How many troponins should we measure to get a clinically significant result?

Sir,

Rapid and accurate risk stratification, appropriate and institution-specific triage to interventional vs. medical strategies, and optimal pharmacological therapy are all major goals in the management of acute coronary syndrome.1 Ramsay et al. recently concluded in QJM that the Global Registry of Acute Coronary Events (GRACE) score was superior to electrocardiogram and troponin findings alone in predicting major cardiac events in unselected patients presenting to a large teaching hospital with suspected cardiac pain.2 Since the implementation of algorithms based on the measurement of cardiospecific troponins is a well-established diagnostic strategy for risk stratification and treatment guidance in acute coronary syndrome,1 we found this conclusion intriguing. The outcome of their investigation, along with evidence that current approaches for diagnosing myocardial injury frequently result in the unnecessary use of laboratory resources,3,4 prompted us to analyse the percentage of clinically significant troponin T (TnT) values among the total measurements for this analyte in the stat laboratory of our University hospital between January and December 2006. Since serial TnT measurement is an essential part of routine clinical practice in our hospital, results below the decision-making threshold represent potentially avoidable expenditures and/or inappropriate test requests.

We therefore searched the database of our laboratory information system for all available results using the fourth-generation TnT assay on the Elecsys 2010 (Roche Diagnostics). When the same patient underwent multiple TnT tests, the highest test result was considered for our evaluation. Overall, 5648 patients with clinical symptoms suggestive of acute coronary syndrome (1282 in-patients and 4366 patients from the emergency department) had at least one TnT measurement. Since troponins are conventionally released as complexes, leading to various cut-off values depending on the extent of the myocardial damage and assay methodology,1 test results were stratified according to the decision-making threshold corresponding to the lowest TnT concentration associated with a 10% total imprecision in the assay (>0.03 μg/l).5

The percentage of clinically significant TnT values (>0.03 μg/l) recorded over the 1-year period was low (15.0%) and rather different between in-patients vs. patients admitted to the local emergency department (40.8% vs. 7.5%, respectively) (Table 1). The overall cost for the national healthcare system associated with the 4798 non-diagnostic TnT test requests was estimated at approximately 86 604 Euros (GBP 57 955) per year.

The consensus recommendations of the Joint European Society of Cardiology (ESC) and American College of Cardiology (ACC) committee for the redefinition of myocardial infarction promoted biochemical markers, particularly cardiac troponins, to a pivotal role in the diagnostic approach to the acute coronary syndrome.1,6 Although the measurement of cardiospecific troponins may thus appear unavoidable, the use of the new diagnostic criteria could lead to a substantial increase, up to 30%, in the number of infarctions in patients with acute coronary syndrome. The recent investigation of Ramsay et al. indicates that isolate or indiscriminate testing may led to the potential wastage of several economical and organizational resources for the

Table 1 Troponin T (TnT) stat measurements for in-patients and patients admitted to the local emergency department with suspected acute coronary syndrome over a 1-year period

<table>
<thead>
<tr>
<th>TnT (μg/l)…</th>
<th>≤0.03</th>
<th>&gt;0.03</th>
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<tbody>
<tr>
<td>Total</td>
<td>4798 (85.0%)</td>
<td>850 (15.0%)</td>
</tr>
<tr>
<td>Emergency department</td>
<td>4039 (92.5%)</td>
<td>327 (7.5%)</td>
</tr>
<tr>
<td>In-patients</td>
<td>759 (59.2%)</td>
<td>523 (40.8%)</td>
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healthcare systems. This is noteworthy, since a variety of additional variables may contribute to adverse risk besides the elevation of cardiac biomarkers and the presence of suggestive electrocardiogram changes. Our results support this hypothesis, underlining that a strategy aimed at rationalizing troponin testing, such as that proposed by Ramsay et al., based on the application of a validated risk assessment, would be far more cost-effective for identifying patients at higher risk for subsequent cardiac events, especially those presenting at the emergency department, than simply doing an isolated troponin measurement at admission.

With pressure from cost containment and reimbursement policies worldwide, expenditure on non-diagnostic results also highlights the need to identify diagnostic strategies based on something more concrete than simple clinical suspicion. In addition, a positive troponin result in a patient in whom the test was inappropriate in the first instance, may generate other unfavourable consequences, including decreased specificity, costs and health risk from further investigations, and unnecessary patient anxiety.

G. Lippi,
G.L. Salvagno,
M. Montagnana,
G.C. Guidi
Sezione di Chimica e Microscopia Clinica
Dipartimento di Scienze Morfologico-Biomediche
Università degli Studi di Verona
Verona
Italy
email: ulippi@tin.it; giuseppe.lippi@univr.it

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Estimated glomerular filtration rates (eGFR): predicting progression is dependent on accuracy

Sir,
In a recent paper, Hemmelgarn et al. introduced a potentially important clinical risk score for the prediction of progression amongst patients with chronic kidney disease (CKD). The use of readily available clinical data to allow risk stratification of patients would represent a significant advance in the practical management of CKD. However, the study has a number of potentially problematic methodological issues. The authors chose to limit their study population to those with an eGFR <90 ml/min/1.73 m², because of concerns regarding the validity of the MDRD eGFR estimate above that level of function. These validity concerns continue to be a problem when using the MDRD estimation equation between 60 and 90 ml/min/1.73 m², and this concern has become so prominent within the nephrology community that the equation’s creators have recommended reporting eGFR estimates as simply >60 ml/min/1.73 m², rather than giving specific estimates above that level.

Recent advances have improved the accuracy of the MDRD equation (traceable by isotope dilution mass spectrometry IDMS), but (as recently discussed in QJM) these corrections are dependent on central laboratory validation and provision of correction factors. Regardless of the methodology, there remains significant concern over the clinical relevance of an estimated GFR between 60 and 90 ml/min/1.73 m², particularly in the