

CLINICAL RESEARCH STUDY

THE AMERICAN
JOURNAL of
MEDICINE®

'Chest Pain Typicality' in Suspected Acute Coronary Syndromes and the Impact of Clinical Experience

Edward W. Carlton, MBChB,^{a,b} Martin Than, MBBS,^c Louise Cullen, MBBS,^d Ahmed Khattab, PhD,^a Kim Greaves, MD^e

^aCentre of Postgraduate Medical Research and Education, Faculty of Health and Social Services, Bournemouth University, Poole, Dorset, UK; ^bEmergency Department, Southmead Hospital, Bristol, UK; ^cEmergency Department, Christchurch Hospital, Christchurch, New Zealand; ^dEmergency Department, Royal Brisbane and Women's Hospital, Herston, Queensland, Australia; ^eSunshine Coast Hospital and Health Services, University of the Sunshine Coast, University of Queensland, Australia.

ABSTRACT

BACKGROUND: Physicians rely upon chest pain history to make management decisions in patients with suspected acute coronary syndromes, particularly where the diagnosis is not immediately apparent through electrocardiography and troponin testing. The objective of this study was to establish the discriminatory value of "typicality of chest pain" and the effect of clinician experience, for the prediction of acute myocardial infarction and presence of significant coronary artery disease.

METHODS: This prospective single-center observational study was undertaken in a UK General Hospital emergency department. We recruited consecutive adults with chest pain and a nondiagnostic electrocardiogram, for whom the treating physician determined that delayed troponin testing was necessary. Using their own clinical judgment, physicians recorded whether the chest pain described was typical or atypical for acute coronary syndrome. Physicians were defined as "experienced" or "novice" according to post-graduate experience. Acute myocardial infarction was adjudicated using a high-sensitivity troponin (hs-cTn) assay, whereas coronary artery disease was adjudicated angiographically.

RESULTS: Overall, 912 patients had typicality of chest pain assessed, of whom 114/912 (12.5%) had an acute myocardial infarction and 157/912 (17.2%) underwent angiography. In patients undergoing angiography, 90/157 (57.3%) had hs-cTn elevation, of whom 60 (66.7%) had significant coronary artery disease. Sixty-seven of 157 (42.7%) patients had angiography without hs-cTn elevation; of these, 31 (46.2%) had significant coronary artery disease. For the diagnosis of acute myocardial infarction, chest pain typicality had an area under the curve (AUC) of 0.54 (95% confidence interval [CI], 0.49-0.60). For the prediction of significant coronary artery disease with hs-cTn elevation AUC: 0.54 (95% CI, 0.40-0.67), and without hs-cTn elevation AUC: 0.45 (95% CI, 0.31-0.59). When assessed by experienced physicians, specificity for the diagnosis of acute myocardial infarction was higher at 65.8% (95% CI, 63.1%-68.7%) vs 55.4% (95% CI, 53.9%-56.8%) for novices.

CONCLUSIONS: Subjective interpretation of "typicality of chest pain" is of limited discriminatory value in the assessment of suspected acute coronary syndromes, in the context of a nondiagnostic electrocardiogram. Greater clinical experience improves accuracy as a rule-in tool but does not improve overall discriminatory ability.

© 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). • *The American Journal of Medicine* (2015) 128, 1109-1116

KEYWORDS: Acute coronary syndrome; Chest pain; Clinical experience; Coronary artery disease; Emergency department; High-sensitivity troponin; Myocardial infarction

Funding: See last page of article.

Conflict of Interest: See last page of article.

Authorship: See last page of article.

Requests for reprints should be addressed to Edward Carlton, MBChB, Department of Emergency Medicine, North Bristol NHS Trust, Southmead Road, Westbury-on-Trym, Bristol BS10 5NB, UK.

E-mail address: eddcarlton@gmail.com

Patients with chest pain symptoms suggestive of acute coronary syndromes account for 10% of all emergency department attendances.¹ Yet, only 15%-20% have a final diagnosis of acute coronary syndrome.² In the remainder, distinguishing whether a patient presenting with chest pain has an acute coronary syndrome or a non cardiac problem is difficult.³ While some alternative diagnoses become apparent using history alone, the ongoing diagnostic uncertainty in the remainder of patients has been shown to lead to emergency department overcrowding, higher levels of resource use, and increased health care costs.⁴⁻⁶

In patients with chest pain and potential acute coronary syndrome, clinical assessment includes electrocardiography and the results of cardiac troponin testing.⁷ However, over half of patients will have a nondiagnostic electrocardiogram (ECG),² and at least 10% with unstable angina will not have troponin elevations, even in the era of high-sensitivity assays.⁸ This sizeable group of patients represents a significant diagnostic and resource challenge. In these situations, physicians often use the perceived discriminatory value of the chest pain history. This will assist in deciding whether a patient is more or less likely to have cardiac chest pain, and the subsequent need for further observation and investigation.⁹

Published data demonstrate that typical symptoms provide useful diagnostic information in patients with stable coronary artery disease.¹⁰⁻¹² In contrast, evidence examining the value of typical symptoms in patients presenting with chest pain in the acute setting have demonstrated a poor correlation with the final diagnosis of acute coronary syndrome.^{3,13-19} However, these studies have tended to either include patients with diagnostic ECG changes, focus on specific chest pain characteristics rather than overall typicality, or use research nurses to extract this information. Although it is evident that unstructured clinical judgment, or gestalt, has an important role to play in the overall risk assessment of acute chest pain patients,²⁰ the subjective interpretation of typicality of chest pain and the impact that clinical experience may have upon its diagnostic accuracy remain poorly understood.

This study therefore aimed to establish, in patients presenting with chest pain and potential acute coronary syndrome with a nondiagnostic ECG, the discriminatory value of "typicality of chest pain" and the effect of clinical experience, for the prediction of acute myocardial infarction and presence of significant coronary artery disease.

METHODS

Study Design and Setting

This was a planned substudy of a single-center prospective diagnostic cohort study undertaken from July 2012 to August 2013. This study was designed to assess physician risk assessment of emergency department patients with chest pain using an accelerated diagnostic pathway, the results of which have been published previously.²¹ It was approved by the UK National Research Ethics Service, registered with the Controlled Trials Database (ISRCTN No. 21109279), and designed using the Standards for Reporting Diagnostic Accuracy.²² All patient participants provided written informed consent. The study institution's Emergency Department was situated within a UK District General Hospital and has approximately 62,000 new patient attendances per year.

CLINICAL SIGNIFICANCE

- In emergency patients being assessed for potential acute coronary syndromes with a nondiagnostic electrocardiogram, where troponin results are not yet available, typicality of chest pain is of limited discriminatory value in the prediction of acute myocardial infarction or the presence of significant coronary artery disease.
- The diagnostic accuracy of chest pain typicality for the rule-in of acute myocardial infarction appears to be greater with a higher level of clinical experience, but this effect is small.

Selection of Participants

We recruited consecutive adults of at least 18 years of age, who had a primary complaint of chest pain, and for whom the treating physician in the Emergency Department determined that delayed (6 hours post attendance) troponin testing was required for the assessment of an acute coronary syndrome. Clinical protocols at the time of the study did not include troponin testing at presentation, unless >12 hours had elapsed since peak symptoms, therefore, assessing physicians were blinded to initial troponin results. In order to focus upon the patient group that provides the greatest diagnostic challenge to physicians, patients were recruited only if they had a nondiagnostic ECG. Patients who were discharged directly from the emergency department at the discretion of the treating physician without delayed troponin testing were not recruited. All patients who required 6-hour troponin testing were admitted to an inpatient assessment unit under the care of an acute general internist; the decision to admit was at the discretion of the assessing physician in the emergency department. Onward cardiology consultation, stress testing, or discharge for outpatient follow-up was at the discretion of the acute internist. Referral for invasive angiography was at the discretion of cardiologists. Recruitment was undertaken 24 hours a day, 7 days a week. Patients were screened by a dedicated researcher and assessed for eligibility and consented in collaboration with the treating physician. Patients were excluded if any of the following were present: ST-segment elevation myocardial infarction or left bundle branch block not known to be old, ECG changes diagnostic of ischemia (ST-segment

depression ≥ 1 mm or T-wave inversion consistent with the presence of ischemia), arrhythmias (new-onset atrial fibrillation, atrial flutter, sustained supraventricular tachycardia, second-degree or complete heart block, or sustained or recurrent ventricular arrhythmias), troponin not suitable for analysis (eg, hemolysis), age ≥ 80 years, a clear nonacute coronary syndrome cause for chest pain was found at presentation (eg, pulmonary embolism, pneumonia, aortic dissection), another medical condition requiring hospital admission, refusal or inability to give informed consent, non-English-speaking, pregnancy, renal failure requiring dialysis, or inability to be contacted after discharge.

Methods and Measurements

On-duty Board Certified Attendings, Senior Emergency Medicine Residents, and Junior Residents all undertook assessments of pain typicality during the study period and completed standardized data collection forms after genuine clinical consultations and before obtaining results of diagnostic tests (other than the initial ECG). To standardize recruitment, ECG evaluation was undertaken by members of the research team. A trained researcher reviewed the hospital record to collect data on the level of clinical experience of the assessing physician, cardiovascular history, cardiac risk factors, and all investigations related to the visit according to standardized data definitions.²³

We instructed clinicians to record whether they thought the chest pain described was typical cardiac chest pain in a “yes” or “no” tick box, using their own clinical judgment and taking into account all factors from history and examination. The level of experience for assessing physicians was recorded. Clinical experience was defined a priori as either “experienced” or “novice.” Experienced physicians were either Board Certified Attendings (Fellows of the UK College of Emergency Medicine) or Senior Residents with at least 2 years of emergency department experience. Novice physicians were Junior Residents with <1 years’ emergency department experience. During the study period there were 12 experienced physicians and 32 novice physicians undertaking clinical assessments.

Each participating patient had pain typicality assessed by only one treating physician. As such, if a patient had a primary consultation with a novice physician, followed by a review by an experienced physician, only the interpretation of the primary assessing physician was recorded.

The fifth-generation Roche ELECSYS high-sensitivity troponin-T assay (Roche, Basel, Switzerland), which has a 99th percentile reference limit of 14 ng/L and 10% coefficient of variation of $<10\%$ at 9 ng/L, was used for both presentation and 6-hour samples. All serum samples were tested in real time.

In order to provide a quantitative measure of pretest probability and ensure provider groups were similar in this regard, researchers calculated the Thrombolysis in Myocardial Infarction (TIMI) Score²⁴ for each patient. This was assessed from data available at presentation and without

knowledge of either the treating physicians’ interpretation of chest pain typicality or troponin results.

Outcomes

The primary endpoint was the diagnosis of fatal or nonfatal acute myocardial infarction occurring during the index visit. The presence of acute myocardial infarction was defined according to the Third Universal Definition, which states that an increase or decrease in troponin with at least one value above the 99th centile value in the context of a patient with ischemic symptoms or signs (ECG changes or imaging evidence) would satisfy the diagnosis.²⁵ Based on current consensus guidance for high-sensitivity troponin assays, an increase or decrease of 20% (delta) was considered statistically significant and consistent with a diagnosis of acute myocardial infarction.²⁶ Adjudication of this endpoint was carried out by 2 local cardiologists blinded to the physician interpretation of typical pain, but whom had access to the in-hospital clinical record, General Practitioner records, ECG, troponin, and angiography results.

In order to overcome the diagnostic adjudication challenges associated with high-sensitivity troponin assays, such as small elevations in troponin,²⁷ and evaluate those patients without troponin elevation that have clinically relevant coronary artery disease, we also included a secondary diagnostic outcome measure for those patients assessed angiographically. This was categorized into the presence of significant coronary artery disease with or without high-sensitivity troponin-T elevation (hs-cTnT ≥ 14 ng/L at either presentation or 6 hours later vs hs-cTnT <14 ng/L at presentation and 6 hours later). Significant coronary artery disease was defined as $\geq 70\%$ luminal diameter narrowing of at least one major coronary artery as reported on visual assessment by the operator.

Analysis

As this was a planned substudy, no formal power calculation was undertaken, however, previous observational studies reporting the diagnostic utility of chest pain characteristics have typically recruited upwards of 400 participants.^{13,14,16-19} Chi-squared analyses were used to generate 2×2 tables for the calculation of sensitivity and specificity; 95% confidence intervals (CI) are reported. Receiver-operating characteristic curves were obtained by plotting sensitivity against 1-specificity. The area under the receiver-operating characteristic curve (AUC) was chosen as the primary measure of discriminatory value, as it gives a global measure of diagnostic test performance. The AUC was tested against the null hypothesis that typicality of chest pain has no discriminatory ability in determining the presence or absence of acute myocardial infarction or significant coronary artery disease, and therefore the true AUC was 0.50, with a significance of $<.05$. AUC equals 0.5 when the diagnostic test corresponds to random chance (null hypothesis) and 1.0 indicates perfect diagnostic accuracy. For

analysis of the effect of clinical experience, sensitivity (ability of the test to rule out a condition) and specificity (ability of the test to rule in) were compared. All reported *P*-values are 2-tailed. Statistical analysis was carried out using SPSS version 20 (IBM, Armonk, NY).

RESULTS

Characteristics of Study Subjects

Overall, 912 patients had typicality of chest pain assessed, of whom 394 (43%) were recorded as having had typical chest pain (Figure 1). Acute myocardial infarction occurred in 114/912 (12.5%), and 157/912 (17.2%) underwent angiographic assessment. In those undergoing angiography, 90 (57.3%) had hs-cTnT elevation, of whom 64 (71.1%) had significant coronary artery disease. In the 67 (42%) patients who had angiography without hs-cTnT elevation, 28 (41.7%) had significant coronary artery disease, of whom 21 (67.7%) required percutaneous coronary intervention.

Of the assessments for typicality of chest pain, 227 (24.9%) were made by experienced emergency department physicians and 685 (75.1%) were made by novices. Table 1 summarizes recruited patient demographics according to physician experience; there were no significant differences in clinical characteristics or outcomes ($P > .05$ for all). When assessed by experienced physicians, a lower proportion of patients were identified as having typical chest pain when compared with novices (35.2% vs 45.8%, $P = .005$).

Table 2 demonstrates that there was no significant difference in quantitative pretest probability between

provider groups when assessed using the TIMI score (in the absence of troponin results).

Contingency tables showing the occurrence of acute myocardial infarction and significant coronary artery disease, with and without hs-cTn elevation according to the presence or absence of typical chest pain, are shown in the Appendix (available online).

Discriminatory Value of Typicality of Chest Pain

The receiver-operating characteristic curves demonstrating the discriminatory ability of typicality of chest pain as assessed by all physicians in the emergency department, either as a diagnostic tool for acute myocardial infarction, or significant coronary artery disease both with and without hs-cTn elevation, are presented in Figure 2. Below this are also listed the values for AUCs according to specific provider groups. When tested against the null hypothesis that the true AUC is 0.50, the *P*-value for all providers is $>.05$, suggesting that typicality of chest pain has limited discriminatory ability in the diagnosis or exclusion of acute myocardial infarction and significant coronary artery disease with or without hs-cTn elevation in this cohort across all providers.

Diagnostic Accuracy and Impact of Clinical Experience

Figure 3 presents the sensitivity and specificity of typicality of chest pain for the diagnosis of acute myocardial infarction and significant coronary artery disease both with and without hs-cTn elevation, according to provider groups. As a rule-in tool,

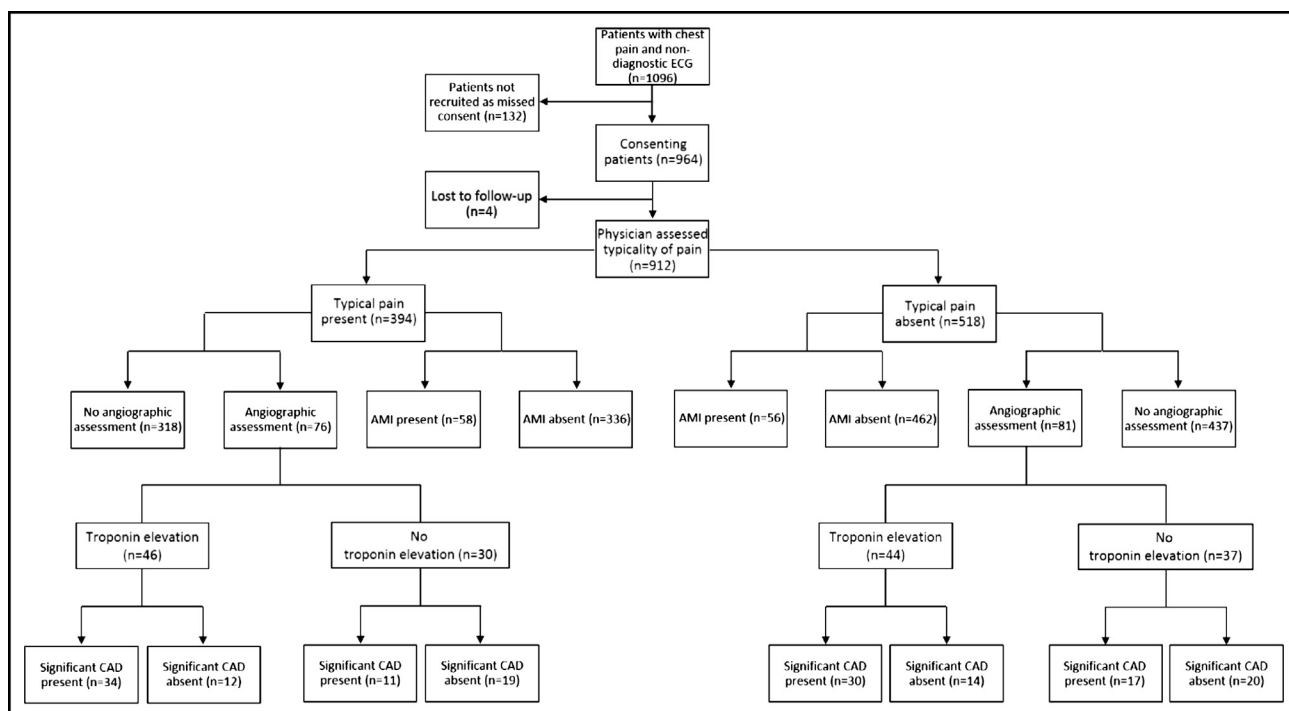


Figure 1 Participant recruitment flow chart. AMI = acute myocardial infarction; CAD = coronary artery disease; ECG = electrocardiogram.

Table 1 Patient Characteristics According to Provider Groups

	Total (N = 912)	Experienced Physicians (n = 227)	Novice Physicians (n = 685)
Age, y (Mean/SD)	58.0/13.3	58.5/12.8	57.8/13.4
Male sex (%)	546 (59.9)	137 (60.4)	409 (59.7)
Ethnicity (% White British)	869 (95.3)	219 (96.5)	650 (94.9)
Risk factors, n (%)			
Hypertension	505 (55.4)	126 (55.4)	379 (55.3)
Hyperlipidemia	601 (65.9)	154 (67.8)	447 (65.3)
Smoking Current	219 (24.0)	61 (26.9)	158 (23.1)
Diabetes	152 (16.7)	31 (13.7)	121 (17.7)
Family History of CAD	340 (37.3)	78 (34.4)	262 (38.2)
Medical history			
Angina	238 (26.1)	51 (22.5)	187 (27.3)
Myocardial infarction	194 (21.3)	42 (18.5)	152 (22.2)
Percutaneous coronary intervention	173 (19.0)	40 (17.6)	133 (19.4)
Atrial arrhythmia	115 (12.6)	26 (11.5)	89 (13.0)
Stroke/TIA	62 (6.8)	14 (6.2)	48 (7.0)
Coronary artery bypass graft	47 (5.2)	11 (4.8)	36 (5.3)
Typical chest pain present	394 (43.2)	80 (35.2)	314 (45.8)
Outcomes			
Fatal/nonfatal AMI	114 (12.5)	34 (14.9)	80 (11.6)
Significant CAD with troponin elevation	64 (7.0)	19 (8.3)	45 (6.5)
Significant CAD without troponin elevation	28 (3.1)	10 (4.4)	18 (2.6)

No significant difference seen between physician groups; *P* > .05 for all variables.
 AMI = acute myocardial infarction; CAD = coronary artery disease; TIA = transient ischemic attack.

specificity of typical chest pain for all outcomes, when adjudicated by physicians as a whole, ranged from 51.3%-57.9% (95% CI, 40.8%-70.8%). However, when assessing the ability of typicality of chest pain as a rule-in tool according to physician experience, the specificity for the diagnosis of acute myocardial infarction was higher for experienced physicians, at 65.8% (95% CI, 63.1%-68.7%), compared with novices at 55.4% (95% CI, 53.9%-56.8%). Similarly, in patients with significant coronary artery disease without hs-cTnT elevation, there was a trend toward higher specificity when assessed by experienced physicians: 66.7% (95% CI, 48.8%-89.5%) vs 46.7% (95% CI, 34.8%-58.6%). It is important here to note that this finding was not statistically significant due to wide and overlapping 95% confidence intervals. In patients with significant coronary artery

disease and hs-cTnT elevation, there was no difference in test specificity between physician groups: 54.5% (95% CI, 28.8-79.4) vs 53.3% (95% CI, 29.6-75.9).

As a rule-out tool for all outcomes, sensitivity of typicality of chest pain ranged from 39.3%-53.1% (95% CI, 24.7%-60.6%). There was no significant difference in the ability of typicality of chest pain to act as a rule-out tool for any outcome measure when comparing experienced and novice physicians.

DISCUSSION

Physicians rely upon chest pain history to make management decisions in patients with suspected acute coronary syndromes,

Table 2 Quantitative Estimates of Pretest Probability Using the TIMI Risk Score,²⁴ in the Absence of High-sensitivity Troponin Results, According to Provider Groups

TIMI Score*	Total (n = 912)	Experienced Physicians (n = 227)	Novice Physicians (n = 685)	Significance of Difference Between Experienced and Novice Physicians (<i>P</i> -value)
0	210 (23)	50 (22)	160 (23.4)	.680
1	285 (31.3)	80 (35.2)	205 (29.9)	.134
2	157 (17.2)	33 (14.5)	124 (18.1)	.218
3	175 (19.2)	42 (18.5)	133 (19.4)	.762
4	77 (8.4)	20 (8.8)	57 (8.3)	.818
5	8 (0.9)	2 (0.9)	6 (0.9)	.990

*The Thrombolysis in Myocardial Infarction (TIMI) Score²⁴ was calculated from the following 5 parameters from data available at presentation and without the knowledge of troponin results: 1) Age 65 years or older; 2) Three or more risk factors for coronary artery disease (family history, hypertension, hyperlipidemia, diabetes or being a current smoker); 3) Use of aspirin in the past 7 days; 4) Significant coronary artery stenosis; 5) Severe angina (2 or more angina events in the past 24 hours). One point was assigned for each variable present.

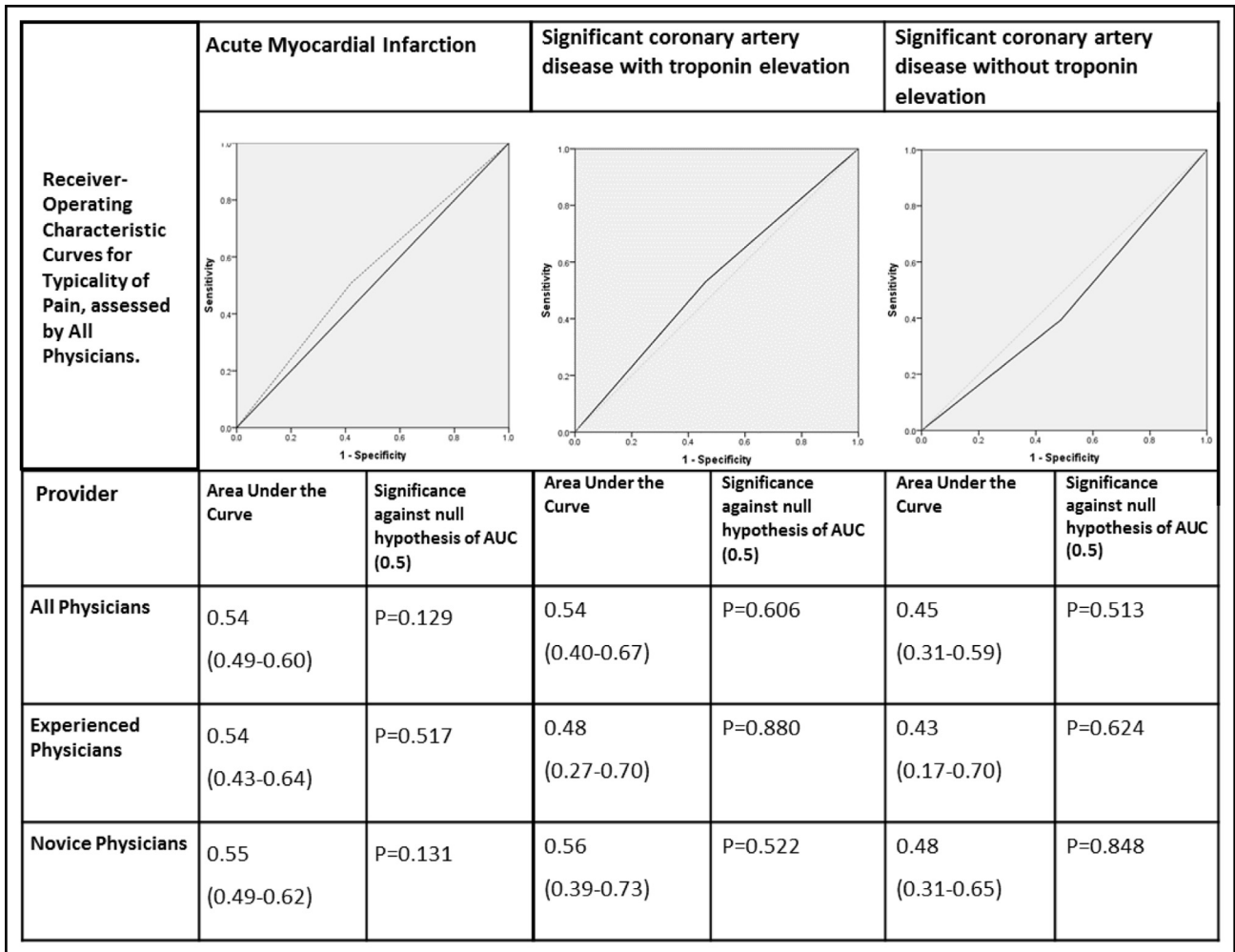


Figure 2 Discriminatory ability of the typicality of chest pain for either acute myocardial infarction, or significant coronary artery disease with and without high-sensitivity troponin-T elevation.

where the diagnosis is not immediately apparent through ECG and troponin testing. Our results show that in emergency patients being assessed for a potential acute coronary syndrome with a nondiagnostic ECG, where troponin results are not yet available, typicality of chest pain is of limited discriminatory value in the prediction of acute myocardial infarction or the presence of significant coronary artery disease. With regard to clinician experience, the diagnostic accuracy for the rule-in of acute myocardial infarction appears to be greater with more experience, but this difference is small and therefore likely to have limited clinical applicability.

Our report has several important implications. Physicians intuitively adopt a *Bayesian* approach to diagnosis, making an initial diagnosis based on probabilities, then adjusting these probabilities as more information becomes available.²⁸ This diagnostic approach is applied readily in the risk assessment of patients with acute chest pain. In the absence of diagnostic ECG changes, physicians weigh up all the information gathered from the history and physical assessment to establish pretest probability before the results of troponin testing. Chest pain typicality has been traditionally

central to this assessment, yet our results bring its value into question.

Until recently, contemporary cardiac troponin assays could be used reliably to identify those patients with a non-ischemic ECG who were at high risk for acute myocardial infarction and adverse events with low false-positive rates.⁷ However, the development of high-sensitivity cardiac troponin assays, which can detect troponin in over 50% of apparently illness-free individuals,²⁶ has raised concerns around binary positive and negative interpretation of results. The potential for multiple acute conditions to cause elevations in hs-cTn²⁹ has necessitated better estimates of pretest probability to allow improved management decisions based on elevated hs-cTn results. Our results suggest that chest pain typicality may also be of limited use in this regard.

With the advent of high-sensitivity assays, there was the potential that in clinical practice, their use may make the diagnosis of unstable angina obsolete.³⁰ By using hs-cTn to adjudicate our primary endpoint and confirm the findings in a subset of patients who have undergone angiographic assessment, we have demonstrated an important finding. In our cohort, over 40% of

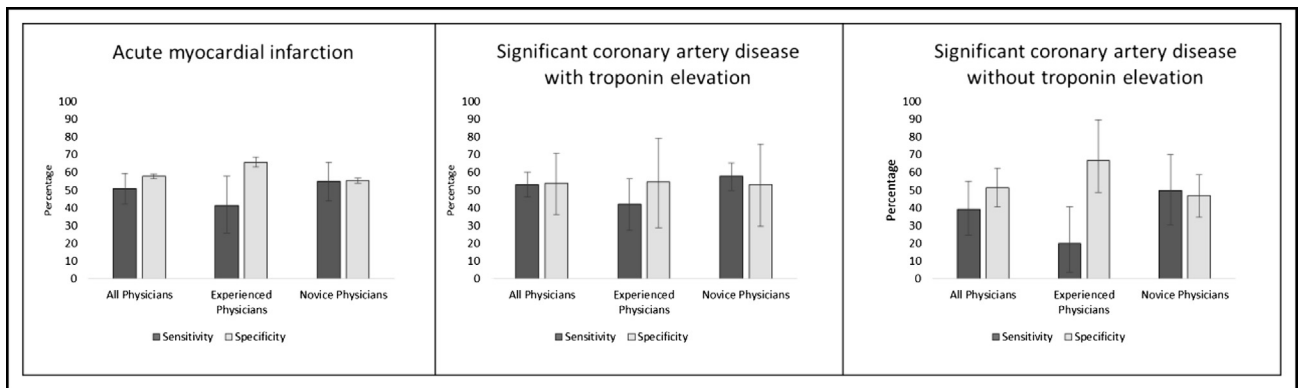


Figure 3 Sensitivities and specificities of typicality of chest pain for the diagnosis of acute myocardial infarction and significant coronary artery disease with and without high-sensitivity troponin elevation.

patients assessed angiographically had significant coronary artery disease, in the absence of high-sensitivity troponin elevations, and two-thirds of these required intervention. It is these patients in whom treating physicians most rely on the discriminatory value of the chest pain history, yet we demonstrate that typicality may again be of limited use.

We therefore suggest that there should be a focus on the clinical application of accelerated diagnostic protocols, which combine risk scores with high-sensitivity troponin testing^{21,31-34} rather than unstructured subjective clinical assessment or gestalt.²⁰

Importantly, this study included only patients with chest pain and a potential acute coronary syndrome with a non-diagnostic ECG who were admitted to a ward for delayed biomarker testing. As a result, the treating clinician had already used clinical judgment to identify patients with chest pain in whom there was a high level of suspicion for acute coronary syndrome and therefore required further inpatient evaluation. Those patients with diagnostic ECGs and those discharged directly from the emergency department with “non-concerning” histories were, as a result, intentionally excluded from analysis. Although our population therefore may be subject to significant selection bias, we have focused intentionally on a cohort of patients that provide the greatest diagnostic challenge for acute physicians on a day-to-day basis. It is possible that the discriminatory value of typicality of chest pain would have improved if patients with clinically evident acute coronary syndromes also had been recruited for analysis. However, the exclusion of those patients in whom there was no diagnostic uncertainty has allowed us to provide novel insight into an everyday and highly relevant clinical problem.

There are some limitations to this study. The applicability of the results may be limited by the characteristics of the population selected. The inclusion of predominantly white patients may limit the applicability to international settings, especially as cross-cultural differences in symptom reporting exist.¹⁸ The upper age cut-off of ≥ 80 years was chosen for pragmatic institutional reasons, as patients were cared for by different inpatient teams. This may limit further the general applicability of the findings, as firstly, older individuals are more likely to report atypical symptoms³⁵ and secondly, older cohorts are

known to have high proportions of patients with elevated hs-cTn assay results, often due to subclinical disease.³⁶

CONCLUSION

Physician interpretation of “typicality of chest pain” is of limited discriminatory value in patients being assessed for potential acute coronary syndromes, in the context of a nondiagnostic ECG. Greater clinical experience improves accuracy as a rule-in tool for acute myocardial infarction, but this does not improve overall discriminatory ability.

References

- Nawar E, Niska R, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. *Adv Data*. 2007;386:1-32.
- Goodacre S, Cross E, Arnold J, Angelini K, Capewell S, Nicholl J. The health care burden of acute chest pain. *Heart*. 2005;91(2):229-230.
- Swap C, Nagurney J. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes. *JAMA*. 2005;294(20):2623-2629.
- Pines J, Pollack C, Diercks D, Chang A, Shofer F, Hollander J. The association between emergency department crowding and adverse cardiovascular outcomes in patients with chest pain. *Acad Emerg Med*. 2009;16(7):617-625.
- Hwang U, Baumlin K, Berman J, et al. Emergency department patient volume and troponin laboratory turnaround time. *Acad Emerg Med*. 2010;17(5):501-507.
- Thokala P, Goodacre S, Collinson P, et al. Cost-effectiveness of presentation versus delayed troponin testing for acute myocardial infarction. *Heart*. 2012;98(20):1498-1503.
- Panju A, Hemmelgam B, Guyatt G, Simel D. The rational clinical examination. Is this patient having a myocardial infarction? *JAMA*. 1998;280(14):1256-1263.
- Reichlin T, Twerenbold R, Maushart C, et al. Risk stratification in patients with unstable angina using absolute serial changes of 3 high-sensitive troponin assays. *Am Heart J*. 2013;165(3):371-378.
- Amsterdam E, Kirk J, Bluemke D, et al. American Heart Association. Testing of low risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. *Circulation*. 2010;122(17):1756-1776.
- Diamond G, Forrester J. Analysis of probability as an aid in the clinical diagnosis of coronary artery disease. *N Engl J Med*. 1979;300(24):1350-1358.
- Pryor D, Shaw L, McCants C, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med*. 1993;118(2):81-90.

12. Genders T, Steyerberg E, Alkadhi H, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. *Eur Heart J*. 2011;32(11):1316-1330.
13. Goodacre S, Locker T, Morris F, Campbell S. How useful are clinical features in the diagnosis of acute undifferentiated chest pain? *Acad Emerg Med*. 2002;9(3):203-208.
14. Henrikson C, Howell E, Bush D, et al. Chest pain relief by nitroglycerin does not predict active coronary artery disease. *Ann Intern Med*. 2003;139(12):979-986.
15. Chun A, McGee S. Bedside diagnosis of coronary artery disease: a systematic review. *Am J Med*. 2004;117(5):334-343.
16. Goodacre S, Pett P, Arnold J, et al. Clinical diagnosis of acute coronary syndrome in patients with chest pain and a normal or non-diagnostic electrocardiogram. *Emerg Med J*. 2009;26(12):866-870.
17. Body R, Carley S, Wibberley C, McDowell G, Ferguson J, Mackway-Jones K. The value of symptoms and signs in the emergent diagnosis of acute coronary syndromes. *Resuscitation*. 2010;81(3):281-286.
18. Greenslade J, Cullen L, Parsonage W, et al. Examining the signs and symptoms experienced by individuals with suspected acute coronary syndrome in the Asia-Pacific Region: a prospective Observational Study. *Ann Emerg Med*. 2012;60(6):777-785.
19. Rubini-Gimenez M, Reiter M, Twerenbold R, et al. Sex-specific chest pain characteristics in the early diagnosis of acute myocardial infarction. *JAMA Intern Med*. 2014;172(2):241-249.
20. Body R, Cook G, Burrows G, Carley S, Lewis P. Can emergency physicians 'rule in' and 'rule out' acute myocardial infarction with clinical judgement? *Emerg Med J*. 2014;31(11):872-876.
21. Carlton E, Cullen L, Than M, Gamble J, Khattab A, Greaves K. A novel diagnostic protocol to identify patients suitable for discharge after a single high-sensitivity troponin. *Heart*. 2015. doi: 10.1136/heartjnl-2014-307288 [Epub ahead of print].
22. Bossuyt PM, Reitsma JB, Bruns DE, et al. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. *Ann Intern Med*. 2003;138:40-44.
23. Cullen L, Than M, Brown A, et al. Comprehensive standardized data definitions for acute coronary syndrome research in emergency departments in Australasia. *Emerg Med Australas*. 2010;22(1):35-55.
24. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA*. 2000;284(7):835-842.
25. Thygesen K, Alpert J, Jaffe A, Simoons M, Chaitman B, White H. Third universal definition of myocardial infarction. *Circulation*. 2012;126(16):2020-2035.
26. Thygesen K, Mair J, Giannitsis E, et al. Study Group on Biomarkers in Cardiology of ESC Working Group on Acute Cardiac Care. How to use high-sensitivity cardiac troponins in acute cardiac care. *Eur Heart J*. 2012;33(18):2252-2257.
27. Mills N, Churchhouse A, Lee K, et al. Implementation of a sensitive troponin I assay and risk of recurrent myocardial infarction and death in patients with suspected acute coronary syndrome. *JAMA*. 2011;305(12):1210-1216.
28. Sackett D, Straus S, Richardson S, Rosenberg W, Haynes B. *Evidence-Based Medicine. How to Practice and Teach EBM*. 2nd ed. London: Churchill Livingstone; 2011.
29. Newby L, Jesse R, Babb J, et al. ACCF 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation task force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2012;60(23):2427-2463.
30. Twerenbold R, Jaffe A, Reichlin T, Reiter M, Mueller C. High-sensitivity troponin T measurements: what do we gain and what are the challenges? *Eur Heart J*. 2012;33(5):579-586.
31. Cullen L, Mueller C, Parsonage W, et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *J Am Coll Cardiol*. 2013;62(14):1242-1249.
32. Cullen L, Greenslade J, Than M, et al. The new Vancouver Chest Pain Rule using troponin as the only biomarker: an external validation study. *Am J Emerg Med*. 2014;32(2):129-134.
33. Body R, Carley S, McDowell G, et al. The Manchester Acute Coronary Syndromes (MACS) decision rule for suspected cardiac chest pain: derivation and external validation. *Heart*. 2014;100(18):1462-1468.
34. Than M, Flaws D, Sanders S, et al. Development and validation of the Emergency Department Assessment of Chest Pain score and 2 h accelerated diagnostic protocol. *Emerg Med Australas*. 2014;26(1):34-44.
35. Horne R, James D, Petrie KW, Weinman J, Vincent R. Patients' interpretation of symptoms as a cause of delay in reaching hospital during acute myocardial infarction. *Heart*. 2000;83(4):388-393.
36. Eggers K, Al-Shakarchi J, Berglund L, et al. High-sensitive cardiac troponin T and its relations to cardiovascular risk factors, morbidity, and mortality in elderly men. *Am Heart J*. 2013;166(3):541-548.

Funding: This study was supported by a research grant from the College of Emergency Medicine of the United Kingdom and research fellowship funding from Bournemouth University, UK.

Conflict of Interest: EC has received funding from Abbott in support for related research. MT has received funding from Alere, Abbott, Beckman, and Roche for speaking and support for other research. LC has received funding from Abbott, Roche, Alere, Siemens, and Radiometer Pacific for clinical trials, and from Alere, Boehringer Ingelheim, Pfizer, AstraZeneca, Abbott, Novartis, and Radiometer Pacific for speaking and education. AK has no conflicts of interest. KG has received funding from AstraZeneca and Takeda UK for related research.

Authorship: Each author has contributed to the analysis and interpretation of the data, drafting and approval of the final manuscript. All authors have also contributed to the conception/design of the study reported in this manuscript.

SUPPLEMENTARY DATA

Supplementary tables accompanying this article can be found in the online version at <http://dx.doi.org/10.1016/j.amjmed.2015.04.012>.

APPENDIX

Contingency tables showing the occurrence of acute myocardial infarction (**Supplementary Table 1**) and significant coronary artery disease with and without troponin elevation (**Supplementary Table 2**) according to the presence or absence of typical chest pain.

Supplementary Table 1 The occurrence of acute myocardial infarction according to the presence or absence of typical chest pain

	Acute Myocardial Infarction	No Acute Myocardial Infarction	Total
All physicians			
Typical chest pain present	58	336	394
Typical chest pain absent	56	462	518
Total	114	798	912
Experienced physicians			
Typical chest pain present	14	66	80
Typical chest pain absent	20	127	147
Total	34	193	227
Novice physicians			
Typical chest pain present	44	270	314
Typical chest pain absent	36	335	371
Total	80	605	685

Supplementary Table 2 The occurrence of significant coronary artery disease with and without troponin elevation according to the presence or absence of typical chest pain

	Significant Coronary Artery Disease and hs-cTnT \geq 14 ng/L	No Significant Coronary Artery Disease and hs-cTnT \geq 14 ng/L	Total
All physicians			
Typical chest pain present	34	12	46
Typical chest pain absent	30	14	44
Total	64	26	90
Experienced physicians			
Typical chest pain present	8	5	13
Typical chest pain absent	11	6	17
Total	19	11	30
Novice physicians			
Typical chest pain present	26	7	33
Typical chest pain absent	19	8	27
Total	45	15	60
	Significant Coronary Artery Disease and hs-cTnT $<$ 14 ng/L	No Significant Coronary Artery Disease and hs-cTnT $<$ 14 ng/L	Total
All physicians			
Typical chest pain present	11	19	30
Typical chest pain absent	17	20	37
Total	28	39	67
Experienced physicians			
Typical chest pain present	2	3	5
Typical chest pain absent	8	6	14
Total	10	9	19
Novice physicians			
Typical chest pain present	9	16	25
Typical chest pain absent	9	14	23
Total	18	30	48

Hs-cTnT = high-sensitivity troponin-T elevation.