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Commentary on sudden unexpected death in a middle-aged woman - spontaneous coronary artery dissection (SCAD), myocardial infarction and cardiac biomarkers.

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SCAD is an uncommon cause of myocardial infarction (MI). It presents clinically either as sudden cardiac death, as in this case, or as an acute coronary syndrome (ACS) with clinical symptoms, changes in the electrocardiogram (ST segment elevation MI or non-ST elevation MI) and a rise in cardiac biomarkers. Although initially thought to be very rare, SCAD is increasingly recognised as a cause of MI in women. Both clinical awareness of SCAD as a clinical diagnostic entity and the use of a sex-specific 99th centile may improve the rate of diagnosis. Investigation is by angiography but treatment is conservative although this approach is based on expert consensus rather than clinical trial evidence [1].

The measurement of "cardiac enzymes" for the diagnosis of MI has now been entirely replaced by the use of immunoassay for the cardiac troponins (cTn) and resulted in a paradigm shift in the diagnosis of MI. Approximately 33% of patients with a diagnosis of unstable angina by conventional "cardiac enzymes" had an elevated cTn, associated with a significant risk of a major adverse cardiac events (sudden cardiac death, myocardial infarction, readmission with unstable angina, need for urgent cardiac revascularisation) on follow-up[2]. This was a consistent finding across range of studies[3] and lead to debate about the most appropriate biochemical tests for MI, culminating in a proposal to redefine MI with cTn as the gold standard for diagnosis and effectively the arbiter as to whether or not an MI had occurred[4]. This proposal was then adopted after consultation as the universal definition of MI which emphasised the primary role of cTn[5]. However, it must be remembered that MI is a clinical diagnosis and requires the demonstration of a dynamic change in cTn in patients with appropriate clinical features as well as evidence from the electrocardiogram.

The redefinition of MI shifted the diagnostic threshold from twice the upper reference limit

of CK or CK-MB (both less sensitive and specific for myocardial injury than cTn) to the 99th percentile for cTn with two unforeseen problems. First, it had already been reported that cTn elevation occurred in other medical conditions than MI, compensated for by using a cTn threshold equivalent to the WHO diagnosis and the relative insensitivity of early cTn assays[6]. Second, a shift from a WHO diagnostic threshold of twice the URL (where an elevated value in a healthy individual will occur in only 0.0044% of cases) to a 99th percentile cut off (where, by definition elevated values occur in 1% of healthy individuals) meant that a large number of cTn elevations occurred in a range of other clinical conditions. To encompass this, a second category of MI was proposed, type 2 MI where the underlying pathophysiology was not plaque rupture but supply/demand mismatch causing myocyte necrosis.

There are problems with the concept of type 2 MI as originally proposed. The universal definition of type 2 MI is inconsistent and too complicated. The definition is subject to interpretation with different series recording widely different prevalence. Although type 2 MI was acknowledged as associated with an adverse prognosis, there are no agreed treatment strategies[7]. Although logically treatment of the primary cause is important there is often underlying coronary disease which is ignored. Where there is diagnostic uncertainty, patients have worse outcomes. The current definition of type 2 MI potentially leads to mismanagement and does not result in improvements in care[8].

The redefinition of MI did not take into account that cTn elevation was reported in conditions without obvious ischaemic aetiology, such as envenomation. This was rectified in the 4th universal definition of MI[9] but the problems in the definition of type 2 MI remain. A more simplified clinical classification that recognises myocardial infarction can occur by different

mechanisms with different treatment implications is required. This would recognise the difference between primary myocardial infarction, myocardial infarction secondary to other pathophysiology as well as other causes of acute myocardial injury such as trauma or envenomation. SCAD results in partial or complete occlusion of the coronary artery and requires angiography. Inclusion within the category of type 2 MI does not make sense and SCAD should be included in a similar category to atherothrombosis due to embolism, vasospasm or similar acute events [10]. However, it can be argued that the concept of Type 2 MI as a whole should be discarded in favour of a category of secondary ischaemic myocardial injury.

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References

1. Saw J, Mancini GBJ, Humphries KH. Contemporary Review on Spontaneous Coronary Artery Dissection. *J Am Coll Cardiol* 2016; 68:297-312.

2. Stubbs P, Collinson P, Moseley D, Greenwood T, Noble M. Prospective study of the role of cardiac troponin T in patients admitted with unstable angina. *BMJ* 1996; 313:262-4.

3. Heidenreich PA, Alloggiamento T, Melsop K, McDonald KM, Go AS, Hlatky MA. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. *J Am Coll Cardiol* 2001; 38:478-85.

4. 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. Thygesen K, Alpert JS, White HD et al. Universal definition of myocardial infarction. *Circulation* 2007; 116:2634-53.

6. Collinson PO, Hadcocks L, Foo Y et al. Cardiac troponins in patients with renal dysfunction. *Ann Clin Biochem* 1998; 35 (Pt 3):380-6.

7. Collinson P, Lindahl B. Type 2 myocardial infarction: the chimaera of cardiology? *Heart* 2015; 101:1697-703.

8. Eggers KM, Baron T, Chapman AR, Gard A, Lindahl B. Management and outcome trends in type 2 myocardial infarction: an investigation from the SWEDEHEART registry. *Sci Rep* 2023; 13:7194.

9. Thygesen K, Alpert JS, Jaffe AS et al. Fourth universal definition of myocardial infarction (2018). *Eur Heart J* 2019; 40:237-69.

10. Lindahl B, Mills NL. A new clinical classification of acute myocardial infarction. *Nat Med* 2023; 29:2200-5.