patients. We investigated the use of a POC cTnI assay in ACS patients.

Methods: We studied consecutive patients (n = 367) presenting with symptoms suggestive of ACS who were admitted through the emergency department. We measured plasma cTnl with the i-STAT assay. Patients were risk-stratified based on cTnl concentrations defined by the predetermined 99th percentile reference limit for plasma (0.04 μg/L). Patients were followed for 60 days. We computed survival and event curves with the Kaplan–Meier method and compared risk stratification groups with the log-rank test.

Results: Acute myocardial infarction (MI) was diagnosed in 8.1% of patients. Odds ratios and 95% confidence intervals for all-cause death (ACD), MI or ACD, MI or cardiac death, and cardiac death at 60 days were all statistically significant after adjustment for age, diabetes, hypertension, and history of renal failure as follows: 2.54 (1.24–5.20), P = 0.009; 2.76 (1.37–5.58), P = 0.003; 5.98 (1.65–21.7), P = 0.008; and 2.54 (1.24–5.20), P = 0.009. Kaplan–Meier curves showed early separation between patients with increased vs. reference concentrations before 30 days for ACD, MI or ACD, and MI or cardiac death.

Conclusion: The i-STAT POC cTnl assay can be added to the list of assays for risk stratification. © 2006 American Association for Clinical Chemistry

Numerous studies have evaluated cardiac troponin I (cTnI) and cardiac troponin T (cTnT) as markers for risk stratification of acute coronary syndrome (ACS) patients. Metaanalyses have demonstrated that cTnI or cTnT concentrations measured at the time of admission can be used to predict adverse outcomes (1). Increased cardiac troponins in ACS patients have been correlated with severity of coronary artery stenosis (2). Because analytical and clinical differences exist among cardiac troponin assays (3, 4), cardiology (5, 6) and laboratory medicine (4, 7) have endorsed the need for evidence-based studies before individual assays are accepted into clinical practice. In a 2000 consensus document from the European Society of Cardiology (ESC) and the American College of Cardiology (ACC), myocardial infarction (MI) was redefined as any amount of myocardial necrosis in the presence of myocardial ischemia, as indicated by an increased cardiac troponin above the 99th percentile of a reference population (5, 6). Although assay precision is important for risk stratification (8), recent data have demonstrated that assay imprecision of 10% to 25% will not significantly misclassify patients by ruling out MI (9).

Few studies have investigated the role of point-of-care (POC) testing for assessing adverse outcomes in ACS patients. One study using qualitative POC assays for cTnI and cTnT showed both assays to be independent predictors of cardiac events in ACS patients 30 days after admission (10). Although patient risk was successfully stratified with both qualitative assays, higher concentra-
tions more equivalent to ROC curve cutoffs were used as decision cutoffs, a limitation of qualitative assays. Several studies have since documented that lowering cutoff concentrations to the 99th percentile reference limit will identify additional patients at risk (11–13). Furthermore, 2 quantitative whole-blood POC cTnI assays have recently been used successfully for risk stratification for all-cause death (ACD) or cardiac events in patients presenting with symptoms suggestive of ACS (14, 15).

We investigated the prognostic value of a quantitative POC cTnI assay (i-STAT) for risk stratification using the 99th percentile cutoff concentration for ACD and cardiac events in ACS patients admitted in routine clinical practice.

This prospective study, performed at one site in 2001–2002, was approved by the hospital’s Human Subject Research Institutional Review Board. We studied 400 consecutive patients presenting with symptoms suggestive of ACS who were admitted through the emergency department and evaluated through the cardiac short-stay or telemetry units for ruling in and ruling out MI over a minimum of 8 h after presentation. Plasma (heparin) was collected at presentation (baseline).

Specimens were collected and frozen at –70 °C until analysis within 1 year. Using the Dade Dimension assay, we determined that cTnI was stable in specimens frozen for up to 3 years in our laboratory with <10% variance in over 200 specimens. For the i-STAT cTnI assay, we have determined stability only to 6 months, with <12% variance in 25 plasma specimens over a concentration range of <0.04 to 3.5 μg/L without positive/negative crossovers around the 99th percentile cutoff. We have no reason to believe that stability would be different over a 1-year period, but we do recognize this as a potential limitation of the study. Because of analytical problems, results were not obtained on 11 specimens, and 19 patients were lost to follow-up. Therefore, data analysis was based on 367 patient samples. The median time from onset of symptoms to hospital presentation was 3.5 h. cTnI was measured by the i-STAT 1, 300 series POC system (i-STAT Corporation; now owned by Abbott Laboratories), as recommended by the manufacturer. Patients were risk-stratified at 60 days (prospectively designated) based on cTnI concentrations defined by the predetermined 99th percentile reference limit for plasma of 0.04 μg/L (16).

The lower limit of detection was 0.02 μg/L. Total imprecision (%CV), determined in our laboratory, was 10% and 20% at 0.09 and 0.07 μg/L, respectively. Patient demographics and endpoint outcomes data were collected for all 367 participants by review of medical records (without knowledge of cTnI results) at least 60 days after baseline blood sampling. The primary endpoints were ACD, cardiac death, and MI. We used the χ² test to compare dichotomous variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated and adjusted for age, diabetes, hypertension, and history of renal failure. Differences in 60-day event rates were compared between patients with increased and reference cTnI concentrations using the 99th percentile. After censoring first for a length of time interval of interest (60 days), we computed exposure from the time of blood draw until the date of event. We computed survival and event curves with the Kaplan–Meier method and compared risk stratification groups with the log-rank test (17). Cumulative event rates were taken from the Kaplan–Meier survival curves. Statistical significance was accepted at 0.05, and all statistical tests were two-sided. Statistical analysis was performed with SPSS for Macintosh, Ver. 10.

All 367 ACS patients presented with ischemic symptoms suggestive of MI; 53% (194) had documented chest pain, and 8.1% (30) had a diagnosis of acute MI at presentation. The patients were 56% male with a median age of 58.3 years (range, 18.6–95.8 years) and were 52% Caucasian, 30% African American, 3% Hispanic, 3% Asian, 8% Native American, and 4% mixed/other ethnicity. A history of coronary artery disease was present in 70% of patients, with 21% having had a previous MI. In 68% of patients no electrocardiographic (ECG) changes were noted; 7% had ST elevations, 4% ST elevations, 3% new Q-waves, and 18% right or left bundle branch block. A history of renal failure, diabetes, or hypertension was present in 7%, 26%, and 60%, respectively. Baseline cTnI was >0.04 μg/L in 21% of patients (n = 77). Thirty-nine (10.6%) of the patients died within 60 days.

ORs with 95% CIs for an increased baseline plasma cTnI above the 99th percentile for ACD, MI or ACD, MI or cardiac death, and cardiac death at 60 days were all statistically significant after adjustment for age, diabetes, hypertension, and history of renal failure as follows: 2.54 (1.24–5.20), P = 0.009; 2.76 (1.37–5.58), P = 0.003; 5.98 (1.65–21.7), P = 0.008; 2.54 (1.24–5.20), P = 0.009. Kaplan–Meier curves (Fig. 1) by baseline cTnI showed early separation between patients with increased concentrations vs concentrations within reference limits before 30 days for ACD (top, log-rank P <0.001), MI or ACD (middle, log-rank P = 0.003), and MI or cardiac death (bottom, log-rank P = 0.002). Similar findings were observed for cardiac death alone; P = 0.01 (graph not shown).

The current study demonstrates that patients who present through the emergency department with symptoms suggestive of ACS and with an increased POC plasma cTnI at presentation have a significant increase in risk over 60 days for ACD and cardiac events. These findings add to the evidence-based literature reporting cardiac troponin measured predominantly with central laboratory instrumentation (1) and demonstrating that increased cTnI and cTnT predict the risk of adverse outcomes in ACS patients. Our observation of a median time of presentation of 3.5 h is comparable to other outcome studies (1, 8, 10, 11). Our findings also complement the analytical specification study recently published for the i-STAT POC assay (16). Thus, the current study provides evidence in support of the ESC/ACC consensus document for use of the 99th percentile cTnI cutoff for risk assessment (5, 6).

A limitation of our study is the small sample size, but our data support numerous trials that examined several cTnI and cTnT assays, demonstrating that increases of
cardiac troponin above the 99th percentile are predictors of adverse cardiac events and ACD (1, 11, 13). In addition, we did not document clinical data regarding ECG changes, medications, and current renal function (creatinine). However, risk stratification by cTnI was significant after adjustments for age, diabetes, hypertension, and history of renal failure. Other limitations were that only the baseline admission specimen was studied, because additional samples were not available, and that stability of cTnI at >6 months was not assessed for the i-STAT assay. Thus, minor instability might possibly have led to a small number of misclassifications around the 99th percentile cutoff between 6 months and 1 year. Finally, the 19 patients (4.7%) lost to follow-up might possibly have biased the findings; 2 of 19 (10.5%) had an increased cTnI.

Laboratory medicine (NACB, IFCC) and cardiology (ESC, ACC, AHA) guidelines and consensus documents have all recognized the need to provide rapid cardiac troponin turnaround times from blood draw to result reporting to care giving of <60 min and preferably <30 min (5, 6, 18). Rapid turnaround times assist in more appropriate patient triage, diagnostics, management, therapy, and risk stratification for adverse outcomes, improving clinicians’ ability to evaluate patients’ clinical features both in emergency medicine and in cardiology chest-pain and monitoring units. The i-STAT POC cTnI assay, designed to use both whole-blood specimens and plasma (current study), can be reliably added to the growing list of assays for diagnostic and risk stratification use in emergency, cardiology, and laboratory inpatient and outpatient settings.

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References


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Background: The aim of this study was to explore whether electronically retrieved laboratory data can predict mortality in internal medicine departments in a regional hospital.

Methods: All 10 308 patients hospitalized in internal medicine departments over a 1-year period were included in the cohort. Nearly all patients had a complete blood count and basic clinical chemistries on admission. We used logistic regression analysis to predict the 573 deaths (5.6%), including all variables that added significantly to the model.

Results: Eight laboratory variables and age significantly and independently contributed to a logistic regression model (area under the ROC curve, 88.7%). The odds ratio for the final model per quartile of risk was 6.44 (95% confidence interval, 5.42–7.64), whereas for age alone, the odds ratio per quartile was 2.01 (95% confidence interval, 1.84–2.19).

Conclusions: A logistic regression model including only age and electronically retrieved laboratory data highly predicted mortality in internal medicine departments in a regional hospital, suggesting that age and routine admission laboratory tests might be used to ensure a fair comparison when using mortality monitoring for hospital quality control.

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Monitoring hospital mortality rates is used to evaluate and improve the quality of healthcare (1) and is one measure of the performance monitoring systems required by hospital-accrediting organizations for quality control (2). This process requires adjustment for differences in severity of illness and other risk factors to ensure a fair comparison. Many attempts worldwide have used readily available independent variables to predict in-hospital mortality (3–5). Among these variables are the diagnostic codes listed in the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), which are often used for billing. These codes can only be applied retrospectively because they are based on the final discharge diagnosis. This method, however, has been criticized because, although widely available and inexpensive, it lacks clinical details necessary to permit adequate adjustment for each patient’s underlying medical condition (6, 7) and does not differentiate between diseases on admission and hospital-acquired complications, such as shock, that often precede death. Risk-adjustment models that include hospital-acquired complications could therefore overestimate the predictive value of the model and could mask inadequate care by increasing the measured risk of patients whose health deteriorated during hospitalization. In fact, Pine et al. (1), using ICD codes after excluding diagnoses that may have been hospital-acquired, found that the mean areas under the ROC curves in a logistic regression model decreased from 0.87 to 0.75.

Electronically retrieved laboratory data might be useful in predicting mortality because the tests are done routinely on admission, are unbiased by clinical evaluation, and reflect, at least to some extent, disease severity. We explored whether electronically retrieved laboratory data not requiring any data abstraction could predict mortality in internal medicine departments in a regional hospital.

All patients presenting to the internal medicine emergency room at Laniado Hospital over a 1-year period (starting from January 3, 2003) were included in the cohort. Of 23 397 patients, 10 308 (44.1%) were hospitalized in 4 internal medicine departments, which included intensive care patients (not surgical patients). All results of clinical chemistry and hematology tests done on admission are stored electronically. There is no hospital...