Redefining myocardial infarction

Sir,

The editorial by Dr Birkhead (Vol 62(5), 2001, p. 260) focused on a recent proposal for a new definition of myocardial infarction and its potential implications. The proposal was made in a so-called 'consensus statement' from a joint committee of the European Society of Cardiology and the American College of Cardiology. Because of their high sensitivity to and specificity for myocyte necrosis, cardiac troponin assays are a pivotal feature of the redefinition. As a consequence, it is expected that widespread adoption of the new definition will lead to a swell in the number of reported cases of acute myocardial infarction.

In our own centre, data on all cases of admission with suspected acute coronary syndrome, over a 6-month period, reveal that the redefinition would lead to a 54% increase in the number of patients diagnosed as having had an acute myocardial infarction.

It has come to be accepted that there exists a wide and continuous spectrum of acute coronary syndromes. At one end of that spectrum is unstable angina without troponin release and at the other is an extensive, full-thickness myocardial infarction with consequent left ventricular systolic dysfunction. Moreover, the prognosis across this spectrum has also been shown to be continuous in its adversity and to be predictable by serum levels of cardiac troponin (Antman et al, 1996).

For patients, doctors and society in general, however, the label of myocardial infarction has well-defined and far-reaching implications. A select group of clinicians has decided that the goal posts for this label should be moved. Before imposing this authoritative opinion on clinical colleagues, wouldn't a wider discussion have been a wise and prudent move? Surely the views of employers and insurers, as well as physicians, are crucial to the application of the suggested change in definition.

One possibility would be to identify a serum troponin level which would approximate to the currently accepted thresholds of creatine kinase (or creatine kinase-MB isoenzyme), above which infarction is diagnosed. Clinical events associated with serum troponin levels below this ceiling might attract a different diagnostic label which is less emotionally charged. The difference between unstable angina with minimal myocardial injury and myocardial infarction may be a semantic one for the purist on board the 'Troponista' battle bus, but if you're the bus driver, there is a wide gulf between the two.

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Antman EM, Tanasijevic MJ, Thompson B et al (1996) Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Engl J Med* **335**(18): 1342–9

Sir,

Definitions in medicine should be based on sound pathophysiology and should be of practical value for classification and audit. The new proposed definition for myocardial infarction (Joint European Society of Cardiology/ American College of Cardiology Committee, 2000), which is based on 'a typical rise and gradual fall' in troponin T or troponin I concentrations rather than the generally accepted rise in creatine kinase (CK) activity, fulfils neither of these criteria.

Pathophysiology

Acute myocardial infarction is a discrete clinical event caused by occlusive coronary thrombosis resulting in macroscopic myocardial necrosis. Unstable angina is characterized clinically by repeated prolonged attacks of cardiac pain, is caused by non-occlusive coronary thrombosis and typically leads to myocardial ischaemia without necrosis. Some cases of unstable angina, however (about 30–40%) (Hamm et al, 1992; Stubbs et al, 1996), do show biochemical evidence of necrosis, evidenced by a rise in troponin without a rise in CK. The reason is almost certainly that microemboli from an unstable atheromatous plaque are causing downstream microinfarcts. This is different from occlusive coronary thrombosis and requires a different management strategy.

Practical considerations

The advent of clinical governance, national medical audit and performance indicators forces clinicians to realize what epidemiologists have known for years — that generally agreed definitions are essential. If some UK hospitals abandon measurement of CK in favour of troponin, about one third of cases previously diagnosed as unstable angina may now be labelled infarction.

Unstable angina, defined clinically, is now at least 50% more common than infarction. Thus, hospitals using troponin solely as a serum marker are likely to inflate their numbers of cases of infarction by 50% or more. As case fatality for infarction is typically 15–20% and for unstable angina 2–4%, clinical performance for hospitals using troponin will appear to be better than it really is, and comparisons with hospitals using CK will be invalid.

Conclusion

In the opinion of this author, measurement of both troponin and CK is essential for proper management of the acute ischaemic syndromes. For the diagnosis of myocardial infarction, the conventional definition, including a rise in CK activity to greater than twice normal, should be retained.

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Hamm CW, Ravkilde J, Gerhardt W et al (1992) The prognostic value of troponin T in unstable angina. *N Engl J Med* **327:** 146–50

Joint European Society of Cardiology/ American College of Cardiology Committee (2000) Myocardial infarction redefined — a consensus document of the joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction. *Eur Heart J* **21:** 1502–13

Stubbs P, Collinson P, Moseley D et al (1996) Prospective study of the role of cardiac troponin T in patients admitted with unstable angina. *Br Med J* **313:** 262–4

Sir,

While it may be true that the new biochemical definition of myocardial infarction could distort the data on prevalence and incidence of this disorder, slavish adherence to the 'conventional' biochemical confirmation of infarction (utilized in Dr Birkhead's hospital) could distort the data in the opposite direction for the following reasons: the kinetics of creatine kinase (CK) release mean that the enzymatic peak can be easily missed if blood samples are not taken every 4–6 hours on the first day or two (Yusuf et al, 1987) (or, at the very least, 8-hourly for the first 24 hours; Dufour et al, 1989). This is what makes a mockery of the time-honoured diagnostic cut-off level of a total CK of >2 times the upper limit of the normal range in those hospitals which do not adhere to this time-consuming sampling protocol.

Furthermore, in some patients with authenticated myocardial infarction, the typical rise and fall in total CK (characterized by doubling of enzyme levels) takes place entirely within the normal range (Yusuf et al, 1987).

The validity of utilizing the criterion of doubling of the enzyme level (regardless of its location in the 'normal' range) is supported by a study in which patients who manifested a doubling of their lowest CK-MB level proved to have myocardial necrosis (on the basis of the electrocardiographic microsphere technique) despite having failed the criterion of CK-MB >2 times the upper limit of the normal range. The authors of that study concluded that 'by conventional enzymatic approach, diagnosis of non-Q wave infarction can be missed in a sizeable number of patients' and present important clinical implications (Carpeggiani et al, 1989).

Owing to its more advantageous diagnostic time window, extending 12–24 hours after symptomatic presentation of myocardial infarction (de Winter et al, 1995; Chiu et al, 1999), troponin levels do not require frequent sampling in order to enhance sensitivity, but the problem that is increasingly being recognized is one of spurious elevation of this parameter (Ng et al, 2001).

This can be mitigated by serial testing of troponin I, CK-MB and myoglobin during the first 90 minutes following clinical assessment, with consequent accuracy of 91% in predicting whether the troponin level is indicative of myocardial infarction in the individual case (Ng et al, 2001).

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Carpeggiani C, L'Abbate A, Marzullo P et al (1989) Multiparametric approach to diagnosis of non-Q wave acute myocardial infarction *Am J Cardiol* **63:** 404–8

Chiu A, Chan WK, Cheng SH, Leung CK, Cho CH (1999) Troponin-I, myoglobin, and mass concentration of creatine kinase-MB in acute myocardial infarction. *Q J Med* **92:** 711–8

de Winter RJ, Koster RW, Sturk A, Sanders GT (1995) Value of myoglobin, troponin T, and CK-MBmass in ruling out an acute myocardial infarction in the emergency room. *Circulation* **92:** 3401–7

Dufour DR, LaGrenade A, Guera J (1989) Rapid serial enzyme measurements in evaluation of patients with suspected myocardial infarction *Am J Cardiol* **63:** 652–5

Ng SM, Krishnaswamy P, Morrisey R, Clapton P, Fitzgerald R, Maisel AS (2001) Mitigation of the clinical significance of spurious elevations of cardiac troponin I in settings of coronary ischemia using serial testing of multiple cardiac markers. *Am J Cardiol* **87:** 994–9

Yusuf S, Collins R, Lin L et al (1987) Significance of elevated MB isoenzyme with normal creatine kinase in acute myocardial infarction. *Am J Cardiol* **59:** 245–50

Sir,

I read Dr Jolobe's letter with interest. He reiterates the point that CK is not as sensitive as troponin assay but is not correct in suggesting that slavish adherence to the conventional definition will distort the data in the opposite direction. Slavish adherence will provide the incidence of the condition as defined. What it will not do is include cases where microembolization from unstable plaque thrombus results in elevation of troponin but does not cause sufficient necrosis to produce elevation of CK. The point raised that there has to be repeated sampling for CK over 24 hours is correct, however. The papers quoted by Dr Jolobe (Yusuf et al, 1987; Dufour et al, 1989) are from the pre-troponin era but remind us that CK-MB isoenzyme is also more sensitive than CK.

My concern in writing this editorial differs from that expressed by Dr Jolobe. It was to express the concern that a diagnosis of infarction should not be made on the basis of any elevation of troponin. Whether at some time in the future a global, rather than a European/American axis definition, can be based on an agreed multiple of the threshold value of a standardized assay remains to be seen; this should be the goal. Until this is achieved, I believe we should continue to use CK and troponin together.

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Ascitic fluid analysis: the role of imaging

Sir,

The review article by Drs Jeffery and Murphy (Vol 62(5), 2001, p. 282) on the analysis of ascitic fluid was a comprehensive review of the laboratory-based analyses that are commonly used. The radiological investigations were not mentioned, and yet it is vital that these are used as complementary investigations alongside biochemistry and haematology.

Ultrasound examination allows for confirmation of the diagnosis and also for clues as to the aetiology by assessing the characteristics of the intra-abdominal organs and appearance of the fluid. Doppler ultrasound is essential to establish hepatic and portal vein patency. Computed tomography scanning further visualizes the solid intra-abdominal organs. These modalities should be used in conjunction with laboratory-based investigations to establish the cause of ascites.

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