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Role of Monitoring Changes in Sensitive Cardiac Troponin I Assay Results for Early Diagnosis of Myocardial Infarction and Prediction of Risk of Adverse Events

Fred S. Apple,[1*] Lesly A. Pearce,[1] Stephen W. Smith,[1] Jason M. Kaczmarek,[1] and MaryAnn M. Murakami[1]

BACKGROUND: We sought to determine the diagnostic accuracy of the cardiac troponin I (cTnI) VITROS® Troponin I-ES assay for early detection of acute myocardial infarction (AMI) and for risk prediction of adverse events in patients with symptoms of acute coronary syndrome (ACS).

METHODS: cTnI was measured on admission and approximately 6 h postadmission in 381 patients. The 99th percentile cTnI concentration (0.034 μg/L) and change [delta (δ)] between admission and follow-up concentrations were evaluated in diagnostic sensitivity and specificity calculations. Risk of cardiac event or death within 60 days was evaluated by Cox proportional hazards regression.

RESULTS: AMI occurred in 52 patients. Diagnostic sensitivities (95% CI) of admission and follow-up cTnIs for AMI were 69% (55%–81%) and 94% (84%–99%), respectively. The corresponding specificities (95% CI) were 78% (73%–82%) and 81% (77%–85%), and ROC curve areas were 0.82 vs 0.96 ($P < 0.001$). Deltas between admission and follow-up cTnI >30% had a sensitivity of 75% (95% CI 61%–86%) and a specificity of 91% (95% CI 87%–94%). During follow-up, 1 cardiac death, 2 noncardiac deaths, 52 AMIs, 6 coronary artery bypass grafts, and 43 percutanous coronary interventions occurred in 62 patients. A δ cTnI >30%, when added to either initial cTnI >0.034 μg/L or follow-up cTnI >0.034 μg/L, improved risk stratification for cardiac event or death ($P < 0.001$).

CONCLUSIONS: Admission cTnI measured by the VITROS ES assay is a sensitive biomarker for detection of AMI. Utilizing >30% cTnI δ in addition to either the baseline or follow-up concentration improved both specificity and risk assessment in patients presenting with symptoms of ACS.

The "Universal Definition of Myocardial Infarction" recommendation published on behalf of the joint European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation Task Force for the redefinition of acute myocardial infarction (AMI)[2] is predicated on the detection of an increase or decrease of cardiac troponin (cTn), with at least one value above the 99th percentile reference value in patients with evidence of myocardial ischemia *(1)*. Blood samples for measurement of cTn are recommended to be drawn at presentation and 6–9 h later to optimize both clinical sensitivity for ruling in AMI and clinical specificity for ruling out AMI. These concepts were supported by the National Academy of Clinical Biochemistry (NACB) Laboratory Medicine Practice Guidelines *(2, 3)*. The NACB further suggested that a rapid rule-in protocol with frequent early sampling of myocardial necrosis biomarkers may be appropriate if tied to therapeutic strategies. With improvements in commercial cTn assays, cTnI can be measured with lower limits of detection and improved precision at the 99th percentile reference value concentrations. The potential diagnostic and prognostic implications of monitoring lower concentrations coupled with smaller increases in cTn to improve diagnostic sensitivity and risk stratification have been exemplified in a recent study based on the second-generation Advia Centaur TnI-Ultra assay *(4)*. The findings of this study demonstrated that any measurable cTnI value in patients with symptoms suggestive of ACS was an independent predictor of adverse events, supporting recent studies based on the Beckman Accu cTnI assay for de-

[1] Hennepin County Medical Center and University of Minnesota, Department of Laboratory Medicine and Pathology and Emergency Medicine, Minneapolis, MN.
* Address correspondence to this author at: Hennepin County Medical Center, Clinical Laboratories P4, 701 Park Ave., Minneapolis, MN 55415. Fax 612-904-4229; e-mail apple004@umn.edu.

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[2] Nonstandard abbreviations: AMI, acute myocardial infarction; cTn, cardiac troponin; NACB, National Academy of Clinical Biochemistry; CK-MB, creatine kinase isoenzyme fraction MB; LoD, limit of detection; ECG, electrocardiogram; RR, relative risk.

tecting an increased risk of adverse events in a cohort of elderly individuals with and without coronary artery disease *(5, 6)*. Taken together, these findings support the recommendations of the NACB that encourage cTn as the preferred biomarker for risk stratification and recommend its measurement in all patients suspected to have ACS. Concentrations of cTn exceeding the 99th percentile are indicative of increased risk of death and recurrent ischemic events *(2, 3)*.

The concept of using a δ biomarker approach has been previously explored. In 1998 Fesmire et al. first reported that at 2 h postadmission a δ concentration change for creatine kinase isoenzyme fraction MB (CK-MB) >1.6 μg/L was more sensitive for detection of AMI than a concentration that exceeded the 6-h reference value of 6.0 μg/L *(7)*. Furthermore, the 2-h δ for CK-MB mass initially outperformed the 2-h δ for the first-generation cTnI assay *(8)*, but was surpassed by δ calculations performed with the second-generation cTnI assay *(9)* used for both emergency room rule-out of AMI and prediction of adverse outcomes. Other studies have also demonstrated that use of δ cTnIs obtained with a sensitive, newer generation cTnI assay (Beckman AccuTnI) in specimen sets with a time interval of ≥3 h or in 1 specimen ≥6 h after onset of symptoms gave a prevalence of AMI equivalent to that obtained using the American Hospital Association definition of AMI *(10, 11)*. More recently, NACB guidelines have suggested that in patients with baseline increases of cTn who present with possible ACS, changes in cTn concentrations of ≥20% should be used to define patients with an AMI *(2)*. However, no studies to date have examined the implications of δ cTnI for both accuracy of detecting AMI and risk assessment using the newer generation cTnI assays.

The purpose of this study was to determine both the diagnostic accuracy for AMI and the prognostic value for assessing risk of short-term adverse events when the second-generation VITROS® Troponin I ES assay is used to measure cTnI concentrations in a nonselected heterogeneous population of patients presenting with ischemic symptoms suggestive of ACS. Several sets of criteria were evaluated, including cTnI concentrations at the limit of detection (LoD) and the 99th percentile reference value, as well as δ criteria of 10%, 20%, and the optimal cutpoint determined by ROC curve analysis (30%) with specimens drawn at baseline and approximately 6 h later.

Materials and Methods

After institutional review board approval of this study, leftover plasma (heparin) specimens were prospectively collected from 397 patients who presented with symptoms suggestive of ACS and were admitted through the emergency department at Hennepin County Medical Center (Minneapolis, MN) to rule in or rule out AMI between September 27, 2005, and June 2, 2006. Specimens for each patient were obtained at the time of presentation (baseline) and at a follow-up time a minimum of 4 h (and maximum of 10 h) after the presentation sample. Timing of the follow-up sample was dependent on execution of standing orders for samples collected at 4, 8, and 12 h and availability of leftover samples. Sixteen patients did not have a second sample available and were excluded from the study; none of the excluded patients ruled in for AMI.

Plasma was initially stored refrigerated at 4 °C, and was frozen at −80 °C within 48–72 h. cTnI was measured by the second-generation Ortho-Clinical Diagnostics VITROS Troponin I ES assay according to the manufacturer's recommended procedure. cTnI values used for diagnostic and risk-assessment calculations were those designated in the manufacturer's package insert (cleared by the US Food and Drug Administration): LoD 0.012 μg/L, 99th percentile reference value 0.034 μg/L, and total imprecision of 10% at 0.034 μg/L. All of these criteria were confirmed in our laboratory. Values observed below the LoD were coded as 0.011 μg/L in the analyses. Additionally, δ criteria of 10%, 20%, and the optimal δ as determined by ROC analysis (30%) were evaluated for diagnostic and risk-assessment accuracy.

Patient demographic data and clinical diagnoses were obtained by chart review following patient enrollment into the study. Record review was carried out blinded to the VITROS Troponin I ES results and included gathering up-to-date medical history of previous medical conditions. Criteria for AMI were defined according to the European Society of Cardiology/American College of Cardiology redefinition of myocardial infarction guidelines *(1)*, for which diagnosis of AMI is based on evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia at presentation. Diagnosis of AMI required the following: detection of a rising or falling increase of cTnI (as measured by the Siemens Dade Behring Dimension or Stratus CS assays in use in the Hennepin County hospital laboratories) above the 99th percentile reference value (<0.1 μg/L; total imprecision 12% at 0.12 μg/L) with at least one of the following: symptoms of ischemia, new ST-T changes on electrocardiogram (ECG), development of Q waves on ECG, or imaging evidence of new loss of viable myocardium.

Chart reviews or telephone follow-up interviews (performed without knowledge of the cTnI findings) were used to determine clinical outcomes during a 60-day follow-up period. Clinical sensitivities and specificities for AMI as well as area under the ROC curves were computed and compared to assess diagnostic ac-

curacy, whereas diagnostic specificity was assessed using the McNemar test. The primary endpoint for assessing prognostic risk of short-term adverse events was the combined endpoint of first cardiac event (MI, percutanous coronary intervention, coronary artery bypass graft; including events at the index hospitalization) or death within 60 days. Exposure was computed from date of blood draw until date of first event, with censoring at time of last contact if <60 days. Cumulative event rates were estimated by use of the Kaplan-Meier method and compared by using the log-rank statistic. Relative risks (RR) and 95% CI were estimated by using Cox proportional hazards models with stepwise forward and backwards modeling to identify independent predictors. Statistical significance was accepted at the 0.05 level, and all statistical tests were 2 sided. Statistical analyses were performed with MedCalc 9.6.0.0 (www.medcalc.be) and SPSS for Windows version 15.0 (SPSS).

Results

Patients included in this study were diverse in racial make-up (42% white, 48% African American, 7% Native American, 1% Hispanic, and 2% other/mixed ethnicity) and had a mean age of 54 years (range 23–95 years). By medical history, 35% of patients had coronary artery disease, 22% MI, 29% diabetes, 66% hypertension, and 8% renal disease. The mean estimated glomerular filtration rate was 84 mL/min/1.73 m^2 (range 5 to >60 mL/min/1.73 m^2). Median time between reported onset of symptoms and presentation was 3.9 h, and median time between presentation and initial blood draw was 0.8 h (87% ≤2 h). Time between baseline and follow-up blood draws averaged 6 h (78% ≤ 6h).

AMI was clinically diagnosed in 52 (13.6%) of patients during initial hospitalization. Clinical sensitivities and specificities for AMI based on the 99th percentile of cTnI concentration (0.034 μg/L) were 69.2% and 77.5%, respectively, at baseline and 94.2% and 81.2% at follow-up (Table 1), with no difference in specificity between sample times ($P = 0.99$). For comparison, the initial Stratus CS specimen results demonstrated accuracy similar to the baseline VITROS ES results: 59.6% (95% CI 45.1–73.0) sensitivity and 88.0% (95% CI 84.0–91.3) specificity with an area under the ROC curve of 0.77 (95% CI 0.73–0.82). The VITROS ES cTnI assay with the follow-up specimen demonstrated a higher diagnostic accuracy ($P < 0.001$) for AMI than with the baseline sample, as evidenced by a higher area under the ROC curve (baseline 0.82, 95% CI 0.77–0.85; follow-up 0.96, 95% CI 0.94–0.98; Fig. 1). Use of the LoD concentration cutoff (≥0.012 μg/L) as the diagnostic threshold increased sensitivity for both baseline and follow-up samples to 90.4% and 98.1%, respectively, but reduced specificity from approximately 80% to approximately 50% (each $P < 0.001$).

Table 1. Clinical sensitivities and specificities of the VITROS ES cTnI assay for detection of AMI in 381 patients.

	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Baseline sample		
cTnI >0.012 μg/L	90.4 (79.0–96.8)	46.2 (40.7–51.8)
cTnI >0.034 μg/L	69.2 (54.9–81.3)	77.5 (72.6–81.9)
Follow-up sample		
cTnI >0.012 μg/L	98.1 (89.7–99.7)	55.3 (49.5–60.5)
cTnI >0.034 μg/L	94.2 (84.0–98.7)	81.2 (76.5–85.2)
Delta criterion		
Increase >10%	75.0 (61.1–86.0)	81.5 (76.8–85.5)
Increase >20%	75.0 (61.1–86.0)	86.6 (82.5–90.1)
Increase >30%	75.0 (61.1–86.0)	90.6 (86.9–93.5)

A δ cTnI of >30% was determined by ROC curve analysis as the optimal cutpoint for classification of AMI. No δ criterion had a higher diagnostic sensitivity than criteria based on a single absolute concentration (Table 1). Diagnostic specificity was similar between baseline cTnI >0.034 μg/L and δ > 10% ($P = 0.42$)

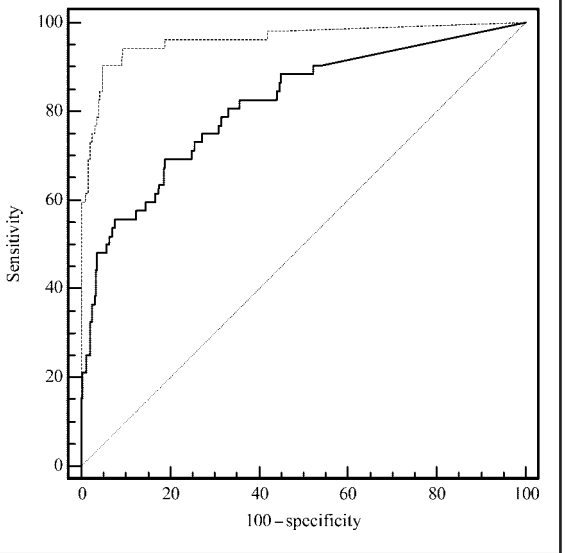

Fig. 1. ROC curves for baseline (solid line) and follow-up (dashed line) data obtained with the VITROS ES cTnI assay.

Sensitivity and specificity are given in percentages.

Table 2. Stratification for AMI by initial cTnI and delta criterion.

cTnI, μg/L	Patients with AMI
Initial <0.034	
Increase <20%	2 of 226 (0.9%)
Increase >20%	14 of 45 (31%)
Initial >0.034	
Increase <20%	11 of 72 (15%)
Increase >20%	25 of 38 (66%)
Initial <0.034	
Increase <30%	2 of 223 (0.9%)
Increase >30%	14 of 38 (37%)
Initial >0.034	
Increase <30%	11 of 78 (14%)
Increase >30%	25 of 32 (78%)

with an increased specificity observed for deltas >20% ($P = 0.02$), and >30% ($P < 0.001$). Specificity was also significantly higher for δ >20% ($P = 0.001$) and >30% ($P < 0.001$) vs cTnI >0.034 μg/L at the time of follow-up. Results were similar when the follow-up draw was performed 4–6 h (n = 299) vs >6 h (n = 82) after the initial draw. Addition of a δ >20% or >30% criterion to results of the initial sample improved identification of AMI patients relative to a single baseline sample (Table 2).

cTnI concentrations in AMI patients (n = 52) ranged from 0.011–347 μg/L at baseline (median 0.084 μg/L) and 0.011–264 μg/L at follow-up (median 2.73 μg/L). An additional 11 AMI patients would have been detected at baseline using the 0.012 μg/L LoD cutoff compared to the 99th percentile cutoff. The diagnoses of patients who had an increased cTnI >0.034 μg/L at baseline or follow-up but did not have an AMI (n = 89) included congestive heart failure, other acute and subacute ischemic heart disease, dysrrhthmia, prior MI, chronic renal disease including end-stage renal disease, hypernatremia, hyponatremia, stroke, and cancer.

Overall 1 cardiac death, 2 noncardiac deaths, 52 MIs, 6 coronary artery bypass grafts, and 43 percutanous coronary interventions occurred in 62 patients during the first 60 days following presentation. No AMIs were related to percutanous coronary intervention or coronary artery bypass graft procedures for outcomes assessment. Patients who had increased cTnI concentration on the initial sample or follow-up sample or had evidence of change in cTnI at follow-up exceeding the 10%, 20%, or 30% criterion (each $P < 0.0001$) had higher 60-day rates of cardiac events and death (Table 3). Patients in the intermediate group tended to have higher rates than the reference group according to any of the criteria except that based on 10% δ, though none of these differences was statistically significant. The reference and intermediate groups were thus combined to calculate RR of cardiac event and death. Patients identified by any of the criteria of initial draw >0.034 μg/L, follow-up draw >0.034 μg/L, and δ >10%, >20%, or >30% were at significantly increased risk for cardiac events and death (Table 3). The single most predictive of the 4 criteria for increased risk was follow-up cTnI >0.034 μg/L. Patients with follow-up cTnI ≤0.034 μg/L were the largest group and had the lowest event rate, and those with follow-up cTnI >0.034 μg/L had the highest adjusted RR.

Adding the criterion of an increase in cTnI >30% on follow-up draw improved the risk stratification for cardiac event and death (Table 4, Fig. 2). Both initial cTnI >0.034 μg/L (adjusted RR 3.2, 95% CI 1.9–5.5, $P < 0.001$) and an increase >30% on follow-up sample (adjusted RR 9.1, 95% CI 5.3–15.9, $P < 0.001$) were independently predictive of risk of adverse cardiac event or death. Follow-up cTnI >0.034 μg/L (adjusted RR 8.9, 95% CI 3.9–20.7) and change >30% (adjusted RR 3.8, 95% CI 2.1–6.9) were also independently predictive of risk, and this combination was the more powerful of the 2 models for risk stratification.

Discussion

The current study provides evidence demonstrating that the second-generation VITROS Troponin I ES assay offers both improved sensitivity for detection of AMI at the 99th percentile and better risk stratification of adverse events in a heterogeneous patient population presenting at an urban medical center with symptoms suggestive of ACS. We demonstrated the potential utility of δ cTnI >30% for improved diagnostic clinical specificity for ruling out AMI compared to the absolute cTnI concentration from the first or second specimen and improved risk stratification when the δ is used with the absolute concentration from the second specimen. Our data reinforce the growing evidence-based literature supporting use of more analytically sensitive cTn assays for improved diagnostic accuracy for detecting patients at risk for cardiac events *(2–6, 13)* and also provide preliminary information on the value of a rising δ pattern in serial cTn concentrations over time as an indicator of acute injury.

The diagnostic sensitivity of cTnI >0.034 μg/L for detection of MI at patient presentation, a median of 3.9 h after onset of symptoms, was 69% and increased to 94% when a second specimen was taken approximately 6 h later. Patients with an initial cTnI concen-

Table 3. VITROS ES cTnI assay results and 60-day event rates and RR for cardiac events and death.

		Cardiac + all-cause death		
cTnI, μg/L	n	Events, n	60-Day cumulative event rate, % (95% CI)	Adjusted RR[a]
Initial <0.012	156	9	5.9 (2.2, 9.6)[b]	Reference group
Initial 0.012 to 0.034	115	13	11.4 (5.5, 17.2)[c]	
Initial >0.034	110	40	36.9 (27.8, 46.0)[d]	4.3 (2.5, 7.4)
Follow-up <0.012	181	3	1.7 (0.0, 3.6)[b]	Reference group
Follow-up 0.012 to 0.034	89	5	5.7 (0.8, 10.6)[c]	
Follow-up >0.034	111	54	49.2 (39.8, 58.6)[d]	18.3 (8.6, 39.2)
Decrease >10%	112	8	7.3 (2.4, 12.1)[b]	Reference group
Change <10%	169	11	6.8 (2.9, 10.6)	
Increase >10%	100	43	43.4 (33.6, 53.2)[d]	6.5 (3.8, 11.3)
Increase >20%	84	2	2.4% (0.0, 5.6)[b]	Reference group
Change <20%	214	18	8.7% (4.9, 12.6)[c]	
Increase >20%	83	42	51.0% (40.1, 61.8)[d]	8.2 (4.7, 14.0)
Decrease >30%	65	1	1.5% (0.0, 4.5)[b]	Reference group
Change <30%	246	19	8.0% (4.5, 11.4)[c]	
Increase >30%	70	42	60.5% (48.9, 72.0)[d]	10.5 (6.1, 18.2)

[a] RR adjusted for age, estimated glomerular filtration rate, history of hypertension, MI, and diabetes.
[b] Reference group.
[c] $0.05 < P < 0.10$ compared to reference group.
[d] $P < 0.0001$ compared to reference group.

Table 4. Serial VITROS ES cTnI assay results and 60-day event rates.

cTnI, μg/L	n	No. of events	60-Day cumulative event rate, % (95% CI)
Initial <0.034			
Increase <30%	233	5	2.2 (0.2, 4.1)
Increase >30%	38	17	45.2 (29.2, 61.1)[a]
Initial >0.034			
Increase <30%	78	15	19.8 (10.8, 28.9)
Increase >30%	32	25	78.1 (63.8, 92.4)[a]
Follow-up <0.034			
Increase <30%	258	6	2.4 (0.5, 4.3)
Increase >30%	12	2	17.5 (0.0, 39.6)[b]
Follow-up >0.034			
Increase <30%	53	14	27.2 (14.9, 39.4)
Increase >30%	58	40	69.4 (57.4, 81.3)[a]

[a] 2.2 vs 45.2, $P < 0.001$; 19.8 vs 78.1, $P < 0.001$; 27.2 vs 69.4, $P < 0.001$.
[b] 2.4 vs 17.5, $P < 0.01$.

tration >0.034 μg/L were also at 4-fold greater risk of a cardiac event or death within 60 days following presentation. These results add to the growing literature on the power of newer generation, more analytically sensitive cTn assays to aid in clinical triage and risk management *(2–6, 12, 13)*. Diagnostic specificity tends to be lower with the more analytically sensitive cTnI assays, as reflected in the 78% specificity at presentation we obtained for the VITROS ES assay. Although some medical specialists may have concern that the lower specificity confounds the diagnostic picture, we support the view that any amount of myocardial damage as detected by cTn signals an impaired clinical outcome for the patient *(12, 14)*. In the current study the increased cTnI values observed that were not indicative of MI were associated with other pathophysiologic processes, such as congestive heart failure, renal disease, drug toxicity, and cancer, which are well described in the literature and understood to be caused by different mechanisms than AMI. These findings must also be considered important in the patient's differential diagnosis, and depending on the clinical status of the patients, possibly followed up in an outpatient setting.

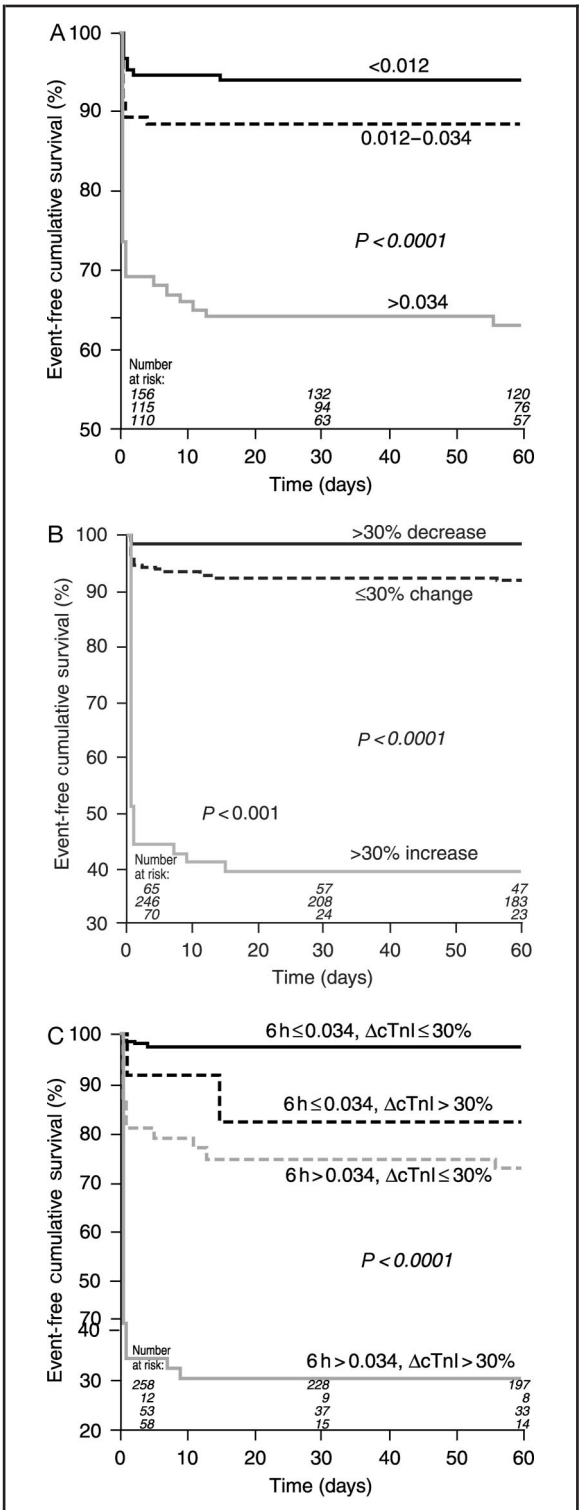

Fig. 2. 60-Day risk for cardiac event and all-cause death according to VITROS ES cTnI assay data for (A), initial sample, (B), δ > 30%, and (C), combined absolute follow-up cTnI concentration and 30% δ value.

Evaluating for a 30% cTnI change over time improved risk stratification of patients for cardiac events and death regardless of admission cTnI concentration. The concept of a δ value has been more and more embraced by expert opinions of laboratorians, emergency medicine physicians, and cardiologists. The ability to follow a rising and changing biomarker pattern demonstrates the acuity of the myocardial injury and assists in narrowing the differential diagnosis. Although several previous studies have demonstrated the use of δ values for both CK-MB and cTnI *(7–9)*, the current study is the first to provide δ data based on the newer generation, more analytically sensitive cTnI assays. One goal is to shorten the window for the follow-up sample from a 6 h period, as shown in the current study, to a time approaching 2 h. More analytically sensitive assays have been shown to have LoDs <0.001 μg/L (1 pg/mL) in proof-of-principle studies *(15, 16)*. Further studies are required to determine whether these assays provide further diagnostic accuracy with higher analytical precision.

The δ criteria we used, i.e., >10%, >20%, and >30% change, were based on the concepts that at the 99th percentile, a 10% total imprecision has been demonstrated, and that the expected biological variation for the current generation of cTnI assays has been suggested to be 15% to 20% *(3)*. Our data support and operationalize the observations of Wu et al. *(17)* demonstrating that biological variability for a research, high-sensitive cTnI assay is approximately 46% for increasing cTnI concentrations and that our ROC-curve–derived δ of 30% obtained with a contemporary assay was optimal for interpretation of serial draws for diagnostic accuracy. Conceptually we hypothesized that a rising cTnI pattern would be indicative of an acute process, whereas a static pattern would be indicative of a chronic process. However, an acute injury showing a rising cTnI can be associated with a non-AMI diagnosis *(18)*. The biomarker, along with the clinical history and findings, the ECG, and imaging evidence must all be considered when treating the patient and discerning the correct diagnosis. Our findings of both comparable diagnostic accuracy (with improved clinical specificity) and improved risk stratification for adverse events support the use of a 30% δ value, but our results must be confirmed with additional studies and with the use of different cardiac troponin assays.

This study had several limitations. Optimal timing of blood draw for measurement of cTnI in the AMI patient requires an interval of at least 6 h between onset of symptoms and time the sample is obtained. Although the time of sample collection is easily determined, ascertaining exact onset of symptoms is difficult in our population and can be regarded only as a best guess. Although our goal for time between samples

was 6 h, control over timing of the follow-up draw was limited by the clinical environment of the patient and the availability of a leftover specimen, such that we cannot rule out a possible bias attributable to the timing of the samples. The possibility of an actual false-positive cTnI result cannot be ruled out, but these types of findings are becoming increasingly rare with the newer generation of assays, which have been better optimized to avoid false positives and false negatives attributable to antibody interferences. When such findings do occur, however, they are most often single or isolated increases that do not fit the patient's clinical picture. The evidence-based literature does not report a substantial incidence of false-positive findings that would affect diagnosis at 99th percentile cTnI concentrations or risk stratifications of ACS patients, providing that assay imprecision falls in the 10% to 25% range *(19–21)*.

Our data included the 52 AMIs occurring before discharge (part of index hospitalization), and we used the initial plasma sampling before clinical diagnosis rather than discharge sample in our 60-day risk analysis, so our results cannot be interpreted as representative of strictly short-term postdischarge risk stratification. We understand that the Universal Definition of MI is predicated on a standard that employs cTnI as an integral part of the diagnosis. Because both ECG and non-ECG MIs are reported in our study population, it is impossible to define a gold-standard MI definition without the use of cTn. Our study had limited power to detect a difference in 60-day event rates between patients with cTnI below the LoD ($<$0.012 μg/L) and between the LoD and the 99th percentile (0.012–0.034 μg/L) for either the initial sample or the follow-up sample. Our results showed a trend for increased risk with the intermediate level cTnIs but were not definitive.

In conclusion, we have demonstrated acceptable clinical diagnostic accuracy for MI detection and risk stratification by use of the VITROS ES Troponin I assay. We recommend that optimal cTn δ criteria be developed and evaluated assay by assay before use in clinical practice to assist in diagnosis as well as in risk assessment for ACS patients. We believe the use of analytically sensitive cTn assays in conjunction with shorter-timed δ values will be a future diagnostic tool for improved patient management.

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