Direct comparison of high-sensitivity-cardiac troponin I vs. T for the early diagnosis of acute myocardial infarction

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Aim
It is unknown whether cardiac troponin (cTn) I or cTnT is the preferred biomarker in the early diagnosis of acute myocardial infarction without ST segment elevation (NSTEMI).

Methods and results
In a prospective multicentre study, we measured cTnI and cTnT using clinically available high-sensitivity assays (hs-cTnI Abbott and hs-cTnT Roche) and compared their diagnostic and prognostic accuracies in consecutive patients presenting to the emergency department with acute chest pain. The final diagnosis was adjudicated by two independent cardiologists using all information pertaining to the individual patient. The mean follow-up was 24 months. Among 2226 consecutive patients, 18% had an adjudicated final diagnosis of NSTEMI. Diagnostic accuracy at presentation as quantified by the area under the receiver-operating-characteristics curve (AUC) for NSTEMI was very high and similar for hs-cTnI \[\text{AUC: } 0.93, \text{95\% confidence interval (CI) 0.92–0.94}\] and hs-cTnT \[\text{AUC: } 0.94, \text{95\% CI: 0.92–0.94}\] \(P = 0.62\). In early presenters (\(< 3\) h since chest pain onset) hs-cTnI showed a higher diagnostic accuracy (AUC: 0.92, 95\% CI: 0.89–0.94) when compared with hs-cTnT AUC (0.89, 95\% CI: 0.86–0.91) \(P = 0.019\), while hs-cTnT was superior in late presenters \(\text{AUC hs-cTnT 0.96 (95\% CI: 0.93–0.95) vs. hs-cTnI 0.94 (95\% CI: 0.93–0.95); P = 0.007}\). The prognostic accuracy for all-cause mortality, quantified by AUC, was significantly higher for hs-cTnT (AUC: 0.80; 95\% CI: 0.78–0.82) when compared with hs-cTnI (AUC: 0.75; 95\% CI: 0.73–0.77; \(P < 0.001\)).

Conclusion
Both hs-cTnI and hs-cTnT provided high diagnostic and prognostic accuracy. The direct comparison revealed small but potentially important differences that might help to further improve the clinical use of hs-cTn.

Keywords
Acute myocardial infarction \• High-sensitive cardiac troponin

Introduction
Acute myocardial infarction (AMI) is a major cause of death and disability worldwide. Patients with symptoms suggestive of AMI account for \(~ 10\%\) of all emergency departments (ED) consultations, even though only 10–20\% of them eventually suffer from AMI. Rapid identification of AMI is of paramount clinical importance for early treatment and management.1

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Cardiac troponins (cTn) I and T are proteins unique to heart and specific sensitive biomarkers of myocardial damage.\textsuperscript{1–4} Cardiac troponin and 12-lead electrocardiogram (ECG) complement patient history and physical examination in the evaluation of patients, presenting with acute chest pain.\textsuperscript{5,6} A limitation of conventional cTn assays is their low sensitivity at the time of patient presentation, owing to a delayed increase in circulating levels requiring serial sampling for 6–9 h in a significant number of patients.\textsuperscript{2} Recent studies found that more sensitive cTn assays can improve the accuracy of the diagnosis of AMI at the time of presentation to the ED.\textsuperscript{7,8}

The cTn complex is immobilized on the thin filament of the contractile apparatus and plays a critical role in the regulation of excitation–contraction coupling in the heart.\textsuperscript{6} In AMI, cTnI and cTnT are released from necrotic myocardium both as intact proteins and degradation products.\textsuperscript{6} The clinical availability of fully developed high-sensitivity assays for both cTnI (Abbott) and cTnT (Roche) in Europe and other countries now for the first time provides the methodological requirement to appropriately test the hypothesis whether the substantial biochemical differences including molecular weight between cTnI (~23 kDa) and cTnT (~35 kDa) could result in different diagnostic and prognostic performances for both biomarkers.\textsuperscript{6,9} This hypothesis is based on preliminary findings from subgroup analyses as well as very recent observations with pre-commercial and still experimental hs-cTn assays.\textsuperscript{10–12}

The aim of our large prospective multicentre study was to directly compare the diagnostic accuracy of clinically available hs-cTnI and hs-cTnT for NSTEMI, as well as their prognostic accuracy for all-cause mortality during 24-month follow-up, in consecutive patients presenting to the ED with acute chest pain.

**Methods**

**Study design and population**

Adverse Predictors of Acute Coronary Syndrome Evaluation (APACE) is an ongoing prospective international multicentre study (performed in nine different study centres in Switzerland, Spain, and Italy) designed and coordinated by the University Hospital Basel Switzerland to advance the early diagnosis of AMI.\textsuperscript{7,10–12} From April 2006 to August 2012, consecutive patients older than 18 years presenting to the ED with symptoms suggestive of AMI with an onset or peak within the last 12 h were recruited, after informed consent was obtained.

Patients with terminal kidney failure requiring regular dialysis were excluded. For this analysis, patients were also excluded if (i) hs-cTnI (Abbott) or hs-cTnT (Roche) levels were not available (n = 661) or (ii) the final diagnosis remained unclear after adjudication and at least one cTn or hs-cTnT level was elevated (possibly indicating the presence of AMI) (n = 69) (iii) patients with a final diagnosis of ST segment myocardial infarction (STEMI) (n = 75).

The study was carried out according to the principles of the Declaration of Helsinki and approved by the local Ethics Committees. The authors designed the study, gathered, and analysed the data, vouch for the data and analysis, wrote the paper, and decided to publish.

**Routine clinical assessment**

All the patients underwent a clinical assessment that included medical history, physical examination, 12-lead ECG, continuous ECG monitoring, pulse oximetry, standard blood test, and chest radiography. Levels of cTn were measured at presentation and serially thereafter as long as clinically indicated. Timing and treatment of patients were left to discretion of the attending physician.

**Adjudicated final diagnosis**

Adjudication of the final diagnosis was performed centrally in the core lab (University Hospital Basel) for all patients twice: Once according to conventional cTn levels used onsite (this method was used in the initial analyses to examine the performance of hs-cTn assays\textsuperscript{7,11–13} and once including levels of Roche hs-cTnT in order to also take advantage of the higher sensitivity and higher overall diagnostic accuracy offered by hs-cTn assays.\textsuperscript{14,15} This allows the additional detection of small AMIs that were missed by the adjudication based on conventional cTn assays. Two independent cardiologists reviewed all available medical records—patient history, physical examination, results of laboratory testing, radiological testing, ECG, echocardiography, cardiac exercise test, lesion severity, and morphology in coronary angiography—pertaining to the patient from the time of ED presentation to 90-day follow-up. In situations of disagreement about the diagnosis, cases were reviewed and adjudicated in conjunction with a third cardiologist.

Non-ST segment myocardial infarction was defined and cTn levels interpreted as recommended in current guidelines.\textsuperscript{16,17} In brief, NSTEMI was diagnosed when there was evidence of myocardial necrosis in association with a clinical setting consistent with myocardial ischaemia. Myocardial necrosis was diagnosed by at least one cTn value above the 99th percentile (or for the conventional cTn assays above the 10% precision value if not fulfilled at the 99th percentile) together with a significant rise and/or fall.\textsuperscript{9,18,19} The criteria used to define rise and/or fall in conventional cTn and hs-cTnT are described in detail in the Supplementary material online, Methods.

All other patients were classified as ‘No NSTEMI’ for this analysis, including in this group the categories of unstable angina (UA), non-cardiac chest pain (NCCP), cardiac but non-coronary disease (e.g. tachyarrhythmias, perimyocarditis), and symptoms of unknown origin with normal levels of cTn and hs-cTnT (thereby ruling-out AMI).

Unstable angina was defined according to recent guidelines as follows: (i) new onset (de novo) of severe angina, or recent destabilization of previously stable angina with at least severe (class III) angina characteristics (crescendo angina), or post-MI angina, and (ii) either coronary artery stenosis >70% on angiogram, or positive cardiac exercise testing, or in ambiguous cases when AMI or sudden death occurred within 60 days, and (iii) absence of alternative diagnosis.\textsuperscript{20}

**Measurement of high-sensitivity cardiac troponin I and high-sensitivity cardiac troponin T**

Blood samples for determination of hs-cTnI (Abbott) and hs-cTnT (Roche) were collected at presentation to the ED, in serum and EDTA plasma tubes for hs-cTnT, and in serum for hs-cTnI. Additional samples were collected at 1, 2, 3, and 6 h. When treatment required transferring the patient to the catheter laboratory or coronary care unit, because the diagnosis of AMI was certain, serial sampling was disrupted. After centrifugation, samples were frozen at ~80°C until assayed in a blinded fashion in a dedicated core laboratory. The Abbott hs-cTnI assay used was the final pre-commercial release version of the ARCHITECT High Sensitive STF Tropion I assay (Abbott Laboratories, Abbott Park, IL, USA). Samples were thawed, mixed, and centrifuged (for 30 min at 3000 RCF and 4°C for serum samples or for 10 min, twice, at 3000 RCF for plasma samples) prior to analysis and according to manufacturer’s instructions. The hs-cTnI assay has a 99th percentile concentration of 26.2 ng/L with a corresponding coefficient of variation (CV) of <5% and a limit of detection (LoD) of 1.9 ng/L.\textsuperscript{21} The Roche hs-cTnT assay...
was measured on the Elecsys 2010 (Roche Diagnostics). The limit of blank and LoD were determined to be 3 and 5 ng/L, respectively. The 99th-percentile of a healthy reference population was reported at 14 ng/L with an imprecision corresponding to 10% CV at 13 ng/L. This study does not include any measurements with hs-cTnT lots that required the revision of the calibration curve. Calculation of the glomerular filtration rate was performed using the abbreviated Modification of Diet in Renal disease formula.

Follow-up and prognostic endpoints

After hospital discharge, patients were contacted by telephone interview or written form after 3, 12, and 24 months of follow-up. In case of reported clinical events—in particular cardiovascular events—since presentation to the ED, details were reviewed by asking the patients and traced by establishing contact with the respective family physician or treating institution. The primary prognostic endpoint was all-cause mortality during 24-month follow-up; non-fatal AMI during the follow-up was a secondary prognostic end-point. Information regarding death and AMI was obtained from the national registry on mortality, the hospital’s diagnosis registry or family physician’s records.

Statistical methods

The data are expressed as medians ± IQR for continuous variables, and for categorical variables as numbers and percentages. Continuous variables were compared with the Mann–Whitney U test, and categorical variables using the Pearson χ² test. Receiver-operating-characteristics (ROC) curves were constructed to assess the sensitivity and specificity of both assays to compare their ability to diagnose AMI and UA, as well as their prognostic accuracy. Prognostic accuracy was quantified by three complementary methods: AUC using the dichotomy of survival, AUC using survival analysis techniques and estimate the concordance index (Harrell’s c) using the survival model, and a Cox proportional-hazard model. The comparison of areas under the ROC curves (AUC) was performed as recommended by deLong et al. Pre-defined subgroups include patients with recent onset of symptoms (< 3 h).

All hypothesis testing was two-tailed and P-value of < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows 21.0 (SPSS, Inc., Chicago, IL, USA) and MedCalc 9.6.4.0 (MedCalc software, Mariakerke, Belgium).

Results

Patient characteristics

The baseline characteristics of 2226 patients with suspected NSTEMI are shown in Table 1. The adjudicated final diagnosis was NSTEMI in 18% of patients, UA in 10%, cardiac but non-coronary symptoms in 13%, non-cardiac cause in 54%, and symptoms of unknown origin in 5%. Among the 399 NSTEMI patients, 85% had type I AMI and 15% had type II AMI.

Diagnostic performance of high-sensitivity cardiac troponin I and T for acute myocardial infarction

As shown in Figure 1, levels of the two hs-cTn at presentation were significantly higher among the 399 patients who had NSTEMI compared with the 1827 patients in the no-NSTEMI group (hs-cTn median 115.4 ng/L (IQR: 21.7–627.9) vs. 3.5 ng/L (IQR: 2.2–7.2) P < 0.001; hs-cTnT median 65.0 ng/L (IQR: 28.0–152.5) vs. 7.0 ng/L (IQR: 4.0–12.4) P < 0.001). Diagnostic accuracy of hs-cTn for NSTEMI, as quantified by the AUC, was similar for hs-cTn and hs-cTnT (AUC hs-cTn 0.93, 95% CI: 0.92–0.94; AUC hs-cTnT 0.94, 95% CI: 0.92–0.94; P = 0.619; Figure 2A).

Diagnostic performance of high-sensitivity cardiac troponin I and T in early presenters

Among patients presenting to the ED with chest pain onset within 3 h (representing 25% of the overall cohort), hs-cTn showed a significantly higher diagnostic accuracy for NSTEMI compared with hs-cTnT (Table 2). As shown in Figure 2B, among the early presenters the AUC at presentation for hs-cTn was 0.92, 95% CI: 0.89–0.94 vs. hs-cTnT 0.89, 95% CI: 0.86–0.91 (P = 0.019). In patients presenting to the ED with chest pain onset of > 3 h the AUC for hs-cTn was significantly lower compared with hs-cTnT [0.94 (95% CI: 0.93–0.95) vs. 0.96 (95% CI: 0.94–0.96)] (P = 0.007).

Diagnostic performance of high-sensitivity cardiac troponin I and high-sensitivity cardiac troponin T for unstable angina

Among all consecutive patients, 9.7% had a final diagnosis of UA. Levels at presentation of both hs-cTn assays were significantly higher among patients whose final diagnosis was UA compared with those with NCCP, hs-cTn median 6.4 ng/L (IQR: 3.6–12.1) vs. 3.0 ng/L (IQR: 1.9–5.1) P < 0.001; hs-cTnT median 10.7 ng/L (IQR: 6.9–15.9) vs. 6.0 ng/L (IQR: 3.9–9.7) P < 0.001. High-sensitivity-cTn had a slightly higher diagnostic accuracy for UA as quantified by the AUC compared with hs-cTnT (0.74, 95% CI: 0.72–0.77, vs. 0.72, 95% CI: 0.69–0.74; P = 0.07).

Correlation with angiographic findings

Among all patients in whom coronary angiography was performed (n = 530), 83% (n = 441) had positive angiographic findings (one vessel, two vessels or three vessels disease). The accuracy to predict a positive angiographic finding as quantified by the AUC was significantly higher for hs-cTn when compared with hs-cTnT (0.82, 95% CI: 0.78–0.84, vs. 0.79, 95% CI: 0.76–0.81; P < 0.001).
Prognostic accuracy of high-sensitivity cardiac troponin I and T for mortality

Patients were followed during a mean period of 24 months. During this time a total of 153 patients died, 44% of them had a diagnosis of NSTEMI and 56% had a different diagnosis than NSTEMI (P = 0.001). Prognostic accuracy as quantified by the AUC was high for both and significantly higher for hs-cTnT when compared with hs-cTnI (0.80, 95% CI: 0.77–0.83, vs. 0.75, 95% CI: 0.73–0.79; P = <0.001; Figure 4). The prognostic superiority of hs-cTnT was consistent in the NSTEMI group (P = <0.001) and in the non-NSTEMI group (P = 0.001).

Similar findings were obtained regarding cardiac death. Among all patients 3% (n = 69) suffered from a cardiac death during the follow-up. The accuracy to predict cardiac death as quantified by the AUC was significantly higher for hs-cTnT when compared with hs-cTnI (0.82, 95% CI: 0.80–0.84, vs. 0.79, 95% CI: 0.78–0.81; P = 0.004).

Prediction of acute myocardial infarction in the future

Among all patients in the no-NSTEMI group (n = 1827), 3.6% (n = 65) suffered an AMI during the follow-up. The accuracy to predict AMI among these patients as quantified by the AUC was
moderate for both and slightly higher for hs-cTnI when compared with hs-cTnT (0.70, 95% CI: 0.68–0.72 vs. 0.66, 95% CI: 0.64–0.68; P = 0.07. Among all patients in the NSTEMI group (n = 399), 14.8% (n = 59) suffered an AMI during the follow-up. The accuracy to predict AMI among these patients as quantified by the AUC was very low for both (hs-cTnI 0.56, 95% CI: 0.51–0.61 vs. hs-cTnT 0.54, 95% CI: 0.49–0.59; P = 0.49).

**Discussion**

While hs-cTn assays still await approval for clinical use in the USA, two fully developed hs-cTn assays have become clinically available in Europe and many other countries in 2010 (hs-cTnT, Roche) and 2013 (hs-cTnI, Abbott). This large prospective multicentre study directly compared the diagnostic and prognostic accuracy of these clinically available hs-cTn assays in consecutive patients presenting to the ED with acute chest pain. We report six major findings.

First, in our analysis both hs-cTnI and hs-cTnT showed very high diagnostic accuracy for NSTEMI (AUC 0.93 and 0.94) already at presentation, confirming and extending similar previous findings for both clinically available as well as pre-commercial s-cTn and hs-cTn assays.7,8,29 Secondly, in the overall group diagnostic accuracy at presentation for NSTEMI was similar with both assays. This finding is of major clinical relevance for clinicians, laboratory experts, and hospital administrators as it will help these decision-makers in planning the future laboratory strategies of their institutions. However, our data also suggested that time from symptom onset may impact on the respective diagnostic superiority of either test over the other: hs-cTnI seemed to be superior in early presenters, while hs-cTnT seemed to be superior in late presenters. It is important to highlight that the diagnostic superiority of hs-cTnI vs. T in early presenters methodologically is very sound, as our methodology introduced a small but unavoidable bias in favour of hs-cTnT regarding diagnostic accuracy. While local levels of both cTnI and cTnT were used for the adjudication, only hs-cTnT levels were available for the additional adjudication of small AMIs and more patients were enrolled in sites using (hs-)cTnT rather than cTnI. In addition, the finding of diagnostic superiority of hs-cTnI in early presenters is supported by similar recent observations with s-cTnI in critical subgroups such as the elderly and patients with pre-existing coronary artery disease.11,12

**Figure 1** Levels of high-sensitivity cardiac troponin according to final diagnoses. Troponin levels at the time of patients’ presentation to the emergency department. The boxes represent median and inter-quartile ranges. hs-cTn, high-sensitivity cardiac troponin; AMI, acute myocardial infarction; CAD, coronary artery disease.

**Figure 2** Diagnostic performance of high-sensitivity cardiac troponins I and T. Receiver-operation-characteristic curves show the diagnostic accuracy of high-sensitivity cardiac troponins I and T for non-ST segment myocardial infarction at presentation to the emergency department with acute chest pain in the overall cohort (A) and in the patients with a chest pain onset within 3 h (B).
and therefore quite certainly real. Although early presenters can be assumed to derive the greatest benefit from early revascularization, it remains uncertain whether the magnitude of the difference is sufficient to achieve clinical relevance. Even small differences in the diagnostic accuracy for AMI in early presenters may have sufficient effect on the early management of patients. In addition, these differences may impact also on, e.g. the negative predictive value of specific rule-out algorithms. For their acceptance and adoption, clinicians might see a difference between an algorithm that offers, e.g. a NPV of 99.9% vs. an algorithm that offers an NPV of 99.5%. Thirdly, during serial sampling, diagnostic accuracy of both hs-cTnI and hs-cTnT further increased. While the direct comparisons of hs-cTnI and hs-cTnT at the individual later time points showed similar accuracy for both, the comparison of the respective combinations of levels at presentation with serial measurements showed a very small but statistically significant higher diagnostic accuracy of hs-cTnT vs. hs-cTnI. Fourthly, comparing the diagnostic accuracy of both assays to differentiate UA from NCCP, hs-cTnI was slightly

### Table 2  Diagnostic accuracy of changes in high-sensitivity cardiac troponin I vs. changes in high-sensitivity cardiac troponin T in early presenters

<table>
<thead>
<tr>
<th>Time point</th>
<th>AUC (95% CI) hs-cTnI</th>
<th>AUC (95% CI) hs-cTnT</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0h*</td>
<td>0.92 (0.89–0.94)</td>
<td>0.89 (0.86–0.91)</td>
<td>0.019</td>
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<tr>
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<td>0.95 (0.92–0.96)</td>
<td>0.97</td>
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<td>0.94 (0.92–0.96)</td>
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<tr>
<td>1h+Δ0h−1h*</td>
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<td>0.95 (0.93–0.97)</td>
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<tr>
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<td>0.97 (0.95–0.98)</td>
<td>0.88</td>
</tr>
<tr>
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<td>0.96 (0.94–0.98)</td>
<td>0.05</td>
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<tr>
<td>2h+Δ0h−2h*</td>
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<tr>
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</tr>
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<tr>
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<td>0.98 (0.95–0.99)</td>
<td>0.99 (0.96–0.99)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

a = 558; b = 456; c = 385; d = 181.
*Comparisons between hs-cTnI vs. hs-cTnT.

### Table 3  Diagnostic accuracy of changes in high-sensitivity cardiac troponin I vs. changes in high-sensitivity cardiac troponin T

<table>
<thead>
<tr>
<th>Time point</th>
<th>AUC (95% CI) hs-cTnI</th>
<th>AUC (95% CI) hs-cTnT</th>
<th>P-value*</th>
</tr>
</thead>
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<td>0.95 (0.94–0.96)</td>
<td>0.92</td>
</tr>
<tr>
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<td>0.96 (0.95–0.97)</td>
<td>0.05</td>
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<tr>
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<td>0.032</td>
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<td>0.97 (0.96–0.98)</td>
<td>0.017</td>
</tr>
</tbody>
</table>

a = 2226; b = 1735; c = 1374; d = 642.
*Comparisons between hs-cTnI vs. hs-cTnT.

![Figure 3](https://academic.oup.com/eurheartj/article-abstract/35/34/2303/2481219)  
**Figure 3** Diagnostic performance of high-sensitivity cardiac troponin T and I within time. Receiver-operation-characteristic curves displaying the diagnostic accuracy for non-ST segment myocardial infarction of serial sampling of high-sensitivity cardiac troponin I vs. high-sensitivity cardiac troponin T.

![Figure 4](https://academic.oup.com/eurheartj/article-abstract/35/34/2303/2481219)  
**Figure 4** Prognostic performance of high-sensitivity cardiac troponin T and I. Receiver-operation-characteristic curves displaying the prognostic accuracy for all-cause mortality during the 24-month follow-up of high-sensitivity cardiac troponin I and high-sensitivity cardiac troponin T.
superior to hs-cTnT. However, it is important to highlight that overall the diagnostic accuracy of hs-cTn for UA was only moderate, corroborating the data reported in earlier pilot studies in which the adjudication of the final diagnosis was based on conventional cTn assays only. Further studies are needed to define the best possible clinical use of hs-cTn in conjunction with all other clinical information in the differentiation of UA from NCCP. Fifthly, prognostic accuracy for all-cause mortality during 24-month FU was high for both hs-cTnI and T. In fact, hs-cTnT was significantly superior compared with hs-cTnI. Our data corroborate and extend recent studies in which hs-cTnT was compared with cTnI and hs-cTnI assays and shown to be the better prognosticator. As follow-up was performed blinded to levels of both hs-cTnT and hs-cTnI and revealed a substantial number of deaths, and was consistent using three different statistical models to quantify prognostic accuracy, also the finding of prognostic superiority of hs-cTnT over hs-cTnI methodologically seems very robust. The observed difference in prognostic accuracy (ΔAUC 0.05) was consistent in the NSTEMI and non-NSTEMI group and clearly seems clinically meaningful. Sixthly, prognostic accuracy to predict non-fatal AMI during 24-month FU among patients in the no-NSTEMI group was low-to-moderate for both biomarkers, and slightly higher for hs-cTnI compared with hs-cTnT. This finding is supported by a similar observation in another chest pain cohort and highlights the fact that different pathophysiological signals may be helpful in the prediction of death vs. the prediction of acute plaque rupture resulting in non-fatal AMI.

We can only speculate which pathophysiological differences between cTnI and T or the specific hs-cTn assays used were the major drivers for the observed differences. First, release of cTn occurs first from the early appearing cytosol pool and subsequently from the structural pool. Release from the latter is the reason for the sustained elevations observed clinically in AMI and is a surrogate for irreversible break down of sarcomeric proteins. It is conceivable that the early appearing pool contains larger amounts of cTnI than cTnT, which would explain that cTnI seems to be the superior signal in early presenters. On the other hand, if the cTnT signal results to large extent from the irreversible break down of sarcomeric proteins, this more profound injury could then be well understood to be more closely linked to mortality when compared with a signal that may be induced also from less severe injury. Recent observations from studies of exercise-induced myocardial ischaemia support this hypothesis. Silent coronary plaque rupture with subsequent microembolization may be the possible mechanisms linking hs-cTn with the risk of AMI in the future. As microembolization represents a minor injury, it may result in a predominate release of cTn from the early appearing cytosol pool and may therefore be better reflected by levels of hs-cTnI. Patients experiencing silent plaque rupture with microembolization may well be considered at an increased risk of subsequent plaque ruptures that may not heal spontaneously and that may result in clinically apparent AMI. Secondly, we think it is unlikely that pre-analytical or analytical issues of one of the assays played a relevant role as each assay proved superior in at least one category. Measurements of hs-cTnT were performed from two types of samples (serum and EDTA plasma), while hs-cTnI was measured from only one type (serum). While these sample types have been shown to reveal very high correlations close to 1, the use of two sample types might have introduced a minor disadvantage for the hs-cTnT assay.

The observed differences should not distract from the enormous amount of similarities between hs-cTnI and hs-cTnT, neither should they be misinterpreted as a suggestion to use two hs-cTn assays in parallel. In addition, it is important to highlight that hs-cTn must always be used and interpreted in conjunction with all other clinical information.

Some limitations of this study merit to be considered. First, we analysed the diagnostic and prognostic performance of cTnI and cTnT using the two clinically available hs-cTn assays. Future studies will need to evaluate whether our findings also apply to other hs-cTn assays once they will become clinically available. Second, since our study was prospective and observational, we cannot determine with precision the clinical benefit associated with the clinical use of either hs-cTnI or hs-cTnT. Thirdly, as patients with terminal kidney failure requiring dialysis were excluded from this study, we cannot comment on the diagnostic and prognostic performance of cTnI or cTnT in those patients. Fourth, our data set does not allow to address the question whether and if to what extent the difference in molecular weight (23 vs. 35 kDa) between cTnT and cTnT contributed to our findings.

In conclusion, both hs-cTnI and hs-cTnT provided high diagnostic and prognostic accuracy. The direct comparison revealed small but potentially important differences between the performance of the cTnI and cTnT molecule and the cTnT molecule that might help to further improve the clinical use of hs-cTn in the management of patients presenting with suspected AMI.

Supplementary material

Supplementary material is available at European Heart Journal online.

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