Ninety-Minute Accelerated Critical Pathway for Chest Pain Evaluation

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Rapid, efficient, and accurate evaluation of chest pain patients in the emergency department optimizes patient care from public health, economic, and liability perspectives. To evaluate the performance of an accelerated critical pathway for patients with suspected coronary ischemia that utilizes clinical history, electrocardiographic findings, and triple cardiac marker testing (cardiac troponin I [cTnI], myoglobin, and creatine kinase-MB [CK-MB]), we performed an observational study of a chest pain critical pathway in the setting of a large Emergency Department at the Veterans Affairs Medical Center in 1,285 consecutive patients with signs and symptoms of cardiac ischemia. The accelerated critical pathway for chest pain evaluation was analyzed for: (1) accuracy in triaging of patients within 90 minutes of presentation, (2) sensitivity, specificity, positive predictive value, and negative predictive value of cTnI, myoglobin, and CK-MB in diagnosing acute myocardial infarction (MI) within 90 minutes, and (3) impact on Coronary Care Unit (CCU) admissions. All MIs were diagnosed within 90 minutes of presentation (sensitivity 100%, specificity 94%, positive predictive value 47%, negative predictive value 100%). CCU admissions decreased by 40%. Ninety percent of patients with negative cardiac markers and a negative electrocardiogram at 90 minutes were discharged home with 1 patient returning with an MI (0.2%) within the next 30 days. Thus, a simple, inexpensive, yet aggressive critical pathway that utilizes high-risk features from clinical history, electrocardiographic changes, and rapid point-of-care testing of 3 cardiac markers allows for accurate triaging of chest pain patients within 90 minutes of presenting to the emergency department. ©2001 by Excerpta Medica, Inc.

Methods

Preliminary studies with cTnI were approved by the University of California, San Diego, Committee on Human Subjects. From this initial research, a critical pathway utilizing a cardiac marker algorithm was established as the standard of care and implemented at the San Diego Veterans’ Affairs Hospital. During a 9-month period from July 1998 to April 1999, we analyzed the diagnoses, triage patterns, and medical outcome of 1,285 consecutive patients who presented to the emergency department with symptoms of cardiac ischemia. Patients who had symptoms or signs consistent with a possible diagnosis of acute MI, “rule-out MI,” or unstable angina were admitted to the Cardiac Care Unit (CCU). All MIs were diagnosed within 90 minutes of presentation (sensitivity 100%, specificity 94%, positive predictive value 47%, negative predictive value 100%). CCU admissions decreased by 40%. Ninety percent of patients with negative cardiac markers and a negative electrocardiogram at 90 minutes were discharged home with 1 patient returning with an MI (0.2%) within the next 30 days. Thus, a simple, inexpensive, yet aggressive critical pathway that utilizes high-risk features from clinical history, electrocardiographic changes, and rapid point-of-care testing of 3 cardiac markers allows for accurate triaging of chest pain patients within 90 minutes of presenting to the emergency department. ©2001 by Excerpta Medica, Inc.

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patients to either the intensive care unit, the direct observation unit (DOU), the ward, or home. Patients who had chest pain were directed into 1 of 5 pathways based on history, electrocardiogram, and clinical suspicion of MI. A cardiac marker algorithm was incorporated into this pathway, which tested myoglobin, cTnI, and CK-MB at time of presentation (time 0), and at 30, 60, and 90 minutes to help determine patient diagnosis. When indicated, subsequent measurement of the cardiac enzymes at 3 and 6 hours were made to substantiate a final diagnosis of MI. In most cases, emergency department physicians were able to evaluate patients and determine patient triage destination within 90 minutes.

**Assays:** Whole blood (about 2 to 3 ml) was collected in green top tubes by nursing personnel and assayed using the Triage Cardiac Panel (Biosite Diagnostics, San Diego, California) by intensive care unit gas laboratory technicians. This point-of-care instrument, approved by the Federal Drug Administration, compared with other platform-based assays, provides a rapid, quantitative analysis of 3 cardiac markers (CK-MB, myoglobin, and cTnI) using either heparinized whole blood or plasma. Results were available in ~15 minutes. All assays were based on the principle of a 2 site or sandwich fluorescence immunoassay using a pair of polyclonal and monoclonal antibodies selected to recognize different polypeptide segments unique to the cardiac isoforms of free and complexed troponin I, CK-MB, or myoglobin. The analytic sensitivity of the cTnI test was 0.4 ng/ml, and the analytic sensitivity of the CK-MB mass assay was 0.6 ng/ml. There was no significant cross-reactivity to CK-BB at levels up to 5,000 ng/ml and 0.03% cross reactivity with CK-MM at 10,000 ng/ml. Upper limits of normal for CK-MB in this study for subjects without MI was ≤8.9 ng/ml. The threshold for detection for the myoglobin assay was 1.0 ng/ml. The upper limits of normal was higher than with most other assays at ≤170 ng/ml. This was determined by preliminary studies comparing readings to those on the Opus Machine (Dade Behring, Westwood, Massachusetts). MIs were classified using criteria established by the World Health Organization (characteristic chest pain, electrocardiographic changes [new Q waves or ST-segment elevation or depression of >1 mm in 2 contiguous leads], and biochemical markers [elevation of serial CK-MB mass level above the decision threshold of >8.9 mg/l]) in all cases where patients had chest pain within <6 hours. ASA = acetylsalicylic acid; CAD = coronary artery disease; PTCA = percutaneous transluminal coronary angioplasty.

**FIGURE 1.** Accelerated critical pathway for chest pain evaluation. Patients are directed into pathways as indicated by their electrocardiographic (ECG) changes, symptom duration, and cardiac ischemic probability. Risk-stratification markers at 3 and 6 hours may be done in the emergency department, at the physician’s discretion. *Definitions of positive markers: (1) sustained (+) CK-MB at 3 or 6 hours; and (3) increasing myoglobin >25% over 90 minutes with a final value of >150 ng/ml if the patient had chest pain within <6 hours. ASA = acetylsalicylic acid; CAD = coronary artery disease; PTCA = percutaneous transluminal coronary angioplasty.*
correlations between the Opus Machine (previously used for cardiac marker analysis at the San Diego Veteran’s Affairs Medical Center) and the Triage Cardiac Panel machine used for this critical pathway showed the upper limits of normal in the Triage machine to be 170 ng/ml, roughly twice that of the Opus. This was further substantiated in preliminary studies over 6 months. The level of 150 ng/ml, which is higher than that used in other studies, was chosen to avoid missing an MI in patients who may have had low baseline myoglobin levels and whose proportional increase during an MI may not have been detectable if the upper limit was too high. The 25% increase in myoglobin was chosen based on preliminary studies in which myoglobin in patients with MI was observed to increase acutely 25% to 50% over 90 minutes. Patients with sustained positive cTnI <1.0 ng/ml (threshold for MI) who have chest pain were considered to have possible myocardial ischemia and were grouped with the unstable angina patients.

**Coronary Care Unit utilization:** According to the chest pain critical pathway, criteria for admission into the coronary care unit (CCU) included any one or a combination of the following: chest pain with ST-segment elevation or depression; chest pain unrelieved by usual measures such as aspirin or nitrates in the emergency room; or sustained, positive cardiac markers (see above).

CCU bed utilization during this study was compared with CCU bed utilization during a period of time before the critical pathway implementation. From October 1996 to March 1997, 505 consecutive patients were prospectively evaluated for chest pain in the emergency department. During this 6-month period, cardiac markers were tested at 0, 2, 6, and 12 hours, and CCU admission was at the discretion of the house officer or attending physician. The triage destination of these patients compared with the triage of patients managed under the critical pathway demonstrated how this new pathway impacted patient care and hospital costs.

**Statistical analysis:** Accuracy of individual or combined myocardial markers by each measured time period was determined by comparisons of patients actually diagnosed with MI to that indicated by cardiac marker concentration. The clinical sensitivity and specificity of the cardiac marker algorithm at the various times were calculated as a percentage. The 95% confidence intervals are included. Comparisons between the different combinations of markers were made using the McNemar test using an α ≤0.05 to designate statistical significance.

**RESULTS**

**Patient characteristics:** The clinical characteristics of the 1,285 patients enrolled in this study are shown in Table 1. Patients without a subsequent diagnosis of MI or unstable angina more commonly waited >6 hours before presenting to the emergency department. Patients diagnosed with MI or unstable angina were likely to have new onset of chest pain at rest as well as a history of MI. In the 66 patients with acute MI confirmed by elevated CK-MB, the electrocardiogram was diagnostic (ST-segment elevation) in only 17% of them. Of the 138 patients with unstable angina, 11 had minimally elevated values of cTnI that were >0.6 ng/ml but less than the diagnostic cut-off of 1.0 ng/ml used to diagnose MIs. These patients were classified as having “minor myocardial injury” and categorized with the unstable angina patients. MI, minor myocardial injury, and unstable angina patients were all triaged to the CCU and received the same clinical treatment according to the critical pathway. Of the 5 different critical pathways patients were triaged into (Figure 1), ≈4% were initially in the MI/ST elevation pathway; about 6% were in the second pathway with ST depression and unrelenting chest pain; 38% were in the probable and possible unstable angina group; and the remaining 63% of the 1,285 patients were in the noncardiac chest pain pathway.

**Sensitivity and specificity:** Figure 2 compares the clinical sensitivity and specificity of each marker alone and combined for the diagnosis of MI from time of presentation to 90 minutes after first cardiac markers are drawn. A diagnosis of MI was considered if any or all markers were positive for a MI. A MI was “ruled out” only if all markers were negative. cTnI was specific and sensitive for the diagnosis of MI, approaching 100% sensitivity by 6 hours. When cTnI was combined with positive delta myoglobin (25% increase over 90 minutes), 94% of MIs were detected by 90 minutes, with a negative predictive value of 99.7%. Delta myoglobin and cTnI, used separately, each had sensitivities of 29% and 86%, and negative predictive values of 96% and 99%, respectively. Using the algorithm criteria, 4 patients could not be diagnosed definitely with MI until after the initial 90-minute draws. All 4 of these patients, however, had electrocardiographic changes that slated them for admission to the CCU. Two patients had high myoglobin levels that did not increase further over 90 minutes.

### Table 1 Clinical Characteristic of Patients With Chest Pain

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (n = 1,285)</th>
<th>MI (n = 66)</th>
<th>Unstable Angina (n = 138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>64 ± 13</td>
<td>65 ± 11</td>
<td>64 ± 13</td>
</tr>
<tr>
<td>Men (%)</td>
<td>98</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>Duration of pain onset &gt;6 h (%)</td>
<td>50.2</td>
<td>34.8</td>
<td>34.1</td>
</tr>
<tr>
<td>New pain at rest (%)</td>
<td>19.1</td>
<td>30.3</td>
<td>30.4</td>
</tr>
<tr>
<td>Prior MI/CABG (%)</td>
<td>30.6/19.5</td>
<td>42.4/16.7</td>
<td>54.3/34.8</td>
</tr>
<tr>
<td>ECG findings (%)</td>
<td>Normal 70.9</td>
<td>19.7</td>
<td>64.5</td>
</tr>
<tr>
<td></td>
<td>ST-segment elevation</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td>ST-segment depression</td>
<td>5.7</td>
<td>10.9</td>
</tr>
<tr>
<td></td>
<td>T-wave inversion</td>
<td>5.7</td>
<td>17.4</td>
</tr>
<tr>
<td></td>
<td>New bundle branch block</td>
<td>0.93</td>
<td>4.5</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; ECG = electrocardiographic.
CK-MB was already elevated in these patients. Another patient had ST elevation and did not require further testing over 90 minutes. The final patient presented 5 hours after symptom onset, likely passing the window in which myoglobin increases. The combination of all 3 markers, cTnI, CK-MB, and delta myoglobin, allowed 100% sensitivity at 90 minutes irrespective of electrocardiographic changes.

We analyzed the difference in using purely positive myoglobin (>170) to detect MI versus using positive delta myoglobin (increasing >25%, with value(s) ≥150). For myoglobin >170, the positive predictive value was 16%, and the negative predictive value was 98% at 90 minutes. Because myoglobin is very nonspecific, it has relatively low sensitivity and specificity. Delta myoglobin was less sensitive and more specific (29% and 98%, respectively) than single myoglobin values at time points up to 90 minutes, but had high sensitivity and specificity when combined with cTnI, CK-MB, or both. Among the various combinations of markers, positive delta myoglobin was present in association with other markers 23% of the time. When only cTnI and myoglobin were evaluated in the first 90 minutes, positive delta myoglobin preceded and predicted subsequent elevations of cTnI in nearly 10% of cases.

**Symptom to presentation delay:** Of the entire patient population, 50% presented at ≥6 hours after symptom onset, 29% presented at <6 hours, and 21% had unknown delay times. In the patients subsequently diagnosed with MI, 35% presented at ≥6 hours, 45% presented at <6 hours, and 21% had unknown symptom onset-to-presentation delays. In the non-MI subset, 51% presented at ≥6 hours, 28% at <6 hours, and 21% were unknown. In the patients with known symptom onset to presentation delays, 63% presented ≥6 hours. Patients with MI with known symptom onset times tended to present earlier (44% ≥6 hours), whereas those without MI tended to present later (64% ≥6 hours).

**Cardiac marker testing frequency:** The average number of blood draws per patient was 2.18. Only 24% of patients required all 4 blood draws to rule in MI. Patients subsequently diagnosed with MI had more draws than patients without MI, with average draws of 3.11 and 2.13, respectively. Patients who presented >6 hours after onset of symptoms and elicited low suspicion of cardiac ischemia were more likely to have their cardiac markers tested only once as directed by the critical pathway. Those presenting within <6 hours of chest pain or had high likelihood of cardiac ischemia were likely to have been tested more often. In general, these patients had ≥3 of the 4 sets of cardiac markers drawn in the first 90 minutes after presentation. Some patients also had markers drawn after the first 90 minutes after presentation, (as indicated by the critical pathway) if physicians believed another value was needed to confirm the diagnosis or to follow the trend of the cardiac markers in a patient with MI.

**CCU admission:** Using the present critical pathway, there was a ≥40% decrease in CCU bed utilization compared with a baseline period during which no definitive criteria were established for admission, and early, repetitive evaluation of the cardiac markers was not utilized (p <0.001). Figure 3 shows the disposition of patients from the emergency department during each period.

**Disposition:** Hospitalization: Table 2 shows the disposition of admitted patients along with their final diagnosis, complications, and subsequent interventions. More than 95% of all patients with MIs were admitted to the CCU; all were able to be triaged by the 90-minute time point according to the critical pathway. The only patients with MIs admitted elsewhere (n = 3) were patients whose infarcts were >2 days old or who chose not to be resuscitated and were designated to be “no code” status. Of these 3 patients, 1 died while in the ward. Hospital mortality was 4.9%, whereas direct cardiac mortality from MI was 0.9%. Significantly more CCU patients died or had subsequent cardiac intervention (pacemakers, percutaneous transluminal coronary angioplasty, or stents) or coronary artery bypass grafting compared with patients admitted to the DOU or the ward (p <0.001).

**Patient discharge from the emergency department:** Patients could be sent home at the discretion of the emergency department physician after consultation with the CCU team. As per the critical pathway, patients not sent to the CCU on admission or not sent home after the first negative set of cardiac markers were to be reevaluated after 90 minutes. The critical pathway allowed physicians to make triage decisions at the 90-minute point (CCU, DOU, ward, home, or further testing). For those patients ultimately discharged home, Table 2 shows the time point in the critical pathway at which this decision was made. Of the 1,285 patients who presented to the emergency department with chest pain, 508 (40%) were discharged home. In 90% of this group, the decision to discharge the patient home was made at or before the 90-minute marker results were evaluated. Of this group, 13 patients returned to the emergency depart-
ment within a 30-day time period. One patient (0.2%) was subsequently diagnosed with MI, and 12 others (2%) were admitted for unstable angina.

**DISCUSSION**

Using the critical pathway in this study, all patients who “ruled in” with an acute MI were identified within a 90-minute time period. The negative predictive value of early repetitive cardiac marker testing in this setting was 100% using a combination of 3 markers. Although not all patients were discharged at 90 minutes, the results of this study indicates that rapid triage of all patients, including high- and low-risk patients is possible within 90 minutes of presentation. This critical pathway decreased CCU admissions by 40% while still triaging the sickest patients to the CCU. This decrease, along with its likely associated cost savings with regard to intensive care unit costs, may even be underestimated because at several time points during our study a shortage of DOU beds may have falsely elevated the CCU admission rate. It is nearly impossible to account for this number, although we estimate that approximately 10% of the CCU patients would have been sent to DOU, had space been available. In nearly 90% of cases in which patients were ultimately discharged home, the decision for discharge was made by evaluating physicians within 90 minutes of presentation. In the 30-day follow-up period, only 1 patient who was discharged home returned to the emergency department with an acute non-Q-wave MI on day 12. Twelve others were admitted for “unstable angina.” Admission is the standard practice at this Veteran’s hospital whenever a patient returns with chest pain ≤1 month of an emergency room visit.

The critical pathway in this study relies strongly on the cardiac marker algorithm to diagnose MI. Kost et al. developed a strategy for using myoglobin and CK-MB mass to diagnose acute MI. He tested myoglobin and CK-MB in all MI possible patients but reserved serial markers for those with heightened clinical suspicion. Troponin I was tested only for specific confirmation, late presentation, or risk stratification. In this study, the negative predictive value of cTnI combined with delta myoglobin was 99.7%, making the routine measurement of CK-MB possibly dispensable; however, as CK-MB has been historically used as the gold standard for diagnosis, it served to substantiate necrosis of myocardium when cTnI leaks. Although multiple cardiac markers can be of tremendous value in the early and accurate diagnosis of MIs, there is also dismay about the cost of performing multiple biochemical tests as part of the routine workup for MI. Clinicians have aimed efforts at finding alternative cost-effective strategies to exclude MIs aimed at low-risk patients.

In our study, we hypothesized that using a cardiac panel that simultaneously tests for all 3 markers using a small point-of-care instrument with rapid turnaround time facilitates the diagnosis of acute MI. Our
results agree with the recent study by Newby et al.,23 which prospectively compared bedside quantitative marker testing with local laboratory results in 10,005 patients in 6 chest pain units. They found that rapid analysis of the same markers used in this study identifies positive patients earlier and provides better risk stratification for mortality than a local, laboratory-based single marker approach. Other studies using multiple markers support this idea7,16,24–26 and confirm the recommendations of the National Academy of Clinical Biochemistry.13–15

Although aggressive testing of 3 markers may mean that some patients are tested multiple times, using a point-of-care testing device that tests all 3 cardiac markers together helped to eliminate the total number of blood draws a patient had to undergo, as well as decreased the cost of materials and labor compared with testing each marker separately. In addition, the machine’s ability to test whole blood facilitated rapid testing results. If patients presented with >6 hours of chest pain and suspicion of cardiac ischemia was low, the critical pathway indicated that no further testing was needed; thus, not all patients underwent multiple testing. In this study, the average number of times a patient was tested was 2.2, with average draws of 3.2 and 2.1 times in patients with and without MI, respectively. We believe the cost of testing cardiac enzymes an average of 2.2 times should be more than adequately justified when compared with the savings associated with a 40% reduction in CCU admissions, shorter emergency department visits, and early and accurate patient triage. Our critical pathway eliminates the prolonged waiting period when MI confirmation, late presentation assessment, or risk stratification needs arise.

Study limitations: Secondary to the demographics of the Veteran’s Affairs patient population, 98% of our study population was male, making it difficult to extend our results to the general population. Next, our study showed a low incidence of infarction in our population (5%). Several possible explanations exist for this low value. Patients who were transferred from other hospitals for care in the Veteran’s Affairs Hospital with a previously established diagnosis of MI were not included in our study because their diagnosis and triage decisions were made before their presentation to our hospital. A low incidence of MI may also be explained by a possible overuse of cardiac markers in patients who had possible ischemic symptoms but not necessarily chest pain. In our study, we included all patients who had cardiac markers drawn and evaluated using the critical pathway because a certain fraction of MIs may present atypically or asymptptomatically. Finally, in our study, patient presentation to the emergency department was often on the late side (>50% presented within >6 hours of chest pain), which may not reflect the general population as a patient population characteristic. If patients presented earlier, the sensitivities of the markers when used alone would shift relative to one another.

In summary, our critical pathway, developed and implemented at the San Diego Veteran’s Affairs Hospital, is a simple, yet aggressive, critical pathway that allows accurate triaging of patients with chest pain within 90 minutes of presenting to the emergency department. This pathway, which uses high-risk features from patients’ histories and electrocardiograms along with rapid, point-of-care testing of a panel of myocardial markers, has the advantage of being simple to follow, inexpensive, and available to any emergency department or urgent care clinic.

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References