Early Dynamic Change in High-Sensitivity Cardiac Troponin T in the Investigation of Acute Myocardial Infarction

Sally J. Aldous,1* A. Mark Richards,1,2 Louise Cullen,3 and Martin P. Than1

BACKGROUND: The definition of acute myocardial infarction (AMI) requires a rise and/or fall in troponin with 1 or more results ≥99th percentile of the reference range. How much troponin must change has not been specified. We ascertained whether dynamic changes (Δ) in high-sensitivity troponin T (hs-cTnT) improved diagnostic and prognostic test performance in the emergency department.

METHODS: We recruited 939 patients with symptoms suggestive of acute coronary syndrome (without ST elevation). hs-cTnT was measured at 0 h and 2 h after presentation. End-points were admission diagnosis of AMI and 1-year adverse events (composite of death, AMI, revascularization).

RESULTS: Diagnostic specificity of 0–2-h hs-cTnT for AMI (incurred by 200 patients) improved from 79.8% (78.8%–80.5%) by using the 99th percentile alone to 94.2% (92.9%–95.4%) when we also included a Δ ≥20%, but diagnostic sensitivity decreased from 94.5% (90.7%–96.9%) to 49.5% (44.6%–53.9%). With the inclusion of those patients with a Δ ≥20% when 0–2-h hs-cTnT was <99th percentile, in addition to any with concentrations ≥99th percentile, diagnostic sensitivity increased to 97.5% (94.4%–98.9%), hs-cTnT ≥99th percentile predicted adverse events (incurred by 111 patients), adjusted hazard ratio 1.9 (1.2–2.8), whereas a Δ ≥20% did not, hazard ratio 1.1 (0.7–1.7).

CONCLUSIONS: Diagnostic specificity of hs-cTnT improved with the use of a Δ ≥20% in those patients with concentrations ≥99th percentile, but at a cost of a large reduction in sensitivity. Diagnostic specificity improved with the use of a Δ ≥20% in patients with 0–2-h concentrations <99th percentile. Both approaches may be required for optimum rule-in and rule-out strategies, respectively. The Δ criteria seem to be less useful for medium-term risk stratification.

© 2011 American Association for Clinical Chemistry

High-sensitivity cardiac troponin assays in cohorts with potential acute coronary syndromes (ACS)4 have improved the diagnostic sensitivity for the early diagnosis of acute myocardial infarction (AMI) (1–3). Increasing the diagnostic sensitivity for myocardial injury may be accompanied by loss of diagnostic specificity for the diagnosis of AMI, given that many other insults, both acute and chronic, can result in increased cardiac troponin concentrations (4). Although in practice AMI is often diagnosed on the basis of ischemic symptoms with ≥1 cardiac troponin value ≥99th percentile, the formal definition requires a rise and/or fall in cardiac troponin (4,5). If this dynamic change is not present, nonacute cardiac conditions such as heart failure and valvular disease should be considered. However, a dynamic pattern may occur with other cardiac injuries, including takotsubo syndrome, pulmonary embolism, arrhythmia, and sepsis (4–9).

The combination of a cardiac troponin value ≥99th percentile and dynamic change should improve the diagnostic specificity of cardiac troponin, but the absolute or proportional change for optimal diagnostic performance and the ideal timing of samples have not been determined. In addition, these values are likely assay dependent. Changes in troponin must exceed combined background biological and analytical variability before they can be confidently ascribed to a pathological event. This minimum significant change is 46%, or a decrease of 32% from previous measurements for a high-sensitivity cTnI assay (8), and 84% for short-term changes (0–4 h) in high-sensitivity cardiac troponin T (hs-cTnT) (10). These limits are derived

1 Christchurch Hospital, Christchurch, New Zealand; 2 Cardiovascular Research Center, National University Health System, Singapore; 3 Department of Emergency Medicine, Royal Brisbane and Women’s Hospital, Brisbane, Australia.

* Address correspondence to this author at: Cardiology department, Christchurch Hospital, Riccarton Road, Christchurch, New Zealand. E-mail sally.aldous@cdhb.govt.nz.

Received January 5, 2011; accepted June 3, 2011.

Previously published online at DOI: 10.1373/clinchem.2010.161166

4 Nonstandard abbreviations: ACS, acute coronary syndrome; AMI acute myocardial infarction; hs-cTnT, high-sensitivity cardiac troponin T; AUC area under the curve; HR, hazard ratio.
from measurements in healthy populations, who by definition have cardiac troponin concentrations within the normal range 99% of the time. The National Academy of Clinical Biochemistry has recommended the use of a 20% δ in sensitive (but not specifically high sensitivity) assays (11, 12) when cardiac troponin is within the pathological range (≥99th percentile). There is a paucity of published data to validate this approach.

Our primary aim was to assess the diagnostic and prognostic test performance of early (0 h and 2 h) measurements of hs-cTnT (Roche assay) within the emergency department. We assessed if the dynamic change (δ) between the 2 measurements could improve diagnostic sensitivity when early hs-cTnT values were <99th percentile (and thus “rule out” of AMI) and/or improve diagnostic specificity when early hs-cTnT values were ≥99th percentile (and thus “rule in” of AMI). A secondary aim was to investigate the value of the percent δ hs-cTnT in the prediction of adverse events at 1 year.

Materials and Methods

This was a prospective observational cohort study and includes a secondary analysis from a multinational Asia-Pacific collaboration involving measurement of cardiac biomarkers at 0 and 2 h (13). Concurrent samples were collected to assess the early performance of hsTnT.

Consecutive patients who visited the emergency department at Christchurch Hospital, New Zealand, between 0530 and 2000 with symptoms suggestive of ACS were prospectively recruited (November 2007 to December 2009). Patients were included if there was suspicion of ACS in the absence of objective evidence of an alternative diagnosis and excluded if they were younger than 18 years, unable to provide informed consent, unwilling to participate, transferred from another hospital, or not available for follow-up. Patients with ST elevation AMI were recruited but excluded from this analysis.

Research nurses identified eligible patients, and blood samples were collected at 0 h and 2 h. Patients also had samples sent for serial core laboratory cardiac troponin analysis at 0 h and ≥6 h later. Further investigations and treatments were at the discretion of the attending clinician. Routine (0 h and ≥6 h) and research (2 h) samples were collected in lithium heparin tubes and sent to the core laboratory for measurement of cTnI, which was performed on an Architect system (Abbott Diagnostics) with a limit of detection of 0.005 μg/L, 99th percentile of 0.014 μg/L, and CV <10% at 0.032 μg/L, as per the manufacturer. Research samples were collected into EDTA tubes at 0 h and 2 h after presentation and centrifuged, and the plasma was stored frozen at −80 °C for later assay in a blinded fashion in batches in a dedicated research laboratory by use of an hs-cTnT assay (Elecsys system, Roche Diagnostics) with a limit of detection of 0.005 μg/L, 99th percentile of 0.014 μg/L, and CV <10% at 0.013 μg/L. In-house precision data showed CVs of 12.7% for the low-concentration QC at a mean concentration of 0.055 μg/L (n = 79) for cTnI and 5.8% for the calibrator QC at a mean value of 0.023 μg/L (n = 62) for hs-cTnT.

The research protocol was approved by the Upper South A Regional Ethics Committee of the New Zealand Ministry of Health, and all participants gave informed consent. Compared with the use of the 99th percentile alone, the δ criteria investigated were:
1. The ≥99th percentile and percent δ of ≥10%, 20%, and 30% to look for improvement in early diagnostic specificity and assess diagnostic sensitivity;
2. The ≥99th percentile or percent δ of ≥10%, 20%, and 30% or the biological and analytical variability of hs-cTnT of 84% to look for improvement in early diagnostic sensitivity and assess diagnostic specificity.

Patients were followed for 1 year for adverse events after discharge by means of the New Zealand death registry, patient notes review, and “National Health Events Search” in addition to telephone calls to the patient by research nurses. The primary end points were index admission diagnosis of AMI and 1-year adverse events: composite of all-cause mortality, non-fatal AMI (spontaneous/type 1 AMIs only), and revascularization.

All investigations and final diagnoses were reported independently by a cardiologist (S.J. Aldous) who was blinded to the investigative assay results but had knowledge of the serial core laboratory cTnI (Abbott Architect) and used a predefined structured adjudication process. Patient risk factors and diagnoses were based on 2001 American College of Cardiology definitions (14) and the 2007 redefinition of AMI (5). In conjunction with symptoms suggestive of ACS, AMI was diagnosed if there was a rise and/or fall of the cTnI (≥20%) with ≥1 value ≥99th percentile. When cTnI exceeded the 99th percentile but there was no rise or fall, AMI was diagnosed if there was objective evidence of myocardial ischemia, including new ischemic electrocardiogram changes, positive stress testing, or significant coronary artery disease detected with coronary angiography (1 or more coronary stenoses of ≥70% or revascularization procedure) and no clear alternative cause for the cardiac troponin elevation.

Continuous variables are presented as medians and interquartile ranges and categorical variables as numbers and percentages. The percent dynamic
change in cardiac troponin was calculated by subtracting the 0 h value from the follow-up value (2 h for hs-cTnT and 2 h and 6 h for cTnI) divided by the lower of the 2, multiplied by 100 (8).

ROC curves were constructed by plotting the percent calculation for each patient against the outcome of AMI. The resulting area under the ROC curve (AUC) was compared with the AUC generated by plotting peak values of hs-cTnT and cTnI against the outcome of AMI. Diagnostic sensitivities, diagnostic specificities, positive predictive value, and negative predictive value were calculated for each proposed diagnostic strategy. Diagnostic sensitivities and specificities were compared by using the McNemar test. Hazard ratios (HR) were determined, and by use of Cox proportional hazard modeling were adjusted according to the patient characteristics in Table 1 by the forward conditional method. Those with negative strategies were the reference groups. All hypothesis testing was 2 tailed, and $P$ values $<0.05$ were considered statistically significant. All statistical analyses were performed with the use of SPSS for windows (www.spss; 1999–2004; version 13.0).

### Results

A total of 939 patients were recruited. Two hundred patients (21.3%) had non–ST elevation AMI, 83 (8.8%) had definite unstable angina, 54 (5.7%) had other cardiac diagnoses, 257 (27.4%) had definite non-cardiac chest pain, and 345 (36.7%) had undifferentiated chest pain. There were 284 patients (30.2%) who underwent coronary angiography and 163 (17.4%) were revascularized, with the 2-h sample collected before angiography in all patients.

We adjudicated AMI using the core laboratory cTnI (using the samples collected at 0, 2, and 6–12 h). Of the 200 patients with AMI, 181 had increased ($99$th percentile) hs-cTnT at 0 h and 189 patients (94.5%) by 2 h. Of the 739 patients without AMI, 134 (18.1%) had increased hs-cTnT at 0 h and 149 (20.2%) were negative.
by 2 h. This resulted in diagnostic sensitivity and specificity of hs-cTnT for AMI at 0 h of 90.5% (86.1%–93.7%) and 81.9% (80.7%–82.7%), respectively, and at 2 h of 94.5% (90.7%–96.9%) and 79.8% (78.8%–80.5%), respectively.

The median percent δ for hs-cTnT between 0 h and 2 h for those patients with AMI was 20.4% (7.4%–66.6%) and for those without AMI was 1.2% (0%–15.7%). The ROC AUC for AMI was 0.92 (0.90–0.95) as determined by using values obtained at 0 h, and 0.95 (0.93–0.97) by using the peak of values of the 0 h and 2 h samples. ROC curves plotting percent δ between 0 h and 2 h for the diagnosis of AMI had an AUC of 0.78 (0.75–0.81), which was inferior to that obtained by using the absolute values (P = 0.001). With the use of ROC curves, a diagnostic specificity of >90% for the diagnosis of AMI was achieved at a percent δ of ≥39.7%, but a diagnostic sensitivity of >90% was achieved at a percent δ of only ≥2.5%. The ROC curve derived optimum δ was 10%.

The diagnostic sensitivities, diagnostic specificities, positive predictive values, and negative predictive values of 0–2-h hs-cTnT with and without δ criteria are shown in Table 2. Addition of a ≥10%–30% δ criterion to those patients with increases in hs-cTnT improved diagnostic specificity compared with the 99th percentile alone (P = 0.001 for all). Adding a ≥20% δ criterion was more specific than ≥10% δ (P = 0.001), and ≥30% δ was more specific than ≥20% δ (P = 0.001). However, diagnostic sensitivity was reduced (P < 0.001 for all comparisons). When we added a δ criterion to those without increased 0–2-h hs-cTnT, diagnostic sensitivity was increased by δ criteria of ≥10%–30% δ (P = 0.031 compared with the 99th percentile alone) but not by ≥84% δ (P = 0.500). A ≥84% δ had higher diagnostic sensitivity than ≥30% δ, although this result was not statistically significant (P = 0.125). A ≥30% δ was not more sensitive than a ≥20% δ (P = 1.0), and a ≥20% δ was not more sensitive than a ≥10% δ (P = 1.0). Specificity was reduced (P < 0.001 for all comparisons). Similar calculations for cTnI are provided in the Supplemental Data file that accompanies the online version of this article at http://wwwclinchem.org/content/vol57/issue8.

There were 259 patients with a ≥20% δ over 2 h, of which 179 were increases and 80 were decreases. For the 200 patients with AMI, there were 105 patients (52.5%) with a ≥20% δ (91 increases and 9 decreases). Six of these decreases were in patients who presented within 6 h of symptom onset. The diagnostic sensitivity of hs-cTnT ≥99th percentile fell from 94.5% to 49.5%, and diagnostic specificity improved from 79.8% to 94.2%. The influence of time from symptom onset to presentation (as reported by the patient) on diagnostic sensitivity and specificity for hs-cTnT ≥99th percentile and a δ of ≥20% is shown in Fig. 1. The δ criteria provided high diagnostic specificity irrespective of time from symptom onset. However, diagnostic sensitivity was superior for earlier presentations.

Complete 1-year follow-up was obtained for 100% of patients. By 1 year 111 patients (11.8%) experienced adverse events; 40 (36.0%) of these patients had AMI on the index admission and 63 (56.8%) had increased hs-cTnT, with 35 patients (31.5%) having a δ of ≥20%. Absolute values of hs-cTnT yielded an AUC of 0.67 (0.60–0.72) for adverse events at 1 year, which was superior to the percent change in hs-cTnT between 0 h and 2 h, which showed an AUC of 0.60 (0.55–0.67) (P = 0.049). The ROC-curve–derived optimum percent δ for the prediction of adverse events was 3%.

### Table 2. Diagnostic sensitivity and specificity of 0–2-h hs-cTnT with and without δ criteria.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV*</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥99th percentile</td>
<td>94.4 (90.7–96.9)</td>
<td>79.8 (78.8–80.5)</td>
<td>55.9 (53.7–57.3)</td>
<td>98.2 (96.9–99.0)</td>
</tr>
<tr>
<td>AND ≥10%</td>
<td>69.0 (63.7–73.8)</td>
<td>89.7 (88.3–91.0)</td>
<td>64.5 (59.6–68.9)</td>
<td>91.4 (90.0–92.8)</td>
</tr>
<tr>
<td>AND ≥20%</td>
<td>49.5 (44.6–53.9)</td>
<td>94.2 (92.9–95.4)</td>
<td>69.7 (62.9–75.8)</td>
<td>87.3 (86.1–88.4)</td>
</tr>
<tr>
<td>AND ≥30%</td>
<td>30.0 (33.8–41.5)</td>
<td>96.6 (95.5–97.6)</td>
<td>75.2 (66.9–82.2)</td>
<td>85.2 (84.2–86.0)</td>
</tr>
<tr>
<td>OR ≥10%</td>
<td>97.5 (94.4–98.9)</td>
<td>55.9 (55.0–56.3)</td>
<td>37.4 (36.2–38.0)</td>
<td>98.8 (97.3–99.5)</td>
</tr>
<tr>
<td>OR ≥20%</td>
<td>97.5 (94.4–98.9)</td>
<td>64.8 (64.0–65.2)</td>
<td>42.9 (41.5–43.5)</td>
<td>99.0 (97.7–99.6)</td>
</tr>
<tr>
<td>OR ≥30%</td>
<td>97.5 (94.4–98.9)</td>
<td>69.7 (68.9–70.1)</td>
<td>46.5 (45.1–47.2)</td>
<td>99.0 (97.9–99.6)</td>
</tr>
<tr>
<td>OR ≥84%</td>
<td>95.5 (91.9–97.6)</td>
<td>76.3 (75.3–76.9)</td>
<td>52.2 (50.2–53.3)</td>
<td>98.4 (97.2–99.2)</td>
</tr>
</tbody>
</table>

* PPV, positive predictive value; NPV, negative predictive value.
<table>
<thead>
<tr>
<th>δ criterion</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV*</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10%</td>
<td>94.4 (90.7–96.9)</td>
<td>79.8 (78.8–80.5)</td>
<td>55.9 (53.7–57.3)</td>
<td>98.2 (96.9–99.0)</td>
</tr>
<tr>
<td>≥20%</td>
<td>69.0 (63.7–73.8)</td>
<td>89.7 (88.3–91.0)</td>
<td>64.5 (59.6–68.9)</td>
<td>91.4 (90.0–92.8)</td>
</tr>
<tr>
<td>≥30%</td>
<td>49.5 (44.6–53.9)</td>
<td>94.2 (92.9–95.4)</td>
<td>69.7 (62.9–75.8)</td>
<td>87.3 (86.1–88.4)</td>
</tr>
<tr>
<td>≥40%</td>
<td>30.0 (33.8–41.5)</td>
<td>96.6 (95.5–97.6)</td>
<td>75.2 (66.9–82.2)</td>
<td>85.2 (84.2–86.0)</td>
</tr>
<tr>
<td>≥50%</td>
<td>97.5 (94.4–98.9)</td>
<td>55.9 (55.0–56.3)</td>
<td>37.4 (36.2–38.0)</td>
<td>98.8 (97.3–99.5)</td>
</tr>
<tr>
<td>≥60%</td>
<td>97.5 (94.4–98.9)</td>
<td>64.8 (64.0–65.2)</td>
<td>42.9 (41.5–43.5)</td>
<td>99.0 (97.7–99.6)</td>
</tr>
<tr>
<td>≥70%</td>
<td>97.5 (94.4–98.9)</td>
<td>69.7 (68.9–70.1)</td>
<td>46.5 (45.1–47.2)</td>
<td>99.0 (97.9–99.6)</td>
</tr>
<tr>
<td>≥84%</td>
<td>95.5 (91.9–97.6)</td>
<td>76.3 (75.3–76.9)</td>
<td>52.2 (50.2–53.3)</td>
<td>98.4 (97.2–99.2)</td>
</tr>
</tbody>
</table>

* PPV, positive predictive value; NPV, negative predictive value.

AND, hs-cTnT must be elevated above the 99th percentile by 2 h in addition to the percent δ criteria being above threshold; OR, either hs-cTnT must be elevated above the 99th percentile by 2 h (irrespective of the % δ achieved) or have a δ criteria value above threshold.

Marked values for delta criteria are statistically more sensitive or specific compared with hs-cTnT ≥99th percentile alone (P < 0.05).
Adjusted HR for hs-cTnT ≥99th percentile (without \( \delta \) criteria) and for \( \delta \) changes obtained by using hs-cTnT are shown in Table 3.

Discussion

In this study we investigated the diagnostic utility of the change in hs-cTnT between 0 h and 2 h in patients presenting with possible ACS, and specifically assessed whether \( \delta \) changes obtained by using hs-cTnT are shown in Table 3.

Table 3. HRs comparing different percent \( \delta \) values in predicting adverse events.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>HR</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥99th percentile alone</td>
<td>1.9 (1.2–1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥10% ( \delta )</td>
<td>0.9 (0.6–1.3)</td>
<td>0.636</td>
</tr>
<tr>
<td>≥20% ( \delta )</td>
<td>1.1 (0.7–1.7)</td>
<td>0.736</td>
</tr>
<tr>
<td>≥30% ( \delta )</td>
<td>1.2 (0.7–1.8)</td>
<td>0.527</td>
</tr>
<tr>
<td>≥3% ( \delta * )</td>
<td>1.6 (1.0–2.7)</td>
<td>0.052</td>
</tr>
</tbody>
</table>

* ROC curve derived optimum percent \( \delta \) for adverse events.

hs-cTnT had high diagnostic sensitivity (94.5%) by 2 h but its diagnostic specificity was not optimal (79.8%). The results of this study confirmed that a \( \delta \) of ≥10% in addition to early values of ≥99th percentile increased diagnostic specificity for AMI significantly (79.8%–91.5%), corroborating the findings of Apple et al. (15) and Giannitsis et al. (3). However, in accordance with other reports (1–3, 9, 15, 16), diagnostic sensitivity was reduced to 69.0% with further reductions if larger \( \delta \) values were applied.

We have demonstrated that a \( \delta \) criterion is more likely to be fulfilled in patients presenting earlier after symptom onset (Fig. 1). Although those patients presenting later are more likely to have increased cardiac troponin on presentation, the already increased concentration is likely to reduce the proportional increment in cardiac troponin between measurements. In addition, 2 h may also be too short a time period in which to demonstrate significant changes in cardiac troponin. Because of loss in diagnostic sensitivity, \( \delta \) calculations for the rule in of AMI may be relevant only when other chronic conditions known to increase cardiac troponin are present.

The false-negative rate of hs-cTnT can be reduced from 5.6% to 2.5% by including not only those patients with hs-cTnT ≥99th percentile, but also those with hs-cTnT <99th percentile with a \( \delta \) criterion of ≥30%. It would be reasonable to repeat hs-cTnT at a later time point to finally rule out AMI in patients with \( \delta \) of ≥30% in whom neither of the early (0 h or 2 h) values exceed the 99th percentile. When initial hs-cTnT falls within the normal range, very small absolute shifts may exceed 10%–30%, which may fall within the imprecision of the assay at these concentrations. However, repeat measurement of hs-cTnT at a later time point to
differentiate biological and analytical variation from pathological changes is still a valid approach.

It is unclear why those patients who present soon after onset of symptoms would have a fall in cardiac troponin after such a short time period. However, a fall in hs-cTnT still appears to be very specific for AMI and identifies a small but significant number of those patients with AMI, suggesting that both a rise and/or fall should be included.

hs-cTnT was superior to cTnI in risk stratification for 1-year adverse events. Previous studies in which there were more patients with adverse events at follow-up are identified by the cardiac troponin assay with the highest analytical sensitivity (17–19). The finding of an increased hs-cTnT alone was superior to any strategy involving percent δ change. Apple et al. (15) found that an increase in cardiac troponin of >30% improved risk stratification for cardiac events or death at 60 days, but Kavsak et al. (20) found that for long-term prognosis, with up to 8 years follow-up, an acute change in cardiac troponin did not appear to be prognostically informative. In the study we report, although the percent δ was predictive of adverse events by ROC analysis, the AUC was lower than the peak hs-cTnT and did not yield a significant HR. This result may be due to the fact that δ changes aid only in short-term risk stratification; this prognostic utility may be lost by 1 year. It may also be due to an underpowering of the study for this end point.

STUDY LIMITATIONS

1. hs-cTnT by 2 h had lower diagnostic sensitivity for AMI than cTnI at 0–6 to 12 h. This may in part be due to the early timing of the second sample but also because the test performance of hs-cTnT was adjudicated by using a less analytically sensitive cardiac troponin assay. This is standard for such investigations, but there is inherent difficulty in assessing a new test with possibly equal or better performance than the standard against which it is being assessed. In addition, no 2 assays are completely concordant.

2. Performance characteristics of δ criteria may also change if AMI was adjudicated according to hs-cTnT measured over longer intervals, but samples for later measurements were not collected.

3. It is unlikely that the optimum timing over which to calculate a dynamic change in hs-cTnT is 2 h. This period may be too small to detect significant changes in cardiac troponin. However, it is in the early hours after presentation that criteria to improve diagnosis are required.

4. The performance of early cTnI (see the Online Supplemental Data file) is likely overestimated because these and later cTnI results were used for adjudication.

In conclusion, δ values can improve early diagnosis of AMI, but different δ values are needed for rule-in or rule-out strategies. However, these results should not be used in isolation because clinical evaluation is vital for correct interpretation. Prognostically, δ criteria are unlikely to offer additional information beyond that of values ≥99th percentile alone in identifying those patients who are at risk for adverse events.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

References

5. Thygesen K, Alpert JS, White HD. Joint ESC/ACCF/

7. Parmar MS. We need to address the issue of "mild troponinaemia". BMJ 2009;338:769.