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Clinical predictors of acute coronary syndromes in patients with undifferentiated chest pain

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Summary

Background: Patients with acute, undifferentiated chest pain present a frequent diagnostic challenge to clinicians. Clinical features are often used to determine which patients may have acute coronary syndrome (ACS).

Aim: To identify clinical features that independently predict ACS in patients with acute, undifferentiated chest pain.

Design: Prospective study of patients enrolled in a randomized controlled trial.

Methods: The presenting characteristics of participants in the ESCAPE randomized trial of chest pain unit vs. routine care were recorded in a standardized manner. Follow-up consisted of troponin T measurement at 2 days, postal questionnaire at 1 month, and telephone contact at 6 months. ACS was defined as elevated troponin T at 2 days or major adverse cardiac event within 30 days of presentation. Multivariate analysis identified independent clinical predictors of ACS.

Results: ACS was diagnosed in 77 (7.9%) of the 972 patients recruited. The following characteristics were independent predictors of ACS (odds ratio, p): age (1.09, $p<0.001$), male gender (8.6, $p<0.001$), indigestion or burning-type pain (3.0, $p=0.034$), pain radiating to the left (2.4, $p=0.013$) or right (5.7, $p<0.001$) arm, vomiting (3.5, $p=0.007$), and previous (5.1, $p<0.001$) or current (3.7, $p<0.001$) smoking.

Discussion: In addition to previously recognized predictors of ACS, it appears that indigestion or burning type pain predicts ACS in patients attending the emergency department with acute, undifferentiated chest pain. Diagnosis of acute 'gastro-oesophageal' chest pain should be avoided in this setting.

Introduction

Approximately 700 000 patients attend an emergency department in England or Wales each year with acute chest pain.[1] After initial assessment, including an electrocardiogram (ECG) and chest radiograph, one quarter will be left with no clear diagnosis.[1] These patients may be defined as having acute, undifferentiated chest pain, and present a difficult challenge to the clinician. Most will have a benign cause for their pain,[2] so admission for further investigation may be wasteful, but to discharge them home risks inadvertently discharging patients with acute coronary syndrome (ACS).[3] Decision-making in these patients will thus often rely upon clinical prediction of ACS, using presenting characteristics such as the nature of symptoms or risk factors for coronary heart disease (CHD).

There is a substantial literature relating to the predictive value of presenting characteristics for

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ACS, and it has recently been summarized in a systematic review.[4] This concluded that pain radiating to the left arm, right shoulder or both arms, the presence of diaphoresis, auscultation of a third heart sound, or hypotension, all predicted acute myocardial infarction (AMI). Meanwhile, presentation with pain described as pleuritic, sharp or stabbing, positional, or pain reproduced by palpation were all associated with a decreased likelihood of AMI.

However, subsequent data has questioned the value of these predictors in the group of patients for whom clinical predictors are likely to be most useful: those with acute, undifferentiated chest pain.[5] These patients are cardiovascularly stable and have a normal or non-diagnostic ECG. Many of the recognized clinical predictors are therefore unlikely to be present. In addition, earlier studies[6,7] examined predictive value for acute myocardial infarction according to old diagnostic criteria.[8] The development of newer cardiac markers for ACS has increased sensitivity for detecting prognostically significant myocardial damage.[9]

We aimed to measure the predictive value of a number of presenting characteristics in patients attending the emergency department with acute, undifferentiated chest pain to determine which characteristics were independent predictors of ACS.

Methods

The Northern General Hospital Emergency Department is the only adult emergency department serving the 530 000 population of Sheffield in the UK. From 5 February 2001 to 5 May 2002, the department was the location for the ESCAPE randomized controlled trial of chest pain unit versus routine care.[10] All patients attending with chest pain or a related complaint were screened for eligibility. They were excluded if they had ECG evidence of ACS (>1 mm ST elevation or depression, T wave inversion >3 mm, bundle branch block, tachyarrhythmia, second or third degree heart block), a clear clinical diagnosis of ACS (known CHD with prolonged or recurrent pain typical of their angina), co-morbidity or suspected alternative pathology requiring admission (such as heart failure or pulmonary embolus), a clear non-cardiac cause (such as pneumothorax or chest pain only present on chest wall movement), or if they were unable to provide informed consent to participate. Eligible patients were asked to provide written consent. The North Sheffield Research Ethics Committee approved the ESCAPE trial.

Specialist Chest Pain Nurses recorded the patient's presenting characteristics on a standardized data collection sheet. These were senior nurses, with experience in cardiac and emergency care, who were responsible for managing patients with suspected ACS and assessing patients with undifferentiated chest pain on the emergency department chest pain unit. The following characteristics were determined, *a priori*, to be of potential value in predicting ACS: age, gender, nature, site and radiation of pain, nausea, vomiting, sweating, dyspnoea (defined as a subjective feeling of dyspnoea), past history of CHD, diabetes, hypertension, hyperlipidaemia, current or previous smoking, family history of CHD, and chest wall tenderness on palpation.

Patients were managed either on a chest pain unit or by routine care according to the day of week, as determined by the trial randomization schedule. All patients were invited to attend a review clinic two days after initial presentation for troponin T measurement. At one month, they were sent a postal questionnaire and at six months they were contacted by telephone. On each occasion they were asked to report any adverse events or hospital attendances.

ACS was defined as any elevation of troponin T at two-day follow-up, or if any of the following events were recorded in the 30 days after initial presentation: cardiac death (death certified as being due to an underlying cardiac cause), non-fatal myocardial infarction (as defined by current guidelines[9]), new-onset heart failure requiring hospital admission, life-threatening arrhythmia, or coronary revascularization procedure.

Statistical analysis

Univariate logistic regression was used to determine the association between each clinical feature and ACS. Any clinical feature that predicted ACS ($p<0.1$) was entered into a multivariate logistic regression model to determine which features were independent predictors of ACS ($p<0.05$). These analyses were performed using SPSS for Windows.[11] Likelihood ratios with 95%CIs were calculated for any categorical clinical feature that was an independent predictor of ACS using Confidence Interval Analysis (CIA) statistical software.[12]

Results

During the study period, there were 6957 presentations with chest pain or related complaint to the emergency department. Of these, 764 (11.0%) had ECG evidence of ACS, 2402 (34.5%) had known

CHD with prolonged or recurrent anginal pain, 869 (12.5%) had co-morbidity or suspected alternative pathology requiring admission, and 1291 (18.6%) had a clear non-cardiac cause. Thus 1631 (23.4%) had acute, undifferentiated chest pain. Consent to participate was requested from 1118, of whom 972 agreed. The recruited patients were younger (49.5 vs. 52.5 years, $p=0.001$) and more likely to be male (57.7% vs. 64.0%, $p=0.01$) than those who declined or were unable to consent.

Hospital computer records and case notes were reviewed for all patients, 851 (87.6%) attended the review clinic and had their troponin T level measured, 679 (69.9%) returned the postal questionnaire at one month, and 680 (70.0%) were contacted by telephone at 6 months. Overall, 43 patients (4.4%) were followed up by computer and case note review only.

ACS was recorded in 77 patients (7.9%): 65 patients had only one criterion for ACS, while 12 patients had multiple criteria. At two day follow-up 70 patients had an elevated troponin T. At 30 days the following events had been recorded: one cardiac death, five non-fatal MI (all identified by troponin T elevation and ECG changes), one life-threatening arrhythmia (ventricular fibrillation), one new-onset heart failure, and 13 revascularization procedures (eight coronary stents, three angioplasties and two bypass grafts).

The mean age of the study population was 49.5 years and 622 (64%) were male. Some 254 patients (26.1%) were referred by their General Practitioner, 334 (34.4%) called an emergency ambulance, 328 (33.7%) were self-referred, and 56 (5.8%) used another route of referral. The other presenting characteristics are outlined in Table 1.

The following characteristics were univariate predictors of ACS: gender ($p<0.001$), nature of pain ($p=0.006$), site of pain ($p=0.014$), pain radiation ($p=0.001$), nausea ($p=0.039$), vomiting ($p<0.001$), sweating ($p=0.086$), smoking ($p=0.037$), ex-smoker ($p<0.001$), chest wall tenderness ($p=0.053$) and age ($p<0.001$). Other characteristics were not predictive: dyspnoea ($p=0.260$), past history of CHD ($p=0.361$), diabetes ($p=0.842$), hypertension ($p=0.507$), hyperlipidaemia ($p=0.317$), and family history of CHD ($p=0.496$).

The results of multivariate analysis are shown in Table 2. The reference categories were: 'non-specific/other' for nature of pain, 'central' for site of pain, and 'none' for radiation. The following factors were independent predictors of ACS: older age, male gender, indigestion/burning type pain, radiation to the left or right arm, vomiting, and current or past history of smoking. Likelihood ratios for categorical clinical features are shown in Table 3.

Table 1 Presenting characteristics of the study population

Presenting characteristic	*n*	Percentage
Nature of pain		
Indigestion/burning	116	11.9
Stabbing/sharp	229	23.6
Aching/dull/heavy	356	36.6
Gripping/crushing	125	12.9
Non-specific/other	128	13.2
Not recorded	18	1.9
Site of pain		
Central	652	67.1
Left	254	26.1
Right	35	3.6
Other	16	1.6
Not recorded	15	1.5
Pain radiation		
None	372	38.3
Left arm	260	26.7
Right arm	57	5.9
Neck	44	4.5
Jaw	28	2.9
Back	123	12.7
Other	57	5.9
Not recorded	31	3.2
Other		
Nausea	290	29.8
Vomiting	56	5.8
Dyspnoea	387	39.8
Sweating	402	41.4
Past history of CHD	43	4.4
Diabetes	46	4.7
Hypertension	247	25.4
Hyperlipidaemia	128	13.2
Current smoker	312	32.1
Ex-smoker	95	9.8
Family history of CHD	389	40.0
Chest wall tenderness	137	14.4

Discussion

Age, male gender, indigestion or burning pain, radiation to either arm, vomiting, and current or previous smoking were predictive of ACS in patients presenting with acute, undifferentiated chest pain. These characteristics can be used to identify patients who are at higher risk of ACS and thus require more cautious management.

The predictive value of age, gender and smoking status reflects known risk factors for CHD and has

Table 2 Results of multivariate analysis

Clinical feature	Odds ratio	95%CI	*p*
Pain radiation			
Left arm	2.4	1.2–4.9	0.013
Right arm	5.7	2.4–13.8	<0.001
Neck	0.2	0.1–2.3	0.198
Jaw	2.3	0.6–9.4	0.250
Back	0.4	0.1–1.8	0.231
Nature of pain			
Indigestion/burning	3.0	1.1–8.4	0.034
Stabbing/sharp	1.1	0.4–3.5	0.848
Aching/dull/heavy	1.5	0.6–3.9	0.422
Gripping/crushing	1.8	0.6–5.4	0.321
Site of pain			
Left	0.7	0.3–1.6	0.465
Right	0.3	0.1–2.4	0.231
Other			
Chest wall tenderness	0.8	0.3–2.3	0.731
Nausea	1.4	0.7–2.6	0.340
Vomiting	3.5	1.4–8.5	0.007
Ex smoker	5.1	2.4–11.0	<0.001
Smoker	3.7	1.9–7.0	<0.001
Sweating	1.1	0.6–2.0	0.636
Gender	8.6	3.6–20.7	<0.001
Age	1.09	1.06–1.12	<0.001

Table 3 Likelihood ratios (LRs) for independent predictors of ACS

Clinical feature	LR of positive test (95%CI)	LR of negative test (95%CI)
Male gender	1.47 (1.35–1.61)	0.24 (0.12–0.48)
Indigestion/burning pain	2.28 (1.48–3.51)	0.85 (0.74–0.96)
Radiation to left arm	1.29 (0.93–1.80)	0.90 (0.76–1.06)
Radiation to right arm	3.78 (2.17–6.60)	0.86 (0.77–0.96)
Vomiting	3.51 (1.98–6.25)	0.87 (0.79–0.97)
Current smoker	1.37 (1.04–1.81)	0.83 (0.68–1.01)
Ex-smoker	2.53 (1.58–4.05)	0.85 (0.76–0.96)

been reported previously.[6] However, we found no predictive relationship for other risk factors for CHD: hyperlipidaemia, hypertension, diabetes and family history of CHD. It may be that patient awareness of some risk factors (particularly hypertension and family history) results in a lower threshold for presentation with non-cardiac chest pain, whereas others (age, gender and smoking) do not.

That vomiting and pain radiating to the arm are predictive of ACS confirms existing findings.[4,13] The important new finding of this study is that pain described as indigestion or burning in nature is predictive of ACS. This contradicts traditional teaching that associates such pain with gastro-oesophageal reflux, but reflects the anecdotal experience of many clinicians.[14] Perhaps we should now consider that presentation to the emergency department with indigestion or burning pain is typical for ACS. Since diagnostic testing for gastro-oesophageal disease is unlikely to be available in the acute setting, diagnosis of acute gastro-oesophageal chest pain should be avoided.

Caution should be observed in extrapolating these findings outside the emergency department. This cohort was deliberately selected to identify a patient group with a specific diagnostic problem. Patients attending the emergency department are likely to be highly self-selected. Hence the finding

that indigestion or burning pain predicts ACS may be explained by patient selection rather than pathophysiology. Patients with such pain are likely to attend the emergency department only if it is exceptional or severe, if not they would more likely self-medicate with an antacid. This study provides no evidence that indigestion or burning pain predicts ACS in primary care or in non-acute chest pain.

Other limitations should also be appreciated, particularly in relation to some of the negative findings of this study. Although the sample size was reasonably large, it was determined by the trial requirements rather than the measurements being estimated by this study. Hence it is possible that weaker predictors may have been rejected due to lack of statistical power. Also, limits upon the amount of data collected mean that some potentially useful features of the patient history were not recorded. For example, the time from symptom onset to presentation may be a useful predictor of ACS, but was not recorded in this study.

A substantial proportion of patients with undifferentiated chest pain were excluded from this study, predominantly due to inability or unwillingness to provide consent. This means that two important patient groups may be under-represented. Firstly, Sheffield has a wide variety of small populations of ethnic minorities. This makes it very difficult to arrange translation facilities, particularly in the emergency setting. Hence non-English speakers were effectively excluded. This severely limits our ability to extrapolate these findings to ethnic minorities. Indeed, the interpretation of clinical predictors among ethnic minorities is a specific area requiring further research. Secondly, the study cohort was relatively young, with older patients more likely to be unable or unwilling to participate. Exclusion of older people was particularly likely to apply to those with cognitive or physical impairments that limited their ability to provide written consent or take part in the trial. Hence we should be cautious about applying these findings to older people, particularly those with cognitive or physical impairment.

Finally, the limited predictive power of the characteristics we have identified needs to be appreciated. Likelihood ratios between 2 and 5 are useful, but certainly not diagnostic.[15] Likelihood ratios between 0.5 and 2 offer little additional diagnostic information.

Patients with acute, undifferentiated chest pain remain a great diagnostic challenge. Guidelines for the diagnostic management of suspected ACS have been published,[16,17] but these guidelines assume that patients with suspected ACS form a distinct, well-defined group. In practice, however, the decision to suspect ACS in a patient with undifferentiated chest pain (and thus undertake further diagnostic testing) is likely to be based upon clinical characteristics. Indeed, a recent survey of emergency department management of undifferentiated chest pain in the UK[18] revealed substantial variation in reported practice, with many patients being discharged home without observation or further testing. Our study suggests that clinical characteristics are an unreliable means for selecting patients for further investigation. If we want to avoid inappropriate discharge of patients with ACS, we must retain a high index of suspicion and a low threshold for diagnostic testing.

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