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Accuracy of history and physical examination for detecting acute myocardial infarction – a hospital based diagnostic accuracy study

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Abstract

Although acute myocardial infarction (AMI) is a common disorder that makes people seek emergency healthcare, there is little evidence on the diagnostic accuracy of symptoms and signs, for the diagnosis of acute myocardial infarction. This study was conducted in Intensive Care Unit of a rural teaching hospital in central India. It was a hospital based cross-sectional diagnostic accuracy study. We followed STARD guidelines for conducting and reporting the study: (i) we consecutively enrolled all inpatients suspected to have and admitted to intensive care unit during a specified period. (ii) We did a blind and independent comparison of the index tests (symptoms and signs) with the reference standard (ECG). (iii) Every patient received both index test as well as reference standard regardless of the results of the either. 450 patients aged 30 years and over (279 men and 171 women) admitted with acute chest pain to the intensive care unit and suspected to have acute myocardial infarction were finally included.

Index tests: 1. History: Chest pain (character, location, radiation, aggravating and relieving factors)

2. Risk factors: Personal history of hypertension, diabetes, angina, smoking 3. Physical examination: Third heart sound, crackles, chest tenderness 4. ECG: ST-segment elevation or depression, T waves peaking or inversion, Q waves

Reference standard: 12-lead electrocardiogram (ECG) for history and physical examination; discharge diagnoses for ECG

Statistical Software: Stata, version 12 (Stata Corporation, Texas, USA). The results of the final model are presented as adjusted odds ratios (OR) with 95% confidence intervals.

Results: Of the 481 patients enrolled, we evaluated 450 patients (279 (62%) men and 171 women (38%); aged 20 years to 90 years [mean 57.7(SD 12.9) years]. In a multivariate logistic regression model, following features of history and physical examination emerged as independent predictors of AMI: crushing chest pain (OR 10.3), pain radiating to the right arm (OR 5.4), heavy chest (OR 3.3), burning character of chest pain (OR 3.3), male sex (OR 2.0), sweating (OR 1.9), apprehension (OR 1.7), pain relieved with nitroglycerine (OR 1.8), and pain radiating to both shoulders (OR 1.6). Third heart sound and crackles were both associated with OR of 2.3 each while chest tenderness yielded an OR of 0.25. **Conclusion**: Even in a high prevalence setting, no sign or symptom exhibited by patients presenting with possible

acute MI proved effective enough alone to rule in or out AMI.

Key Words: Physical signs, History, Acute myocardial infarction, Chest pain

Introduction

Acute myocardial infarction (AMI) is an important cause of admission in intensive care unit in hospitals. Despite advances in diagnosis, physicians miss up to 10% of AMI presenting with acute chest pain (1-4). Conversely, a large proportion of people with chest pain who are admitted, do not turn out to AMI. According to the American Heart Association criteria (2010), patients with proven AMI must receive thrombolysis within 30 minutes of their arrival to the hospital (door to needle time). To ensure that patients with AMI receive evidence-based therapies, it is important that AMI is ruled in or ruled out, quickly and accurately. History and physical examination are key elements used by physicians to triage patients with acute chest pain. The diagnostic accuracy of signs and symptoms has been examined in several systematic reviews (5-7) and individual studies (5, 8-11).

An updated systematic review (7) concluded that signs and symptoms lack accuracy to confidently rule in or rule out acute myocardial infarction. By contrast, a clinical prediction score(11) that included eight predictors (age, gender, risk factors, history of cardiovascular disorder, duration of pain, substernal location of pain, pain increasing with exertion and absence of tenderness on palpation) could accurately distinguish ACS form other competing disorders (the area under the receiver operating characteristic curve 0.95 (95% confidence intervals 0.92 to 0.97).

It is therefore, important to evaluate diagnostic accuracy of history and physical examination to detect AMI in a resource limited setting. This hospital based study was designed to evaluate the accuracy of history and physical examination to detect acute myocardial infarction in patients presenting with acute chest pain.

Materials and Methods

The study was conducted in an intensive care unit (ICU) of the Department of Medicine after taking approval from the Institutional Ethics Committee over a period of 9 months. It is a prospective cross-sectional study in which consecutive patients with acute chest pain and possible ACS presenting to the intensive care unit were enrolled.

Because no hypothesis was tested in this study, the sample size was based on estimation of the precision of the sensitivity and specificity of the index tests as well as on the precision of the estimates of the logistic regression coefficients(12). Assuming that 20% of all in-patients with acute chest pain will have AMI, the desired sensitivity and specificity was considered as 80%. Seeking 10% absolute precision with 95% CI for each estimate, it was needed to enroll about 300 patients suspected to have the target disorder, of which 60 participants would have to have AMI.

The patients were included on the basis of history, risk factors, physical examination and electrocardiogram. We excluded patients known to have a diagnosis before they were enrolled in the study, those who underwent ECG before they were enrolled, and those who on life support measures at the time of admission and those who died before study data could be collected.

Index Tests

The following data was collected from each enrolled patient- age in years, sex, and previous history of coronary heart disease, diabetes, hypertension, smoking and family history of coronary artery disease, hypertension or diabetes. Within an hour of their arrival the patients were enquired about the characteristics of the chest pain, any precipitating or aggravating factors and any associated symptoms such nausea and/or vomiting and sweating. The various signs with which the patients presented were also recorded. We performed index tests and the reference standard in a blind and independent manner and ensured that ECG is obtained within 30 minutes of the arrival of the patient in the ICU.

Reference Standard

The diagnosis of AMI was based on the criteria proposed by the World Health Organization (WHO). The WHO requires evolutionary changes on serially obtained ECG tracings or an increase or decrease in biomarkers levels, either with typical ischemic like chest symptoms. AMI was defined as any one of the following:

(1) A serum cardiac biomarker: Creatinine Kinase isoenzyme (CK-MB) ≥ 24 Units, or

(2) Following changes on the ECG: ST segment elevation or depression (classified as < 0.05 mV, 0.05 to 0.1 mV, and > 1.0 mV deviation) in at least 2 contiguous leads, development of pathological Q-waves, T-wave inversion (≥ 0.2 mV when isolated or < 0.2 mV when in 2 or more contiguous leads with dominant R waves), new left bundle branch block.

Statistical Analysis

Descriptive analysis

We summarized data with the mean and median as measures of central tendency and standard deviations and interquartile ranges as measures of spread for continuous variables. We described frequencies for categorical variables. To compare demographic, symptoms, signs and laboratory characteristics of AMI and non-AMI, we analyzed continuous variables using 2-sided *t* tests or, if skewed, Wilcoxon rank sum tests. We analyzed categorical predictors using $\chi 2$ or Fisher's exact test. We performed univariate logistic regression to examine the relationship between AMI (the reference standard) and predictor variables (symptoms, signs and risk factors). All tests were two-sided, with a *P* value of 0.05 or less considered statistically significant.

Multivariate regression models

Data were analyzed using STATA software (Version 12, Stata Corporation, Texas, USA). The initial analysis included a comparison of the frequencies of history and physical examination variables among patients with and without AMI. Crude (unadjusted) odds ratios (OR) were computed to assess the strength of association between history, signs and ECG (covariates) and AMI (reference standard). The OR estimates were computed along with 95% confidence intervals (CI).

Bivariate analysis was followed by multivariate analysis. The following steps were used for model development: variables that were statistically significant at the p=0.20 level on bivariate analyses were included in the preliminary model. In addition, other variables that were considered biologically important were forced into the model even if they were not statistically significant. The preliminary full model included all the variables selected using the criteria described above. From this full model, variables that did not contribute significantly were dropped one at a time until all those remaining in the contributed significantly. At each step, the variable with smallest contribution to the model (largest *p*-value) was dropped. The impact of elimination of each variable on the model was evaluated using the likelihood ratio test. The backward, stepwise process was continued until the best fitting, most parsimonious final model was identified. The fit of the final model was assessed using the Hosmer-Lemeshow goodness-of-fit test. The results of the final model are presented as adjusted odds ratios (OR) with 95% confidence intervals.

Results

Of the 481 patients enrolled, we evaluated 450 patients, 279 (62%) men and 171 women (38%); aged 20 years to 90 years [mean 57.7(SD 12.9) years]. The patients with acute myocardial infarction were aged almost similar to those without infarction (58.6 vs. 57.1 years, p= 0.218).

The prevalence of acute myocardial infarction was 41% (187 of 450; 95% CI 37% to 46%).

Patients with AMI were as likely to have similar body mass index (25.5 vs. 24.8; p=0.96) and waist hip ratio (91cm vs. 89cm; p= 0.99) as patients without AMI. Similarly, pulse rate, systolic blood pressure and diastolic blood pressure did not differ between patients with, as opposed to those without, AMI. Patients with AMI had significantly higher creatine phosphokinase - MB levels (90.4 vs. 26.8; p=0.001) compared to patients without AMI. Of the 187 patients with AMI, 145 had ST elevated MI and 42 had non-ST elevated MI. Of the145 patients, 112 had anterior MI and 33 had inferior MI. Of the 450 patients, 47 (10%) died during the hospital stay. Those who died were significantly older than who survived (63.4 vs. 57.01 years; p= <0.001). Patients with MI were more likely to die (38 of 147, 20%) compared to those without MI (9 of 263, 3%; p=<0.001). Of the 187 patients with acute MI, 145 (78%) were assigned a discharge diagnosis of ST elevated myocardial infarction (STEMI) and 42 (22%) were assigned a diagnosis of non-ST elevated myocardial infarction (non-STEMI). A total of 34 of 145 (23%) patients with STEMI died, compared to 4 of 42(10%) patients with non-STEMI. A total of 109 (24%) study patients were diabetic (49 of 187[26%] patients with AMI and 60 of 263 [22%] patients without AMI; p=0.40). A total of 81 patients had a history of high blood pressure (26 of 171 [14%] with AMI; 55 of 263(21%) without AMI; p=0.05). A total of 71 of 450 patients (15 %) were smokers; 26 of 187 (14 %) compared with 45 of 263[21]; 15%; p= 0.35).

Cardiac risk factors including hypertension, smoking, obesity, hypercholesterolemia, diabetes and family history of cardiovascular diseases did not emerge as independent predictors of acute MI. Similarly, levels of glucose and serum cholesterol levels, traditional risk factors of acute myocardial infarction, were almost similar in patients with as against without infarction.

Performance of Index tests: We tested different clinical symptoms (nature of pain, site of pain, radiation of pain, associated symptoms, aggravating and relieving factors) and signs (chest tenderness, third heart sound, crackles)for their diagnostic accuracy.

In a multivariate logistic regression model, following features of history and physical examination emerged as independent predictors of AMI: crushing chest pain (OR 10.3), pain radiating to the right arm (OR 5.4), heavy chest (OR 3.3), burning character of chest pain (OR 3.3), male sex (OR 2.0), sweating (OR 1.9), apprehension (OR 1.7), pain relieved with nitroglycerine (OR 1.8), and pain radiating to both shoulders (OR 1.6). Third heart sound and crackles were both associated with OR of 2.3 each while chest tenderness yielded an OR of 0.25.

Figure 1: Study Flow

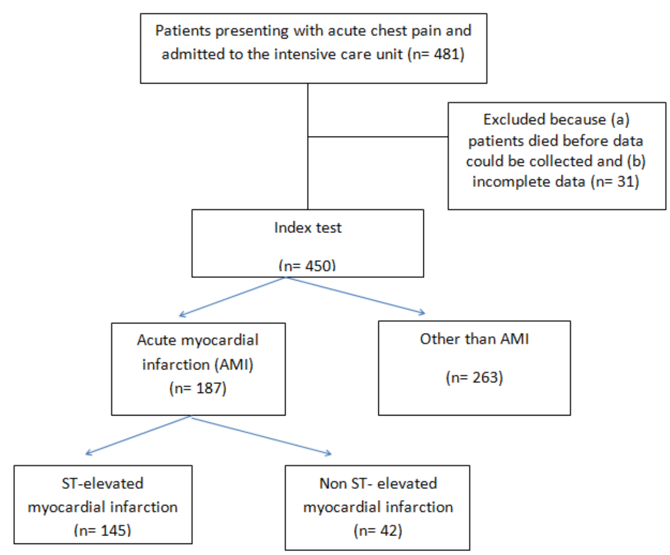

Table 1: Univariate Analysis of Predictors of Acute Myocardial Infarction

Variables	Odds ratio	95 % confidence interval	P value
Sex	1.5	1.0 – 2.3	0.030
Is this a heart attack?	2.4	1.6 – 3.5	<0.001
Characteristics of pain			
Squeezing	6.2	4.1 – 9.5	<0.001
Heavy	0.62	0.42 – 0.92	0.018
Burning	0.72	0.43 – 1.2	0.221
Gastric	0.21	0.08 – 0.54	0.001
Stabbing/sharp	1.0	0.71 – 1.5	0.853
Pleuritic	0.09	0.01 – 0.68	0.020
Worst pain ever	0.24	0.08 – 0.71	0.010
Produced by palpation	0.06	0.01 – 0.44	0.006
Location			
Substernal	1.8	1.2 – 2.6	0.003
Radiation			
Left arm	1.7	0.04 – 3.0	0.082
Right arm	5.5	2.0 – 15.0	0.001
Both arms	3.0	1.7 – 5.3	<0.001
Both shoulders	2.2	1.4 – 3.6	0.001
Left shoulder	2.4	1.3 – 4.5	0.004
Right shoulder	4.8	1.7 – 13.4	0.003
Back	0.72	0.48 – 1.1	0.107
Area of involvement			
A part of chest	1.1	0.74 – 1.6	0.653
All over chest	1.0	0.67 – 1.49	0.986

Pattern of pain			
Intermittent	0.54	0.36 – 0.82	0.003
Continuous	1.7	1.1 – 2.5	0.012
Frequency of pain			
First time	2.3	1.5 – 3.6	<0.001
More than one time	0.43	0.28 – 0.65	<0.001
Aggravating factors			
Emotion	1.0	0.56 – 2.3	0.936
Coughing	0.23	0.11 – 0.49	<0.001
Movement	0.33	0.16 – 0.69	0.003
Relieving factors			
Nitroglycerine	3.1	2.1 – 4.5	<0.001
Antacids	0.60	0.24 – 1.48	0.267
Associated factors			
Nausea	0.90	0.57 – 1.5	0.705
Vomiting	1.2	0.74 – 2.0	0.446
Apprehension	3.3	2.1 – 5.0	<0.001
Physical findings Chest tenderness	0.12	0.04-0.36	0.001
Third heart sound	2.4	1.3-4.6	0.001
Crackles	1.6	0.96-2.6	0.06
Personal history			
Angina	0.61	0.37 – 1.00	0.054
Diabetes	1.2	0.78 – 1.9	0.408
Hypertension	0.61	0.37 – 1.01	0.058
Hyperlipidemia	1.9	0.42 – 8.6	0.407

Smoking	0.78	0.46 – 1.32	0.359
Family history			
Coronary heart disease	1.3	0.48 – 3.3	0.639
Diabetes	0.58	0.20-1.7	0.306

Table 2: Multivariate Analysis of Predictors of Acute Myocardial Infarction

Characteristics	**Odds Ratio**	**95% C I**	**P value**
Sex	2.0	1.2 – 3.2	0.008
Squeezing type chest pain	10.3	4.6 – 22.8	<0.001
Heaviness type chest pain	3.3	1.5 – 7.2	0.003
Burning type chest pain	3.3	1.4 – 7.7	0.006
Pain radiating to right arm	5.4	1.6 – 18.1	0.007
Pain radiating to both shoulders	1.6	0.93 – 2.8	0.089
Relived with nitroglycerin	1.8	1.1 – 2.8	0.020
Associated with sweating	1.9	1.2 – 3.1	0.008
Associated with apprehension	1.7	1.0 – 2.9	0.035
Chest tenderness	0.25	0.08 – 0.82	0.022
Third heart sound	2.3	1.1 – 5.1	0.032
Crackles	2.3	1.2 – 4.4	0.016

Discussion

The main finding of our study is that in patients presenting with-and admitted because of- acute chest pain, the presence of any of the following characteristics of pain increased the likelihood of AMI: male sex, patients perceiving a sense of impending doom, chest pain radiating to either right arm, or to both shoulders, squeezing chest pain, burning pain, chest pain diaphoresis, a third heart sound and crackles. Pain reproduced by palpation or tender chest reduced the probability of AMI. These variables can help physicians rapidly decide about the diagnosis, but of their own are not sufficiently sensitive or specific enough to rule in or rule out acute myocardial infarction.

Our findings (retrosternal pain 95% CI 1.1 to 1.6) are in line with those reported by Everts et al (13) who concluded that a pain location of central or midchest has little value for predicting AMI. Because disorders such as gastro-oesophageal reflux and dyspepsia also produce retrosternal pain, the lack of discriminating power stands to reason.

The prevalence of AMI was almost ten times higher in our study compared to that reported in Goodacre's study but we found that exertional pain and pain radiating to the both arms were poor predictors of acute MI. In another study, Goodacre et al (14) showed that pain radiating to the left (OR 2.4) and pain radiating to the right (OR 5.7) were independent predictors for acute MI.

Our results point out that the radiation of pain to the right arm (LR 5.0) is a much more powerful discriminant for AMI than pain to the left arm (LR 1.6). This finding may seem contrary to the widely held belief by physicians that only left arm radiation is meaningful for a clinical diagnosis of AMI. It is important to realize that right arm pain often co-exists with left arm pain- 45 of 51 patients in a study by Berger(15).The importance of right arm pain was also confirmed in the studies by Goodacre et al (14, 16) indeed, in these studies the right arm pain was an independent marker of acute MI in a multivariate logistic regression analysis and had a higher discriminating ability to rule in acute MI. (OR for left arm pain, 2.4; OR for right arm pain, 5.7).

In our study, pain reported by palpation was found in only 1 of 187 patients with AMI compared to 22 of 263 non-AMI patients.

However, in the study by Goodacre et al (16), vomiting (OR 1.3; 95% CI 0.5 to 3.3) and diaphoresis (OR 1.4; 95% CI 0.7 to 2.3) failed to retain their place in the final multivariate logistic regression model. In our study, nausea and vomiting were poor predictors of AMI but patients with AMI were twice as often likely to sweat compared to non-AMI patients.

In 3 large studies (2, 17,18) of patients presenting to the emergency department with chest pain, none of the classic risk factors emerged as independent predictors of AMI. We too found that angina; history of diabetes, and smoking did not distinguish patients of AMI from those without, AMI. In our study, 26 of 187 AMI patients (14%) vs. 55 of 263 non-AMI patients (21%) reported history of hypertension: thus hypertension was not a significant predictor of AMI in our study.

The most common characteristics included the presence of Q waves, ST-segment elevation or depression and T wave inversion. New ST segment elevation, as shown by previous work (19,20,21,22) is the most important feature in increasing the probability of MI. However, very few patients in our study had had an ECG recorded in the past, and for those who had a previous ECG, ECG was either lost, misplaced, or had faded with the passage of time. New ST segment elevation could be documented in only 4 of 187 patients but the width of 95% confidence intervals suggests a lack of statistical significance (0.43 to 167.8). The width of confidence intervals is driven by the number of patients with past ECG records showing absence of ST elevation- only 3 of 187. We found that any ST-segment elevation (95% CI 6.3 to 14.4), indicated that patients with a discharge diagnosis of AMI were almost 10 times more likely to have elevated ST-segment compared to those without MI. Similarly any Q wave suggested that patients with AMI were about five times as likely to show Q wave in their ECG, compared to those, without AMI. By contrast, the incidence of new Q was only in 4 of 187 suggesting that this ECG feature lacked precision to confidently rule in or AMI.

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