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Impact of serum troponin measurement on triage of chest pain in a district hospital

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SUMMARY

Aim: To evaluate the impact on the clinical service of incorporating cardiac troponin T (cTnT) measurement into the existing chest pain care pathway in our district general hospital.
Methods: We randomised 200 consecutive patients admitted with acute chest pain, but without ST elevation on ECG, either to our existing chest pain care pathway (pathway 1) or to a new pathway incorporating semi-quantitative cTnT measurement (pathway 2).
Results: In comparison with pathway 1, in pathway 2 there was a strong trend towards reduced length of stay (3.13 v 4.36 days, p=0.08), and reduced usage of low molecular weight heparin (LMWH) (4.59 v 5.45 doses per patient, p=0.05). The number of cardiac events at three months in care pathway 1 (14/92) and care pathway 2 (22/108) did not significantly differ, p=0.34. In patients with atypical chest pain, there was a tendency for cardiologists to discharge earlier (1.75 v 2.03 days, p=0.07) and use less LMWH (2.04 v 2.97 doses, p=0.06) than general physicians.
Conclusion: In this study, incorporation of cTnT measurement into a chest pain care pathway resulted in a strong trend towards reduced length of hospital stay and LMWH usage.

INTRODUCTION

Chest pain is one of the commonest presentations to the accident and emergency department. The traditional risk factors obtained from the clinical history and abnormalities on the electrocardiogram (ECG) discriminate poorly between cardiac and non-cardiac pain, resulting in some 4-8% of patients with an acute myocardial infarction being discharged.[1] This may be catastrophic for the individual, and it accounts for 25% of litigation against emergency departments in the US.[2] For this reason, a large proportion of patients presenting with chest pain are admitted, although fewer than half of these have an acute coronary syndrome.[3] As chest pain accounts for 20-30% of acute medical admissions,[3] patients at low-risk of a cardiac event constitute about 10% of all hospital admissions.

Measurement of cardiac troponins may aid risk stratification and triage of this large group of patients. Several studies have shown that elevated troponin levels are associated with increased risk of subsequent cardiac events.[4-7] However most of these studies have been carried out in high-risk populations in clinical trials, or in cardiology units. The true value of a troponin assay in the assessment of unselected patients in a district general hospital is less certain.

In our hospital, as in many district general hospitals, initial management of chest pain has been performed by general physicians, with higher risk patients subsequently being referred to a cardiologist. In order to standardise care, a care pathway for patients admitted with chest pain without ST-elevation on the ECG was in operation. Patients were risk stratified on the

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basis of history, conventional risk factors for coronary disease and presence of ischaemic changes on the ECG. In an effort to improve the efficiency of the service, we devised a new care pathway incorporating serum cardiac troponin T (cTnT) measurement into the risk assessment algorithm. The care pathways represented alternative accepted management strategies for acute chest pain. The purpose of this study was to compare the clinical effectiveness of the pathways in an unselected population presenting to a district hospital. Specifically we sought to address the question of whether inclusion of cTnT in the risk stratification algorithm would influence length of hospital stay or use of low molecular weight heparin (LMWH).

SUBJECTS AND METHODS

Patient selection

The study population consisted of 200 consecutive patients admitted with chest pain to the Mater Hospital between May 22nd and October 12th 2000.The study was designed to be as inclusive as possible; however, patients with a history of myocardial infarction (MI) in the previous two weeks, ST elevation on the admission ECG, pleuritic chest pain, co-morbidity reducing life expectancy (e.g. advanced malignancy) and those unable to give an adequate history were excluded.

Study protocol

This was a prospective, randomised open comparison of two care pathways. Patients were randomised to Pathway 1 or Pathway 2 according to their accident and emergency number: odd numbers were allocated to pathway 1 and even numbers to pathway 2. Page 1 of both care pathways was filled in by the admitting doctor. It directed them to record clinical data, to take appropriate blood tests, and to assess the need for cardiac monitoring. In Pathway 2 they were directed to take two samples for point-of-care serum cTnT measurement: the first at least six hours after the onset of the most severe chest pain, and the second at 12 hours. If the patient presented more than 12 hours after the onset of pain, or if the first sample was positive, a single sample sufficed.

The first senior doctor assessing the patient made the clinical risk assessment. This may have been the registrar on the weekday evening ward-round, or the consultant on the ward round on the following morning. In Pathway 1, the assessment was made according to the character of the chest pain, presence of risk factors for ischaemic heart disease (IHD), and ECG characteristics. In Pathway 2, the assessment was based on character of chest pain, ECG characteristics, and serum cTnT levels. Those deemed to be at low risk were discharged early for outpatient exercise stress testing (EST) if appropriate, whereas those deemed to be at higher risk were kept as inpatients for intensive anti-anginal treatment and EST (see Fig. 1).

Risk factors for IHD were defined as: hypercholesterolaemia: total serum cholesterol >5.2mmol/1 or on statin therapy; hypertension: units mmHg on three occasions or on anti-hypertensive therapy; and diabetes mellitus: fasting blood sugar >7.0mmol/1 or on diabetic diet or medication. The patients were designated as current, ex- or non-smokers, according to their response at the time of admission. Family history of IHD was also obtained from the patient at the time of admission.

Data relating to in-patient episodes were obtained from the clinical notes. Follow-up data was obtained by a research nurse using a standard questionnaire administered by telephone three months post-discharge, and from the patient's GP or hospital records where necessary. Primary end-points were the number of doses of LMWH used and the length of hospital stay. Cardiac events during the follow-up period were a secondary end-point and included death from IHD, readmission with MI or unstable angina, and need for revascularisation. In order to compare our results with previous studies, MI was defined as the combination of typical chest pain with elevation in creatine kinase greater than twice the upper limit of normal, with or without dynamic ECG changes. Unstable angina was defined as a typical history compatible with type IIIB of the Braunwald classification.[8]

Analytical techniques

A semi-quantitative measurement of troponin T was made using the Cardiac Reader (Roche Diagnostics). 150μl of heparinised whole blood was applied to the reader, and a result was available after 12 minutes. A numerical value for cTnT was obtained in the range 0.1-2.0μg/l. Elevations of cTnT either less than 0.1μg/l or greater than 2.0μg/l gave readings LOW or HIGH respectively. If cTnT was not detected, a negative reading was obtained. Although the manufacturers

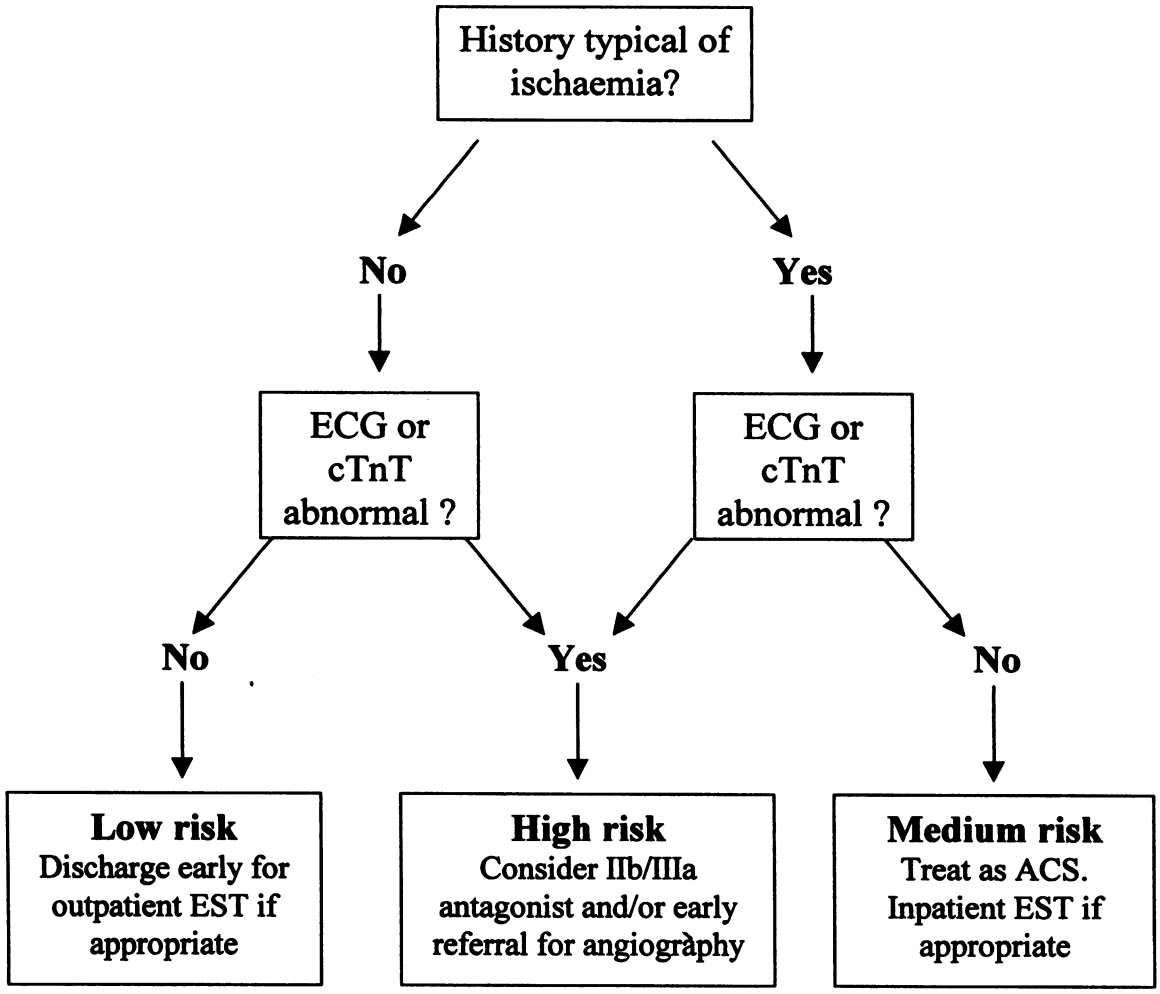

Fig 1. Algorithm for the management of chest pain in Care Pathway 2. (EST – Exercise Stress Test)

cut-off value for a positive result was >0.1μg/l, for this study we designated the test as being positive if any troponin T was detected. This is in light of studies showing that troponin T levels in the range 0.06-0.1μg/l are associated with increased risk of cardiac events,[5] and is consistent with a recent paper that recommended a reduction in the cut-off value to 0.05μg/l.[9] Quality control was assured by testing one kit in each batch of 10 against standards. All house officers were trained to perform the analysis. There are several cardiac Troponin I assays, each with their individual characteristics, available on the market but only one cTnT assay is available. The cTnT assay was chosen so that the current results could be more easily compared with those from previous trials.

Statistical analysis

All results for continuous variables are expressed as means. The student's t-test and the Mann-Whitney test were used to compare continuous variables between groups when the distributions were normal and non-parametric respectively. The χ^2-test with the appropriate number of degrees of freedom was used to compare categorical variables. Analyses were performed on SPSS (version 10.1) software package. Recruitment of 200 patients was sufficient to have 80% power to detect a difference of 1.5 days in length of stay between the groups at the 5% level of significance.

RESULTS

Of the 200 patients enrolled, 92 (46%) were randomised to pathway 1, and 108 (54%) to pathway 2. Baseline characteristics were similar in both groups (Table).

14 patients (7.0%) were diagnosed with myocardial infarction based on elevation of cardiac enzymes within the first 24 hours of admission. Unstable angina was diagnosed in 97 patients (48.5%), and the remaining 89 patients (44.5%) were considered to have non-cardiac chest pain.

TABLE

Patient characteristics at baseline

Characteristic	*All Patients number %*	*Care pathway 1 number %*	*Care pathway 2 number %*	*p-value*
Mean Age (years)	62.3	63.4	61.4	0.28
Male	106(53)	46(50)	60(56)	0.43
Smoking Status				
Current	54(27)	24(26)	30(28)	0.57
Ex-smoker	21(11)	14(15)	7(6)	
Hypertension	78(39)	39(42)	39(36)	0.36
Diabetes mellitus	23(12)	13(14)	10(9)	0.28
Hypercholesterolaemia	118(59)	53(58)	65(60)	0.71
Family history IHD	144(72)	67(73)	77(71)	0.75
Mean no. of risk factors	2.45	2.55	2.36	0.22
Personal history IHD	101(51)	49(53)	52(48)	0.47

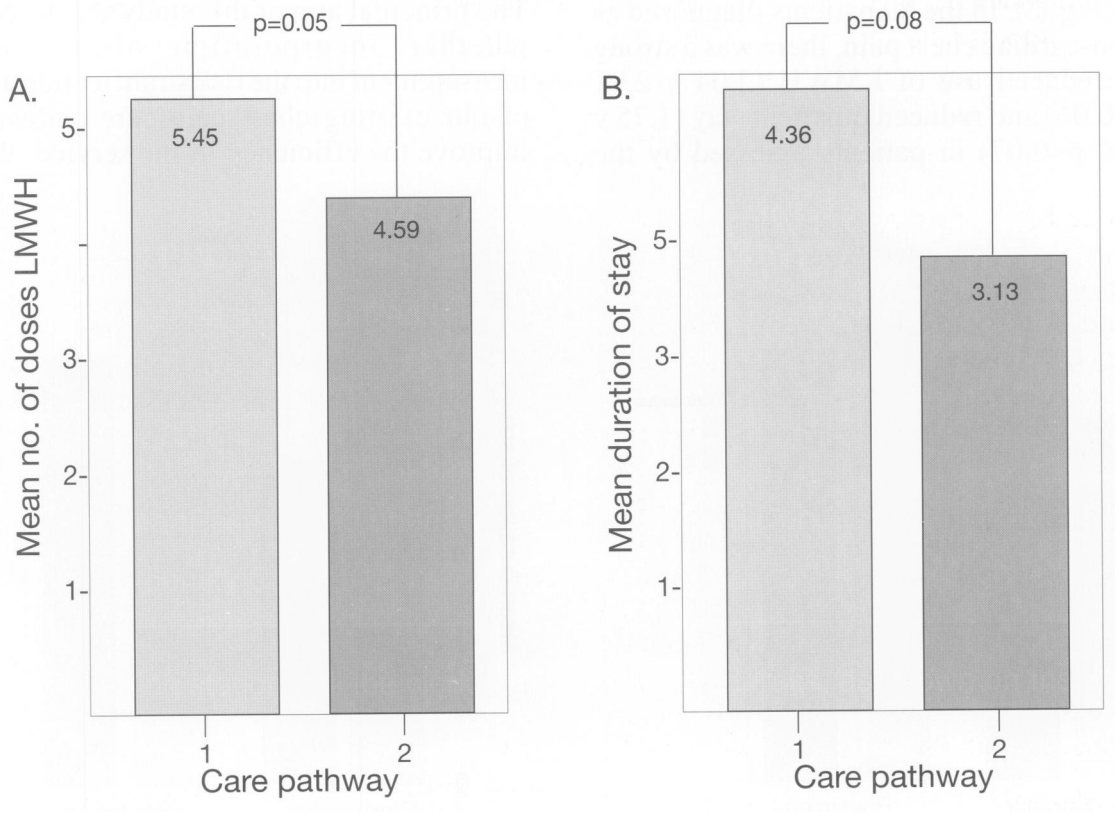

Fig 2. Mean number of doses of Low Molecular Weight Heparin (A) and duration of hospital stay (B) in care pathway 1 compared to care pathway 2.

Troponin T measurements

Of the 108 patients allocated to pathway 2, 106 had serum cTnT testing completed as per protocol. cTnT was positive in 15 (14%), including all five patients with myocardial infarction, and 10 of 48 (21%) with unstable angina. Each patient with an elevated cTnT was subsequently diagnosed as having either a myocardial infarction or unstable angina. Hence, although the sensitivity of cTnT for acute coronary syndromes was low at 28%, it was highly specific (100%).

Three patients who had normal cTnT on initial sampling subsequently developed elevated cTnT on repeat sampling. Of the 15 patients with elevated cTnT levels, five had no rise in creatine kinase, four had no dynamic ECG changes, and a further four had neither a rise in enzymes nor ECG changes, and hence would not have been identified as being at high risk by traditional markers.

Comparison of care pathways and teams

In comparison with pathway 1, in pathway 2 there was a strong trend for a reduction in use of LMWH (p=0.05) and in mean length of stay (p=0.08) (Fig. 2). In the 89 patients diagnosed as having non-cardiac chest pain, there was a strong trend for reduced use of LMWH (2.04 v 2.97 doses, p=0.06) and reduced inpatient stay (1.75 v 2.03 days, p=0.07) in patients assessed by the cardiology team compared with those assessed by general physicians. This trend in the triage of non-cardiac chest pain was particularly evident when cTnT measurements were employed (see Fig. 3).

Follow-up

Cardiac events occurred in 36 patients (18%) in the 3-month follow-up period. 22 of the 106 (21%) patients who had cTnT tested had a cardiac event, including 5 of 15 patients (33%) who were cTnT positive and 17 of 91 (19%) of those testing negative. The excess rate of events in patients testing positive for cTnT failed to reach significance (p=0. 19). The positive and negative predictive values of an elevated cTnT for a cardiac event occurring within 3 months were 33% and 81% respectively.

In the 3-month follow-up, 14 of 92 patients (15%) on pathway 1 had an event, compared with 22 of 108 (20%) patients on pathway 2. There was no significant difference in the frequency of events between the two pathways (p=0.34).

DISCUSSION

The principal aim of this study was to determine whether incorporation of serum cTnT measurement into the risk stratification algorithm of our existing chest pain care pathway could improve the efficiency of the service. We found

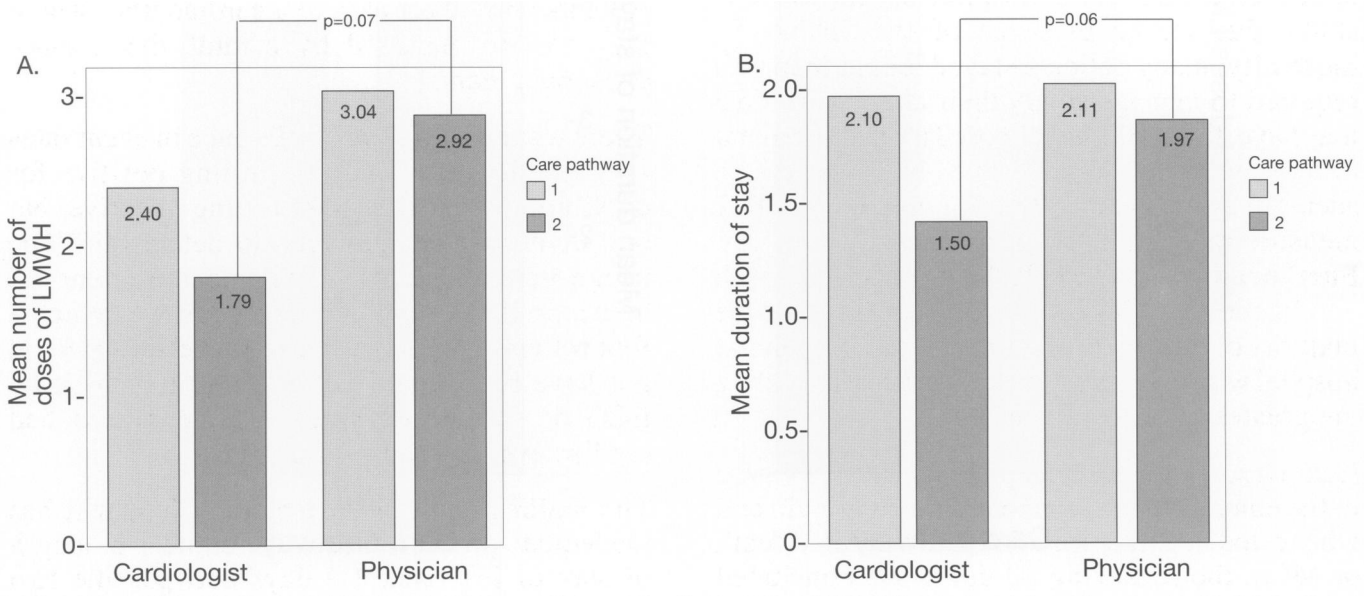

Fig 3. Mean number of doses of Low Molecular Weight Heparin (A) and duration of hospital stay (B) in patients with non-cardiac chest pain assessed by a cardiologist (n=24) compared to those assessed by a physician (n=65). There was a trend towards a greater reduction in these parameters when assessment was made by a cardiologist using pathway 2.

that there was a strong trend, which just failed to reach statistical significance, towards reduced length of hospital stay and usage of LMWH when cTnT measurement was employed.

This has major resource implications for a busy district general hospital. Assuming the pattern of admissions throughout the year was similar to that seen in the current study, over 500 patients with chest pain would be admitted to our hospital. As patients randomised to Care Pathway 2 spent on average 1.23 less nights in hospital, over 600 bed nights would be made available for other patients.

Most previous studies of serum troponin measurements in the assessment of chest pain have been carried out in high risk populations[5-7] or in cardiology units.[10,11] Our study had minimal exclusion criteria and therefore more accurately reflects the characteristics of patients admitted to a district general hospital with chest pain. Elderly patients were included (age range 28-94 years), as were those with significant co-morbidity (other than dementia and advanced malignancy). The difference between our study population and those of previous trials which required dynamic ECG changes for inclusion, is illustrated by a cardiac event rate of 18% at 3-month follow-up in our study, compared with 72% and 52% event rates at 30 days in the GUSTO-IIa and TRIM studies.[6,7] The impact of cTnT measurement in these high risk populations cannot be extrapolated directly to the district general hospital setting. In our study, due to the presence of significant co-morbidity, many patients stayed longer than was required to manage solely their chest pain. This may have diluted the benefit of cTnT measurement in improving efficiency, but would give a more accurate assessment of the true impact of cTnT measurement in a district general hospital. Furthermore, by excluding patients with nondiagnostic ECG's, these studies excluded the majority of patients presenting to a district general hospital with chest pain, including those providing the greatest diagnostic challenge.

Hamm found that 1.1% of patients who presented to the emergency department with chest pain and who tested negative for cTnT had a cardiac death or MI in the following 30 days.[4] He concluded that a negative result could therefore allow rapid and safe discharge of patients from the emergency department. Our study raises some doubts as to the validity of this approach. Firstly, three patients, including one patient with evolving infarction, who tested negative for cTnT greater than six hours after the onset of most severe chest pain subsequently tested positive on repeat sampling at 12 hours. This reflects the delay in release of cTnT from damaged myocardial cells, and is in keeping with other studies.[7] Secondly, a negative cTnT does not rule out the presence of an acute coronary syndrome or the occurrence of subsequent cardiac events. Only 21% of patients diagnosed with unstable angina in our study had raised cTnT levels, a proportion similar to that seen in other studies.[4,6,10] 19% of patients testing negative for cTnT had an event by three months, including one cardiac death in a patient who also had a negative EST pre-discharge. Furthermore, in Hamm's study, all patients diagnosed with unstable angina were admitted and treated with LMWH, including those testing negative for cTnT. The event rate may have been greater if these patients had been discharged directly from the emergency room.

Our study showed that members of the cardiology team tended to be more efficient than general physicians in managing patients with non-cardiac chest pain, particularly when cTnT measurements were employed (see Fig. 3). The addition of cTnT measurement to the decision-making process had little impact in reducing the LMWH usage or the length of stay for patients with non-cardiac chest pain assessed by a general physician. This provides a strong argument for admitting all patients with chest pain to a cardiac unit, where they can be managed by a multi-disciplinary chest pain team.

There was no significant difference in event rates at 3 months in the patients testing positive for cTnT compared with those testing negative, but our study was not powered to detect this. The prognostic value of cTnT measurement is, however, illustrated by the fact that we detected four patients with elevated cTnT levels who would not have been identified as being high risk by ECG or cardiac enzymes. Of these, two had cardiac events during follow-up.

The major limitation of the study is that it has inadequate power to detect differences in length of stay of less than 1.5 days between the two groups. Therefore, although the improvement in efficiency with cTnT measurement fails to reach significance in the study, we feel that if we were to ignore the strong trend towards improved

efficiency, we would be committing a type two error, and be discounting a smaller but still clinically important effect. We had anticipated that the impact of cTnT would have been greater than that seen. A recent randomised trial of patients admitted to a coronary care unit showed a 66% reduction in length of stay when a cTnI-based algorithm was compared with standard risk stratification.[11] However this trial did not include the time spent on the general wards following discharge from the coronary care unit, which as seen in our study, dilutes the impact of troponin measurement on overall length of stay, but more accurately reflects the overall expenditure.

In conclusion, our study supports the hypothesis that incorporating serum troponin measurement into a risk stratification care pathway improves service efficiency and is safe. This is likely to be most efficient in the setting of a chest pain unit or cardiac unit, where patients are assessed by those most experienced in the management of acute coronary syndromes.

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