardial infarction$'' OR MH ''chest pain'' OR TI ''chest pain'' OR AB ''chest pain'' OR MH ''angina pectoris'' OR TI ''angina pectoris'' OR AB ''angina pectoris'' OR TI ''heart attack'' OR AB ''heart attack'') AND (TI ''manchester triage'' OR AB ''manchester triage'' OR TI ''manchester protocol'' OR AB ''manchester protocol'' OR TI ''manchester triage system'' OR AB ''manchester triage system'' OR TI ''manchester risk classification'' OR AB ''manchester risk classification''))

Web of Science (webofknowledge.com), searched on February 28, 2016

Topic:((''acute coronary syndrome$'') OR Topic: (''myocardial infarction$'') OR Topic: (''chest pain'') OR Topic: (''angina pectoris'') OR Topic: (''heart attack'') AND (Topic: (''manchester triage'') OR Topic: (''manchester protocol'') OR Topic: (''manchester triage system'') OR Topic: (''manchester risk classification''))

Scopus (scopus.com), searched on November 15, 2015

((TITLE-ABS-KEY (''heart attack'') OR TITLE-ABS-KEY (''acute coronary syndrome$'') OR TITLE-ABS-KEY (''myocardial infarction$'') OR TITLE-ABS-KEY (''chest pain'') OR TITLE-ABS-KEY (''angina pectoris'')) AND ((TITLE-ABS-KEY (''manchester triage'') OR TITLE-ABS-KEY (''manchester protocol'') OR TITLE-ABS-KEY (''manchester triage system'') OR TITLE-ABS-KEY (''manchester risk classification'')))

Cochrane Central Register of Control Trials (cochranelibrary.com), searched on January 28, 2016

((''acute coronary syndrome'':ti,ab,kw (Word variations have been searched) OR ''acute coronary syndrome'' OR ''myocardial infarction'':ti,ab,kw (Word variations have been searched) OR ''myocardial infarction'' OR ''chest pain'':ti,ab,kw (Word variations have been searched) OR ''chest pain'' OR ''angina pectoris'':ti,ab,kw (Word variations have been searched) OR ''angina pectoris'' OR ''heart attack'':ti,ab,kw (Word variations have been searched)) AND (''manchester triage'':ti,ab,kw (Word variations have been searched) OR ''manchester protocol'':ti,ab,kw (Word variations have been searched) OR ''manchester triage system'':ti,ab,kw (Word variations have been searched) OR ''manchester risk classification'':ti,ab,kw (Word variations have been searched)))

Embase (embase.com), searched on January 28, 2016

((''acute coronary syndrome''/exp OR ''heart infarction''/exp OR ''acute heart infarction''/exp OR ''thorax pain''/exp OR ''angina pectoris''/exp OR ''myocardial infarction'' OR ''chest pain'' OR ''heart attack''/exp) AND (''manchester triage'' OR ''manchester protocol'' OR ''manchester triage system'' OR ''manchester risk classification''))

Bandolier (medicine.ox.ac.uk), searched on January 28, 2016
((''acute coronary syndrome'' OR ''myocardial infarction'' OR ''chest pain'' OR ''angina pectoris'' OR ''heart attack'') AND (''manchester triage'' OR ''manchester protocol'' OR ''manchester triage system'' OR ''manchester risk classification''))

Science Direct (sciencedirect.com), searched on January 28, 2016
((''acute coronary syndrome'' OR ''myocardial infarction'' OR ''chest pain'' OR ''angina pectoris'' OR ''heart attack'') AND (''manchester triage'' OR ''manchester protocol'' OR ''manchester triage system'' OR ''manchester risk classification'')) – All fields

BMJ Clinical Evidence (bmj.com), searched on November 15, 2015
Free strategy

IBECS (bases.bireme.br), searched on January 28, 2016

Banco de teses USP (teses.usp.br), searched on January 28, 2016

Google Scholar (scholar.google.com), searched on January 28, 2016
((''acute coronary syndrome'' OR ''myocardial infarction'' OR ''chest pain'' OR ''angina pectoris'' OR ''heart attack'') AND (''manchester triage'' OR ''manchester protocol'' OR ''manchester triage system'' OR ''manchester risk classification''))

