BRIEF REPORT

Effectiveness to identify acute myocardial infarction using the Manchester screening in patients with chest pain at the emergency service

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Background: Among cardiovascular diseases (CVD), acute coronary syndrome (ACS) is the main manifestation, corresponding to signs and symptoms that occur with ischemia and outcome of angina or acute myocardial infarction (AMI). The aim of this study was to investigate the performance of biochemical markers eligible in a chest pain protocol, using Point of care Test (POCT), in patients in a reference emergency room.

Methods: In this study, 1380 medical records of patients of both genders were evaluated, ranked by applying chest pain protocol using the Manchester Triage System (MTS). Markers for myocardial injury were measured in serial analysis including myoglobin (Mgb), creatine kinase MB fraction mass (CK-MB), and cardiac troponin I (cTnI).

Results: Acute myocardial infarction was predominant in males ($P < .001$), in patients with hypertension ($P < .001$), and in those with previous myocardial infarction ($P < .026$) and significant electrocardiogram (ECG) data for AMI screening ($P < .001$). A multivariate regression model showed as predictors for AMI the variables ECG data by admittance at the emergency room, previous AMI history, levels of both Mgb at the third hour, and cTnI at the sixth hour after admission.

Conclusion: This study showed the importance of a rapid and serial test as a cardiac marker for AMI screening, as well as has indicated the importance of time between the onset of chest pain and admission to the emergency room as an efficient aid in diagnosing this life-threatening disease.

KEYWORDS

acute myocardial infarction, cardiac troponin I, creatine kinase MB mass, Manchester Triage System, myoglobin

1 | INTRODUCTION

Acute myocardial infarction (AMI) is the most common event among cardiovascular diseases. In Brazil, AMI is the main cause of mortality.¹ Among other risk factors, in addition to genetic predisposition, are smoking, dyslipidemia, diabetes mellitus, and lifestyles, that is, anxiety, stress, diet rich in animal fat, and sedentary lifestyle.² AMI is considered a public health problem, and many individuals are not diagnosed

correctly and or not treated properly, thus increasing the risk of acute coronary syndrome (ACS).³ Patients evaluation with chest pain (CP) or other symptoms that suggest myocardial ischemia remains a major challenge for health professionals at the emergency services.

The cardiac troponins are proteins involved in myocardial contraction and exhibit high specificity to cardiac damage.⁴ Troponins are used as tissue necrosis markers and redefinition of criteria for AMI diagnosis. A major challenge for manufacturers has been the

development of rapid, safe, and sustainable cost markers that do not require very complex technologies and easy-to-interpret. For AMI cases in which the ECG is not conclusive, markers of cardiac injury contribute to the inclusion diagnosis.⁴ Classification risk is a tool used in service room in several countries to ensure agility to take care people at high risk of death. Among the different classification systems already applied for AMI risk classification, the Manchester Triage System (MTS)⁵ is one of the most widely used. In this context, the objective of this study was to investigate the impact of implementing a rapid Point of care Test (POCT) in patients presenting chest pain admitted to the emergency room of a cardiologic hospital whose AMI classification risk was performed according to the MTS.

2 | MATERIAL AND METHODS

This study was conducted by investigating medical records of 1380 adult patients over 18 years old who presented CP classified according to the MTS protocol. These patients were attended at Madre Teresa Hospital emergency room in Belo Horizonte, Brazil, from January 2013 to March 2014. This study was approved by both Ethics Committees of the Federal University of Minas Gerais and Hospital Madre Teresa. Cases suggesting sepsis and other cardiovascular diseases, such as pulmonary thromboembolism, congestive heart failure were not included for evaluation of myocardial necrosis markers in this study. In the first hour of emergency care, some patients were redirected to other clinical care once it was ruled out that CP was associated with cardiovascular etiology.

2.1 | Manchester triage system protocol

Manchester Triage System color scale is used to classify the severity of attendance, that is, red (emergency: immediate clinical attention); orange (very urgent: evaluation within 10 minutes); green

(not urgent: within 120 minutes); and blue (less urgent: within 240 minutes).

2.2 | Laboratory evaluation

Patients admitted with CP and suspected of AMI were submitted to conventional ECG. They were also assessed using POCT including troponin I (cTnI), creatine kinase MB fraction mass (CK-MB), and mioglobina (Mgb) after the admission at the emergency room at the first (1h), third (3h), and sixth (6h) hours. Blood samples were collected in EDTA, and the dosages were obtained through immunofluorometric assay (Triage Meter Pro equipment-Alere®). Data were analyzed by comparing the groups of patients according to the outcome, that is, acute myocardial infarction presence ("AMI") or not ("NO AMI"). Figure 1 illustrates the study design as shown below.

2.3 | Statistical analysis

Univariate logistic regression analysis was performed for each variable in order to identify those related to AMI outcome. Variables with *P*-value lower than .20 were considered for the multivariate logistic regression model. Only variables independently associated with AIM were kept, with a *P* < .05. Efficiency measures of tests for AMI diagnosis were also calculated for each laboratorial marker such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The receiver operating characteristic (ROC) curve was performed for quantitative laboratory markers Mgb (3h) and cTnI (6h). Statistical analysis was performed using SPSS version 22.0 program.

3 | RESULTS

From the 1380 patients screened for CP, 274 (19.8%) had ACS, of which 107 (7.8%) had AMI and 167 (12.1%) had unstable angina.

FIGURE 1 The Flow Diagram explains the study design mentioning eligible patients taken at the beginning and so the outcome patients suffering from AMI or NO AMI. AMI, acute myocardial infarction, PTE, pulmonary thromboembolism, CHF, congestive heart failure, POCT, point of care test, CK-MB, creatine kinase MB fraction mass

TABLE 1 Risk Route according to the AMI and NO AMI groups

	Route Care				Total
	Red N (%)	Orange N (%)	Green N (%)	Blue N (%)	N (%)
No AMI	6 (0.5)*	16 (1.3)	48 (3.4)	1182 (94.4)**	1252 (100.0)
AMI	42 (40.8)**	23 (22.3)	12 (11.6)	26 (25.2)*	103 (100.0)
Total	48 (3.5)	39 (2.9)	60 (4.4)	1208 (89.2)	1355 (100.0)

AMI, Acute myocardial infarction.

Data presented in absolute values (N) and percentage (%).

Pearson's chi-square test *P*-value = .001.

Significance level residues (r): *less frequent; **most frequently.

Among the infarcted patients, the mean age was 66.2 ± 13.2 years and among the non-infarcted group, 58.9 ± 18.0 years old. A higher probability of myocardial infarction was observed in patients with age ranging from 68 to 85 years old.

According to gender, 708 were women and 672 men. Among AMI group, the frequency of men (69 cases) was higher when compared to women (38 cases) ($P < .001$). Fourteen (13%) infarcted patients with history of previous AMI that occurred more than one year earlier ($P = .026$) were observed. From all 107 AMI cases, 75 (70%) were classified as hypertensive against, 674 (53%) in NO AMI group ($P < .001$) (Data not shown). AMI and NO AMI groups defined according to MTS color scale, used to classify the severity of attendance showed to be, significantly different between them ($P = .001$) (Table 1).

From the 102 AMI cases evaluated by ECG, 13 (13%) had normal ECG reading, 35 (34%) had alterations in non-specific segments for myocardial infarction (inconclusive result), and 54 (53%) had reading suggestive of AMI with changes in the ST segment/Q wave (SSTQ), ($P < .001$) (data not shown).

Myocardial injury markers including Mgb, CK-MB, and cTnI were performed serially following patient admission to the emergency room. The results were stratified according to the cutoff of 107 ng/mL for Mgb, 4.3 ng/mL CK-MB mass, and 0.390 ng/mL for cTnI.

The serial sensitivity, specificity, PPV, and NPV values for blood hypertension, ECG, and myocardial necrosis markers for AMI detection. Myocardial necrosis markers were also evaluated in cases in which the ECG result was inconclusive for AMI screening. In 980 cases in which ECG reading was inconclusive, cardiac necrosis markers were performed to confirm or not AMI cases. The efficiency of the myocardial necrosis markers was evaluated serially in cases wherein ECG reading was inconclusive for AMI and checked through

the tests of sensitivity, specificity, PPV, and NPV presented in percentage (%), measured serially in the (1h), (3h), and (6h) hour after admission (Table 2).

To perform the multiple logistic regression the variables age, gender, AMI previous report, abnormal ECG, blood hypertension, and Mgb, CK-MB, cTnI in (1h), (3h), and (6h) were initially included in the analysis from 328 cases. After the logistic regression, the variables that continued significant and that better explained the AMI event in this study were abnormal ECG, previous AMI reported by the patient, Mgb (3h) and cTnI (6h) (Table 3).

TABLE 2 Results independence and efficiency tests for the variables studied

Variable	SENS (%)	SPEC (%)	PPV (%)	NPV (%)	P
Blood hypertension	70	47	11	95	.001
ECG	53	93	39	96	.001
Mgb (1h)	60	82	22	96	.001
Mgb (3h)	73	78	22	97	.001
Mgb (6h)	61	74	17	96	.001
CK-MB (1h)	39	98	59	95	.001
CK-MB (3h)	66	95	55	97	.001
CK-MB (6h)	71	94	52	98	.001
cTnI (1h)	39	99	75	93	.001
cTnI (3h)	67	98	79	97	.001
cTnI (6h)	77	98	73	98	.001

NPV, negative predictive value; PPV, positive predictive value; SENS, sensitivity; SPEC, specificity.

Pearson's chi-square test *P*-value < .05.

TABLE 3 Final model for multiple logistic regression by evaluating infarction event

Variable	BETA	SE	P-value	OR	95% CI for OR	
					LI	LS
Constant	-3.417	0.380	.000	0.033		
ECG	1.483	0.483	.002	4.406	1.710	11.348
Previous AMI	1.601	0.549	.004	4.958	1.690	14.549
Mgb (3h)	0.919	0.444	.038	2.507	1.050	5.984
cTnI (6h)	4.636	0.560	.000	103.146	34.417	309.120

AMI, Acute myocardial infarction; LI, lower limit; LS, upper limit; OR, odds ratio; SE, standard error.

Using the variables Mgb (3h) and cTnI (6h), π value was calculated using the logistic regression formula below, whose β_0 is the constant of the multiple logistic regression formula, β_1/β_2 the constant for each variable, and the "X" the variable value for each patient:

$$\pi = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x_1 + \beta_2 x_2)}}$$

Receiver operating characteristic curve was constructed based on the π values for each patient and AMI as the outcome. ROC curve showed an area under the curve (AUC) equal to 0.930 (95% CI 0.891 to 0.970; standard error 0.020; *P*-value .001), showing an effective observation for discerning AMI from NO AMI. The cutoff point for the breakdown of these cases was $\pi = 0.833$. Using this cutoff point, classification accuracy rate for AMI was 71.1% and only 0.8% of misclassification (healthy patients as AMI patients) (Figure 2).

4 | DISCUSSION

According to our data, the number of deaths in the AMI group was 8.4% lower than the national rate.¹ Based on data from 2011, 300 to 400 thousand cases a year of heart attack are estimated, as well as the occurrence of one death in every 5-7 cases of heart attack.¹ According to the data from hospitalized patients in Brazil, the incidence of death due to cardiovascular events was (11%).⁶ At the present study, 12.1% of cases related to unstable angina with a 2.4% death rate were observed. In fact ACS represents 4.7% of the deaths rate in this population. However, the incidence of approximately 5% of death at Madre Teresa Hospital, in Brazil, is similar to data found in developed countries.⁷ The lower death rate recorded in the

present study for a small sample of the Brazilian population may be explained by the high standard of care provided at the Madre Teresa Hospital, which makes it a reference hospital in Cardiology. Better socioeconomic conditions, access to health insurance, and a very fast care through the application of MTS may also have influenced the lower death rate found.

Thirty-one percent of the population in screening for CP sought the emergency department within 12 hours after the onset of pain and 25%, 13-24 hours after of onset of pain. The attendance time at screening using the MTS recommends that patients should be investigated within of a maximum of 120 minutes which can reduce the mortality rate. MTS methodology in attendance for ACS influences the initial and likely final prognosis as reported by Dias (2013).⁸

According to the data obtained in the present study, the number of men who suffered AMI was 1.82 times greater than the number of women. Age is another important prognostic factor related to cardiovascular risk especially when comparing mortality due to AMI between men and women.⁹ However, the extent of gender disparity varies widely between the countries.¹⁰ Higher mortality rate in women has been linked to the fact that they are older and have a higher prevalence of comorbidities, such as hypertension and diabetes mellitus, in comparison with men.¹¹

In our study, a large number of hypertensive patients in AMI when compared to NO AMI group were found. However, high blood pressure data are consistent to other studies related to the Brazilian population as well as in developed countries for evaluating AMI in emergency room.^{7,12}

Manchester Triage System is used to classify individuals particularly those with highest risks to ensure AMI diagnosis with greater efficiency, effectiveness, and speed. Of the 274 cases of ACS evaluated, 54 cases of AMI representing one-fifth of the patients, presented changes in the ST segment, indicating a lower incidence of AMI compared to that reported by the ACS Protocol of the Brazilian Ministry of Health (2011).¹ Half (1/2) of AMI cases treated in the emergency room at Madre Teresa Hospital presented a suggesting ECG reading with ST-elevation resulting in acute Q-wave myocardial infarction. Consequently, biomarkers can be highly important and effective in assessing myocardial necrosis in half the cases of non-conclusive ECG readings in the emergency room.

A greater sensitivity in the third and sixth hours observed for CK-MB and cTnI evidences the necessity to serial analysis for those parameters after the first hour. Literature also reports greater precision in the diagnosis of AMI when using necrosis markers in serial analyzes, as low cTnI values allow the exclusion of false-positives.^{13,14} In the first hour of screening for AMI, cTnI showed better PPV when compared to Mgb and CK-MB markers according to Thygesen, et al (2012)⁴ by confirming the better accuracy for this marker in the case of individuals with ACS. Although cTnI did not present a diagnostic advantage for PPV at 3rd and 6th hours in relation to the first-hour screening, it should be emphasized that the serial analysis of this marker makes it possible to minimize failures in relation to the early discharge of patients after care.

FIGURE 2 Receiver operating characteristic curve π values obtained by application of the multivariate model formula, and the outcome Acute myocardial infarction AMI or NO AMI

Therefore, by taking Figiel data (2008),¹⁵ these serial analyses are mainly important in inconclusive ECG reading cases for AMI in CP screening. According to our study, the myocardial necrosis markers data taken together, evaluated in serial analysis, showed increased sensitivity and specificity with a better accuracy at the third hour compared to data from the same patient when admitted. Thus, it might minimize undue cases of hospital discharge in the early hours.^{13,14}

Using a logistic regression model with an independent variable for the occurrence of AMI, it was possible to observe that the variables ECG, previous AMI, Mbg (3h), and cTNI (6h) were associated to the event. An analysis of the model allowed to conclude that, in the study population, patients with abnormal ECG presented 4.4 times more chance of AMI diagnosis, whereas patients with previous AMI presented 4.9 times more chance of a new AMI. On the other hand, alterations in Mbg levels at the third hour and cTNI at the sixth hour resulted in 2.5 and 103.1 times more chance of AMI, respectively.

The ROC curve showed that the model is able to discriminate AMI and NO AMI individuals. The cutoff value chosen for the final model in ROC curve in the present study included few false-positive values. Nevertheless, other precautions must be taken to minimize improper AMI inclusion. Algorithms or score graduation risks can be constructed by customer service to enhance security in the improper exclusion of AMI in screening.

In conclusion, the dynamics and efficiency of an emergency room can be improved to discriminate patients with AMI through the MTS application and knowing the main variables involved in this disease such as hypertension, diabetes, and dyslipidemia, as well as levels of appropriate biomarkers. ECG, Mbg (3h), and cTNI (6h) levels and patient's cardiac history are important tools that can effectively predict AMI in a population. It is still worth noting that in cases of inconclusive AMI through the electrocardiographic profile, the application of POCT assumes importance as a fast, and conclusive aid for the diagnosis of this potentially fatal disease.

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