How Useful Are Clinical Features in the Diagnosis of Acute, Undifferentiated Chest Pain?

STEVE GOODACRE, MB, CHB, MRCP, FFAEM, MSC,
TOM LOCKER, MB, CHB, FRANCIS MORRIS, MRCP, FRCS,
STEPHEN CAMPBELL, BSC, MD, FRCP

Abstract. **Objectives:** To measure the predictive value and diagnostic performance of clinical features used to diagnose coronary syndromes in patients presenting with acute, undifferentiated chest pain. **Methods:** The clinical features of patients presenting to the authors' chest pain unit with acute, undifferentiated chest pain were prospectively recorded on a standard form. Admitted patients were followed up by case note review. Discharged patients were followed up as outpatients three days later. Six months after the emergency department visit, evidence of adverse events was searched for from the hospital computer database, case notes, and the patient's primary care physician. The authors tested the power of each feature to predict: 1) acute myocardial infarction (AMI) by World Health Organization criteria, and 2) any acute coronary syndrome (ACS), evidenced by cardiac testing, AMI, arrhythmia, death, or revacsularization procedure within six months. **Results:** Eight hundred ninety-three patients were assessed, 34 (3.8%) with AMI and 81 (9.1%) with ACS. Features useful in the diagnosis of AMI were exertional pain [likelihood ratio (LR) = 2.35], pain radiating to the shoulder or both arms (LR = 4.07), and chest wall tenderness (LR = 0.3). Features useful in the diagnosis of ACS were exertional pain (LR = 2.06) and pain radiating to the shoulder, the left arm, or both arms (LR = 1.62). The site or nature of pain and the presence of nausea, vomiting, or diaphoresis were not predictive of AMI or ACS. **Conclusions:** Important differences exist when clinical features are specifically investigated in patients with acute chest pain and a nondiagnostic electrocardiogram. Clinical features have a limited role to play in triage decision making. **Key words:** chest pain; myocardial infarction; diagnosis; emergencies; clinical features. ACADEMIC EMERGENCY MEDICINE 2002; 9:203–208

THE patient with acute chest pain, who is clinically stable and has a nondiagnostic electrocardiogram (ECG), is a frequent challenge for the emergency physician. The initial ECG has a sensitivity of 20% to 60% for acute myocardial infarction (AMI),[1] so it cannot be relied upon to rule out AMI. The sensitivity of a single set of biochemical markers of AMI at typical time of presentation to hospital is poor.[2] Clinical features may therefore have a key role in determining the likelihood of AMI or acute coronary syndromes (ACSs).

The value of clinical features in the diagnosis of AMI was reviewed several years ago.[3] Panju et al. reviewed the literature for papers reporting cohorts of patients attending hospital with symptoms suggestive of ACS. They found that 1) the presence of pain radiating to the left arm, radiating to the right shoulder, or radiating to both arms; 2) the presence of diaphoresis; 3) auscultation of a third heart sound; or 4) hypotension all predicted AMI. Meanwhile, presentations with pain described as pleuritic, sharp or stabbing, or positional or pain reproduced by palpation were all associated with a decreased likelihood of AMI.

These data mostly originate from large, unselected cohorts of patients and include those who are clinically unstable or have diagnostic ECG changes. It is likely that at least some of these findings, such as the relationship between auscultation of a third heart sound or hypotension and AMI, may not be relevant to the situation in which clinical features are most likely to be of value, as in the low-risk patient who is stable and has a nondiagnostic ECG. Previous work has shown that patients with missed AMI are less likely to have "typical" symptoms or ECG evidence of ischemia or infarction.[4]

We aimed to measure the performance of clinical features used in the diagnosis of chest pain specifically in patients who were clinically stable, with a nondiagnostic ECG, and thus determine which features allow early recognition and appropriate triage of patients with AMI and ACS.

From the Medical Care Research Unit, University of Sheffield (SG), and the Northern General Hospital (TL, FM, SC), Sheffield, United Kingdom.
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Address for correspondence and reprints: Dr. S. W. Goodacre, 87A Sydney Road, Sheffield, S6 3GG, United Kingdom. Fax: 0114-222-0749; e-mail: s.goodacre@sheffield.ac.uk

METHODS

Study Design. This was a prospective, observational cohort study. The study procedures were approved by the hospital research ethics committee. Routine hospital consent procedures were used.

Study Setting and Population. The study was undertaken in a large urban teaching hospital emergency department (ED) receiving 75,000 patients per year, of whom approximately 4% present with chest pain. Approximately 25% of patients attending with chest pain are assessed on a chest pain observation unit (CPOU).[5] The remaining 75% are excluded for the following reasons: 1) new ECG changes consistent with ischemia, defined as >1 mm ST elevation or depression, or >3 mm T-wave inversion in two contiguous leads, or new left bundle branch block (approximately 10%); 2) comorbidity (such as heart failure or arrhythmia) or alternative serious pathology (such as pulmonary embolus) necessitating admission (18%); 3) definite unstable angina, defined as known coronary heart disease (CHD) with prolonged or recurrent episodes of typical anginal pain (35%); and 4) minimal risk of CHD, e.g., age less than 25 years, pain related to recent trauma (12%).

Study Protocol. From March 1, 1999, to September 30, 2000, data were prospectively collected from all patients undergoing assessment on the CPOU. History, examination, ECG, and x-ray findings were recorded on a standard form by a specialist chest pain nurse prior to any further diagnostic testing. All patients were then assessed with ST-segment monitoring for two to six hours, creatine kinase [CK-MB(mass)] measurement at baseline and at least two hours later, and troponin T measurement at least six hours after symptom onset. If these tests were negative, the patient then underwent exercise stress testing (EST), unless he or she was physically unable to exercise or had recently undergone a similar, or more definitive, test for CHD. The decision to perform an exercise test was thus not based on presenting clinical features, once the patient has been accepted onto the CPOU. Those with positive tests were admitted to hospital after assessment, while those with negative tests were discharged.

After CPOU assessment, all discharged patients were invited to attend follow-up three days later for clinical assessment, ECG, and troponin T measurement. The case notes of those admitted were reviewed and the results of all diagnostic tests were recorded. Six months after initial attendance the hospital computer database was searched for any ED visits, hospital admissions, or outpatient visits. Case notes were retrieved and details of diagnostic tests and procedures were recorded. For the first 12 months of the study, this search was supplemented by a letter to the patient's primary care physician to identify any relevant details not recorded in the case notes. It was found that, for local patients, this did not produce any information not already identified by case note review. Therefore, for the last six months, this procedure was limited to patients residing outside the area served by the hospital.

Measurements. The clinical features we examined were pain site, radiation, nature, and duration; presence of nausea or vomiting; diaphoresis; pain described as pleuritic or exertional; pain relieved by glyceryl trinitrate (GTN); and chest wall tenderness. Data relating to these features were retrieved from the standard form by the chest pain nurses and categorized according to predefined criteria. Chest wall tenderness was the only feature of physical examination evaluated. The requirement that patients be clinically stable effectively excluded all but a few with positive examination findings.

We defined two endpoints that we believed would be valuable to identify using clinical features: 1) AMI by World Health Organization (WHO) criteria identified by ECG changes and cardiac enzyme rise after initial presentation;[6] 2) ACS as evidenced by AMI at presentation or at any time over the following six months; subsequent diagnostic test result predictive of adverse outcome [troponin T > 0.1 ng/mL at presentation or three-day follow-up, or early positive exercise stress test (>1 mm ST elevation; or >1 mm horizontal or down-sloping ST depression occurring at stages I or II of the Bruce protocol)]; or subsequent cardiac death, arrhythmia, or revacsularization procedure within six months.

Data Analysis. Analysis was undertaken using SPSS for Windows version 9 (SPSS Inc., Chicago, IL). Univariate logistic regression was used to determine how well each clinical feature predicted AMI or ACS. Any feature that appeared to predict AMI or ACS (p-value <0.20) in the univariate analysis was entered into a multivariate model to determine which features were independent predictors. Sensitivity, specificity, positive and negative predictive values, and likelihood ratios with 95% confidence intervals were calculated for those features shown to have multivariate significance ($p < 0.05$).

RESULTS

During the study period 893 patients were assessed on the CPOU. Mean age was 52.6 years,

62% were male, and 18% had previous evidence of CHD. All underwent cardiac enzyme testing and ECG monitoring: 34 met the WHO criteria for AMI, 14 had an elevated troponin T level without meeting WHO criteria, and two had an episode of arrhythmia recorded. Of the remainder, 599 (71%) underwent EST. The result was negative in 468, inconclusive in 82, late positive in 43, and early positive in six.

Following testing, 131 (15%) were admitted after assessment and 762 (85%) were discharged. Of those discharged, 665 (87%) attended the three-day follow-up appointment. There was no case of missed AMI among those discharged, but one patient had an elevated troponin T level without WHO criteria for AMI. Overall, therefore, 796 of 893 (89%) received follow-up diagnostic testing for AMI with a final diagnosis of AMI made in 34 (3.8%). A total of 57 patients had an endpoint after review of their initial presentations.

At six months all 836 patients without an endpoint after the initial visit were identified on the computer database. One hundred (12%) had been admitted to hospital with a potentially cardiac-related complaint. Case notes were traced for all of these. Twenty-one patients were recorded as having a cardiac event: six cases of AMI, one arrhythmia, two cardiac deaths, and 12 revascularization procedures. Three further patients had attended hospital as outpatients with cardiac arrhythmia but were not admitted. Therefore, ACS was ultimately diagnosed in 81 patients (9.1%).

Letters were sent to the primary care physicians of 444 patients who attended during the first 12 months of the study and were not recorded as having any subsequent hospital contact. Replies were received from 376 (85%). No evidence of missed cardiac pathology was recorded. During the last six months of the study, 23 letters were sent to primary care physicians of patients living outside the hospital catchment area. Replies were received from 18 (78%), again providing no evidence of missed cardiac pathology.

The results of univariate analysis of prediction of AMI at initial presentation are shown in Table 1. Pain site had multiple categories, but no specific site of pain predicted outcome. Odds ratios for pain radiation compare each specific category with a reference category of no radiation of pain. Odds ratios for each type of pain compare each specific category with a reference category consisting of all other types of pain. The following features were entered into the multivariate model: radiation of pain, type of pain, nausea/vomiting, exertional pain, and chest wall tenderness. The results are shown in Table 2. Pain radiation to the shoulder,

TABLE 1. Univariate Analysis of Predictors of Acute Myocardial Infarction

Clinical Feature	Odds Ratio	95% Confidence Interval	p-value
Pain site	—	—	0.79
Radiation to shoulder	6.0	2.0, 17.6	0.0012
Radiation to left arm	1.5	0.6, 4.0	0.38
Radiation to right arm	3.2	0.4, 27.4	0.28
Radiation to throat	2.6	0.3, 21.9	0.37
Radiation to neck	—	—	0.72
Radiation to back	1.1	0.2, 5.3	0.86
Radiation to both arms	7.7	2.7, 21.9	0.0001
Sharp/stabbing pain	0.5	0.1, 2.8	0.41
Burning/indigestion pain	4.0	0.8, 20.1	0.09
Ache	1.9	0.4, 9.4	0.41
Crushing/gripping pain	0.9	0.1, 6.5	0.91
Heavy/pressing pain	1.1	0.2, 5.1	0.90
Pain duration	1.0	0.995, 1.005	0.94
Nausea/vomiting	1.8	0.9, 3.6	0.10
Diaphoresis	1.4	0.7, 2.9	0.29
Exertional pain	3.1	1.5, 6.4	0.0025
Pleuritic pain	0.5	0.1, 2.1	0.34
Relief after taking glyceryl trinitrate	2.1	0.4, 10.9	0.38
Tender chest wall	0.2	0.1, 1.0	0.05

TABLE 2. Multivariate Analysis of Predictors of Acute Myocardial Infarction

Clinical Feature	Odds Ratio	95% Confidence Interval	p-value
Radiation to shoulder	5.7	1.5, 21.4	0.009
Radiation to both arms	4.9	1.3, 19.4	0.02
Burning/indigestion pain	3.4	0.4, 31.0	0.27
Nausea/vomiting	1.3	0.5, 3.3	0.54
Exertional pain	3.3	1.3, 8.4	0.014
Tender chest wall	0.2	0.05, 0.97	0.045

TABLE 3. Diagnostic Characteristics of Clinical Features Predictive of Acute Myocardial Infarction

Clinical Feature	Pain Radiating to Shoulders or Both Arms	Exertional Pain	Absence of Chest Wall Tenderness
Sensitivity	38.2% (23.9, 55.0)*	35.3% (21.5, 52.1)	91.7% (74.2, 97.7)
Specificity	90.6% (88.5, 92.4)	85.0% (82.4, 87.2)	27.8% (24.6, 31.2)
Positive predictive value	14.0% (8.4, 22.5)	8.6% (5.0, 14.4)	4.2% (2.8, 6.3)
Negative predictive value	97.3% (96.0, 98.3)	97.0% (95.6, 98.0)	99.0% (96.3, 99.7)
Positive likelihood ratio	4.07 (2.53, 6.54)	2.35 (1.45, 3.80)	1.27 (1.12, 1.44)
Negative likelihood ratio	0.68 (0.52, 0.89)	0.76 (0.59, 0.98)	0.30 (0.08, 1.14)

*Numbers in parentheses are 95% confidence intervals.

TABLE 4. Univariate Analysis of Predictors of Acute Coronary Syndrome

Clinical Feature	Odds Ratio	95% Confidence Interval	p-value
Pain site			0.51
Radiation to shoulder	3.4	1.5, 7.8	0.004
Radiation to left arm	1.7	0.9, 3.1	0.084
Radiation to right arm	2.5	0.5, 11.9	0.24
Radiation to throat	2.0	0.4, 9.4	0.37
Radiation to neck	0.8	0.2, 3.3	0.72
Radiation to back	0.8	0.3, 2.5	0.74
Radiation to both arms	6.0	2.8, 12.8	<0.0001
Sharp/stabbing pain	0.8	0.3, 2.1	0.61
Burning/indigestion pain	1.5	0.5, 4.5	0.50
Ache	1.0	0.4, 3.3	0.95
Crushing/gripping pain	0.9	0.4, 2.9	0.63
Heavy/pressing pain	0.9	0.3, 2.2	0.73
Pain duration	1.0	0.996, 1.002	0.60
Nausea/vomit	1.0	0.6, 1.7	0.86
Diaphoresis	1.2	0.8, 1.9	0.44
Exertional pain	2.5	1.5, 4.2	0.0005
Pleuritic pain	0.5	0.2, 1.3	0.15
Relief after taking glyceryl trinitrate	2.0	0.6, 4.9	0.27
Tender chest wall	0.6	0.3, 1.2	0.13

pain radiation to both arms, exertional pain, and chest wall tenderness were independent predictors of AMI. The diagnostic parameters of these features are shown in Table 3. Pain radiation to the shoulder or both arms, or exertional pain, increases the probability that pain is due to AMI. The absence of these features reduces the probability of AMI but does not rule the diagnosis out. The presence of chest wall tenderness reduces the probability of AMI.

The results of the univariate analysis of predictors of ACS are outlined in Table 4. As above, pain site had multiple categories, but no specific site of pain predicted outcome. The following features were entered into the multivariate model—radiation of pain, exertional pain, pleuritic pain, and chest wall tenderness. The results are shown in Table 5. Radiation to the shoulder, radiation to the left arm, radiation to both arms, and exertional pain were all independent predictors of ACS. The diagnostic parameters of these features are shown in Table 6. These features add useful diagnostic information but have insufficient sensitivity or specificity to either rule out or rule in ACS.

DISCUSSION

This study has shown that, in patients with a normal or nondiagnostic ECG, exertional pain and pain radiating to the shoulder, left arm, or both arms are predictors of AMI and ACS. These features may therefore assist in the diagnosis of AMI and ACS, but do not have sufficient sensitivity or specificity to rule out or rule in these diagnoses on their own. Chest wall tenderness predicts a reduced likelihood of AMI. Combined with a low prior probability of AMI, this sign could effectively rule out this diagnosis. Absence of chest wall tenderness has little diagnostic value.

We found that many commonly used clinical features were not independent predictors of AMI or ACS in our cohort of selected, low-risk patients. Before rejecting the use of these clinical features, we must consider why they do not appear to be predictive. When multivariate analysis is used to investigate the association between many predictors and a relatively uncommon outcome, statistical power may be inadequate, even in a relatively large cohort such as this. The failure to demonstrate an association between pleuritic chest pain and either AMI or ACS may be explained by inadequate statistical power. The odds ratios for these associations are well below 1, but confidence intervals are wide.

This explanation seems less likely for other features, particularly those relating to the nature of pain. Indeed, "burning" or "indigestion" type pain, often used to diagnose gastroesophageal reflux, appears to be associated with an increased risk of AMI (although not statistically significant). The doubts we have cast over the diagnostic value of the nature of pain are consistent with previous data showing that patients inadvertently discharged from the ED often have atypical symptoms.[4]

We also found no evidence that the site of pain, the presence of nausea, vomiting, or diaphoresis, and the duration of the pain were at all useful in predicting whether the pain was likely to be cardiac or not. This is in contrast to the previous studies that found a positive association between nausea and vomiting, or diaphoresis, and AMI;[7] and a negative association between sharp or stabbing pain and AMI.[8,9]

The failure of nausea, vomiting, or diaphoresis to predict AMI or ACS in our study may reflect that these features are typically associated with ECG changes and are consequently of little value in undifferentiated chest pain. The lack of sharp or stabbing pain to predict the absence of AMI or ACS in our study may reflect the exclusion of very-low-risk patients from our study. Many of these patients may have sharp, stabbing pain and test negative for AMI and ACS. Other studies including these very-low-risk patients have found absence of these symptoms predictive of AMI and ACS.[8,9]

The importance of evaluating the diagnostic value of clinical features lies in their role in improving triage of patients with acute chest pain and avoiding inappropriate discharge of those with AMI or ACS. It is estimated that 2% to 4% of pa-

tients attending hospital with AMI are inadvertently discharged home after initial assessment.[8,10] Conversely, triage of patients with noncardiac chest pain to the coronary care unit represents a considerable waste of resources.[11]

Our data suggest that clinical features have a limited role to play in informing triage decisions and should be used with caution in the patient with a nondiagnostic ECG. Pain that is related to exertion or radiates to the arms or shoulder should prompt triage to a higher level of care, but absence of these features should not be used to justify discharge home. Likewise, the nature of the pain (particularly "burning" or "indigestion" type pain) and the absence of nausea, vomiting, or diaphoresis should not be used to justify discharge home. For patients with a low prior probability of AMI, such as young patients with no CHD risk factors, the presence of chest wall tenderness could be used to allow discharge home without further testing.

In an attempt to improve triage, a number of predictive instruments based on clinical and ECG features have been developed. The most widely used are the Goldman chest pain protocol[12] and the acute cardiac ischemia time insensitive predictive instrument (ACI-TIPI).[13] Despite being shown to effectively risk-stratify patients with acute chest pain, the Goldman protocol did not affect management of patients in the routine clinical setting.[14] Use of the ACI-TIPI led to more appropriate triage decisions and a reduction in unnecessary hospitalizations.[15] Both of these instruments incorporate ECG criteria to predict AMI and ACS. Neither instrument relies upon the nature of the pain or the presence of nausea, vomiting, or diaphoresis to assist risk stratification.

Strategies to improve triage of acute chest pain are now focusing upon the use of early biochemical cardiac markers, either in accelerated protocols[16,17] or in combination with risk stratification protocols,[18] to achieve rapid, appropriate triage. Our results suggest that patients with exertional pain, or pain radiating to the shoulder or both arms, may be too high-risk for such protocols, whereas clinical features are unlikely to be useful in predicting patients who are too low a risk to warrant such evaluation.

LIMITATIONS AND FUTURE QUESTIONS

This was a deliberately selected cohort; it must be stressed that these findings are specific to the context of the investigation, i.e., the clinically stable patient with acute chest pain and no diagnostic ECG change. They may not be relevant to other health care environments, such as primary care, where the selection of patients may be very different.

TABLE 5. Multivariate Analysis of Predictors of Acute Coronary Syndromes

Clinical Feature	Odds Ratio	95% Confidence Interval	p-value
Radiation to shoulder	5.2	2.0, 13.4	0.0008
Radiation to left arm	2.1	1.0, 4.4	0.042
Radiation to both arms	4.8	1.8, 13.2	0.002
Exertional pain	2.4	1.3, 4.5	0.005
Pleuritic pain	0.6	0.2, 1.7	0.34
Tender chest wall	0.6	0.3, 1.2	0.18

TABLE 6. Diagnostic Characteristics of Clinical Features Predictive of Acute Coronary Syndromes

Clinical Feature	Pain Radiating to Shoulder, Left Arm or Both Arms	Exertional Pain
Sensitivity	55.6% (44.7, 65.9)*	29.6% (20.8, 40.3)
Specificity	65.6% (62.3, 68.8)	85.6% (83.0, 87.8)
Positive predictive value	13.9% (10.5, 18.1)	17.0% (11.7, 24.1)
Negative predictive value	93.7% (91.4, 95.4)	92.4% (90.3, 94.1)
Positive likelihood ratio	1.62 (1.30, 2.01)	2.06 (1.41, 2.99)
Negative likelihood ratio	0.68 (0.53, 0.87)	0.82 (0.71, 0.95)

*Numbers in parentheses are 95% confidence intervals.

The definition of outcomes of interest is problematic. Acute myocardial infarction is clearly a valuable outcome to be able to diagnose, but evaluation also needs to identify non-AMI coronary syndromes. Yet simply identifying the presence of CHD may not be useful if the patient is presenting with stable symptoms, or the pain is due to another cause and the presence of CHD is coincidental. We therefore attempted to define ACS to include an element of prognostic value (e.g., by including only early positive EST results or troponin T levels greater than 0.1 ng/mL). However, it is possible that this definition includes cases for whom identification of CHD was of limited prognostic importance and may miss some cases where identification of CHD was valuable.

As mentioned earlier in the discussion, although our cohort is reasonably large, the prevalence of AMI is relatively low. We deliberately chose a high threshold for significance to avoid dismissing potentially valuable clinical features. Nevertheless, it remains possible that the failure of some clinical features to predict AMI may represent inadequate statistical power to detect a weak association. Finally, it is possible that bias may have been caused by misclassification of patients with AMI or ACS as negative for these endpoints because they did not attend for follow-up, did not seek help for further symptoms, or sought help elsewhere.

We have shown that clinical features of chest pain are of limited value for those patients where they have the greatest potential role to play—patients with a nondiagnostic ECG. Investigation in a larger cohort might determine whether some clinical features, such as pleuritic pain or chest wall tenderness, have a significant association with outcome. However, ensuring rigorous follow-up of a low-risk group of patients is a demanding task. Future research efforts are probably better directed at developing diagnostic technology that is quick, convenient, cheap, and accurate in the emergency setting.

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