

## Clinicians ignore best practice guidelines: Prospective audit of cardiac injury marker ordering in patients with chest pain

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**Background.** Chest pain is a frequent presenting symptom and is a diagnostic challenge. Recent recommendations state that high-sensitivity cardiac troponin assays are the only biochemical test required in the diagnosis of acute coronary syndrome (ACS) and that other biomarkers such as myoglobin or creatine kinase (CK)-MB isoform are not indicated.

**Objective.** To establish whether clinician ordering in the setting of suspected ACS was in keeping with recent recommendations.

**Methods.** A prospective audit was undertaken of all requests for cardiac troponin I (cTnI) and CK-MB received at a large tertiary hospital in Durban, South Africa, during a 20-day period in December 2012.

**Results.** A total of 193 cardiac marker requests were received: 12 (6.2%) requests were for cTnI alone; 8 (4.1%) were for CK-MB alone; and the remaining 173 (89.7%) were for both cTnI and CK-MB. Therefore, a total of 181 (93.8%) incorrect requests were received during this period. A total of 103 (53.4%) patients had values below the cut-off point of 40 ng/l for cTnI, i.e. ACS was ruled out. Of these, 15 had CK-MB values above the reference interval. A total of 12 (6.2%) patients had cTnI values >500 ng/l, i.e. ACS was ruled in; 33.3% of this group had normal CK-MB values.

**Conclusion.** Ordering patterns in the setting of ACS did not reflect current recommendations and were wasteful and potentially dangerous.

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Chest pain is common and frequently presents a diagnostic challenge.<sup>[1]</sup> Acute coronary syndrome (ACS) is a cause of significant morbidity and mortality if unrecognised, yet effective treatment is available.<sup>[2]</sup>

Recent rationalisation of biomarker investigation has occurred, with serial measurements of troponins using highly sensitive assays being advised while other biomarkers such as creatine kinase (CK) or myoglobin are no longer indicated, given the limited evidence of

their additional benefit.<sup>[3]</sup> However, evidence shows that uptake of guidelines by clinicians is suboptimal.<sup>[4]</sup>

Anecdotal experience in the laboratory was that clinicians were continuing to order cardiac troponin I (cTnI) together with the CK-MB isoform in cases of suspected ACS. We undertook a prospective audit of requests in the setting of chest pain to ascertain the validity of this suspicion.

## Methods

The National Health Laboratory Service (NHLS) chemistry laboratory based at King Edward VIII Hospital (KEH) provides routine and urgent investigations of a biochemical nature. KEH is a large public hospital that provides tertiary-level care in Durban, KwaZulu-Natal Province, South Africa (SA). A prospective audit of all requests for CK-MB and/or cTnI received at the NHLS chemistry laboratory for a 20-day period during December 2012 was undertaken; this period was chosen for convenience, as it was a quiet time because most outpatient clinics were closed. All requests for this period were examined. Both cTnI and CK-MB were measured on a Beckman-Coulter UniCel DxI 600. Troponin I was determined using the Access Accu-TnI assay, a highly sensitive troponin assay,<sup>[5]</sup> while CK-MB was measured using a mass assay. Data analyses were performed using MS Excel.

## Results

A total of 193 cardiac marker requests were received during the study period; 12 (6.2%) requests were for cTnI alone, eight (4.1%) were for CK-MB alone and the remaining 173 (89.7%) were for both cTnI and CK-MB. Therefore, a total of 181 (93.8%) incorrect requests were received during this period.

For cTnI, 103 (53.4%) patients had values below the cut-off point of 40 ng/l, i.e. ACS was ruled out depending on the time frame from onset of pain to sample collection. Of these, 15 had CK-MB values above the reference interval.

A total of 12 (6.2%) patients had cTnI values >500 ng/l, i.e. ACS was ruled in. Four (33.3%) of this group had normal CK-MB values. If CK-MB had been the sole investigation in this group, ACS would not have been detected and appropriate therapy would not have been instituted.

## Discussion

The diagnosis of ACS is now largely biochemical. Patients can be discharged safely if certain criteria are met,<sup>[6]</sup> as the negative predictive value of this highly sensitive troponin assay is 97% and the negative likelihood ratio is 0.25.<sup>[7]</sup> There is little role for CK-MB, myoglobin or other proteins as markers. There are appropriate times to measure CK-MB, but in general these should follow discussion with the laboratory. Proponents of the CK-MB assay argue that CK-MB is released earlier from damaged cardiac myocytes than troponin is and that the assay is useful in cases of 'false-positive' troponin elevation such as renal failure or cardiac myopathies. Cardiac troponin is released as early as 3 hours after injury,<sup>[8]</sup> and serial measurements of troponin are advocated to identify chronic causes of troponin elevation.<sup>[9]</sup> The use of CK-MB as seen in this study may cause confusion for the inexperienced clinician as there were several instances of discordant troponin and CK-MB measurements.

Troponin measurements from patients that fall between the rule-in and rule-out cut-off points should be repeated in 3 hours to demonstrate a rise and/or fall in levels, to differentiate between ACS and chronic or false-positive causes of elevated troponin blood results. This is often viewed as financially unrealistic as it is an expensive test compared with the CK-MB assay. Serial measurements are therefore said not to be feasible in our resource-constrained environment.

Simple arithmetic, using the state price list, reveals this argument to be fallacious – if the wasteful CK-MB requests had been avoided, the potential savings would have been sufficient for the required serial cTnI measurements. The burden of cardiac disease is predicted to increase in developing countries and rational approaches are required.

Why this pattern of ordering exists remains unknown. The failure of clinicians to take up guidelines has been extensively documented and results from many factors, including the sheer numbers thereof.<sup>[10,11]</sup> Anecdotal evidence suggests that requests are driven by historical practice and, on direct questioning, most clinicians are unable to justify this. Despite *ad hoc* education sessions conducted by JCS and memos distributed to clinicians, there was a persistence in this practice; however, these methods are ineffective in changing ordering behaviour permanently.<sup>[12]</sup> Poorly designed test request forms may drive inappropriate ordering and the request form may need to be redesigned to remove the tick-box options provided for CK and CK-MB.<sup>[13]</sup> An alternative strategy called gatekeeping, used by several institutions, limits the tests or test repertoire that clinicians are permitted to order.

## Study limitations

The clinical outcomes of the patients involved were unknown. This study was not designed to address the question of the clinical utility of the highly sensitive troponin assays, which is well established, but rather to determine the current investigative behaviour at a single centre. This raises the question of whether this study suffers from selection bias. In truth, it does, but discussion with colleagues at other centres reveals similar anecdotal evidence; whether this is generalisable to other clinical settings would be an area of potential future exploration. In addition, this study should be revisited once an intervention has been developed and implemented to assess its effectiveness.

## Conclusion

This audit of laboratory test requests at an academic centre in Durban, SA, revealed that local ordering behaviour was at odds with current recommendations.

**Author contributions.** UB obtained and analysed the data. JCS reviewed the data and wrote the manuscript

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