

ORIGINAL ARTICLE

Troponin I, laboratory issues, and clinical outcomes in a district general hospital: crossover study with "traditional" markers of myocardial infarction in a total of 1990 patients

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Aims: Review of the clinical outcomes and practical issues of replacing traditional cardiac enzymes with troponin I (cTnI) in a district general hospital.

Methods: Crossover study of three sequential three month stages during which serial cardiac enzymes were replaced with a single cTnI measurement available at three set times within 24 hours for the duration of the second three month stage. The study was carried out in a 630 bed district general hospital with 1990 admissions of suspected cardiac ischaemia over the study period as a whole. Account was taken of seasonal factors.

Results: The introduction of troponin was associated with 8.5% more patients with non-ischaemic heart disease (IHD) being discharged on the day after admission, saving approximately 107 bed days each year. Approximately 50% more patients were diagnosed with myocardial infarction during the cTnI stage. There was no increase in readmission within one month or early death with cTnI. Approximately 3% false positive and 1.5% false negative cTnI results were recorded. All false positive cTnI results were coding errors or attributable to known assay interference effects. All false negatives were potentially explained by sample timing factors. The lack of standardisation in troponin assay services impacts clinically.

Conclusion: Younger patients without IHD were discharged earlier during the cTnI stage in apparent safety. Blood sample timing needs to be verified when cTnI is used as an adjunct to early discharge. There were no unexplained false positives or negatives. Standardisation related issues arose.

There are approximately 335 National Health Service clinical laboratories (personal communication, 2003, Institute of Biomedical Sciences, www.ibms.org). Of laboratories registered with the United Kingdom National External Quality Assessment Scheme for Cardiac Markers (UKNEQAS, www.ukneqas.org.uk), 83 are listed for troponin T (cTnT) and 114 for troponin I (cTnI) provided on 11 different analytical platforms. An informative survey on the use of cardiac markers during 2003¹ found that under half of the responding laboratories offered troponin as a routine cardiac marker, whereas 26% based their service upon total creatine kinase (CK) and aspartate aminotransferase (AST). A further quarter included the cardiac specific isoenzyme of creatine kinase. Two thirds of troponin publications have taken place within the past 10 years, and with increasing evidence of improved risk stratification of the acute coronary syndrome (ACS)² by troponin, many hospitals have replaced CK and AST with troponin as the primary marker of myocardial injury. As the range of factors appearing to influence troponin increases, and with the current pressure to optimise hospital bed occupancy, we evaluated the clinical impact and laboratory practicalities of introducing a routine troponin service. Few exclusively district general hospital studies³⁻⁴ have examined such issues on a large numerical scale. Most studies incorporating district general hospitals⁵⁻⁷ have simultaneously measured both enzyme markers and troponin. We have designed a novel CK/AST crossover study with troponin, comparing three months of an established CK/AST service with three months of a troponin only service, followed by return to the CK/AST service for a final three months.

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The consequences of introducing a new test in specialist centres may differ from those in a district general hospital. Some aspects of examining the effects of new tests cannot be addressed by study design where focus upon clinical process may significantly "sharpen" up relevant management and invalidate comparison. We have tried to address some of these issues within a relatively simple protocol. Our end-points included length of hospital stay, rates of death (including a consideration of seasonal influences on death rates), and readmission at one month. Clinicians are familiar with the limitations of traditional cardiac markers, but have much less practical experience of the range of possible anomalies that may affect troponin results. Issues relating to the measurement of troponins have been reviewed.⁸ There is familiarity with the possible consequences of renal insufficiency⁹ and rheumatoid factor¹⁰ on troponin, but interference in assays may be an underestimated problem,¹¹ including negative interference with reference to some cTnI assays.¹² The problems that occur in routine practice are unclear. Therefore, in our study, we have investigated all apparent false positive and false negative test results.

METHODS

Our study was approved by the North East Wales local research ethics committee. All patients with possible cardiac

Abbreviations: ACS, acute coronary syndrome; AST, aspartate aminotransferase; CI, confidence interval; CK, creatine kinase; cTnI, troponin I; ECG, electrocardiogram; ICD, international classification of disease; IHD, ischaemic heart disease; MI, myocardial infarction

Table 1 Diagnostic categories and patient numbers

Diagnosis	Stage 1	Stage 2	Stage 3	Total
Non-IHD	397	238	314	949
MI	85	109	89	283
IHD/non-MI	237	258	263	758
IHD	322	367	352	1041
Total	719	605	666	1990
Study months	Oct-Dec	Jan-Mar	Apr-Jun	Oct-Jun

IHD, ischaemic heart disease; MI, myocardial infarction.

ischaemia admitted under the care of physicians were recruited and the study was undertaken in three stages, each of three months duration.

- Stage 1 (first three months): the base line. Patients were managed according to the hospital guidelines for ACS: up to three consecutive daily cardiac enzymes (CK/AST) were measured.
- Stage 2 (second three months): troponin stage. CK and AST were withdrawn and patients had cTnI measured 12 hours after admission or 12 hours after the definite onset of chest pain. Blood samples for cTnI were assayed in three batches each day at 10.00, 16.00, and 22.00 hours. Individuals with no further chest pain from admission, two normal electrocardiograms (ECGs) (admission and after 12 hours), and a cTnI value of $< 0.5 \mu\text{g/litre}$ were considered for discharge providing all alternative diagnoses had been excluded.
- Stage 3 (third three months): back to baseline stage. The cTnI service was withdrawn and patients were managed with total CK and AST estimation as in stage 1.

Laboratory methods

Cardiac enzymes (total CK and AST) were measured at 37°C (Synchron LX20 analyser; Beckman Coulter (UK) Ltd, High Wycombe, UK) using the manufacturer's recommended protocol. The detection limit for both CK and AST was 5 IU/litre and upper linearity limits on automatic dilution were 4100 and 2600 IU/litre, respectively. The interassay imprecision (coefficient of variation), measured at 117, 264, and 409 IU/litre, did not exceed 2.1% for CK and for AST, measured at 28, 120 and 206 IU/litre, was 3.6%, 1.8%, and 1.7%, respectively. Neither method was International Federation of Clinical Chemistry compliant. Troponin I was measured by a chemiluminescence method at 37°C (ACS 180; Bayer Diagnostics plc, Newbury, UK). The lower limit of detection according to the manufacturer was 0.15 $\mu\text{g/litre}$ with linearity to 50 $\mu\text{g/litre}$. Interassay imprecision was 14.3%, 8.3%, and 6.1% at 0.23, 1.33 and 4.18 $\mu\text{g/litre}$, respectively. Interpretive guidance provided was as follows: cTnI $< 0.5 \mu\text{g/litre}$, minimal myocardial damage; 0.5–1.4 $\mu\text{g/litre}$, suggestive of unstable angina; $\geq 1.5 \mu\text{g/litre}$, myocardial infarction (MI).

Analysis of data

The international classification of disease version 10 (ICD10) coding was used to group patients into three groups according to their discharge diagnosis. The groups were MI (ICD I21, I22), angina (ICD I20), and admission unrelated to ischaemic heart disease (non-IHD); all other codes with the exception of code I2. The hospital patient administration system provided data on length of hospital stay, mortality, and readmission to hospital during the month after discharge, together with overall general medical intake hospital admission and mortality rates.

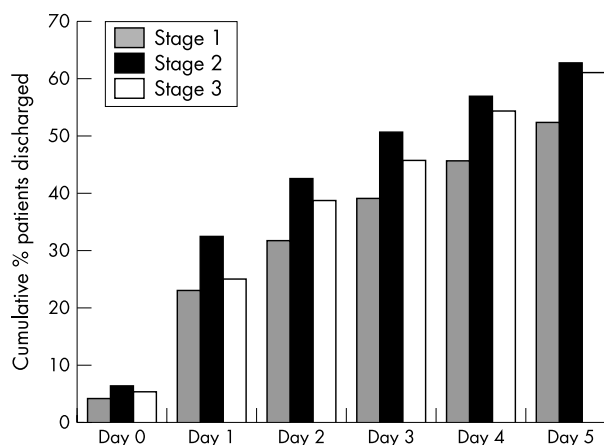


Figure 1 Cumulative percentage of patients without ischaemic heart disease discharged during the five days after admission in stage 1, stage 2, and stage 3 of the trial.

Statistical methods

Median values are presented with interquartile ranges and differences between them assessed by the Wilcoxon-Mann-Whitney test (StatXact version 4; Cytel Software Corporation, USA). Fisher's exact test was used to compare proportions. Confidence intervals for the difference between proportions were calculated using the methods of Gardner and Altman.¹³ To assess the effect of various covariates on length of stay in hospital, a Cox's proportional hazard model was used (Statistica version 6; Statsoft Inc, Tulsa, Oklahoma, USA). Two binary covariates ("stage 1 or 2" and sex) and one continuous covariate (age) were used in the model. Significance is represented by the calculated model parameters, β , SE values, and p values. In addition, a censoring variable was used to indicate those patients who died as inpatients without being discharged.

RESULTS

Patient demographics

There were 1990 patients in total, 1038 men and 952 women. No patients were excluded from our analysis. Seven hundred and nineteen patients were in stage 1, 605 in stage 2, and 666 in stage 3. Median ages of those in stages 1, 2, and 3 were 74.2 (range, 61.2–81.3), 70.9 (range, 58.8–78.7), and 68.7 (range, 56.3–77.8) years, respectively. The median age in stage 1 was higher than that in stage 2 ($p < 0.01$) and the median age in stage 2 was higher than that in stage 3 ($p < 0.02$). The percentages of women in stages 1, 2, and 3 were 51.9%, 45.8%, and 45.3%, respectively. There were more women in stage 1 than in stage 2 ($p < 0.03$) or stage 3 ($p < 0.02$).

Table 2 Number of patients readmitted within one month of each admission

Groups	Stage 1	Stage 2	Stage 3
Total patients	39	37	36
Non-IHD readmitted as non-IHD	9	4	5
Non-IHD readmitted as IHD	1	3	3
Non-IHD readmitted as MI	0	0	0
IHD readmitted as IHD	30	39	32
IHD readmitted as MI	3	2	2
Total episodes	43	48	42

IHD, ischaemic heart disease; MI, myocardial infarction.

Diagnostic categories

Of the 1990 patients, 1041 were categorised as having ischaemic heart disease (IHD). Of these patients, 283 were diagnosed with MI on admission, and 758 as an ACS excluding MI (coded as angina). The remaining 949 patients were diagnosed as a non-IHD related admission. Table 1 shows the breakdown of patients in the three groups according to diagnosis. In stage 2, 18.0% (109 of 605) patients were diagnosed with MI, compared with 11.8% (85 of 719) in stage 1 ($p < 0.01$). This increase of 6.2% (95% CI, 2.4% to 10.1%) reflects just over 50% more patients diagnosed during the troponin stage. Similarly, 13.4% (89 of 666) of patients were diagnosed with MI in stage 3. This fall of 4.9% (95% CI, 1% to 9%) reflects 27% fewer patients being diagnosed with MI in stage 3, compared with stage 2 ($p < 0.01$).

Length of stay

Overall, there were 719, 605, and 666 patients in the three stages, respectively; accumulating 6520, 4780, and 5903 bed days, respectively. The median lengths of stay for the three stages were six (range, 3–11), six (range, 3–10), and six (range, 3–10) days. There were 397, 238, and 314 patients without IHD in the three stages. These low risk patients occupied 3479, 1846, and 2880 bed days, respectively. The median lengths of stay for these patients were six (range, 3–12), five (range, 2–10), and six (range, 3–10) days. Bed occupancy was significantly reduced by at least one day between stages 1 and 2 ($p < 0.01$). Furthermore, a Cox proportional hazard model, with length of stay as the outcome variable and “stage 1 or 2” as a binary covariate appeared to confirm this ($\beta = 0.26$; SE, 0.09; $p = 0.002$). However, because age and the proportion of men and women were different in stages 1 and 2, these were added as additional covariates. This further analysis showed that patient age was the main determinant of the difference in length of stay between stages 1 and 2 ($\beta = -0.030$; SE, 0.003; $p < 0.0001$), with sex having a weaker effect ($\beta = 0.18$; SE, 0.08; $p = 0.04$). Stage number, reflecting the introduction of cTnI testing, had no significant effect on overall length of stay ($\beta = 0.10$; SE, 0.09; $p = 0.25$).

To investigate the possibility that statistics based on overall lengths of stay may be concealing differences at the low end of the length of stay range, the proportions of patients without IHD being discharged in the first few days after admission were examined (fig 1).

Among the patients without IHD, 8.5% more (95% CI, 1.4% to 15.6%) were discharged on the day after admission in stage 2 (73 of 238) than in stage 1 (88 of 397) ($p = 0.02$). There was no difference between the proportion discharged on the day after admission in stage 3 (76 of 314) and stage 2 ($p = 0.10$). There was no difference in the median age of stage 1 (56 years; range, 47–71) and stage 2 (55 years; range, 45–67; $p = 0.4$). The proportions of female patients without IHD in stages 1 and 2 were also similar (51% and 47%, respectively; $p = 0.6$). Overall, there were 949 patients

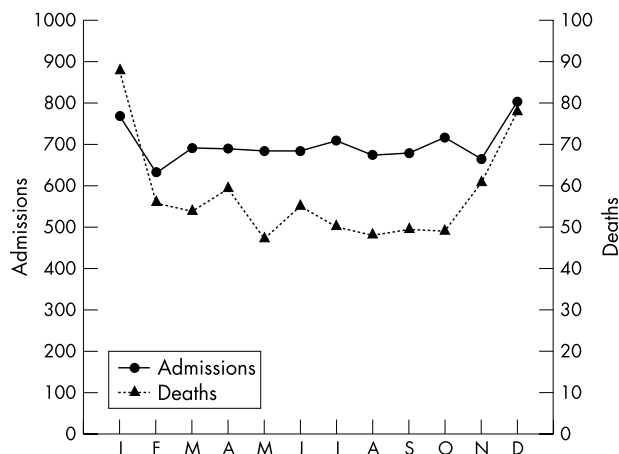


Figure 2 Total number of deaths and medical admissions each month. The data were collected retrospectively for the period 1996 to 2000.

without IHD in stages 1, 2, and 3; equivalent to 1265 patients without IHD each year. If, as was seen, 8.5% of these patients were discharged one day earlier, this would yield an average bed saving of about 107 days each year.

The median lengths of stay among the patients with IHD were six (range, 4–10), seven (range, 4–10), and seven (range, 4–10) days in the three stages. The apparent increase in one day between stages 1 and 2 was not significant ($p = 0.9$).

Readmission within one month

Table 2 shows the number of patients who were readmitted within one month of each admission. Some patients were readmitted more than once.

The readmission rate was similar in all three groups (Fisher’s exact test; $p > 0.05$). Most readmissions were in patients with IHD. There were no patients with a non-IHD diagnosis on the first admission and an MI diagnosis on the second admission. There were a few patients with a non-IHD diagnosis on the first admission and a diagnosis of IHD on the second admission, but the number of these patients was lowest in group 2. There were only seven patients with a diagnosis of IHD on the first admission and a diagnosis of MI on the second admission.

Deaths

There were 170 deaths within one month of admission in the study patients: 67 in patients without IHD, 103 in patients with IHD (49 initially coded as MI, and 54 coded as ACS without acute MI). Table 3 shows a breakdown of the causes of death.

Mortality was highest in stage 1, reflecting the increased admission and mortality in the winter months. Most of the increased mortality in stage 1 was accounted for by deaths in the patients without IHD. There were no differences between

Table 3 Causes of death of patients during the study period

Diagnosis	Stage 1 (%)	Stage 2 (%)	Stage 3 (%)	Total (%)
Non-IHD	41/397 (10.3)	11/238 (4.6)	15/314 (4.8)	67/949 (7.1)
MI	12/85 (14.1)	22/109 (20.1)	15/89 (16.8)	49/283 (17.3)
IHD non-MI	30/237 (12.7)	10/258 (3.8)	14/263 (5.3)	54/758 (7.1)
IHD	42/322 (13.0)	32/367(8.7)	29/352 (8.2)	103/1041 (9.9)
Total	83/719 (11.5)	43/605 (7.1)	44/666 (6.6)	170/1990 (8.5)
Study months	Oct–Dec	Jan–Mar	Apr–Jun	Oct–Jun

Figures in parenthesis are the % of total patients dying within the relevant diagnostic group. IHD, ischaemic heart disease; MI, myocardial infarction.

the mortality of patients admitted with MI in stage 1 (12 of 85), stage 2 (22 of 109), or stage 3 (15 of 89) (Fisher's exact test; $p > 0.05$). In patients without IHD, however, 5.7% (95% CI, 1.7% to 9.7%) more died in stage 1 (41 of 397) compared with stage 2 (11 of 238) (Fisher's exact test; $p = 0.01$).

Seasonal influences

For general comparative purposes, the total number of medical admissions each month, together with the absolute death rates, were collected retrospectively for the period 1996 to 2000 and expressed as numbers for each month of the year (fig 2).

Anomalies in data: false positives and negatives

Patients in stage 2 (troponin stage) were grouped into bands according to their cTnI concentrations and discharge diagnosis (table 4).

False negatives are difficult to define because troponin does not rise in stable angina, so that patients could be diagnosed as having angina and still have troponin concentrations $< 0.5 \mu\text{g/litre}$. However, patients diagnosed with MI, on the basis of history and ECG changes, should have troponin concentrations of at least $0.5 \mu\text{g/litre}$ or more in terms of our assay. For this reason, patients with a diagnosis of MI and troponin concentrations $< 0.5 \mu\text{g/litre}$ were considered to be false negatives. Patients with cTnI values $> 0.4 \mu\text{g/litre}$ and a discharge diagnosis of non-IHD were considered to be false positives. Although there were 20 apparent false positive cases ($\sim 3\%$ of all cTnI tests performed), a retrospective review of case notes and ECGs showed that only two were true false positives, with six thought to represent incomplete or incorrect coding errors. Of the two true false positives (with no clinical evidence of IHD as judged from their clinical notes and ECG), one had rheumatoid arthritis and the other patient was in renal failure. All eight apparent false negatives ($\sim 1.5\%$ of tests) were the result of premature (< 12 hours) blood sampling or late presentation/admission (> 2 weeks) after MI.

Death within one month of discharge and troponin values in patients with IHD

Table 5 describes deaths within one month of discharge according to cTnI concentrations. All except two of these deaths were the result primarily of IHD. One death in the $0-0.4 \mu\text{g/litre}$ subgroup (minimal myocardial damage) was from chronic obstructive airways disease, with IHD contributing to the cause of death, and one death in the $0.5-1.4 \mu\text{g/litre}$ subgroup (suggestive of unstable angina) was caused by a cerebrovascular event, with IHD contributing to the cause of death.

DISCUSSION

We found that the introduction of a troponin I service resulted in a significant increase in early discharge. It did not result in a significant increase in early readmission or death. It is interesting to note that the proportion of patients

discharged early also tended to be greater after withdrawal of the troponin service. This was probably because clinicians became accustomed to discharging patients after single normal "cardiac marker" estimation during stage 2 of the study. Our overall lengths of stay figures were skewed because of the prolonged length of stay of many patients in all three stages and, as an added factor, our data are complicated by seasonal variation in the rate of admissions, with stage 1 having the largest number of patients. Retrospective analysis of whole hospital data of medical admission and death rates over a four year period confirmed a higher rate of admission during the winter months, during which stage 1 of our study was conducted (fig 2). However, the absolute number of patients with suspected cardiac ischaemia remained fairly constant. Therefore, the excess numbers of patients in stage 1 were predominantly patients without IHD. The proportion of patients with IHD diagnosed with MI was higher in stage 2 (cTnI stage) compared with stages 1 and 3, reflecting the greater sensitivity of troponin testing in this setting (table 1).

There was no significant difference in overall mortality in the three stages (table 3), and arguably the introduction of troponin did not benefit coronary patient care. However, the 50% increase in the diagnosis of MI could be considered to be an increase in diagnostic accuracy, and in the long term these patients are likely to benefit from improved risk stratification. The apparent increased mortality in the non-IHD group in stage 1 is consistent with increased mortality during the winter months (table 2). The comparable mortality in stages 2 and 3 supports the hypothesis that early discharge of patients in stage 2 was not at the expense of an increased risk of IDH related death.

"It is interesting to note that the proportion of patients discharged early also tended to be greater after withdrawal of the troponin service"

The reduction in bed occupancy in stage 2 compared with stage 1 as a result of discharging patients early would be of no advantage if they were to be readmitted shortly after. Readmission rates were low in all three stages (table 2); most of the readmission episodes occurred in patients with already correctly identified IHD. There were no patients with a non-IHD diagnosis on first admission and MI on subsequent admission. The number of patients diagnosed as MI on their readmission episode was very small, and in absolute terms lowest in stage 2 (troponin stage); all these individuals had known IHD. A few patients with a non-IHD diagnosis were readmitted with an IHD diagnosis within a month, but these numbers were small and not significantly different in the three stages.

The consensus document of the Joint European Society of Cardiology/American College of Cardiology recommends the use of a cardiac troponin (I or T) for biochemical detection of myocardial damage, the cutoff being greater than the 99th centile value for an appropriate reference control group.¹⁴

Table 4 Anomalies (false positives and negatives). Troponin banding with diagnosis, showing anomalies in data (mismatch of troponin concentrations and diagnosis)

cTnI $\mu\text{g/l}$	Non-IHD	IHD excluding MI	MI	Total
0	85	69	2†	156
0.1-0.4	133	142	6†	281
0.5-1.4	11*	29	7	47
≥ 1.5	9*	18	94	121
Total	238	258	109	605

*Apparent false positives for IHD; †Apparent false negatives for MI.
cTnI, troponin I; IHD, ischaemic heart disease; MI, myocardial infarction.

Table 5 Deaths within one month of discharge and cTnI concentration in patients with IHD

	cTnI 0–0.4 µg/l	cTnI 0.5–1.4 µg/l	cTnI ≥1.5 µg/l
Total IHD patients	230	36	116
Deaths	6 (2.6%)	2 (5.6%)	24 (20.1%)

cTnI, troponin I; IHD, ischaemic heart disease.

Cutoff values for individual manufacturers' assays vary widely,¹⁵ and presently there are three candidates¹⁶ for an international reference preparation, with a crucial need for agreement. In practical terms a local "standard" troponin assay would help in drawing up common guidelines for multiple district general hospitals feeding into their tertiary centre to facilitate clinical dialogue. Using simple criteria, about 3% of cTnI tests in this study were apparently false positive and about 1.5% were false negative. It was reassuring that all of these could be explained. All but two of the false positives were coding errors and illustrate the prevalence of this in hospital practice.¹⁷ The remaining two false positives were probably ascribable to known analytical interference effects. There were no true false negatives on a basis of cTnI measurement 12 hours after the presumed ischaemic event. If normal cTnI is to be an important weighting factor in the early discharge of patients, care must be taken that sample timing has been appropriate. Current National Institute of Clinical Excellence (NICE) guidelines suggest that all patients with raised cTnI in the absence of an ST rise on ECG should be considered for antiplatelet glycoprotein IIb/IIIa treatment.¹⁸ To estimate the number of patients eligible in stage 2, we identified 79 patients (13%) with a 12 hour cTnI value > 0.4 µg/litre and no ST elevation on the admission ECG, as reported previously¹⁹; we do not know what the cTnI concentrations would have been if they had been measured at admission.

In a recent questionnaire,¹ 40% of laboratories undertaking troponin assays provided a random access service. Theoretically, our strategy might have resulted in an eight hour delay in the treatment that has been proved to be of benefit to some individuals. The National Academy of Clinical Biochemistry in their 1999 recommendations²⁰ specify that cardiac markers should be available on a random access basis, with no more than one hour from the time of blood sampling to the result being available. Our "business"

strategy was to focus on the early discharge of patients. In bed saving terms, a cTnI value < 0.5 µg/litre does not rule out the presence of significant but stable coronary artery disease, and troponin should be combined with clinical and ECG findings, along with exercise ECG or isotope heart scan, to risk stratify patients.²¹ However, patients with a cTnI concentration < 0.5 µg/litre may be considered for early discharge with later risk evaluation, assuming that there is no other medical condition requiring continued stay in hospital. We found that the risk of death from cardiovascular cause in these patients is very low (table 5) compared with those with a cTnI concentration > 0.4 µg/litre. There were 15 deaths during stage 2 in patients with cTnI <0.5 µg/litre. Nine of these patients did not have IHD, and of the six with IHD, five were over 80 years old, and IHD was the principal cause of death in only two of these six patients. Both of these patients had MI presenting late, thus yielding a false negative cTnI result. A retrospective district general hospital study from Ireland compared over 200 admissions using traditional cardiac markers with cTnI.⁴ The average length of stay for patients without MI was reduced by two days. A further district general hospital²² study randomly sampling over 200 patients before and after the introduction of cTnI reported a reduction of median length of stay from three to two days in patients with non-diagnostic ECGs and cardiac risk factors/previous history of coronary disease. Troponin was measured on admission and 12 hours later. However, they reported an increase in length of stay from five to eight days for high risk patients presenting with ECG changes. They suggested that prompt transfer to tertiary cardiac centres would result in bed stay savings to district general hospitals. It may be said that this is at the expense of valuable tertiary centre beds, but at the same time, it can be argued that the highest risk patients with acute coronary syndrome in need of such care may be more accurately identified and treated.

In conclusion, three times daily troponin was associated with 8.5% more patients without IHD being discharged on the day after admission, with no evident detriment to their short term well being, saving approximately 107 bed days each year. A greater proportion of patients were diagnosed with MI after the introduction of troponin I and these patients may benefit from better risk stratification. The explanation beyond reasonable doubt of all false positive and negative results enhanced confidence in cTnI. As a discharge tool in patients presenting with chest pain (after verification of blood sample timing), we have shown that replacing traditional cardiac markers with cTnI significantly improves the safe and appropriate discharge of low risk patients, with additional benefits with respect to bed occupancy and health care economics.

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Take home messages

- Replacing traditional markers (cardiac enzymes) of myocardial infarction (MI) with a single troponin I measurement made at one of three fixed times within 24 hours resulted in 8.5% more patients without ischaemic heart disease being discharged on the day after admission, with no evident detriment to their short term well being
- More patients were diagnosed with MI after the introduction of troponin I and these patients may benefit from better risk stratification
- All false positive and negative results could be explained
- For patients presenting with chest pain, replacing traditional cardiac markers with troponin I significantly improves the safe and appropriate discharge of low risk patients, with additional benefits with respect to bed occupancy and health care economics

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ECHO

Age and symptoms predict male NGU best



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Young age and symptoms should be included in predictive algorithms of urethral infection; they are better predictors of urethral infection in men than numbers of urethral polymorphonuclear leucocytes (PMNs), an evaluation study of non-gonococcal urethritis (NGU) has disclosed.

The evaluation substituted the ligase chain reaction for PMN count as the diagnostic test for *C trachomatis* and calculated sensitivity and specificity of the cut offs in PMN count in stained urethral smears as well as the likelihood of PMN count, symptoms, and age predicting *C trachomatis* urethritis. Over 300 men being screened for sexually transmitted infection at one clinic over four weeks were tested; none had gonococcal urethritis.

Age below 30 versus 40 and above increased likelihood of infection with *C trachomatis* 13-fold; PMN count, at ≥ 20 per high power field (hpf), sixfold and 5–9 per hpf, threefold; and dysuria threefold. However, the sensitivity of PMN count at ≥ 5 per hpf was just 63% and specificity 77%. Over a third of the men with *C trachomatis* by ligase chain reaction had PMN counts < 5 per hpf—too many to justify the accepted diagnostic cut off at ≥ 5 . The proportion of men with NGU on a stained urethral smear was 26%, and it was associated with *C trachomatis* in 8%, according to the ligase chain reaction.

With nucleic acid amplification becoming available for *C trachomatis* it made sense to re-evaluate apparent relations between urethral infection and clinical picture, PMN count, and routinely available information like age and symptoms.

▲ Haddow LJ, *et al*. *Sexually Transmitted Infections* 2004;**80**:198–200.



Troponin I, laboratory issues, and clinical outcomes in a district general hospital: crossover study with "traditional" markers of myocardial infarction in a total of 1990 patients

F Jishi, P R Hudson, C P Williams, et al.

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