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The Antibody Configurations of Cardiac Troponin I Assays May Determine Their Clinical Performance

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Background: **Previous studies have shown superior clinical performance of the cardiac troponin I (cTnI) assay from Beckman-Coulter Diagnostics. This assay had a unique combination of monoclonal antibodies with 2 monoclonal antibodies directed against epitopes near the NH_2 terminus of the heart-specific region of troponin I. The approach has been adopted by the new cTnI assay from Abbott Diagnostics. The aim of our study was to investigate whether this approach affects the clinical performance of cTnI assays.**

Methods: **Cardiac troponin concentrations were measured in a random sample of patients with unstable coronary artery disease included in the GUSTO IV trial (n = 696) by the AccuTnI (Beckman-Coulter Diagnostics), Architect cTnI (Abbott Diagnostics), Immulite 2500 cTnI (Diagnostics Products Corporation), and Elecsys 2010 cTnT (Roche Diagnostics) assays and related to the 1-year mortality. The primary cutoff concentrations were based on the 99th percentile upper reference limits and an imprecision (CV) ≤10%.**

Results: **The sensitivities of the AccuTnI and Architect cTnI assays in identifying patients who died within 1 year were equal and were significantly higher ($P < 0.05$) than those of the Immulite 2500 cTnI and the Elecsys cTnT assays. The concordance between the AccuTnI and Architect cTnI assays was 97%, but concordances between the Architect cTnI and the Elecsys cTnT assays were 89%–92% with more at-risk patients ($P < 0.01$ to $P < 0.001$) identified by the Architect cTnI assay.**

Conclusions: **The Architect cTnI assay has clinical performance similar to that of the AccuTnI, probably as a result of the inclusion of a monoclonal antibody against troponin I epitope 41–49 in the assay.**

Modern assays of cardiac troponins specifically reflect the leakage of proteins from myocardial cells *(1–3)*, and any increase of troponin concentrations in the blood seems to be a signal of a poor condition of the myocardium and is related to an unfavorable outcome of the patient *(4–9)*. In a recent report we showed that some assays had superior clinical performance compared with other troponin assays with similar analytic sensitivities and performances *(10, 11)*; the cardiac troponin I (cTnI)[4] assay (AccuTnI) from Beckman Coulter (Fullerton, CA) identified ~10% more patients with an adverse outcome than the AxSYM assay (Abbott, Abbott Park, IL) and the Liaison assay (Diasorin, formerly Byk-Sangtec). In addition, compared with the troponin T assay of Roche, the AccuTnI assay was superior. The choice of antibodies in the cTnI assays was different. The AccuTnI assay is based on a pair of monoclonal antibodies lying next to each other and directed against epitopes in the heart-specific and the stable region of the molecule close to the NH_2 terminus (epitopes 24–40 and 41–49), whereas the 2 other assays incorporate one antibody directed toward the heart-specific region close to the NH_2 terminus (i.e., in the region of epitopes 20-39) and the other antibody directed against epitopes in the stable part closer to the COOH terminus (epitopes 87–91 and 80–110, respectively). With the accumulating knowledge of the presence in blood of many different forms of troponins and interfering factors in the form of autoantibodies *(12–14)*, we postulated that the assay configuration with respect to epitope specificity of

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[4] Nonstandard abbreviations: cTnI and cTnT, cardiac troponin I and T, respectively; GUSTO IV, Global Utilization of Strategies to Open occluded arteries IV; DPC, Diagnostics Products Corporation; URL, upper reference limit; SWISCH, Sweden, Women and Men and Ischemic Heart Disease; and FRISC II, Fast Revascularisation during InStability in CAD trial.

the antibodies determines the clinical performance, possibly because different forms and molecular complexes of troponins are identified by the assays. It appears that epitope 41–49 is critical. Recently, Abbott Diagnostics redesigned their troponin I assay and included in their Architect assay a monoclonal antibody directed toward this epitope. The aim of this study was therefore to determine whether, as a result of these modifications, the Architect assay has achieved clinical performance similar to that of the Beckman Coulter assay. For this purpose, using the Abbott Architect assay and the Beckman Coulter AccuTnI assay, we measured the troponin concentrations in samples from a random group of patients with unstable angina and non–ST-elevation myocardial infarction taken from the Global Utilization of Strategies to Open Occluded Arteries IV (GUSTO IV) trial and related the concentrations to the 1-year mortality. For comparison, we also measured the troponin I concentrations with the Immulite 2500 assay from Diagnostics Products Corporation (DPC, Los Angeles, CA), which has a antibody configuration similar to that of the old AxSYM and Liaison assays, as well as the troponin T concentrations with the Elecsys 2010 assay from Roche (Mannheim, Germany).

Patients and Methods

The GUSTO IV trial included 7800 patients with non–ST-elevation acute coronary syndrome from 458 centers in 24 countries during 1999 and 2000 *(15)*. Briefly, eligible patients were at least 21 years of age with chest pain lasting more than 5 min within 24 h of admission and either a positive cardiac troponin T (cTnT) or cTnI test or 0.5 mm of ST-segment depression. The patients were randomly assigned to abciximab infusion for 24 or 48 h or corresponding placebo infusion. All patients received aspirin for long-term treatment as well as either unfractionated heparin infusion or subcutaneous dalteparin. Coronary angiography was discouraged during or within 12 h after the completion of study agent infusion. Myocardial infarction was defined as either a new Q-wave or creatinine kinase-MB ≥3 times the upper reference limit (URL) as reported previously in detail *(15)*. At 12 months, all-cause mortality data were collected for all patients. From the GUSTO IV trial cohort, 700 samples were randomly selected for the analyses shown in this report. Four samples contained insufficient serum for the analyses.

Blood anticoagulated with EDTA was obtained from a direct vein puncture at randomization, which occurred at a median of 8.5 h from symptom onset in the present subpopulation. Plasma was prepared within 30 min of collection by centrifugation at 2000*g* at room temperature for 20 min.

One reference population consisted of 442 apparently healthy persons participating in the Sweden, Women and Men and Ischemic Heart Disease (SWISCH) case–control study on risk factors for coronary artery disease in elderly men and women during 2001–2002 *(16)*. The Architect assay was used to measure cTnI in EDTA-anticoagulated plasma from 424 of these persons (plasma samples from 18 participants were missing). Written consent was obtained from all participants, and the protocol was approved by the local ethics committee. The second reference population consisted of 747 apparently healthy persons: 435 men [mean (SD) age, 42 (9) years] and 312 women [44 (10) years]. These blood samples had been collected as part of a health screening program of employees at Pharmacia Diagnostics, Uppsala, Sweden. Before use in this study, the samples were deidentified. cTnI in the serum samples of this reference population was measured with the DPC assay. For the preparation of serum, blood was obtained in Vacutainer Tubes (Becton Dickinson) and allow to clot at room temperature for 60–90 min, after which the serum was obtained by centrifugation for 10 min at 2000*g* and thereafter stored at −70 °C until used.

Troponin measurements were made on freshly frozen samples (−70 °C) that had been thawed twice at most. As shown previously with the AccuTnI assay, troponin concentrations are stable in plasma after several freeze–thaw cycles *(17)*. All assays were performed with reagents supplied by the respective companies and performed according to their instructions.

According to the manufacturers, the minimum detectable concentrations of cTnI were 0.01 μg/L for the AccuTnI, ≤0.01 μg/L for the Architect, and 0.10 μg/L for the Immulite 2500. Total imprecision (as CVs) was 4.1%–8% (range, 0.05–11 μg/L) for the AccuTnI, 3%–5.8% (range, 0.1–13.7 μg/L) for the Architect cTnI, and 6.2%–21.7% (range, 0.12–40.9 μg/L) for the Immulite 2500 cTnI assays. The minimum cTnT concentration detectable by the Elecsys assay, according to the manufacturer, was 0.01 μg/L, and total imprecision was 4%–9% (range, 0.4–30 μg/L).

Mortality at 12 months was used as the clinical endpoint in the clinical performance evaluations of the assays.

STATISTICS

The Fisher exact test was used to compare the clinical performances of the assays. Differences in sensitivities were calculated by differences between 2 proportions. Calculations were performed by the statistical software Statistica for Windows (Ver. 7.0; Statistica) and Statistical Package for Social Sciences (SPSS 12.0) software (SPSS Inc.).

Results

The 10% CV imprecision data used in this report were adopted from the manufacturers and previous reports *(17)*. For the AccuTnI assay, the lowest concentration at which the CV was ≤10% was 0.03 μg/L; for the Architect cTnI assay, it was 0.032 μg/L; and for the cTnT assay, it was 0.03 μg/L. With respect to the Immulite 2500 assay, we defined the imprecision profile of the assay from the CV obtained with duplicate measurements of samples

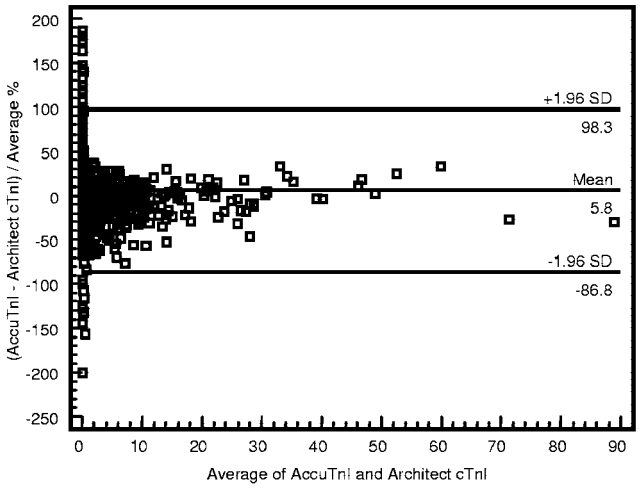

Fig. 1. Bland–Altman plot showing the average difference between the AccuTnI and Architect cTnI assays.

The difference between the assays was 5.8% with the AccuTnI giving higher concentrations.

from a cohort of patients from the GUSTO IV trial (n = 812). The lowest concentration at which the CV was ≤10% was 0.33 μg/L.

The 99th percentile URLs of seemingly healthy reference populations used in this report were partly adopted from the manufacturer and partly from our own results. For the AccuTnI and Architect cTnI assays, the 99th percentile URLs for troponin I were established by means of samples obtained from the SWISCH cohort (n = 424) and were 0.04 and 0.038 μg/L, respectively. For the cTnI assay on Immulite 2500 and for the cTnT assay, the 99th percentile URLs were established in another cohort of seemingly healthy persons (n = 747) and were 0.22 and <0.01 μg/L, respectively. Two different cutoff concentrations were used for the AccuTnI and Architect cTnI assays and were based on the fact that among the 424 persons, 3 had concentrations measured with the Architect assay that were regarded as obvious outliers. The cutoff concentrations based on the 421 persons were 0.027 and 0.032 μg/L, respectively.

The correlation between the Architect cTnI and AccuTnI assays was very good ($r = 0.97$; $y = 1.007x + 0.161$ μg/L; $S_{y|x} = 1.90$ μg/L; n = 802). The overall agreement between the 2 assays is illustrated in Fig. 1 by means of a Bland–Altman plot and shows an overall difference between the methods of 5.8% with the AccuTnI giving the higher concentrations.

The sensitivities for all 4 assays in identifying persons who died within the 1-year follow-up period are given in Fig. 2. As shown, the sensitivities of the Architect cTnI and AccuTnI assays were identical at similar cutoff concentrations, whereas the sensitivities of the cTnT and the Immulite 2500 cTnI assays were lower than the sensitivities of the Architect cTnI and AccuTnI assays ($P = 0.05$) when the 10% CV cutoffs were used. In addition, the sensitivities based on the 99th percentile cutoffs of the cTnT assay and the Immulite 2500 cTnI assay were lower than the sensitivity of the AccuTnI assay when the 99th percentile URL for persons <60 years of age was adopted ($P < 0.05$).

We calculated the concordances between the assays for the Architect cTnI, AccuTnI, and Elecsys cTnT assays, based on either the 10% CV cutoff concentrations or 99th percentile URL for the reference populations. When we used the 10% CV or the 99th percentile URL cutoffs, we found an overall concordance of 97%. As shown in Table 1, with results based on the truncated 99th percentiles, the clinical performances of the AccuTnI and Architect cTnI assays were very similar, with 1.8% and 1.3% of the study population identified only by either the Architect cTnI assay or the AccuTnI assay, of which 1 death had occurred among those individuals identified by the Architect cTnI assay only. The results based on the untruncated 99th percentile URL gave similar results with a 96% concordance. For comparison, we also estimated the concordance based on the lower cutoff limits based on the 99th percentile URL for the persons <60 years of age in the SWISCH cohort as analyzed by AccuTnI (0.02 μg/L) and the 99th percentile URL as reported by the manufacturer of the Architect cTnI assay (0.017 μg/L). The concordance based on these lower cutoff limits was also 97% with similar clinical performances. Also shown in Table 1 is a comparison between the Architect cTnI and the Elecsys cTnT assays; the overall concordance was 92% when the 99th percentile URLs were used as cutpoints. Significantly more individuals were identified by the Architect cTnI assay only than by the Elecsys cTnT assay only ($P < 0.01$, Fisher exact test), with 5 deaths among those identified by the cTnI assay alone but no deaths among those identified by the cTnT assay alone. Thus, 8% of all deaths occurred in the cohort identified only by the Architect cTnI assay. When we used the 10% CV cutoff concentrations, the differences in clinical performances between the cTnI and cTnT assays were even more striking ($P < 0.001$) with an overall concordance of 89%. Comparison of the AccuTnI and the Elecsys cTnT assays gave results identical to those obtained in the Architect cTnI and Elecsys cTnT comparison and were almost identical to previously published results based on the Fast Revascularisation during InStability in CAD trial (FRISC II) cohort *(10, 11)*.

Discussion

We have shown in this report that the choice of antibodies has a great impact on the clinical performance of cTnI assays in the sense that more patients at risk were identified by some assays although the analytical sensitivities of the assays were similar. We also show in this fairly small cohort that the capacity to identify those patients who actually died is greater for some of these assays. Thus, the addition in the Architect cTnI assay of a monoclonal antibody against epitope 41–49 in the heart-specific N-terminal region of the troponin molecule im-

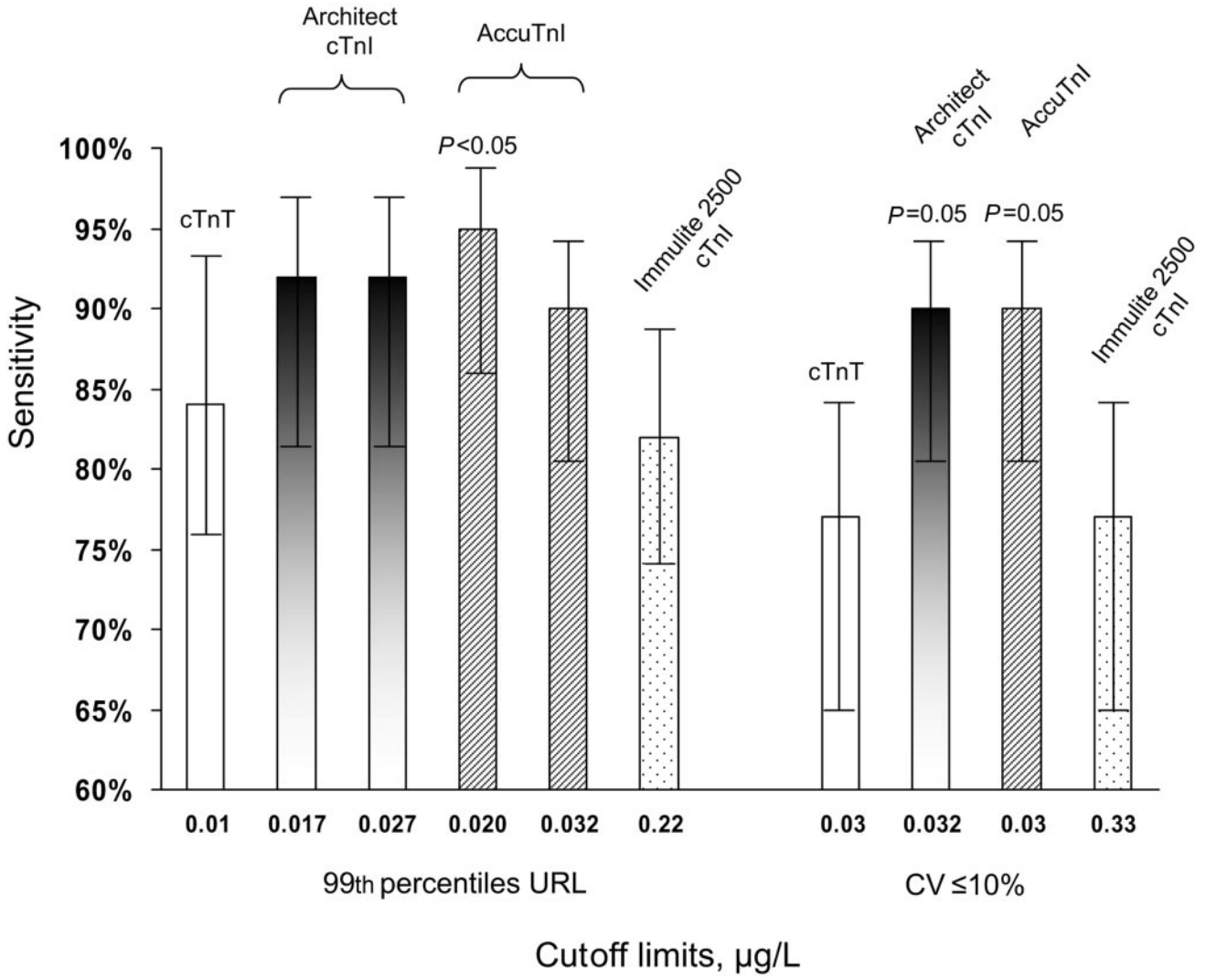

Fig. 2. Sensitivities of cardiac troponin assays in identifying those patients who died within the 1-year follow-up period.

The cutoff concentrations applied (μg/L) are given and correspond to the 99th percentile URLs and the CV ≤10% cutoffs for the respective assays. As indicated by the statistics, the sensitivities of the Architect cTnI and AccuTnI assays at the given cutoffs are significantly higher than the sensitivities of the cTnT or Immulite 2500 cTnI assays whether the cutoffs are based on the 99th percentile URLs or the CV ≤10% cutoffs. The *error bars* indicate the 95% confidence intervals of the proportions.

proved the clinical performance of the assay significantly, and the assay achieved the same sensitivity as the Beckman Coulter AccuTnI assay. On the other hand, the sensitivity of the recently developed cTnI assay performed on the Immulite 2500 (DPC) was lower but was similar to the sensitivities of the cTnT assay and the old AxSYM assay from Abbott *(10)*. The Immulite 2500 cTnI assay is based on an antibody configuration including monoclonal antibodies against epitopes 24–40 and 80–110, but not epitope 41–49, which is similar to the old AxSYM assay. These results lend further support to the notion of the importance of including in assays more than one antibody directed against epitopes in the heart-specific N-terminal region.

The reason for the improvement in clinical performance after inclusion of antibodies against epitope 41–49 in cTnI assays is not entirely clear. From an analytical

Table 1. Concordance between the Architect cTnI assay and the AccuTnI and the Elecsys cTnT assay.

	AccuTnI		Elecsys cTnT	
Architect cTnI	≤0.032 μg/L	>0.032 μg/L	<0.01 μg/L	≥0.01 μg/L
≤0.027 μg/L				
Positive results, n (%)	113 (16.5)	12 (1.8)	126 (18.1)	12 (1.7)
Deaths, n (%)	5 (4.4)	0	5 (4.0)	0
>0.027 μg/L				
Positive results, n (%)	9 (1.3)	549 (80.4)	44 (6.3)	514 (73.8)
Deaths, n (%)	1	56 (10)	5 (11)	52 (10)

[a] Concordance between the AccuTnI and Architect cTnI assays was 97% with similar clinical performances, whereas the concordance between the Elecsys cTnT and Architect cTnI assays was 92% with significantly more persons identified by the Architect cTnI assay ($P < 0.01$).

point of view, the Liaison and Immulite 2500 cTnI assays are very sensitive, well-performing assays and are in that respect comparable to the AccuTnI and Architect cTnI assays; however, their clinical performance is not as high *(11)*. Thus, the question is: What do these different assays measure? Indeed, they seem to identify different molecules at the lower end of the concentration range; we found no correlations between the 2 assay principles, as illustrated by the comparison between the AccuTnI and Liaison cTnI, when results from the reference populations were compared. It is also well documented that cTnI is present in many different forms in the circulation, some of which may be the consequence of truncation of the molecule as a result of proteolytic breakdown and some of which may be the result of complex formations between cardiac troponins I, T, and C in various molecular constellations *(12, 18)*. An interesting observation is the presence of circulating autoantibodies against cTnI in a substantial number of study participants and the possible interference of these antibodies with the assays *(13, 14)* because the autoantibodies seem to be directed preferentially to the more C-terminal regions of the molecule and not to the N-terminal region including epitope 41–49. As shown previously, the concordance between the old AxSYM assay and the Elecsys cTnT assay was very good, ~95%, and with very similar clinical performances for the 2 assays *(10)*. This shows that the 2 assays probably identify the same patients but miss some patients identified by the AccuTnI and Architect cTnI assays. This could indicate that the old AxSYM assay and the Elecsys cTnT assay identify the same molecular complexes of troponins I and T and also suggests that additional unique molecular forms of cTnI are identified by the AccuTnI and Architect cTnI assays.

The study cohort in this report was the GUSTO IV trial patients, who had been recruited as part of a clinical trial of the antithrombotic drug abciximab (ReoPro^{TM}) and were included if they had symptoms and signs of acute coronary syndrome without electrocardiographic indications of ST-segment elevations *(19)*. In our previous report we showed that troponin T concentrations >0.01 μg/L strongly predicted an acute myocardial infarction within the next 30 days *(6)*, whereas troponin T as a risk predictor of death within 1 year was weaker but significant. The present data obtained with improved cTnI assays indicate that the predictive power of cardiac troponins probably was underestimated by the troponin T results. From a clinical point of view, the differences in performance of the different assays should be of considerable interest because the mortality was also high in the cohorts identified with increased concentrations only by the AccuTnI or the Architect cTnI assays. Thus, 1-year mortality was similarly high in patients with Architect TnI concentrations exceeding the 99th percentile cutoff of 0.027 μg/L irrespective of undetectable or detectable troponin T concentrations (11% vs 10%; Table 1). The clinical relevance of identifying patients with very low but increased concentrations of cardiac troponins is also illustrated by the fact that early intervention may reduce the mortality by ~30% in those with increased cTnI concentrations as measured with the AccuTnI assay *(10)*. In our previous study on the FRISC II patient cohort, the average time from symptoms to blood sampling was ~40 h *(5)* and was substantially longer than the 8.5 h in the GUSTO IV trial. In spite of these time differences, we obtained almost identical predictive results in the 2 studies of cardiac troponin measurements, which might indicate that the unique molecular forms of cTnI identified by the assays remained in the circulation for a substantial time period after the acute event.

One limitation of the present study is the exact definition of cutoff concentrations for the fair comparison of different assays. Two criteria for cutoffs were used in this study, and regardless of which principle was adopted, similar results were obtained. The cutoff concentrations at which different assays have a CV ≤10% are based on different criteria: in some reports, they are based on results from 1 center, whereas in others they are based on mean concentrations obtained in multicenter studies *(17, 20, 21)*. Thus, comparisons of assays based on concentrations from such different approaches are obviously quite uncertain. In our study, we therefore preferred to use cutoffs based on the 99th percentile URLs of well-defined reference populations. In this regard, the SWISCH cohort is unique because it was collected randomly in a community but matched with respect to sex and age to the FRISC II cohort of patients. All participants were invited to have a thorough medical examination by a cardiologist, and only those found healthy at this examination were included in the reference cohort. The inclusion criteria for the GUSTO IV trial were similar to those for FRISC II, which means that the SWISCH cohort is well matched to the GUSTO IV cohort as well. Compared with other studies, the 99th percentile of the SWISCH cohort was somewhat higher, which likely is attributable to differences resulting from inclusion of older persons because, as we show in the present study with the Architect cTnI and also in a previous report with the AccuTnI assay, cTnI concentrations tend to increase with age *(11)*. The uncertainty in defining true 99th percentile URLs based on 424 individuals is obvious because the cutoff concentration is equal to the individual having the fifth highest concentration. If 1 or 2 more seemingly healthy individuals with somewhat increased concentrations are included in the reference population, this may have profound consequences on the 99th percentile limit, which is one major reason to eliminate possible outliers from the cohort. We based our evaluations on several cutoff limits ranging from 0.017 μg/L to 0.038 μg/L for the Architect cTnI assay and from 0.02 to 0.04 μg/L for the AccuTnI assay, and the clinical performance results were very similar irrespective of cutoff limit. It should, however, be emphasized that the aim of the present study was not to define the optimal clinical

cutoffs for the different assays, but to illustrate the fact that changes in antibody configurations have impacts on the capacity of the assay to identify patients at risk.

In conclusion, we show that the clinical performance of troponin assays varies. This is true between assays that measure troponin I or T, but also among various cTnI assays. For the measurement of cTnI, inclusion in the assays of at least 2 monoclonal antibodies against epitopes in the N-terminal part of the heart-specific region of the molecule seemed critical to obtaining optimum performance. For as yet unidentified reasons, such cTnI assays also identify more patients at risk than the currently available cTnT assay.

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References

1. Collinson PO, Stubbs PJ. Are troponins confusing? Heart 2003; 89:1285–7.
2. Panteghini M. Role and importance of biochemical markers in clinical cardiology. Eur Heart J 2004;25:1187–96.
3. Apple FS. Analytical issues for cardiac troponin. Prog Cardiovasc Dis 2004;47:189–95.
4. Lindahl B, Venge P, Wallentin L. Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease. The FRISC study group. Circulation 1996;93:1651–7.
5. Lindahl B, Toss H, Siegbahn A, Venge P, Wallentin L. Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. FRISC Study Group. Fragmin during Instability in Coronary Artery Disease. N Engl J Med 2000;343:1139–47.
6. James S, Armstrong P, Califf R, Simoons ML, Venge P, Wallentin L, et al. Troponin T levels and risk of 30-day outcomes in patients with the acute coronary syndrome: prospective verification in the GUSTO-IV trial. Am J Med 2003;115:178–84.
7. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, et al. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med 1996;335:1342–9.
8. Luscher MS, Thygesen K, Ravkilde J, Heickendorff L. Applicability of cardiac troponin T and I for early risk stratification in unstable coronary artery disease. TRIM Study Group. Thrombin Inhibition in Myocardial ischemia. Circulation 1997;96:2578–85.
9. Ohman EM, Armstrong PW, Christenson RH, Granger CB, Katus HA, Hamm CW, et al. Cardiac troponin T levels for risk stratification in acute myocardial ischemia. GUSTO IIA Investigators. N Engl J Med 1996;335:1333–41.
10. Venge P, Lagerqvist B, Diderholm E, Lindahl B, Wallentin L. Clinical performance of three cardiac troponin assays in patients with unstable coronary artery disease (a FRISC II substudy). Am J Cardiol 2002;89:1035–41.
11. Venge P, Johnston N, Lagerqvist B, Wallentin L, Lindahl B. Clinical and analytical performance of the liaison cardiac troponin I assay in unstable coronary artery disease, and the impact of age on the definition of reference limits. A FRISC-II substudy. Clin Chem 2003;49:880–6.
12. Labugger R, Organ L, Collier C, Atar D, Van Eyk JE. Extensive troponin I and T modification detected in serum from patients with acute myocardial infarction. Circulation 2000;102:1221–6.
13. Eriksson S, Halenius H, Pulkki K, Hellman J, Pettersson K. Negative interference in cardiac troponin I immunoassays by circulating troponin autoantibodies. Clin Chem 2005;51:839–47.
14. Eriksson S, Ilva T, Becker C, Lund J, Porela P, Pulkki K, et al. Comparison of cardiac troponin I immunoassays variably affected by circulating autoantibodies. Clin Chem 2005;51:848–55.
15. Simoons ML. Effect of glycoprotein IIb/IIIa receptor blocker abciximab on outcome in patients with acute coronary syndromes without early coronary revascularisation: the GUSTO IV-ACS randomised trial. Lancet 2001;357:1915–24.
16. Johnston N, Jernberg T, Lindahl B, Lindback J, Stridsberg M, Larsson A, et al. Biochemical indicators of cardiac and renal function in a healthy elderly population. Clin Biochem 2004;37: 210–6.
17. Venge P, Lindahl B, Wallentin L. New generation cardiac troponin I assay for the Access immunoassay system. Clin Chem 2001; 47:959–61.
18. Giuliani I, Bertinchant JP, Lopez M, Coquelin H, Granier C, Laprade M, et al. Determination of cardiac troponin I forms in the blood of patients with unstable angina pectoris. Clin Biochem 2002;35: 111–7.
19. Ottervanger JP, Armstrong P, Barnathan ES, Boersma E, Cooper JS, Ohman EM, et al. Long-term results after the glycoprotein IIb/IIIa inhibitor abciximab in unstable angina: one-year survival in the GUSTO IV-ACS (Global Use of Strategies To Open Occluded Coronary Arteries IV–Acute Coronary Syndrome) Trial. Circulation 2003;107:437–42.
20. Uettwiller-Geiger D, Wu AH, Apple FS, Jevans AW, Venge P, Olson MD, et al. Multicenter evaluation of an automated assay for troponin I. Clin Chem 2002;48:869–76.
21. Panteghini M, Pagani F, Yeo KT, Apple FS, Christenson RH, Dati F, et al. Evaluation of imprecision for cardiac troponin assays at low-range concentrations. Clin Chem 2004;50:327–32.