Comparison of Myocardial Perfusion Imaging and Cardiac Troponin I in Patients Admitted to the Emergency Department With Chest Pain

Michael C. Kontos, MD; Robert L. Jesse, MD, PhD; F. Philip Anderson, PhD; Kristin L. Schmidt; Joseph P. Ornato, MD; James L. Tatum, MD

Background—Identification of patients with acute coronary syndromes (ACS) among those who present to emergency departments with possible myocardial ischemia is difficult. Myocardial perfusion imaging with $^{99m}$Tc sestamibi and measurement of serum cardiac troponin I (cTnI) both can identify patients with ACS.

Methods and Results—Patients considered at low to moderate risk for ACS underwent gated single-photon emission CT sestamibi imaging and serial myocardial marker measurements of creatine kinase–MB, total creatine kinase activity, and cTnI over 8 hours. Positive perfusion imaging was defined as a perfusion defect with associated abnormalities in wall motion or thickening. cTnI $\geq 2.0$ ng/mL was considered abnormal. Among the 620 patients studied, 59 (9%) had myocardial infarction and 81 (13%) had significant coronary disease; of these patients, 58 underwent revascularization. Perfusion imaging was positive in 241 patients (39%), initial cTnI was positive in 37 (6%), and cTnI was $\geq 2.0$ ng/mL in 74 (12%). Sensitivity for detecting myocardial infarction was not significantly different between perfusion imaging (92%) and cTnI (90%), and both were significantly higher than the initial cTnI (39%). Sensitivity for predicting revascularization or significant coronary disease was significantly higher for perfusion imaging than for serial cTnI, although specificity for all end points was significantly lower. Lowering the cutoff value of cTnI to 1.0 ng/mL did not significantly change the results.

Conclusions—Early perfusion imaging and serial cTnI have comparable sensitivities for identifying myocardial infarction. Perfusion imaging identified more patients who underwent revascularization or who had significant coronary disease, but it had lower specificity. The 2 tests can provide complementary information for identifying patients at risk for ACS. (Circulation. 1999;99:2073-2078.)

Key Words: imaging □ angina □ myocardial infarction □ troponin

A ccurate diagnosis of acute coronary syndromes in patients presenting to emergency departments (EDs) with chest pain and other symptoms suggestive of myocardial ischemia is difficult. When significant ST-segment changes are present on the ECG, myocardial ischemia is highly likely.1 However, when the is ECG is not diagnostic of ischemia or shows ECG confounders, identification of high-risk patients is more difficult. This leads to the admission of many patients whose symptoms are ultimately attributed to nonischemic causes2–4 and to the inadvertent discharge of patients with myocardial infarction (MI), often with adverse outcomes.5

Recent trends in health care, including increasing costs of inpatient care, have led to investigation of alternative approaches to improve early diagnostic accuracy in patients with possible myocardial ischemia. Two new technologies, myocardial perfusion imaging and assays for cardiac troponin, have both shown promise. Myocardial perfusion imaging with $^{99m}$Tc sestamibi (DuPont Pharma) has a high sensitivity for identifying ED patients at risk for acute coronary events.6,7 Cardiac troponins are sensitive markers for myocardial necrosis; elevations predict an increased risk for cardiac events even in the absence of MI diagnosed by other standards.8,9 The purpose of this study was to compare the ability of early myocardial perfusion imaging and cardiac troponin I (cTnI) assessment to predict short-term cardiac events in patients presenting to the ED with possible myocardial ischemia.

Methods

All patients who present to the ED of the Medical College of Virginia Hospitals with symptoms suggestive of myocardial ische-
mia undergo prompt clinical evaluation by ED house staff and attending physicians. After the initial evaluation, patients thought to be at high risk (ischemic ECG changes or typical symptoms in patients with known coronary disease) are admitted directly to the Coronary Care Unit (CCU), whereas those at low to moderate risk for acute coronary syndromes (eg, typical symptoms in a patient with no history of coronary disease or atypical symptoms in a patient with known coronary disease) undergo further risk stratification according to a protocol that includes early rest myocardial perfusion imaging.10 Patients considered at low risk for ischemia undergo perfusion imaging from the ED and are discharged and scheduled for outpatient stress testing if images are negative. Patients considered at moderate risk for ischemia are observed in the CCU and undergo a rapid rule-in protocol. These guidelines are provided to aid ED physicians with patient assessment but are not intended to replace clinical judgment; therefore, not all patients in the present study were treated in strict accordance with these guidelines. This study includes the initial admission of all patients who were admitted after undergoing ED evaluation and subsequent perfusion imaging. Patients who had undergone cTnI testing within the previous 6 months11 and those in whom serial cTnI samples were not obtained were excluded.

Our technique of early perfusion imaging has been reported previously.10 Briefly, patients were injected with 20 to 30 mCi of redistribution in the ED, and the quality and presence or absence of symptoms were recorded. Approximately 60 minutes after injection, gated single-photon emission CT myocardial perfusion imaging was performed with a triple-headed gamma camera system. Immediately after data acquisition, predefined commercial protocols were used to generate short- and long-axis static reconstructions and multilevel gated cines for visual interpretation. After January 1997, a previously validated automated algorithm was used to obtain a quantitative assessment of ejection fraction.12 All images were performed with gating whenever possible, which allowed assessment of global and regional function. The complementary assessment of function has been shown to improve specificity by differentiating between defects and artifacts.13

Perfusion images were evaluated by an experienced nuclear medicine physician, and all data were made available to the physicians treating the patient. For purposes of this analysis, images were dichotomized as either positive or negative for acute MI or ischemia. Studies showing a discrete perfusion defect with associated abnormalities in wall motion and/or thickening were considered positive. All other studies were considered negative.

After imaging, patients were observed in the CCU and underwent serial sampling of cTnI, total creatine kinase (CK), and CK-MB. Decisions regarding further diagnostic evaluation were made by the attending cardiologist in the CCU. Diagnosis of MI required a validated automated algorithm was used to obtain a quantitative measurement of the operator.13 Spun plasma was filtered before analysis with 0.2-μm sterile filters (Gelman Sciences) fitted to 3-mL Becton Dickinson syringes. The lower limit of detectability for this assay is 0.5 ng/mL. Results were analyzed with the manufacturer’s suggested upper limit of normal, 2.0 ng/mL, as well as a cutoff value of 1.0 ng/mL.

For patients in whom it was indicated, coronary angiography was performed via the Judkins technique, with views of the coronary arteries obtained in multiple projections. Significant coronary artery disease was defined as ≥50% stenosis of the left main artery or ≥70% stenosis in a major coronary artery or its branches.

End points included MI within 1 week of admission, performance of revascularization (CABG or PTCA), or demonstration of significant coronary disease on angiography within 6 weeks of admission. Results are presented as mean±SD. Comparisons were made with Student’s t test or χ2 analysis for categorical and proportional variables, respectively. A P value <0.05 was considered significant. Sensitivity, specificity, and χ-correlation coefficients were calculated in the standard fashion.14 Sensitivities for the end points of significant disease and revascularization were calculated after patients with MI were excluded.

### Results

During the study period, 721 patients were admitted to the CCU who had both myocardial perfusion imaging and cTnI sampling. Of these, 101 patients were excluded: 3 had uninterpretable perfusion images, 71 had cTnI tested only on the initial blood sampling, and 27 underwent PTCA during the 6 months before admission. This left 620 patients who formed the study cohort. Baseline patient characteristics are shown in Table 1.

MI was diagnosed in 59 patients (9%). An additional 140 patients underwent coronary angiography, with 81 (13%) having significant coronary disease. Of the patients with significant coronary disease, 58 (9%) underwent revascularization (39 PTCA and 19 CABG). Myocardial perfusion imaging was positive in 241 patients (39%), the initial cTnI was positive in 37 (6%), and serial cTnI (≥1 sample) was positive in 74 (12%).

Among the 59 patients with MI, 54 (92%) had positive perfusion imaging, 23 (39%) had a positive initial cTnI, and 53 (90%) had positive serial cTnI. The sensitivities of serial cTnI and early perfusion imaging were similar, and both were significantly higher than the sensitivity of the initial cTnI alone for identifying patients with MI (P<0.001) (Table 2; Figure, top panel). Fifty-eight of the 59 patients with MI had either positive perfusion imaging or positive serial cTnI. The remaining patient with MI, whose rest perfusion imaging and serial cTnI assessments were both negative, had normal stress perfusion imaging and normal coronary angiography.

Perfusion imaging was negative in 5 patients with MI. Two of these patients had global hypokinesia but no perfusion defects. The initial cTnI was elevated in 1 of these patients, and serial cTnI was positive in 4 of the 5. The size of the infarctions was small, with a mean peak CK of 318±181 U/L (median, 246 U/L) and CK-MB of 19±8 ng/mL (median, 17 ng/mL).

cTnI was negative in 6 patients with MI. Perfusion imaging was positive in 5 of the 6. The peak cTnI values in these patients were 0.5, 0.5, 1.1, 1.2, 1.4, and 1.9 ng/mL. In 1 patient with a peak cTnI value of 0.5 ng/mL, elevation of CK-MB was not present until the third sample. In the other 5, the mean peak CK was 139±10 U/L (median, 139 U/L).

Of the 81 patients who had significant coronary disease, 61 (75%) had positive perfusion imaging, 6 (7%) had a positive
initial cTnI, and 10 (12%) had positive serial cTnI. There were 58 patients without MI who underwent revascularization, of whom 47 (81%) had positive perfusion imaging, 6 (10%) had a positive initial cTnI, and 10 (17%) had positive serial cTnI. All 10 of the patients with positive serial cTnI values who underwent revascularization also had positive perfusion images.

As shown in Table 2, perfusion imaging had a significantly higher sensitivity than serial cTnI for identifying patients who underwent revascularization (Figure, top panel), experienced an MI, or underwent revascularization or who had either MI or significant coronary disease, although the specificity of perfusion imaging was significantly lower for all end points (Figure, bottom panel). When different end points were used separately or in combination, agreement between perfusion imaging and cTnI was low (Table 3).

Early perfusion imaging was positive in 122 patients who had neither MI nor significant coronary disease. Of these, 81 patients (66%) had evidence of underlying coronary disease: 38 had historical or ECG evidence of prior MI; 30 had moderate to severe systolic dysfunction; and 13 had either fixed perfusion defects on stress imaging or no change from a previous rest study.

Eleven patients (1.8%) without MI or significant coronary disease had positive serial cTnI. The mean value in these patients was 4.9±4.6 ng/mL (range, 2.0 to 17.5 ng/mL; median, 3.1 ng/mL). Perfusion imaging was positive in 5 of these patients. Two patients underwent coronary angiography; neither had coronary disease, although 1 had regional wall motion abnormalities on ventriculography.

Use of an upper limit of 1.0 ng/mL for cTnI did not significantly change the results (Table 2; Figure). Estimates of agreement between cTnI and perfusion imaging were unchanged, with an overall concordance of 71% and a ω-coefficient of 0.28.

**Discussion**

We found that both cTnI and myocardial perfusion imaging had high sensitivities for identifying patients with MI, although the sensitivity of the initial cTnI was significantly lower than that of perfusion imaging. cTnI had a higher specificity for all end points. Myocardial perfusion imaging identified more patients who subsequently underwent revascularization or who had significant coronary disease.

### Table 2. Sensitivity, Specificity, and ORs of Perfusion Imaging vs cTnI

<table>
<thead>
<tr>
<th>End Point</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>92 (81–96)</td>
<td>67 (63–71)</td>
<td>22 (6.2–57)</td>
</tr>
<tr>
<td>Serial cTnI ≥2.0 ng/mL</td>
<td>90 (79–95)</td>
<td>96 (94–98)*</td>
<td>230 (66–590)</td>
</tr>
<tr>
<td>Serial cTnI ≥1.0 ng/mL</td>
<td>97 (88–99)</td>
<td>94 (92–96)*</td>
<td>460 (60–1900)</td>
</tr>
<tr>
<td>Revascularization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion imaging</td>
<td>81 (69–89)</td>
<td>74 (70–77)</td>
<td>12 (4.7–23)</td>
</tr>
<tr>
<td>Serial cTnI ≥2.0 ng/mL</td>
<td>17 (107–29)*</td>
<td>98 (96–99)*</td>
<td>9.3 (3.6–23)</td>
</tr>
<tr>
<td>Serial cTnI ≥1.0 ng/mL</td>
<td>26 (16–39)*</td>
<td>96 (94–98)*</td>
<td>9.4 (4.2–20)</td>
</tr>
<tr>
<td>Combined end point of MI or revascularization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion imaging</td>
<td>86 (79–92)</td>
<td>74 (70–77)</td>
<td>17 (8.2–30)</td>
</tr>
<tr>
<td>Serial cTnI ≥2.0 ng/mL</td>
<td>54 (45–63)*</td>
<td>98 (96–99)*</td>
<td>52 (25–105)</td>
</tr>
<tr>
<td>Serial cTnI ≥1.0 ng/mL</td>
<td>62 (52–70)*</td>
<td>96 (94–98)*</td>
<td>43 (22–79)</td>
</tr>
<tr>
<td>Combined end point of MI or significant coronary disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion imaging</td>
<td>82 (75–88)</td>
<td>75 (70–78)</td>
<td>13 (7.3–22)</td>
</tr>
<tr>
<td>Serial cTnI ≥2.0 ng/mL</td>
<td>45 (37–53)*</td>
<td>98 (96–99)*</td>
<td>35 (17–69)</td>
</tr>
<tr>
<td>Serial cTnI ≥1.0 ng/mL</td>
<td>53 (45–61)*</td>
<td>97 (95–98)*</td>
<td>33 (17–59)</td>
</tr>
</tbody>
</table>

**Numbers in parentheses indicate 95% CI.**

*P*<0.001 compared with perfusion imaging.

**Table 3. Concordance and Agreement Between cTnI and Myocardial Perfusion Imaging**

<table>
<thead>
<tr>
<th>End Point</th>
<th>Concordance, %</th>
<th>ω-Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>92</td>
<td>0.25</td>
</tr>
<tr>
<td>MI or revascularization</td>
<td>67</td>
<td>0.20</td>
</tr>
<tr>
<td>MI or significant coronary disease</td>
<td>62</td>
<td>0.21</td>
</tr>
<tr>
<td>All patients</td>
<td>72</td>
<td>0.31</td>
</tr>
</tbody>
</table>
In the current study, both perfusion imaging and serial cTnI had similar high, although imperfect, sensitivities for MI. Most of the patients not identified by the 2 techniques had small MIs. This finding is not surprising. Perfusion imaging is limited by the threshold of myocardium at risk that is required for detection, which is \( \approx 3\% \) to \( 5\% \). The size of the infarctions (as estimated by peak CK values) in the patients with negative perfusion imaging was within this range.

Troponin values may be negative in patients with MI for a number of reasons, including the size of the infarction, timing of sampling, the threshold value for abnormality, and the particular “gold standard” used to define MI. Release of troponin in patients with MI is proportional to infarct size; therefore, peak troponin values will be low in patients with small MIs. The cutoff values used for markers are often those recommended by the manufacturers of the assays; lowering the cutoff value may improve sensitivity without affecting specificity. In the present study, lowering the normal limit of cTnI to 1.0 ng/mL identified all but 2 of the patients with MI, although sensitivity for the various end points was not significantly improved. If sampling is done early after the onset of necrosis, troponin values may not be detectable; this was seen in 1 patient with MI. Troponin values will be discrepant if the gold standard (in this study, CK-MB) is not perfect, resulting in some patients without necrosis who are incorrectly diagnosed as having MI. This was likely the case in the patient whose serial cTnI, perfusion imaging, and coronary angiography results were all negative.

The proportion of patients with positive serial troponin values in the current study was lower than in some previous studies. This occurred as a result of the overall lower risk of the patients included, as evidenced by the number of cardiac events observed. Most previous studies evaluating troponins in unstable angina required ischemic ECG changes for entry; by definition, this is a group of patients at increased risk for cardiac events. Studies that have examined a broad range of patients presenting to the ED with possible myocardial ischemia have found an incidence of cTnI positivity similar to ours.

We found that the sensitivity of perfusion imaging was significantly higher than that of the initial cTnI. Imaging is typically performed 45 to 60 minutes after injection; with the time required for imaging and processing, the diagnostic information is available within 2 hours of injection. In contrast, optimal sensitivity of cTnI is not reached until 8 to 12 hours after onset of necrosis, with transportation and laboratory processing time causing additional delays. Although the use of bedside or point-of-care testing can minimize these delays, it will not reduce the time required for cTnI to be detectable.

It is important that tools used to identify patients with MI also be able to identify patients with unstable angina. Although the same treatment time demands for MI may not apply to patients with unstable angina, hospital admission and appropriate medical therapy are clearly required to reduce morbidity and mortality, and new therapies offer the potential to improve outcomes. In addition, it is likely that many of the patients who are discharged with a “missed MI” present with unstable angina that subsequently progresses to MI. Finally, early identification of high-risk patients with unstable angina offers the additional advantage of rapid discharge or early stress testing of the remaining low-risk patients.

Numerous studies have demonstrated that cTnT and cTnI can predict cardiac events in both the short-term and the long-term. This prognostic power is evident even in patients without MI, in whom troponin elevations predict an increased rate of later cardiac events. It must be recognized, however, that the lower risk associated with normal troponin values does not necessarily imply “low” risk. Troponin elevations are found in only a minority of patients clinically diagnosed with unstable angina. Those without detectable troponin levels have a low but significant risk for cardiac events, which may be substantial in some subgroups. There is often no difference in the incidence of recurrent ischemia or revascularization between patients with and without elevated troponin values. Similar limitations were seen in the present study, because elevations of cTnI were found in only a minority of patients who underwent revascularization or who had significant coronary stenoses on angiography, even when a lower cutoff value for cTnI was used. Although measurement of troponin allows detection of myocardial cell injury that is undetectable by conventional myocardial markers, myocardial necrosis is still required before troponin is released. Therefore, reliance on assessment of troponin alone is insufficient for identifying most patients with unstable angina. Our results demonstrate that perfusion imaging has an important diagnostic advantage over cTnI in patients with ischemia alone because necrosis is not necessary to cause perfusion abnormalities.

An important limitation of perfusion imaging is the inability to determine whether a perfusion defect is the result of acute infarction, acute ischemia, or old infarction. Myocardial marker sampling of troponin enables definitive identification of myocardial necrosis, as well as detection of small amounts of necrosis that are not sufficient to result in visible perfusion defects. The distinction between old infarction and acute ischemia can often be made on clinical grounds; alternatively, repeat rest imaging after a prolonged pain-free period allows differentiation of the 2 conditions. In this study, a significant number of patients who had positive perfusion imaging without MI or significant coronary disease had evidence of underlying cardiac disease, either from prior MI or significant systolic dysfunction, resulting in a lower specificity. However, considering them “false-positives” is not entirely correct; previous MI is an important risk factor in patients undergoing evaluation for myocardial ischemia, and early discharge is not usually appropriate. The ability of cTnI assessment to identify patients with myocardial necrosis despite negative perfusion imaging and to exclude myocardial necrosis in patients with positive perfusion imaging indicates that the information provided by both tests is complementary. All but 1 patient with MI were identified with the combination of cTnI and myocardial perfusion imaging; given the stress perfusion and coronary angiography results, it is likely that this single patient did not actually have an MI.
Limitations
The results of both cTnI sampling and myocardial perfusion imaging were available to the clinicians caring for the patient and therefore are likely to have affected decisions for further care, such as the decision to proceed with coronary angiography. However, this would not affect the sensitivity for MI. In addition to significant disease on coronary angiography and MI, we used revascularization as an end point. Although there is potential bias in selection of patients for revascularization, all patients had rest angina in combination with significant coronary disease. Unfortunately, there is no gold standard definition for unstable angina. Although “hard” cardiac events such as MI and death are less subject to bias, an important objective in the treatment of patients with unstable angina is prevention of these events. In some groups of patients, early revascularization can reduce the rate of long-term cardiac events.33 Despite its potential limitations, revascularization has been used as an end point in other studies of unstable angina.22,34 The incidence of revascularization in the present study was not excessive and was similar to35 or lower than8,9,34 revascularization rates in other studies of patients with unstable angina.

We examined the predictive ability of cTnI using sampling periods similar to those used for rapid evaluation and triage of patients with chest pain. It is possible that by extending the sampling period, more patients with elevations may have been identified. However, 1 purpose of this study was to examine the predictive ability of serial cTnI when used in a manner found in most chest-pain evaluation protocols.56,37

In conclusion, both cTnI and myocardial perfusion imaging have high sensitivities for identifying patients with MI, although the sensitivity of the initial cTnI was significantly lower than that of perfusion imaging. Although the specificity of cTnI for MI is higher, myocardial perfusion imaging identified more patients who subsequently underwent revascularization or who had significant coronary disease. The 2 techniques offer complementary information when used to identify patients with acute coronary syndromes.

References


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