How do we define myocardial infarction? A survey of the views of consultant physicians and cardiologists

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Abstract

In 2000, the European Society of Cardiology and American College of Cardiology issued a consensus document concerning the redefinition of myocardial infarction (MI). They proposed that the diagnosis of acute MI should be based on the rise and fall of specific markers combined with at least one of the following: ischaemic symptoms, ECG changes consistent with ischaemia or infarction, or coronary intervention. The implications of this redefinition are widespread, and it has been met with mixed opinions from physicians. Here we present the results of a survey, sent to 1,000 consultants in cardiology and general medicine, concerning the availability and their use of cardiac markers and their current working diagnosis of MI. Four case studies were included in the survey. Some 361 responses were analysed. Creatine kinase (CK) remains the most frequently used marker for the diagnosis of MI, but 23% of consultants had moved to a definition based on troponins. Fourteen per cent of consultants no longer used CK in their practice. Ninety-two per cent of consultants had access to troponin assays. Definitions varied widely between consultants, even within individual hospitals, as did the responses to the case studies.

Key words: acute coronary syndrome, myocardial infarction, troponin, biological markers.

Br J Cardiol 2004;**11**:34–8

Introduction

The diagnosis of acute myocardial infarction (MI) defined by the World Health Organisation has required two of three findings from chest pain, development of new Q waves on the electrocardiogram (ECG) and a rise in creatine kinase (CK) to twice the upper limit of normal.[1] Acute coronary syndromes (ACS) that do not fulfil this rigid definition are recognised to be associated with an increased risk of subsequent death and cardiac events.[2,3] The development of assays for troponin T and I, which are highly sensitive and specific for myocyte necrosis, has led to proposals for a new definition of MI encompassing much smaller levels of cardiac damage, but reflecting this risk.

In 2000, the European Society of Cardiology (ESC) and American College of Cardiology (ACC) issued a consensus document concerning the redefinition of MI.[4] They proposed that the diagnosis of acute MI should be based on the rise and fall of specific markers, such as troponins or CK myocardial B fraction (CKMB), combined with at least one of the following: ischaemic symptoms, ECG changes consistent with ischaemia or infarction, or coronary intervention. The implications of this change are widespread, and it has been met with mixed opinions from physicians.

Here we present the results of a postal survey sent to 1,000 UK consultants in general medicine and cardiology. The survey was designed to gauge their working definition of MI and their use of cardiac markers.

Method

A postal survey was sent to 600 consultant cardiologists at 224 UK hospitals (who were identified from the Directory of Cardiology 2001). A further 400 surveys went to consultant physicians in 57 randomly selected UK hospitals. The questionnaires were sent between February and March 2002. Replies were traceable to the hospital to which the questionnaires were sent, but not to individuals.

The survey asked for background details about the hospital, and availability and use of glycoprotein (GP) IIb/IIIa antagonists and cardiac markers. It went on to ask about their current working definition of MI and about guidelines within the hospital. Finally, there were four case studies, and space for comments.

Comparison between numbers of patients with ACS seen by cardiologists and general physicians was made using the Mann-Whitney U Test. Analysis of diagnosis and treatment of ACS according to consultant type (including use of cardiac markers, adoption of a written policy, perception of agreement, use of GP IIb/IIIa antagonists and diagnosis of MI) was carried out by χ^2 analysis.

Results

The overall response rate was 38% (42% from the Directory of

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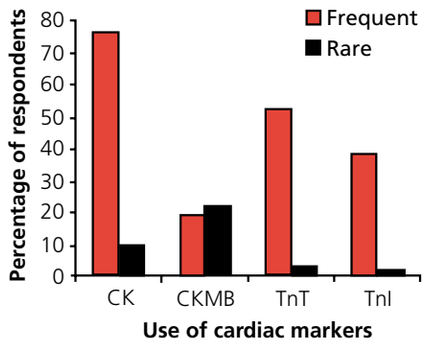
Figure 1. Data and chart for use of cardiac markers (* myoglobin, ALT, AST, LDH, Hbd)

	CK		CKMB		TnT		TnI		Other*
	Frequent	Rare	Frequent	Rare	Frequent	Rare	Frequent	Rare	
No	274	39	69	81	188	9	138	6	61
%	76	10	19	22	52	3	38	2	17



Key: No = number; CK = creatine kinase; CKMB = creatine kinase myocardial B fraction; TnT = troponin T; TnI = troponin I; ALT = alanine aminotransferase; AST = aspartate aminotransferase; LDH = lactate dehydrogenase; Hbd = beta hydroxybutyrate dehydrogenase (LDH isoenzyme)

Table 1. Indication for use of cardiac markers (as percentage of respondents using each marker)

		To define MI %	To estimate size of infarct %	For risk stratification to decide therapy %	To detect early re-infarcts %	For early discharge %
CK	Frequent	86	50	9	30	8
	Rare	18	13	0	54	3
CKMB	Frequent	78	36	13	32	13
	Rare	37	1	0	16	6
Trop T	Frequent	70	14	77	13	77
	Rare	3	0	78	11	44
Trop I	Frequent	64	19	84	9	84
	Rare	50	0	83	17	33

Key: CK = creatine kinase; CKMB = creatine kinase myocardial B fraction; Trop = troponin

Cardiology, 28% of those from randomly selected hospitals). Nineteen replies were not useable, leaving a total of 361 replies for analysis. At least one reply was received from 183 of the 214 hospitals (82% of hospitals).

Consultants and hospitals

Two hundred and twenty-eight (63%) replies were from district general hospitals (DGH), 63 (17%) from teaching hospitals and 70 (19%) from tertiary referral cardiology centres. Of the 361 replies, 159 responders (44%) described themselves as cardiologists, 93 (26%) as cardiologists with general internal medicine (C+GIM) and 109 (31%) as general physicians (GIM). The consultants treated a median of eight patients with ACS a week (range 0–50 patients). GIM consultants saw significantly fewer ACS patients than cardiologists (median three patients for GIM, 10 for C+GIM or cardiology, $p<0.0001$). The number of coronary care unit (CCU) beds varied from two to 32 (median eight).

Availability and use of markers of cardiac damage

CK remains the most widely used marker of cardiac damage and diagnosis of MI, with 76% of respondents using it frequently or routinely (figure 1). However, 14% of respondents no longer use it at all. Other non-specific markers are still used by 17% of respondents.

Ninety-two per cent of respondents have access to measurement of either troponin I or T levels. Troponin T is slightly more widely used than troponin I (197 replies *vs.* 144). Several respondents commented that availability was restricted or that they had to send samples away for analysis, making them less useful for guiding acute management. Common indications included aiding diagnosis of MI, risk stratification and facilitating early discharge (table 1). Eleven per cent of respondents who frequently use troponins stated that they used it to detect early reinfarctions, despite the fact that it is less suitable for this purpose, as levels remain elevated for up to two weeks after MI.[5]

Forty-two per cent of respondents used CKMB, either routinely or rarely. Of the 28 respondents who do not have access to troponins, 16 use CKMB, and 12 state that they have no access to specific markers of cardiac damage. When these replies were cross-checked with other replies from the same hospitals, only one hospital could be identified that genuinely had no access to troponin I, troponin T or CKMB. There was no difference in use of markers between cardiologists or GIM physicians.

Definition of myocardial infarction

Consultants were asked how they currently define acute MI in daily working practice. They were given three options:

A: Two of three: cardiac chest pain/elevated markers/ECG changes
B: Elevated markers plus either chest pain or ECG changes
C: Anyone with elevated markers

They were then asked to state which markers they used as part of their definition.

The majority used one of the first two definitions: A: 163 (45%), B:158 (44%). Twenty-two consultants (6%) defined MI based on markers alone (option C). Of these, eight used levels of troponins, one CKMB, and four CK. Three gave no reply and offered no alternative definition. Sixteen gave alternative definitions, including elevated markers plus ECG changes (five respondents) or all three of pain, ECG changes and markers (three respondents). Four commented that they used different definitions for ST segment elevation MI and non-ST elevation MI.

Overall, 83 consultants (23%) use troponins alone for their definition. Seventy-six (21%) are using just CK or other non-

Box 1. Case scenarios used as part of the questionnaire

Case 1: 68-year-old male with 30 minutes of left submammary pain, not pleuritic or reproducible, but 'like my heart attack, Doc'. No old notes. On ECG, left ventricular hypertrophy with lateral ST depression – no old ECGs for comparison. CK peak 550, troponin T normal on three occasions.

Case 2: 76-year-old woman presenting with pulmonary oedema, old left bundle branch block (LBBB), troponin T 0.12,CK measurements normal. No chest pain, but known diabetic. Known moderately impaired left ventricular function.

Case 3: 54-year-old man with ischaemic heart disease, previous MI, poor left ventricular function presents with ventricular tachycardia. No new changes on ECG after cardioversion with a bolus of amiodarone. No chest pain. Troponin T 0.2, CK normal.

Case 4: As above but required DC cardioversion (2x200J), troponin T 0.2, CK 350.

specific markers. Forty-five hospitals (25%) appear to have adopted troponins as their main marker in the diagnosis of MI. Some of these retain CK for detecting reinfarctions. This includes 24 hospitals from which only one response was received, but it corresponds well with the estimate above, that 23% of consultants are using troponins rather than CK.

There was a large range of troponin levels used as the 'cut-off' for MI (where they were included as part of the definition). This was particularly true for troponin I, for which many assays are available: of those who use it, 41 (45%) replied that they would accept any rise as being abnormal and 36 (39%) stated a definitive figure.

Of the 144 consultants using troponin T to aid definition of MI, 73 (51%) stated that they would consider any rise to be significant and 50 specified a value ranging from > 0.01 to > 1.0 µg/L. The most common value used was 0.1 µg/L (30 replies).

Hospital policies concerning definition of MI

The consultants were asked whether they were aware of a hospital policy (either written or verbal) concerning the definition of MI, and whether there was agreement within the hospital concerning the definition of MI.

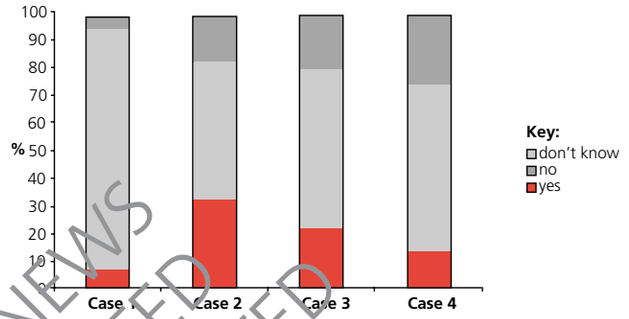
Overall, 46% of respondents had a policy (13% written, 33% verbal). Forty-five per cent said they had no hospital policy, and 9% were uncertain. GIM consultants were significantly less likely to know whether a policy existed (24% GIM *vs.* 3% GIM/cardiology *vs.* 1% cardiology consultants, p<0.001).

There was widespread acknowledgement that disagreement existed between individual consultants within hospitals. Only 47% stated that agreement existed within their hospital. Consultants who were aware that a written policy existed were more likely to consider there to be agreement within their hospital (71% with a written policy *vs.* 60% with a verbal policy *vs.* 31% with no policy, p=0.0004). This would suggest that production of a written policy encourages agreement.

For 45 hospitals there were replies from three or more consultants, enabling some assessment of agreement between doctors within a hospital to be made. Only one hospital had a written policy and all doctors felt there was agreement within the hospital on the definition of MI. At two other hospitals (without a definite written policy) all the respondents said they had agreement.

Figure 2. Data and chart showing responses to the case studies

	Case 1				Case 2				Case 3				Case 4			
	Yes	No	DK	NR	Yes	No	DK	NR	Yes	No	DK	NR	Yes	No	DK	NR
No	24	315	15	6	116	181	56	6	78	209	68	6	47	217	91	6
%	7	87	4	2	32	50	16	2	21	58	19	2	13	60	25	2



Key: No = number; DK = don't know; NR = no reply. In each case, six respondents did not reply.

Case histories

Four brief case scenarios were described, and consultants were asked whether they would diagnose a MI in each instance. The histories are described in box 1, and responses are shown in figure 2.

In case 1, the majority agreed that MI should not be diagnosed (315 responses, 87%). The 24 consultants who said they would diagnose MI included eight cardiologists from tertiary referral centres who used troponins. Two others explained that they would not have measured the troponin and four did not have access to troponin T, and may be unfamiliar with it.

Cases 2, 3 and 4 provided much more diverse responses, in keeping with the 'grey' nature of the cases. Twenty respondents commented that acute left ventricular failure can result in a small rise in troponins. Twenty-three commented that ventricular tachycardia (or other tachyarrhythmias) can result in a troponin rise, but there was less agreement on whether DC cardioversion affects the troponin: seven commented that it could lead to a rise, and six said that it did not.

Responses varied according to the markers and definitions used by the consultants. For example, while 32% of all those who responded said that they would diagnose MI in case 2, this rose to 49% if the responses were limited to the 159 consultants who use troponin T at all, and to 59% of the 49 consultants who

use troponin T as the main marker to diagnose MI. Similar results were seen in cases 3 and 4 (22% *vs.* 34% *vs.* 49%; 13% *vs.* 21% *vs.* 22%, respectively). There was no correlation between consultant type and diagnosis of MI.

Discussion

This survey confirms that the definition of MI varies widely, even between individuals within a hospital. The majority of respondents based their diagnosis on a combination of clinical and biochemical markers. Surprisingly, 6% of consultants define MI on raised levels of markers alone. Definitions ranged from conservative (for example, cardiac chest pain plus ECG changes and CK rise three times the upper limit of normal, or development of new Q waves on ECG), to ready (for example small rises in sensitive markers alone).

Although CK remains the most common biochemical marker used in the definition of MI, approximately 25% of hospitals and consultants have moved towards a definition of MI based on troponins. Only a minority of respondents specified an exact value for the troponin level used in their definition, and when they did they rarely stated the functional sensitivity for their assay. The ACC/ESC guidelines recommend a reading above the 99% functional sensitivity level of the assay as abnormal.[4]

Several comments stated that the 'label' given to the patients was not important, but rather their management. It is true that a precise definition may not affect patient treatment, but the definition of MI is important to patients in other ways. Apart from the psychological implications of the diagnosis, it can affect patients' access to cardiac rehabilitation and other interventions. The implications' of a new definition also reach beyond the immediate management of the patient. In two recent analyses, adoption of the new definition resulted in a significant increase in the number of patients defined as having an MI.[6,7] Epidemiologists require a consistent diagnosis in order to follow trends in disease incidence. Interpretation and application of clinical trial data may be affected, as MI is a common inclusion criterion and end point. From the patient's perspective, the diagnosis influences employment, ability to obtain mortgages and insurance, and continuing to drive.

One problem with the proposed new definition is that it would include a wide spectrum of disease. Thus, many consultants have developed their own definitions, and 75 (20%) were using terms like mini-MI, microinfarction or the vague 'acute coronary syndrome'.

Several consultants called for the term 'myocardial infarction' to be reserved for pathologists, and for the use of new terms reflecting the clinical spectrum of the disease (and the variation in treatment). More, however, simply called for a consensus definition that everyone would apply, to overcome the current confusion.

The case studies prompted interesting results and comments. A surprisingly high number of consultants would diagnose MI in the first case study, despite repeatedly normal troponin levels; these included some who were familiar with regular use of troponin T. In all four case studies, respondents frequently stated that they would check a CKMB in addition to troponin and CK. This is despite the fact that troponin is recognised to be the most specific and sensitive marker of myocyte necrosis, and may reflect respondents' lack of familiarity or comfort with newer assays. Consultants frequently returned to terms such as ACS, rather than committing themselves to a diagnosis of MI.

Case studies 2–4 described patients with elevated troponin levels who presented with pulmonary oedema or ventricular tachycardia (but without other features to confirm MI). These 'grey cases' demonstrate the limits of any rigid definition of MI. In each case, the rise in troponin may reflect an MI (with subsequent ventricular tachycardia [VT] or left ventricular failure [LVF]), or may be the result of insufficient myocardial oxygen supply (as a result of the VT or LVF) leading to secondary myocyte necrosis.

LVF is widely recognised as a cause of troponin release,[8,9] even if it is not due to coronary occlusion. Tachyarrhythmias (in the absence of coronary occlusion) are also associated with troponin rises in animal models,[10] although this is reported less widely in humans.[11] DC cardioversion is rarely associated with elevated troponin levels, and has been extensively reported.[12-14] When a rise does occur, it is more commonly in patients with left ventricular dysfunction, and is usually small.[12,13] CK and CKMB, on the other hand, both increase following DC cardioversion.[13,14] Other causes of rises in troponin not directly attributable to cardiac damage from acute occlusion of a coronary artery include renal failure,[15] drugs (e.g. chemotherapeutic agents), sepsis and subarachnoid haemorrhage.[16,17]

Since this survey was carried out, the British Cardiac Society has published its views.[18] The society believes that the problems

Key messages

- In 2000, the European Society of Cardiology and American College of Cardiology recommended a new definition of myocardial infarction (MI) based on the rise and fall of specific markers of cardiac damage (such as troponins) plus either ECG changes, a history of cardiac chest pain or coronary intervention
- Our postal survey of 1,000 UK cardiologists or general physicians (361 replies) indicates a wide variation in the definition of MI used by consultants
- Creatine kinase (CK) remains the most frequently used marker for the diagnosis of MI, but 23% of consultants had moved to a definition based on troponins
- Only 47% of respondents stated that there was agreement within their hospital over the definition of MI, although this rose to 71% if a written policy was in place
- The wide variety of definitions used will result in patients being given different diagnoses, with implications beyond their immediate management

with the new definition and its implications (as well as concerns over the robustness of the assays) are such that the new definition cannot be recommended. For now, the society recommends that UK doctors continue to define MI according to two out of three of the following: appropriate clinical presentation, typical ECG changes and raised cardiac enzymes (essentially CK or CKMB).

Lack of guidance since the ESC/ACC consensus document was published has led many hospitals to make their own decisions. Where does this latest statement leave the 23% of UK physicians who, we estimate, have moved away from CK? More work is required to standardise troponin assays, to examine the significance of 'false positives', and to bring down costs. If troponins are to be universally accepted as the marker of cardiac damage, further prospective trials are needed to examine their role in managing ACS, and their significance in ST elevation MI will need to be defined.

Limitations of this study include the response rate, and inconsistency in responses from individual consultants within a hospital. However, the study has shown that there is wide variation in diagnostic criteria used. This has major implications for those patients who may have MI diagnosed on doubtful criteria.

References

1. Pedoe-Tunstall H, Kuulasmaa K, Amouyel P *et al*. Myocardial infarction and coronary deaths in the World Health Organisation MONICA project. *Circulation* 1994;**90**:583-612.
2. Antman EM, Tanasijevic MJ, Thompson B *et al*. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Engl J Med* 1996;**335**:1342-9.
3. Lindahl B, Venge P, Wallentin L, for the FRISC study group. Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease. *Circulation* 1996;**93**:1651-7.
4. Alpert JS, Antman E, Apple F *et al*. 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* 2000;**21**:1502-13.
5. Antman EM, Braunwald E. Acute myocardial infarction: pathology. In: Braunwald E, ed. *Heart disease: a textbook of cardiovascular medicine.* 5th edn. Philadelphia: Saunders, 1997.
6. Pell ACH, Pell JP, Simpson E *et al*. Impact of changing diagnostic criteria on the frequency, management and natural history of acute myocardial infarction. *Heart* 2002;**87**(suppl II):P13(abstract).
7. Mudawi T, Bain RJI, Walters M. The impact of cardiac troponins on the incidence and nature of acute myocardial infarction within a district general hospital. *Heart* 2002;**87**(suppl II):P13(abstract).
8. Del Carlo CH, O'Connor CM. Cardiac troponins in congestive heart failure (review). *Am Heart J* 1999;**138**:646-53.
9. Chen YN, Wei JR, Zeng LJ, Wu MY. Monitoring of cardiac troponin I in patients with acute heart failure. *Ann Clin Biochem* 1999;**36**:433-7.
10. Bertsch T, Bleuel H, Aufenanger J, Rebel W. Comparison of cardiac troponin T and cardiac troponin I concentrations in peripheral blood during orciprenaline-induced tachycardia in rats. *Exper Toxicol Pathol* 1997;**49**: 467-8.
11. Luna C, Adie MA, Tessler I, Acherman R. Troponin I elevation after supraventricular tachycardia in a child with hypertrophic cardiomyopathy. *Paediat Cardiol* 2002;**22**:147-9.
12. Allan JJ, Feld RD, Russell AA *et al*. Cardiac troponin I levels are normal or minimally elevated after transthoracic cardioversion. *J Am Coll Cardiol* 1997;**30**:1052-6.
13. Lund M, French JK, Johnson RM, Williams BF, White HD. Serum troponins T and I after elective cardioversion. *Eur Heart J* 2000;**21**:245-53.
14. Vikenes K, Omvik P, Farstad M, Nordrehaug JE. Cardiac biochemical markers after cardioversion of atrial fibrillation or atrial flutter. *Am Heart J* 2000;**140**:690-6.
15. Frankel WL, Herold DA, Ziegler TW, Fitzgerald RL. Cardiac troponin T is elevated in asymptomatic patients with chronic renal failure. *Am J Clin Pathol* 1996;**106**:118-23.
16. Collinson P, Stubbs P. The quest for diagnostic certainty: an unreal expectation in a real world. *Br J Cardiol* 2002;**9**:195-7.
17. Deibert E, Aiyagari V, Diringer MN. Reversible left ventricular dysfunction associated with raised troponin I after subarachnoid haemorrhage does not preclude successful cardiac transplantation. *Heart* 2000;**84**:205-07.
18. Dargie H. Myocardial infarction: redefined or reinvented? *Heart* 2002;**88**:1-3.