Will serum enzymes and other proteins find a clinical application in the early diagnosis of myocardial infarction?

SIR,—Dr Timmis discussed the limited early biochemical diagnosis of acute myocardial infarction in guiding thrombolytic therapy.1 The mortality of infarct patients in Newham General Hospital who present without ST elevation is only a third that of those with ST elevation, none the less about one in 20 of such patients died. In addition, in infarct patients who present with predominant ST depression one year mortality is high (31%).2 De Wood et al’s angiographic study of non-Q wave infarction was performed up to 24 hours after acute myocardial infarction3 and the patency rate caused by spontaneous coronary re-continuation would be expected to be higher than in the first 12 hours, the time window when thrombolytic therapy is believed to be effective.4 Even so, 26% of these patients had occluded coronary arteries and might have benefited from revascularisation treatment. The result of the ISIS-2 trial suggests that patients without ST elevation (except bundle branch block) would not benefit from thrombolytic therapy.5 The inclusion criteria of ISIS-2 raise the possibility that an appreciable number of these patients may not have had a myocardial infarction at all. No definite data are currently available to direct the treatment of patients with early biochemical confirmation of acute myocardial infarction, though the late artery study6 did include patients with old or equivocal electrocardiographic changes and raised concentrations of cardiac enzymes. The LATE study showed a significant reduction in mortality in patients treated with alteplase when thrombolysis was started 6-12 hours after onset of symptoms. Other treatments such as β blockers, ACE inhibition, and aspirin have been shown to be useful in the early management of acute myocardial infarction.7 Early biochemical diagnosis may be useful in guiding this treatment.

Furthermore the use of rapid assays may offer advantages in terms of efficiency. When patients with atrial chest pain may be discharged earlier after negative results. None the less, to exclude acute myocardial infarction, myoglobin should be measured 4-6 hours after the onset of chest pain and creatine kinase MB 6-8 hours after the onset of chest pain.8 Rapid biochemical diagnosis of acute myocardial infarction may be useful in guiding treatment and the more efficient management in coronary care units of patients who present with chest pain.


Letters

SIR,—We studied patients with acute chest pain and transmural ST elevation in the absence of myocardial infarction in the elderly, in whom a rapid diagnostic test would be useful. We studied a group of 2544 patients without ST elevation on the ECG, the 35 day mortality was 7.5% in the placebo group and 6.4% in the group treated with alteplase.
About two thirds of patients who present with ST depression or T wave inversion on an admission ECG will have confirmed acute myocardial infarction on discharge. The patients with a discharge diagnosis of infarction are potentially those who would benefit from thrombolytic therapy. It has been shown in theory and in practice that the use of early immunosassay of creatine kinase MB can achieve 94% sensitivity and specificity for prediction of the discharge diagnosis of infarction.

A subgroup analysis that might yield valuable information could be undertaken by the ISIS-3 coordinators. In ISIS-3, 9158 patients were excluded as having an "uncertain" indication for thrombolytic therapy; 70% of these had an admission ECG criterion other than ST elevation. Fifty nine per cent of the patients in the whole "uncertain" group had a discharge diagnosis of myocardial infarction. Thirty five day mortality was 8.3% in the whole "uncertain" group and 11.4% in those with a discharge diagnosis of infarction. What was the mortality for thrombolytic treatment and what for placebo in this last group? As far as we are aware these figures have never been published.

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These letters were shown to the author, who replies as follows:

Sir.—The concerns of Lee et al are certainly understandable. However, the recent history of cardiac therapeutics is littered with examples of drugs on theoretical grounds should have been beneficial but which, when put to the test of a randomised trial, have proved unhelpful or harmful. Examples include isotopes in heart failure, calcium antagonists in unstable angina, and type 1 antiarrhythmic treatment in the post-infarction period. 1, 2 To this list should perhaps be added thrombolytic therapy in patients with unstable angina and non-Q wave myocardial infarction, following the report of the TIMI-IIIB investigators which concluded that in this group thrombolytic therapy "is not beneficial and may be harmful." 3 In this study presenting ECGs were non-diagnostic in 90% of cases, and in the remaining ST elevation was only transient.

Though I was careful to make implicit in my choice of words that the results of subgroup analyses of randomised trials can provide clues about the likely efficacy of treatment but not provide an answer to the question of how patients are selected for treatment, I may have led some to assume the opposite. An analysis of the trial data from ISIS-3 shows that this is not a reasonable assumption. However, they may make the point that a definitive answer will be obtained only from a randomised trial of treatment in patients who present with a non-diagnostic ECG and then go on to infarction. The TIMI-IIIB trial, while not designed to provide this information, certainly comes close to it. At present, therefore, there seems little justification for selecting patients with cardiac chest pain and a non-diagnostic ECG for thrombolytic therapy on the basis of rapid biochemical assays.

Finally, the assertion of Lee et al that rapid biochemical assays may increase "efficiency" by permitting early discharge of patients with negative results is potentially dangerous if it encourages premature discharge of patients with unstable angina whose need for coronary care is no less than that of patients with acute infarction.

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Haemodynamic deterioration after treatment with adenosine

SRH—It is well known that non-dihydropyridine calcium antagonists, β-blockade, and digitals can lead to an increase in the ventricular rate and haemodynamic deterioration during pre-excitation atrial fibrillation. This is because conduction through the accessory atrioventricular connection is facilitated, and the effect relates to sympathetic activation as well as abolition of retrograde concealed conduction into the accessory pathway. The case reported by Cowell et al illustrates that adenosine is no exception, especially if it is given repeatedly.

Although the very high rate during pre-excited atrial fibrillation may have been the primary cause for the haemodynamic deterioration, another possibility is that the patient's condition worsened after the repeat administration of adenosine for the wrong indication (that is, conversion of atrial fibrillation). In our opinion, Cowell et al should have stressed this fact more than anything else because it illustrates that too enthusiastic and indiscriminate use of adenosine can kill patients with the Wolff-Parkinson-White syndrome. Williams class 1A agent such as pro-cainamide or a 1C agent, rather than adenosine, is indicated for safely terminating rapid pre-excited atrial fibrillation.

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This letter was shown to the author, who replies as follows:

Sir.—We agree with Dr Crijns and Dr Lie that repeat administration of adenosine once atrial fibrillation had been established was inappropriate. However, this patient deteriorated haemodynamically after adenosine because a narrow complex tachycardia converted to more rapid pre-excited atrial fibrillation. There was no evidence of a progressive rate increase when administration of adenosine was repeated; the patient deteriorated after the onset of atrial fibrillation. There was no further deterioration at the time of repeat adenosine administration.

We agree that the agents suggested could be used to convert pre-excited atrial fibrillation chemically but emphasise that electrical cardioversion should be used if there is any evidence of haemodynamic compromise.

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Near miss paradoxical embolism

SRH—In their timely reminder of the importance of a patent forornae ovale as facilitator of paradoxical embolism Prakash et al state...
Will serum enzymes and other proteins find a clinical application in the early diagnosis of myocardial infarction?

I. Gunn, D. Matthews and I. O'Brien

*Br Heart J* 1995 73: 102-103
doi: 10.1136/hrt.73.1.102

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