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Troponin T Levels and Infarct Size by SPECT Myocardial Perfusion Imaging

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OBJECTIVES To evaluate the relationship between serial cardiac troponin T (cTnT) levels with infarct size and left ventricular ejection fraction by gated single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) in patients with acute myocardial infarction (AMI).

BACKGROUND Current guidelines recommend the use of cTnT as the biomarker of choice for the diagnosis of AMI. Data relating cTnT to SPECT-MPI in patients with AMI are limited.

METHODS A subset of patients with their first AMI participating in a community-based cohort of AMI in Olmsted County, Minnesota, were prospectively studied. Serial cTnT levels were evaluated at presentation, <12 h and 1, 2, and 3 days after onset of pain. Peak cTnT was defined as the maximum cTnT value.

RESULTS A total of 121 patients (age, 61 ± 13 years; 31% women) with AMI underwent gated SPECT-MPI at a median (25th percentile, 75th percentile) of 10 (5, 15) days post-AMI. The type of infarct was non–ST-segment elevation myocardial infarction in 61%, and 13% were anterior in location. The median infarct size was 1% (0%, 11%) and the median gated left ventricular ejection fraction was 54% (47%, 60%). Fifty-nine patients (49% of the population) had no measurable infarction by SPECT-MPI. Independent predictors of measurable SPECT-MPI infarct size included cTnT at days 1, 2, and 3 and peak cTnT, but not at presentation or <12 h. In receiver-operator characteristic analysis, the area under the curve was highest at day 3. Receiver-operator characteristic analysis demonstrated a cutoff of 1.5 ng/ml for peak cTnT for the detection of measurable infarct size.

CONCLUSIONS In a community-based cohort of patients with their first AMI, independent predictors of measurable SPECT-MPI infarct size included cTnT at days 1, 2, and 3 and peak cTnT. In contrast, cTnT level at presentation and <12 h was not an independent predictor of myocardial infarction size as assessed by SPECT-MPI. Receiver-operator characteristic analysis demonstrated a cutoff value peak cTnT of 1.5 ng/ml for the detection of measurable infarct. (J Am Coll Cardiol Img 2011;4: 523–33) © 2011 by the American College of Cardiology Foundation

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The American College of Cardiology/European Society of Cardiology diagnostic criteria for acute myocardial infarction (AMI) combine ischemic symptoms and/or electrocardiographic changes with biochemical markers of myocardial necrosis (1). Cardiac troponin (cTn) has been designated as the biomarker of choice for the diagnosis of AMI (1). Serial cTn samples should be acquired at presentation and 6 to 9 h in most patients, with a third sample at 12 to 24 h in the occasional patient in whom the initial measurements are not elevated and the clinical index of suspicion remains high (1,2).

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ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CK-MB = myocardial bound fraction of creatine kinase

cTn = cardiac troponin

cTnT = cardiac troponin T

LVEF = left ventricular ejection fraction

NSTEMI = non–ST-segment elevation myocardial infarction

PCI = percutaneous coronary intervention

ROC = receiver-operator characteristic

SPECT = single-photon emission computed tomography

SPECT-MPI = single-photon emission computed tomography myocardial perfusion imaging

Tc-99m = technetium-99m

Current clinical practice in the United States involves serial cTn measurements during the initial hours after presentation. In the setting of AMI, cardiac troponin T (cTnT) appears in the serum within 1 to 3 h and remains elevated for 4 to 10 days (1). An elevated cTn value establishes the diagnosis of infarction (1), but the clinical significance of the magnitude of elevation of cTn is not clear. Clinicians commonly assume that cTn values measured at presentation and at 6 to 9 h later reflect infarct size. However, only a small number of studies have examined the association between cTn values and infarct size with variable results (3–7). The optimal time to sample cTn that best predicts infarct size is unknown. Nonetheless, cTn release as a reflection of infarct size is already being used as an endpoint to assess the efficacy of therapy in AMI trials (8).

Infarct size can be accurately quantitated by both the size of the perfusion defect on single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) and left ventricular ejection fraction (LVEF) (9). Infarct size measured by SPECT-MPI (10–12) or LVEF (12,13) is a powerful predictor of outcome post-AMI. Accordingly, the aim of this study was to evaluate the associations between serial values of cTnT and nuclear indices of infarct size in a series of patients with their first AMI, diagnosed with the American College of Cardiology/European Society of Cardiology criteria (1).

METHODS

Patients. The study was approved by the Mayo Clinic Institutional Review Board. Patients provided written informed consent. We prospectively recruited a sample of 121 patients hospitalized with their first AMI between November 2002 and October 2007. These patients represented a subset of patients who were enrolled in a prospective, community-based AMI study from Olmsted County, Minnesota, designed to examine changes in the incidence of AMI diagnosis resulting from using cTnT in place of the myocardial bound fraction of creatine kinase (CK-MB). Details of this study have been published elsewhere (14). For myocardial infarction diagnosis, we applied a computerized algorithm that integrated ischemic symptoms, the Minnesota code of the electrocardiograms, and cTnT levels (14). For this algorithm, 3 electrocardiograms were electronically available and were coded using a previously validated electronic coding system. For those patients who were transferred from another medical facility in Olmsted County to the Mayo Clinic Emergency Department (n = 13), the presentation electrocardiograms were not electronically available. For these transferred patients, the clinician's interpretation of the electrocardiogram recorded in the medical record was used for the AMI diagnosis.

Because nuclear indices of infarction cannot separate a past from a current AMI, only patients with a documented first AMI were enrolled in this substudy. The linkage system from the Rochester Epidemiology Project (15) enabled the identification of patients with a previous AMI by history. Electrocardiograms and electronic medical records of all eligible patients were reviewed to exclude patients with significant Q waves on the electrocardiograms or evidence of reduced LVEF, regional wall motion abnormalities, or perfusion defect on any previous cardiac imaging modality (e.g., echocardiography, SPECT-MPI). Because periprocedural AMI can be difficult to diagnose, patients with a history of percutaneous coronary intervention (PCI) or coronary artery bypass surgery were not included in this study. There were 37 patients not included in this study because of a history of myocardial infarction or revascularization, and 78 patients declined to participate in this study.

Clinical data obtained included comorbidities measured by the Charlson index (16) and Killip class. Clinical diagnoses were used to ascertain hypertension, diabetes mellitus, hyperlipidemia, family history of coronary disease, and smoking status. Medications recorded during the hospitalization for the acute event included beta-blockers, angiotensin-converting enzyme inhibitors, angio-

tensin II receptor blockers, statins, and aspirin. Reperfusion or revascularization therapy was defined as the use of thrombolytic therapy, PCI, or coronary artery bypass surgery during the same hospitalization. All decisions regarding patient management were left to the discretion of the attending cardiologists, the vast majority of whom were not investigators in this study.

Serial cTnT. All patients had an increase in cTnT level of >0.03 ng/ml (14). This threshold was the 10% coefficient variation for the assay used at our institution during the time frame of this study. cTnT was measured by the third-generation cTnT assay (17) in the Department of Laboratory Medicine and Pathology, which is certified by the Clinical Laboratory Improvement Act of 1988 and by the College of American Pathologists.

Levels of cTnT were ordered at the discretion of the attending cardiologists. For this reason, cTnT levels were not available at all time points in all patients. Serial cTnT levels were obtained at presentation (n = 121), <12 h (n = 96), 12 to 24 h (99 patients), day 2 (n = 72), and day 3 (n = 45). We performed a preliminary analysis of our data after the evaluation of 53 patients and recognized the potential value of obtaining later measurements of cTnT at ≥4 days. From this time point forward, cTnT values were obtained at ≥4 days when possible but in only 29 patients, and those samples were not included in this analysis due to the small number.

Technetium-99m sestamibi SPECT-MPI. All patients underwent gated SPECT-MPI at a median of 10 days (25th percentile, 75 percentile: 5 days, 15 days) post-AMI. For this study, 45 patients underwent a clinically indicated stress SPECT-MPI, and 76 patients underwent a research SPECT-MPI if not ordered for clinical reasons. All imaging was performed at least 117 h after the onset of symptoms. This time frame was selected because SPECT-MPI performed before the fifth day has been shown to overestimate infarct size. For the clinically indicated stress tests (1 day rest-stress sequence), 8 to 12 mCi of technetium-99m (Tc-99m) sestamibi was administered for the resting images and 32 to 48 mCi of Tc-99m sestamibi for the stress images. For the research scans, patients underwent resting imaging only and received an intravenous injection of 20 to 30 mCi of Tc-99m sestamibi. Infarct size was determined from the resting images. LVEF was calculated from the post-stress gated images.

SPECT images were acquired beginning 45 to 60 min after the Tc-99m sestamibi injection using a rotating gamma camera with a low-energy, all-purpose collimator. Processing and reconstruction were performed using standard back-projection algorithms and a Ramp-Hanning filter. Infarct size was quantitated using established methods (10). Circumferential count profiles were generated for 5 representative short-axis slices of the left ventricle extending from apex to base. Infarct size was quantitated using a threshold value of 60% of peak counts. The defect size was expressed as a percentage of the left ventricle. Gated SPECT LVEF was measured using QGS software (Cedars-Sinai Medical Center, Los Angeles, California) (18). LVEF was not available in 22 patients (18%) due to technical factors.

Coronary angiography. Coronary angiography was performed at the discretion of the attending cardiologist. The angiograms were interpreted by 2 experienced observers according to the CASS (Coronary Artery Surgery Study) coding system: ≥50 left main stenosis or ≥70% stenosis of the left anterior descending, left circumflex, or right coronary arteries or their major branches considered significant (19). The success of PCI was determined by the same individuals.

Follow-up. Follow-up data were obtained at a mean duration of 4.8 ± 1.6 years. Data were obtained by surveillance of medical records. The ascertainment of death incorporated death certificates filed in Olmsted County, autopsy reports, obituary notices, and electronic files of death certificates obtained from the State of Minnesota Department of Vital and Health Statistics (15). The diagnosis of heart failure was validated using the Framingham criteria (20). We previously reported the reliability of the application of these diagnostic criteria in our cohort (21). Major cardiac events at follow-up were defined as death or heart failure.

Statistical analysis. Data are presented as frequencies for categorical variables, as mean ± SD for continuous variables, or as medians with 25th and 75th percentiles for variables with skewed distribution. Time zero was defined as the time of onset of symptoms. cTnT values were categorized using the following approach: <12 h; 12 to 24 h, day 2, day 3, and peak. A value was defined as peak if it was the highest in the time course. In a secondary analysis, models were repeated considering time zero as the time of presentation to the emergency department. For the secondary analysis, we also categorized the time points as <12 h; 12 to 24 h, day 2, day 3, and peak.

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Unadjusted and adjusted logistic regression models were developed to test the associations of measurements of cTnT at each of these time points with SPECT-MPI infarct size of 0% (nonmeasurable infarct) or ≥1% (measurable infarct). The models were adjusted for age, sex, ST-segment elevation myocardial infarction or non–ST-elevation myocardial infarction (NSTEMI), and AMI location. These variables were chosen from those known to be of clinical relevance for post-AMI risk stratification.

Receiver-operator characteristic (ROC) curves were analyzed to evaluate the relationship between cTnT values at the time points and measurable and nonmeasurable SPECT-MPI infarct size. Using ROC analysis, the best cutoff of cTnT for the detection of measurable SPECT-MPI infarct size at each time point was identified.

The correlations between cTnT and SPECT-MPI infarct size and between cTnT and LVEF were analyzed by the Spearman test. The Spearman test was also used to analyze the correlation between infarct size and peak cTnT in patients who underwent PCI ≤9 h versus >9 h from onset of symptoms to first balloon inflation. This time point was used because 9 h was the median time from onset of symptoms to first balloon inflation. There were too few patients to evaluate this issue at multiple time points including very early (within 2 h).

Unadjusted and adjusted Cox proportional hazard regression models were constructed using infarct size or peak cTnT to estimate hazard ratios and 95% confidence intervals for major cardiac events. For all analyses, a p value ≤0.05 was considered statistically significant. SAS software version 9.1 (SAS Institute, Cary, North Carolina) was used for all statistical analyses.

RESULTS

Clinical characteristics. The mean age of the population was 61 ± 13 years, and approximately two-thirds were men. The study cohort was generally a low-risk AMI population: 84% of patients were Killip class I or II, and most (86%) had a low Charlson comorbidity index. The type of infarct was NSTEMI in 61%, and 13% were anterior in location (Table 1).

Patients who had cTnT levels measured at day 2 and later (n = 28) were more likely to have a diagnosis of NSTEMI and more likely to undergo PCI later during hospitalization (median, 38 h; 25th percentile, 75th percentile: 25 h, 53 h) than patients who did not have cTnT levels measured at day 2 and later (median, 11 h; 25th percentile, 75th percentile: 4 h, 27 h) (p = 0.003). All other clinical, biochemical, and angiographic characteristics were similar in these 2 groups of patients.

Table 1. Baseline Clinical Characteristics

Age, yrs	61 ± 13
Men	84 (69)
Killip class	
I	98 (81)
II	4 (3)
III	18 (15)
IV	1 (1)
Comorbidity index	
0	58 (48)
1–2	46 (38)
≥3	17 (14)
Electrocardiogram	
NSTEMI	74 (61)
Infarct location	
Anterior	16 (13)
Inferior	24 (20)
Lateral	8 (7)
Combined	29 (24)
Indeterminate	44 (36)
cTnT, ng/ml	
Presentation (n = 121)	0.04 (0.01, 0.16)
<12 h (n = 96)	0.40 (0.14, 3.31)
Day 1 (n = 99)	0.90 (0.25, 3.01)
Day 2 (n = 72)	1.08 (0.18, 1.92)
Day 3 (n = 45)	1.20 (0.17, 3.08)
Peak (n = 121)	1.46 (0.35, 4.10)
Medications	
Beta-blockers	111 (97)
ACE/ARBs	88 (77)
Statins	96 (83)
Aspirin	114 (99)
Risk factors	
Hypertension	66 (54)
Hyperlipidemia	72 (59)
Diabetes mellitus	21 (17)
Family history of CAD	22 (18)
Current smoker	32 (26)
Reperfusion	93 (77)
Percutaneous coronary intervention	90 (74)*
Coronary artery bypass surgery	2 (2)
Thrombolysis	1 (1)
Coronary angiography	104†
0-vessel CAD	5
1-vessel CAD	46
2-vessel CAD	37
3-vessel CAD	16
Left main CAD	1

Continued on next page

Table 1. Continued

Infarct-related coronary artery	
LAD	71
LCX	40
RCA	53
No. of stents	1.2 ± 0.7
Successful PCI (<20% stenosis)	83 (92)
Percentage of stenosis‡	
Before PCI, median (25th, 75th percentiles)	99 (90, 100)
After PCI, median (25th, 75th percentiles)	0 (0, 0)

Values are mean ± SD, n (%), median (25th percentile, 75th percentile), or n. *Five PCIs were percutaneous transluminal coronary angioplasty only. †Total number of patients who underwent coronary angiography during the same episode of care. ‡$p < 0.001$ for comparison of percentage of stenosis before and after PCI.

ACE/ARB = angiotensin-converting enzyme/angiotensin II receptor blocker; CAD = coronary artery disease; cTnT = cardiac troponin T; LAD = left anterior descending artery; LCX = left circumflex artery; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery.

Seventy-seven percent of patients were treated with reperfusion therapy, most of whom underwent PCI (Table 1). Patients who did not undergo reperfusion (n = 28) were older (68 ± 14 years vs. 59 ± 13 years; $p = 0.002$), were more likely to be women (61% vs. 21%, $p < 0.001$, and have a diagnosis of NSTEMI (89% vs. 53%, $p < 0.001$). In addition, those who did not undergo reperfusion had lower peak cTnT (median, 0.4 ng/ml; 25th percentile, 75th percentile: 0.1 ng/ml, 1.5 ng/ml) than those who underwent reperfusion therapy (median, 1.8 ng/ml; 25th percentile, 75th percentile: 0.6 ng/ml, 4.7 ng/ml; $p < 0.001$).

SPECT-MPI infarct size and LVEF. The median infarct size was 1% (25th percentile, 75th percentile: 0%, 11%). Almost one-half (49%) of patients had no measurable infarct size (Fig. 1). Figure 2 shows an example of no measurable infarct size and Figure 3 shows a measurable infarct size. Only 25% of patients had infarct size >10% of the left ventricle. Among the 99 patients who had a measurable LVEF, the median LVEF was 54% (25th percentile, 47%; 75th percentile, 60%). Of those, nearly two-thirds (62%) had an LVEF >50%. Patients with a measurable infarct size had higher values for peak cTnT (median, 2.9 ng/ml; 25th percentile, 75th percentile: 0.9 ng/ml, 6.2 ng/ml) than those without a measurable infarct (median, 0.7 ng/ml; 25th percentile, 75th percentile: 0.2 ng/ml, 1.8 ng/ml; $p < 0.0001$).

Relationship between cTnT with SPECT-MPI infarct size and LVEF. In the unadjusted logistic regression model, admission cTnT level was not associated with measurable SPECT-MPI infarct size. However, cTnT values at <12 h, days 1, 2, and 3, and peak were all associated with the presence of measurable infarct size (Table 2). After adjusting for age, sex, and type and location of AMI, independent predictors of measurable SPECT-MPI infarct size included cTnT at days 1, 2, and 3 and peak cTnT; cTnT at <12 h was no longer associated with measurable SPECT-MPI infarct size. In ROC analysis, the area under the curve was highest at day 3 (Fig. 4). ROC analysis demonstrated a cutoff of 1.5 ng/ml for peak cTnT for the detection of measurable infarct size (Fig. 4).

There were significant positive correlations of the magnitude of cTnT values at days 1, 2, and 3 and

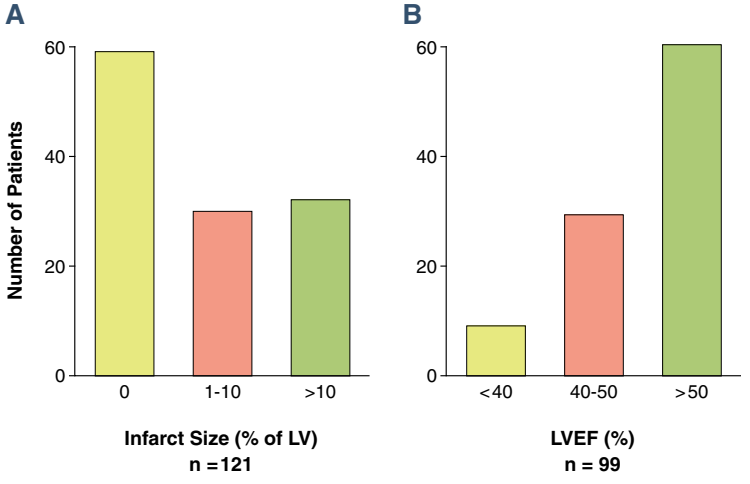

Figure 1. Distribution of SPECT-MPI Infarct Size and LVEF

Almost one-half of patients had no measurable infarct size **(A)**. Most patients had preserved left ventricular ejection fraction (LVEF) **(B)**. LV = left ventricle; SPECT-MPI = single-photon emission computed tomography myocardial perfusion imaging.

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Figure 2. Example of Nonmeasurable Infarct Size

Stress and rest images of an 80-year-old man who presented 2 h after onset chest pain with an anterior wall non–ST-segment elevation myocardial infarction. Initial cardiac troponin T (cTnT) was 0.21 ng/ml. cTnT at day 3 was 1.8 ng/ml. Single-photon emission computed tomography myocardial perfusion imaging showed no perfusion defects. Left ventricular ejection fraction was 55%. HLA = horizontal long axis; SA = short axis; VLA = vertical long axis.

peak with infarct size, but r values were modest (Fig. 5). Of note, SPECT-MPI did not detect infarction in 49% of patients who met the cTnT threshold for infarction. There were significant negative correlations of LVEF and cTnT values at days 1, 2, and 3 and peak cTnT also with modest r values (Fig. 6). There were similar correlations between infarct size and peak cTnT in those patients ≤9 h from onset of symptoms to first balloon inflation ($r = 0.47$, $p = 0.001$) versus those >9 h from onset of symptoms to first balloon inflation ($r = 0.48$, $p < 0.001$).

In a secondary analysis considering time zero as the time of presentation, cTnT level <12 h was associated with SPECT-MPI infarct size in the unadjusted logistic model (odds ratio: 1.22, $p = 0.009$). This association persisted after adjustment (odds ratio: 1.23, $p = 0.03$). For all other time points, the associations were similar to the associations described that used time zero as the onset of symptoms.

Follow-up. During follow-up, 10 patients died and 15 experienced heart failure. Both infarct size (hazard ratio: 1.4; 95% confidence interval: 1.1 to 14.2; $p = 0.006$) and peak cTnT (hazard ratio: 2.8; 95% confidence interval: 1.1 to 6.9; $p = 0.03$) were significantly associated with major cardiac events. The association between infarct size and major cardiac events persisted after adjustment for age ($p = 0.003$) and sex ($p = 0.006$). The association between peak cTnT and major cardiac events also persisted after adjustment for age ($p = 0.003$) and sex ($p = 0.03$).

DISCUSSION

In this community-based cohort of patients with their first AMI defined by contemporary criteria, novel findings include that SPECT-MPI did not detect measurable infarct in nearly half of the patients and that independent predictors of measurable SPECT-MPI infarct size were cTnT levels at days 1, 2, and 3 and peak. In addition, ROC analysis demonstrated a peak cTnT cutoff value of 1.5 ng/ml for the detection of measurable infarct.

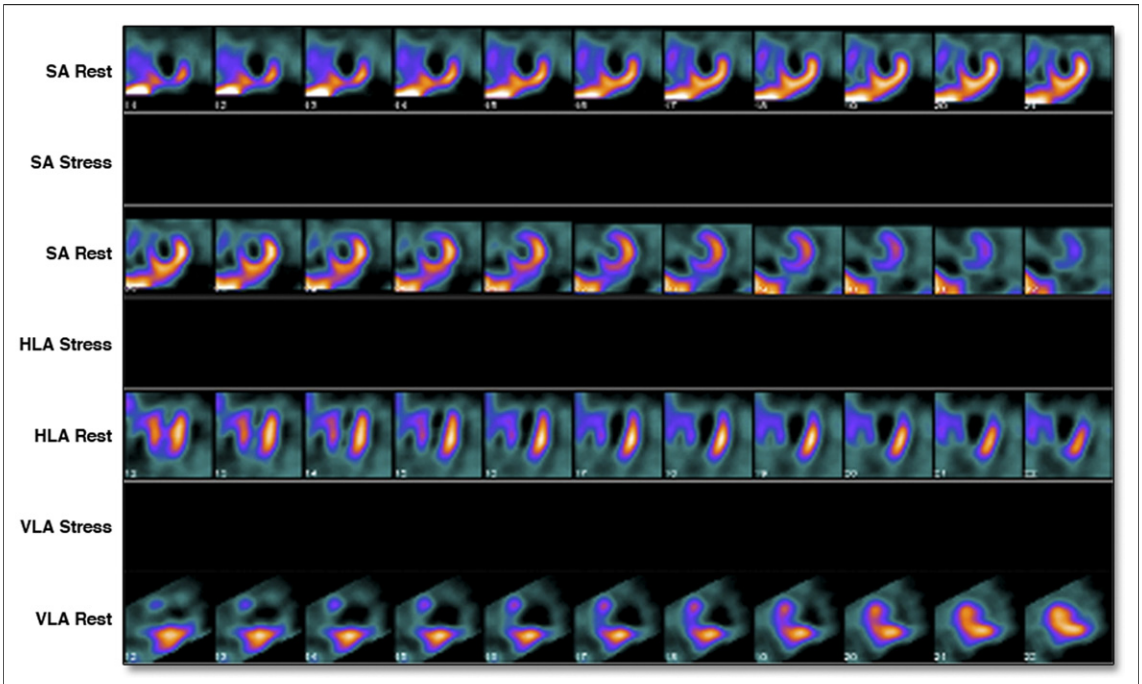

Figure 3. Example of Measurable Infarct Size

Rest-only images of a 47-year-old-man who presented 21 h after the onset of chest pain with an anterior wall ST-segment elevation myocardial infarction treated with direct percutaneous coronary intervention. Initial cardiac troponin T (cTnT) was 4.55 ng/ml. cTnT at day 3 was 7.7 ng/ml. Single-photon emission computed tomography myocardial perfusion imaging showed a large anterior, apical, anterolateral, and anteroseptal perfusion defect. Infarct size was quantitated at 55% of the left ventricle. Left ventricular ejection fraction was 32%. CI = confidence interval; other abbreviations as in Figure 3.

Finally, infarct size and peak cTnT were associated with major cardiac events at follow-up.

cTnT and SPECT for the diagnosis of AMI. In a previous study (14), we reported that implementation of cTnT in place of CK-MB for the diagnosis of AMI resulted in a 74% increase in the number of AMIs with a change in the case mix. Patients with a diagnosis of AMI by cTnT criteria only were less likely to have ST-segment elevation myocardial infarction and had better survival compared with those diagnosed by the traditional CK-MB approach (14). These changes resulted from the increased sensitivity of cTnT versus CK-MB, presumably resulting in the identification of patients with smaller infarcts. The results of the present imaging study support this concept. In this study, 61% of patients had NSTEMI; furthermore, approximately 50% of patients had no measurable infarct by SPECT-MPI and another 25% had an infarct size between 1% and 10% of the left ventricle. SPECT-MPI can detect infarcts as small as 3% of the left ventricle (22) but can miss smaller infarcts, especially nontransmural infarcts involving <50% of the left ventricular wall thickness, as demonstrated by studies using cardiac magnetic resonance (23).

Table 2. Associations Between cTnT and Measurable SPECT-MPI Infarct Size

	Odds Ratio (p Value)	
Time	Unadjusted	Adjusted*
Presentation	1.00 (0.98)	0.97 (0.86)
<12 h	1.17 (0.04)	1.18 (0.10)
Day 1	1.27 (0.01)	1.26 (0.03)
Day 2	1.78 (0.007)	1.66 (0.02)
Day 3	2.03 (0.007)	2.27 (0.008)
Peak	1.33 (<0.001)	1.34 (0.003)

*Adjusted for age, sex, acute myocardial infarction type, and location; odds ratios are expressed per every 1-ng/ml increase in cTnT.
cTnT = cardiac troponin T; SPECT-MPI = single-photon emission computed tomography myocardial perfusion imaging.

Troponin and infarct size. The peak level of CK-MB, the former biomarker for establishing the diagnosis of AMI, was shown to reflect infarct size and was accepted as a clinical method for estimating infarct size (9,24). This measurement is less reliable in patients treated with reperfusion therapy (9). Although an elevated troponin level is currently required for diagnostic purposes (1,2), there are few

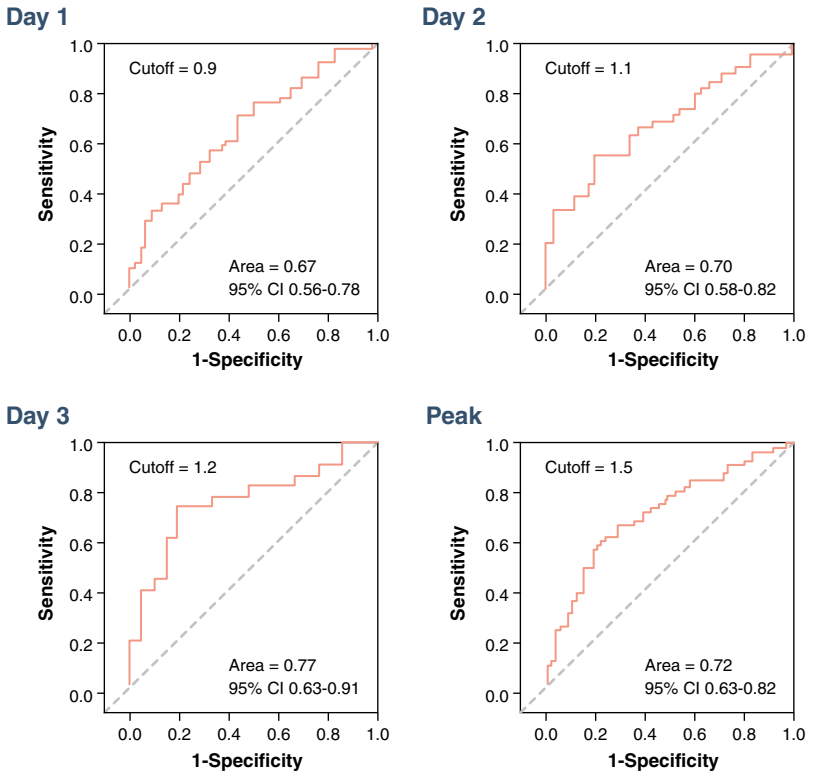

Figure 4. ROC Analysis Displaying the Performance of cTnT to Identify Measurable and Nonmeasurable SPECT-MPI Infarct Size

The area under the curve was highest at day 3. Receiver-operator characteristic (ROC) analysis demonstrated a cutoff of 1.5 ng/ml for peak cardiac troponin T (cTnT) for the detection of measurable infarct size. SPECT-MPI = single-photon emission computed tomography myocardial perfusion imaging.

data examining the optimal timing intervals for obtaining cTn samples or the magnitude of cTn levels for determining infarct size.

In a previous study of 61 patients with AMI (31 ST-segment elevation myocardial infarctions and 30 NSTEMIs) who underwent serial cTnT assay and cardiac magnetic resonance for infarct size, measurements of cTnT within 4 days after the acute event correlated with infarct size except for the admission cTnT (4). In our study, we confirmed these observations in a larger sample size, using a different imaging modality. We observed that cTnT levels measured after the first 24 h post acute event are associated with SPECT-MPI indices of infarct size. The previous study (4) also reported significant but modest correlations (r values of 0.64 to 0.66 for all patients with available cTnT levels between days 1 and 4 and cardiac magnetic resonance infarct mass), with substantially worse r values (r = 0.36 at day 4) for patients with NSTEMI or those with a small infarct mass (r = 0.2 at day 4). In the present study, the majority of patients had NSTEMI or small infarct size, helping to explain the modest r values.

A previous study reported a significant correlation between single time point measurements of cTnT at day 3 post-AMI with infarct size by SPECT-MPI (25). A single measurement of cTnT at day 4 post-AMI was also previously associated with infarct size quantitated by cardiac magnetic resonance (3). In the present study, the correlations between cTnT and infarct size improved as the timing post-AMI increased. However, the subset of patients who had cTnT levels measured at day 2 and later were more likely to receive a diagnosis of NSTEMIs and more likely to undergo reperfusion therapy later during hospitalization. Thus, type of AMI and more prolonged interval for reperfusion therapy in this group of patients may have contributed to the slightly higher correlation of cTnT level with infarct size at later time points (days 2 and 3) observed in our present study.

Prognosis. In the present study, both infarct size and peak cTnT were predictors of major cardiac

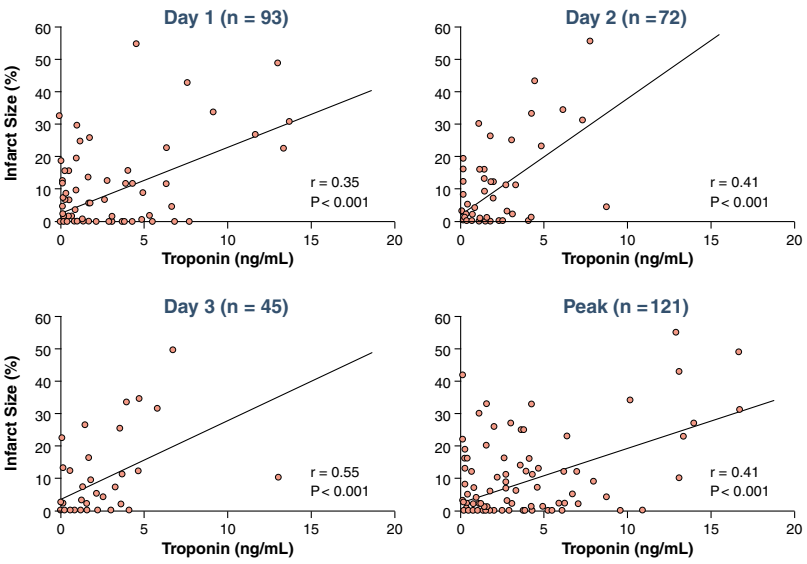

Figure 5. Correlations Between SPECT-MPI Infarct Size and Troponin

There were significant positive correlations of the magnitude of cardiac troponin T values at days 1, 2, and 3 and peak with infarct size, but r values were modest. SPECT-MPI = single-photon emission computed tomography myocardial perfusion imaging.

events at follow-up, also supporting the findings of previous studies. Patients with "microinfarcts" diagnosed by cTnT criteria have a favorable prognosis (14,26). Several studies that enrolled primarily patients with STEMI treated with reperfusion therapy reported that patients with SPECT-MPI infarct size ≤10% of the left ventricle have mortality rates between 0% and 1% during follow-up of 6 months to 2 years (10–12,27,28).

Study limitations. Limitations of this study include the relatively small numbers of cTnT measurements, particularly the later measurements. Enrollment in this study was slower than anticipated and related to the method of screening patients for

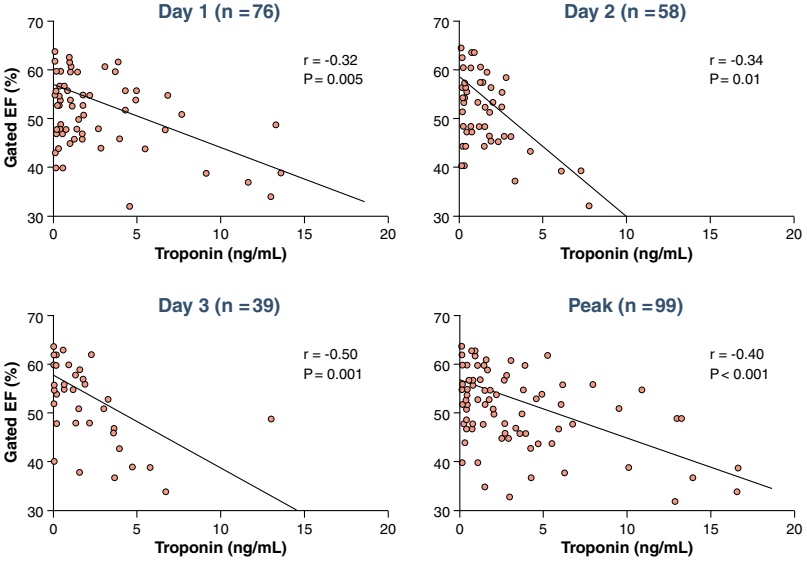

Figure 6. Correlations Between LVEF and cTnT

There were significant negative correlations between left ventricular ejection fraction (LVEF) and cardiac troponin T (cTnT) values at days 1, 2, and 3 and peak cTnT, also with modest r values.

enrollment (cardiovascular research nurses carefully reviewed each potential participant's electronic record and excluded participants with any possible evidence of a previous myocardial infarction on the basis of history, electrocardiography, or imaging study). Also, in the current era of short hospital stay, several patients were unwilling to return for a SPECT study for research purposes 5 days or later after their AMI. Infarct size was quantitated by low-dose Tc-99m sestamibi (8 to 12 mCi) resting images in 45 patients who underwent stress SPECT-MPI. The validation studies of previous applications of this technique were performed in studies in which the resting dose of Tc-99m sestamibi doses was 20 to 30 mCi. Previous work demonstrated that soft-tissue artifact could influence infarct size measurement in some obese patients (10). This issue could potentially play a more important role in this study, given the small median infarct size and the low-dose isotope injection for some of the resting scans. Use of a lower dose increases the "noise" of the images and the possibility that soft-tissue attenuation is incorrectly quantified as infarction.

Study implications. The American College of Cardiology/European Society of Cardiology AMI guideline recommends obtaining cTn samples at presentation and again 6 to 9 h later in patients with suspected AMI. Clinicians commonly view the magnitude of cTnT levels measured at these early time points as indicative of infarct size. The data from the present study indicate that these early measurements of cTnT do not accurately reflect SPECT-MPI infarct size or LVEF, whereas cTnT values after the first 24 h are associated with indices of infarct size. In addition, ROC analysis demonstrated a cutoff value peak cTnT of 1.5 ng/ml for the detection of measurable infarct. Both infarct size and peak cTnT identified patients at increased risk of major cardiac events at follow-up.

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