A Decision Tree for the Early Diagnosis of Acute Myocardial Infarction in Nontraumatic Chest Pain Patients at Hospital Admission*

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**Study objective:** To find an accurate algorithm for the diagnosis of acute myocardial infarction in nontraumatic chest pain patients on presentation to the emergency department.

**Design:** In a prospective clinical study, we compared the diagnostic performances of clinical symptoms, presenting ECG, creatine kinase, creatine kinase MB activity and mass concentration, myoglobin, and cardiac troponin T test results of hospital admission blood samples. By classification and regression trees, a decision tree for the diagnosis of acute myocardial infarction was developed.

**Setting:** Emergency room of a Department of Internal Medicine (University Hospital).

**Patients:** One hundred fourteen nontraumatic chest pain patients (median delay from onset of chest pain to hospital admission, 3 h; range, 0.33 to 22): 26 Q-wave and 19 non-Q-wave myocardial infarctions, 49 patients with unstable angina pectoris, and 20 patients with chest pain caused by other diseases.

**Measurements and results:** Of each parameter taken by itself, the ECG was tendentially most informative (areas under receiver operating characteristic plots: \(0.87 \pm 0.04\) [ECG], \(0.80 \pm 0.05\) [myoglobin], \(0.80 \pm 0.04\) [creatine kinase MB mass], \(0.77 \pm 0.04\) [creatine kinase activity], \(0.69 \pm 0.06\) [clinical symptoms], \(0.67 \pm 0.06\) [creatine kinase MB activity], \(0.67 \pm 0.05\) [troponin T]). In patients presenting 3 h or less after the onset of chest pain, ECG signs of acute transmural myocardial ischemia were the best discriminator between patients with and without myocardial infarction. In patients presenting more than 3 h, however, creatine kinase MB mass concentrations (discriminator value, 6.7 µg/L) were superior to the ECG, clinical symptoms, and all other biochemical markers tested. This algorithm for diagnosing acute myocardial infarction was superior to each parameter by itself and was characterized by 0.91 sensitivity, a 0.90 specificity, a 0.90 positive and negative predictive value, and a 0.90 efficiency.

**Conclusions:** We found an algorithm that could accurately separate the myocardial infarction patients from the others on admission to the emergency department. Therefore, this classifier could be a valuable diagnostic aid for rapid confirmation of a suspected myocardial infarction.

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**Keywords:** acute myocardial infarction; cardiac troponin T; clinical symptoms; creatine kinase; creatine kinase MB; early diagnosis; electrocardiogram; creatine kinase MB activity; myoglobin

**ECG** is the simplest diagnostic modality. Regional ST segment elevations found in the presenting ECG are specific, but they are not very sensitive. Up to 50% of acute myocardial infarction patients may have nondiagnostic ECGs on emergency department admission. In the past, the conventional myocardial markers, creatine kinase and creatine kinase MB activity, proved useful for retrospective confirmation of acute myocardial infarction in these patients, but both are not very helpful for the early diagnosis of acute myocardial infarction. Now, however, new myocardial markers, such as myoglobin and cardiac troponin T, and a new method for measuring the established marker creatine kinase MB have gained increasing interest. Recent creatine kinase MB assays rely on the measurement of creatine kinase MB protein concentration (creatine kinase MB mass), whereas prior assays have measured its enzyme activity. Creatine kinase MB mass concent-

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tration measurement by immunoassays increases the diagnostic sensitivity of this marker for the early diagnosis of acute myocardial infarction considerably. Acute myocardial infarctions may be diagnosed by increased myoglobin or creatine kinase MB mass concentrations when creatine kinase and creatine kinase MB activities are still within their reference intervals. Rapid assays for "stat" determination of myoglobin, creatine kinase MB mass, or cardiac troponin T are already commercially available. Based on clinical symptoms, the presenting ECG recording, and on measurements of the myocardial markers, creatine kinase, creatine kinase MB activity, creatine kinase MB mass, myoglobin, and cardiac troponin T in blood samples drawn at the time of hospital admission, we wanted to develop a diagnostic strategy to rule in acute myocardial infarction on emergency department presentation.

**Methods**

**Patients**

We investigated 114 nontraumatic chest pain patients. They were enrolled nonconsecutively during a 3-month period in 1993. Patients admitted to the hospital between 10 pm and 6 am were usually not included for organizational reasons. The study population consisted of 77 male and 37 female patients about 60 (median) years old (range, 21 to 89 years). The median delay from the onset of chest pain to hospital admission was 3 h with a range from 20 min to 22 h. The median delay of acute myocardial infarction patients was 2 h with a range from 0.33 to 14.5 (Q wave, 1.75, 0.33 to 14.5; non Q wave, 4.5, 0.5 to 14). The patients were classified as having acute myocardial infarction, angina pectoris, and no acute ischemic heart disease. There was a definite other cause for chest pain on hospital admission; it was not caused by coronary artery disease. The final diagnosis was established by an independent cardiologist who was blinded to creatine kinase MB mass, myoglobin, and cardiac troponin T test results. The diagnosis was based on the clinical course and the results of routine diagnostic procedures that were performed during the hospital stay. Forty-five patients had an acute myocardial infarction (prevalence, 0.39); 49 had unstable angina pectoris (16 with transient ST-T alterations), and 20 other diseases that included supraventricular tachycardia (n=3, 1 patient with syncope), pneumonia (n=3), musculoskeletal disorders (n=3), myocarditis (n=2), dilated cardiomyopathy with acute heart failure (n=1), pulmonary embolism (n=5), esophagitis (n=2), and hypertensive crisis (n=1). All myocardial infarction patients did not receive thrombolytic therapy before hospital admission. Therefore, the hospital admission blood samples were drawn and the admission ECGs were recorded before the initiation of thrombolytic therapy in all patients.

The definite diagnosis of acute myocardial infarction was based on standard World Health Organization criteria requiring at least two of the following three clinical criteria to be positive: (1) typical prolonged severe chest pain and related symptoms of more than 20 min duration; (2) the evolution of unequivocal findings indicative for myocardial infarction on serial ECGs in at least two leads of the same vascular territory (ie, diagnostic Q waves or QS complexes); and (3) serial creatine kinase and creatine kinase MB activity elevations with an initial rise and a subsequent fall with peak values of more than twice the upper limit of the reference interval. An acute myocardial infarction was called Q-wave myocardial infarction if there was progression from no Q waves to definite Q waves (≥30 ms) or QS complexes; it was called non-Q-wave myocardial infarction if there were new ST-T alterations (ST-segment depression or elevation of at least 0.1 mV, T-wave inversion or progression) in at least two leads of the same vascular territory of at least 24 h duration.

According to their history and symptoms, chest pain patients were divided into four categories: (1) atypical chest pain; (2) atypical chest pain with symptoms of excessive autonomic nervous system activity (eg, nausea, vomiting, sweating); (3) typical infarct-related chest pain (prolonged pressing, squeezing, and burning pain, which is usually retrosternal, but may radiate or can occur in the lower jaw, back, arms, shoulders, wrist, or epigastrium); and (4) typical infarct-related chest pain with symptoms of excessive autonomic nervous system activity.

**Electrocardiography**

The hospital admission ECG was read by three independent experienced observers who were unaware of the clinical details and had no access to previous ECGs (they were usually not available). If there were discrepancies in the classification among the observers, the decision of the majority was used. The observers classified the ECGs into four groups as follows:

1. **Probable Acute Myocardial Infarction:** These patients showed the typical patterns of acute myocardial ischemia in at least two leads, that are presumable new convex ST-segment elevations (≥0.1 mV limb, ≥0.2 mV precordial leads), ST-segment depression with prominent R in V1, V2, and V3, if this is thought to indicate a posterior infarction, a presumable new left bundle-branch block, and in case of delayed hospital admission, abnormal presumable new Q waves (≥30 ms; amplitude >1/4 R) or QS complexes or hyperacute T waves in case of very early hospital admission (T amplitude ≥1.0 mV in leads V2 to V4, ≥0.75 mV in lead V5, ≥0.5 mV in leads I, II, aVF, V1, or V6, or ≥0.25 mV in leads aV3 or III). ST-segment deviation was always measured 80 ms after the junction point using the PQ segment as the isoelectric line.

2. **Possible Acute Myocardial Infarction:** These patients had ST-segment depression of 0.1 mV or more and/or T-wave flattening or inversion in at least two leads.

3. **Normal ECG.**

4. **Uncodable ECG:** This occurred, for example, because of a ventricular pacemaker.

**Laboratory Analysis**

**Blood Collection:** Immediately after emergency department admission, a single venous blood sample was collected in lithium heparin (final concentration, approximately 20 IU/mL of blood) containing tubes (Sarstedt; Nümbrecht, Germany) and immediately centrifuged at 2,000g for 10 min. Creatine kinase and creatine kinase MB activities were measured without delay; plasma for measurement of all other parameters was frozen in aliquots and stored at −20°C until analysis was performed (within 1 month after blood withdrawal). Creatine kinase and creatine kinase MB activities were repeatedly measured during the hospital stay, which was part of the routine monitoring of patients.

**Creatine Kinase and Creatine Kinase MB Activities:** Creatine kinase and creatine kinase MB activities were measured at 25°C by means of an N-acetylcysteine-activated, optimized ultraviolet test (Merck; Darmstadt, Germany). Creatine kinase MB activity was determined by immunoinhibition. The upper limits of the reference interval of creatine kinase are 70 U/L for women and 80 U/L for men and 10 U/L (for both sexes) for creatine kinase MB activity, respectively.

**Creatine Kinase MB Mass:** Creatine kinase MB mass concentration was measured by a microparticle enzyme immunoassay (Abbott; Abbott Park, Ill) for use with an automated analyzer (Abbott IMx). The upper limit of the reference interval is 5 µg/L.

**Myoglobin:** Myoglobin is an oxygen-binding cytosolic heme pro...
tein (molecular weight, 17.8 kd). It is found in all striated muscle fibers. Myoglobin concentration was determined by a commercially available immunoturbidimetric assay (Turbiquant Myoglobin; Behringwerke AG; Marburg, Germany). The upper limit of the reference interval is 70 µg/L. The detection limit of the assay is 50 µg/L. This assay provides quantitative test results within 1 to 2 min after starting the assay.

Cardiac Troponin T: Cardiac troponin T is part of the troponin complex that consists of three subunits and is involved in the calcium-sensitive switch that regulates the interaction of actin and myosin in striated muscles. Cardiac troponin T (molecular weight, 37 kd) binds to troponymosin. Cardiac troponin T exists in three different isoforms in striated muscles, one for slow-twitch, one for fast-twitch, and one for cardiac muscle. Cardiac troponin T was measured by an enzyme immunoassay (Boehringer Mannheim; Mannheim, Germany) that is specific for the cardiac isofrom and was developed by Katus et al. The upper limit of the reference interval of this assay was 0.2 µg/L; the cross-reactivity with purified skeletal troponin T was less than 1%.5

Statistical Analysis

Sensitivity (true positive test results of all patients with disease), specificity (true negative test results of all patients without disease), efficiency (true positive and negative test results of all positive and negative test results), positive and negative predictive values (true positive test results of all positive test results, true negative test results of all negative test results), and receiver operating characteristic curves with areas under curves were calculated to describe the diagnostic performances of parameters. Receiver operating characteristic curves with area under curves that describe the diagnostic performance of a markers best were calculated by maximum likelihood estimation of binormal receiver operating characteristic curves. Receiver operating characteristic curves were calculated and areas under curves were compared using software (ROCFIT, CLABROC, LABROC1) that was written and provided by Metz et al. (Department of Radiology, University of Chicago). A p value less than 0.05 was considered to indicate statistical significance.

The best combination of ECG and myocardial markers, including all their possible discriminator limits for the early diagnosis of acute myocardial infarction in relation to the time elapsed from the onset of chest pain, was found by the classification and regression trees method. Briefly, the method allows one to construct a binary tree structured classifier. The method starts with all patients and proceeds by repeated splits of patients into two descendant subsets. The fundamental idea is to select such splits that the data in the descendant subsets are "purer" with respect to the classification problem at hand; ie, each subset should contain as many as possible patients belonging to one certain class (eg, acute myocardial infarction) and as few as possible members belonging to all remaining classes (nonacute myocardial infarction). Optimal discriminator values for splits are derived from the data during analysis by testing all possible discriminators and are not settled by the investigators before. The sensitivity, specificity, efficiency, positive, and negative predictive values for this classification procedure were calculated.

Results

Diagnostic Performances of Each Parameter by Itself on Hospital Admission

The ECG was the tendentially most accurate parameter of all tested for the early diagnosis of myocardial infarction on presentation to the emergency department (Tables 1 and 2). The differences of areas under curve of ECG and clinical symptoms, creatine kinase, creatine kinase MB activity, and cardiac troponin T were significant. Within the group of biochemical markers, creatine kinase MB mass concentrations tended to be most accurate. However, only the differences between areas under curves of creatine kinase MB mass and its activity, and cardiac troponin T, were significant. The area under the receiver operating characteristic plot of creatine kinase MB mass concentration was also significantly greater than that of clinical symptoms. All other differences were not significant. Receiver operating characteristic curves of all investigated parameters are shown in Figure 1. Additional parameters that describe the diagnostic performances of parameters are shown in Tables 1 and 2. For the calculation of these parameters for biochemical markers (Table 2), we used optimized discriminator values according to the results of receiver operating characteristics analysis. The optimal discriminator on a receiver operating characteristic curve is the point with the largest deviation from the diagonal line that represents a worthless test in the plot (Fig 1).

The typical manifestations of myocardial ischemia and excessive autonomic nervous system activity are sensitive but not very specific for acute myocardial infarction and the presence or absence of typical infarct-related chest pain with or without symptoms of exces-
Table 2—Diagnostic Performances of Biochemical Markers for the Diagnosis of Acute Myocardial Infarction on Hospital Admission

<table>
<thead>
<tr>
<th>Discriminator Value</th>
<th>CK, 50 U/L</th>
<th>CKMB Activity, 8 U/L</th>
<th>CKMB Mass, 6.7 μg/L</th>
<th>Myoglobin, 50 pg/L</th>
<th>cTnT, 0.32 pg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.63</td>
<td>0.38</td>
<td>0.65</td>
<td>0.50</td>
<td>0.46</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.71</td>
<td>0.90</td>
<td>0.89</td>
<td>0.94</td>
<td>0.85</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.59</td>
<td>0.72</td>
<td>0.82</td>
<td>0.86</td>
<td>0.67</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.74</td>
<td>0.68</td>
<td>0.79</td>
<td>0.83</td>
<td>0.70</td>
</tr>
<tr>
<td>Efficiency</td>
<td>0.68</td>
<td>0.69</td>
<td>0.80</td>
<td>0.77</td>
<td>0.69</td>
</tr>
<tr>
<td>Area under ROC curve (mean±SE)</td>
<td>0.76±0.05</td>
<td>0.67±0.05</td>
<td>0.80±0.04</td>
<td>0.80±0.08</td>
<td>0.67±0.05</td>
</tr>
</tbody>
</table>

*cTnT=cardiac troponin T; CK=creatine kinase.

1Optimal discriminator values according to receiver operating characteristic (ROC) analysis are used. Of all possible discriminator limits of a parameter, these values show the largest deviation on the ROC plot from the diagonal line which represents a worthless test (Fig 1).

sive autonomic activity was of limited value for diagnosis (Table 1). Vice versa the presence of the ECG pattern “probable acute myocardial infarction” (mainly regional ST-segment elevations during the early phase of myocardial infarction) is very specific, but not very sensitive on emergency department admission. Thereby, especially non-Q-wave myocardial infarctions were frequently missed. Using the ECG pattern “possible myocardial infarction” as discriminator increased sensitivity, particularly for non-Q-wave infarctions, but resulted in lower efficiency and considerable loss of specificity (Table 1). The sensitivity of creatine kinase MB activity is too low to considerably support medical decision making on emergency department presentation. By contrast, creatine kinase MB mass concentration was more specific and sensitive than creatine kinase and creatine kinase MB activity (Table 2). The specificity of myoglobin was high, but the overall sensitivity of myoglobin was low. In three of four patients whose hospital admission was delayed for more than 10 h, myoglobin had already returned within the reference interval. All other biochemical markers were increased in these three patients. Cardiac troponin T had a lower sensitivity than creatine kinase MB mass, and its specificity for myocardial infarction was lower as well. Cardiac troponin T was increased in

Table 3—False-Positive Results for the Diagnosis of Myocardial Infarction in Patients Without Acute Coronary Syndromes*

<table>
<thead>
<tr>
<th>CKMB Mass</th>
<th>CKMB Activity</th>
<th>CK</th>
<th>Myoglobin</th>
<th>cTnT</th>
<th>ECG Pattern</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>8</td>
<td>108</td>
<td>&lt;50</td>
<td>0.1</td>
<td>Normal AMI</td>
<td>PE</td>
</tr>
<tr>
<td>9.3</td>
<td>8</td>
<td>61</td>
<td>62</td>
<td></td>
<td>Normal</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>6.6</td>
<td>4</td>
<td>14</td>
<td>68.5</td>
<td></td>
<td>Normal</td>
<td>PE</td>
</tr>
<tr>
<td>5.8</td>
<td>6</td>
<td>42</td>
<td>162</td>
<td>0.2</td>
<td>Uncodable</td>
<td>Arrhythmia with syncope</td>
</tr>
<tr>
<td>1.4</td>
<td>4</td>
<td>77</td>
<td>&lt;50</td>
<td>0.2</td>
<td>Normal</td>
<td>MD</td>
</tr>
<tr>
<td>73.2</td>
<td>13</td>
<td>123</td>
<td>244</td>
<td>2.0</td>
<td>Possible AMI</td>
<td>CMP with acute HF</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>138</td>
<td>&lt;50</td>
<td>0.2</td>
<td>Normal</td>
<td>MD</td>
</tr>
<tr>
<td>20.9</td>
<td>4</td>
<td>106</td>
<td>63</td>
<td>1.0</td>
<td>Probable AMI</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>4.6</td>
<td>3</td>
<td>87</td>
<td>&lt;50</td>
<td>0.2</td>
<td>Normal</td>
<td>Esophagitis</td>
</tr>
</tbody>
</table>

*Optimal discriminator values according to receiver operating characteristic analysis are used. The values given are the results of single measurements in the emergency department. cTnT=cardiac troponin T; CMP=cardiomyopathy; CK=creatine kinase; HF=heart failure; MD=musculoskeletal disorder; PE=pulmonary embolism; AMI=acute myocardial infarction.

The detection limit of the myoglobin assay used was 50 pg/L.
seven patients with unstable angina in whom creatine kinase MB mass and activity were not increased. Five of these seven patients showed ST-segment depression of 0.1 mV or greater in at least two leads of the presenting ECG. In four (three with ST segment depression) of these seven patients, cardiac troponin T was the only biochemical marker that was increased above optimal discriminators obtained by receiver operating characteristics. False-positive results of biochemical markers in patients without acute coronary syndromes are listed in Table 3.

Algorithm for the Early Diagnosis of Myocardial Infarction on Emergency Department Presentation in Relation to the Time From the Onset of Chest Pain

In the next step, we wanted to find the best combination of clinical symptoms, ECG, and myocardial markers for the early diagnosis of acute myocardial infarction in relation to the time elapsed from the onset of chest pain. For this purpose, we used classification and regression trees analysis of our data. The decision tree obtained is shown in Figure 2. Within 3 h after the onset of chest pain, we found that the presence of the ECG pattern “probable myocardial infarction” (that is mostly regional ST-segment elevations) was most accurate for diagnosis of acute myocardial infarction and myocardial markers or the presence or absence of typical clinical symptoms could not provide additional diagnostic information during this time period. However, non-Q-wave myocardial infarctions were frequently missed (Fig. 2). After 3 h, by contrast, creatine kinase MB mass concentration with a discriminator value of 6.7 µg/L was the most informative myocardial marker and was more accurate than the presence or absence of typical infarct-related symptoms and was even more accurate than the ECG. A combination of myocardial markers did not improve diagnostic accuracy. The subsequent split between Q-wave and non-Q-wave infarction was of course based on ECG, that is the presence of the “probable myocardial infarction” pattern. This algorithm could efficiently differentiate acute myocardial infarction patients at the time of hospital admission from the others and had a diagnostic sensitivity of 0.91, a specificity of 0.90, a positive predictive value of 0.90, a negative predictive value of 0.90, and an efficiency of 0.90. Thus, this decision tree allowed us to classify markedly more patients correctly than each tested parameter by itself did (Tables 1 and 2).

Discussion

Based on clinical symptoms, ECG, and measurements of established and new biochemical myocardial markers, we developed an algorithm for the early diagnosis of acute myocardial infarction on emergency department presentation. This classification procedure was clearly superior to each tested parameter by itself. For this novel approach, we used the classification and regression trees method for data analysis that requires
laborious computations in the process of defining the structure of the classification tree. The ability of this method to predict a diagnosis is as high as that of other statistical methods, such as linear discriminant analysis or neuronal nets. Its main advantage over these methods and an attractive feature for everyday clinical decision making is that the result of the analysis (a very simple decision model) can be easily applied for the classification of unknown patients. It involves only a series of simple binary decisions rather than requiring more or less complicated function evaluations such as, for example, linear discriminant models. This is essential for the application of study results in clinical practice. Our findings can be briefly summarized: if a patient is admitted to the hospital within 3 h after the onset of chest pain, one should look for the presence of regional ST segment elevations in the ECG, and if admission is delayed for more than 3 h, one should order creatine kinase MB mass concentration measurement and use ECG for the differential diagnosis of Q-wave and non-Q-wave myocardial infarction. Subsequently serial ECG recordings and creatine kinase MB measurements are required to confirm the diagnosis, because transit or stable ST-segment elevation could be due to other than myocardial infarction mechanisms.

Rapid automated assays (turnaround time, approximately 10 to 20 min depending on the manufacturer; used method, 15 min) for measurement of creatine kinase MB mass concentration are available and are also suitable for “stat” determinations, which are prerequisites for the use of our decision tree in clinical practice. If transportation and centrifugation of the sample, spinning, and reporting are taken with the determination time, the emergency department physician knows the creatine kinase MB mass test result 30 min after blood withdrawal at best, in clinical practice usually after 45 to 60 min. A system suitable for quantitative bedside determinations of creatine kinase MB mass concentrations has been developed by a manufacturer (assay time approximately 10 min). Separation of the plasma from blood cells is also necessary using this system. Therefore, test results are not available before 20 to 30 min. However, rapid whole blood assays will be available in the near future for an even quicker bedside measurement of creatine kinase MB mass and other myocardial markers. One has to be cautious when using the 6.7-μg/L discriminator value that we found with creatine kinase MB mass assays of other manufacturers. Unfortunately, at present, creatine kinase MB mass assays are not yet standardized. Although measuring results of different assays usually correlate very closely, the test results are not identical. As a consequence, the optimal discriminator value for the discrimination acute myocardial infarction/non-

acute myocardial infarction may be different depending on the assay used.

During the first 3 h after the onset of chest pain—not unexpectedly—the diagnostic accuracy of the ECG was superior to all biochemical myocardial markers and biochemical markers are not ideally suited for the diagnosis of acute myocardial infarction during this time interval. Regional ST segment elevations may occur even within 30 s after the onset of coronary occlusion, whereas the release and appearance of myocardial proteins in the peripheral circulation are more time-requiring processes. The sensitivity and specificity of the ECG and of typical infarct-related symptoms for the diagnosis of acute myocardial infarction on hospital admission that we found were in the range of previously reported values for these two parameters. The presence or absence of typical infarct-related symptoms was of limited value for the diagnosis of myocardial infarction in nontraumatic chest pain patients. The biochemical markers could not provide additional diagnostic information to the ECG during the 0 to 3-h period after the onset of chest pain. Recently, Lee et al reported a similar finding. Myoglobin, creatine kinase, and creatine kinase MB activity measurements were not as useful as the ECG for the diagnosis of acute myocardial infarction on admission to a coronary care unit. The mean duration of chest pain of the acute myocardial infarction patients investigated by Lee et al was 3.2 h. In this investigation, creatine kinase MB mass and cardiac troponin T were not measured and the dependence of diagnostic accuracy on the time from the onset of chest pain was not considered. Our study, by contrast, tested the diagnostic performance of a combination of clinical symptoms, ECG, creatine kinase, creatine kinase MB activity, creatine kinase MB mass, myoglobin, and cardiac troponin T in relation to the duration of chest pain. Most interestingly, after 3 h from the onset of chest pain, creatine kinase MB mass concentrations could more accurately separate the myocardial infarction patients from the others than the ECG, clinical symptoms, and all the other biochemical myocardial markers tested. We could confirm that measurement of creatine kinase MB activity is not helpful for the early diagnosis of acute myocardial infarction. The sensitivities of creatine kinase and creatine kinase MB activity were lower compared with creatine kinase MB mass concentration. Interestingly, in this preselected population with nontraumatic chest pain, the specificities of creatine kinase MB and myoglobin were in the same range, because our study population did not include patients with extensive concomitant skeletal muscle damage. However, the overall sensitivity of myoglobin was surprisingly low. This is largely explained by the distribution of the delay of our acute
myocardial infarction patients and the relatively small diagnostic window of myoglobin. About 50% were admitted to the hospital within 2 h after the onset of chest pain, and during this time period, even the sensitivity of myoglobin is not sufficiently high (≤23%). However, in three of four patients whose hospital admission was delayed for more than 10 h, myoglobin had already returned within the reference interval. All other biochemical markers were still increased in these three patients.

The limited analytical sensitivity (detection limit, 50 μg/L) of the rapid assay used may also negatively impair diagnostic sensitivity. Cardiac troponin T had a lower early sensitivity than creatine kinase MB mass, and its specificity for myocardial infarction was somewhat lower as well. The latter is mainly explained by the fact that cardiac troponin T was increased in seven patients with unstable angina in whom creatine kinase MB mass concentrations were not increased. A bias toward creatine kinase MB has to be certainly considered when comparing the specificities of creatine kinase MB and cardiac troponin T for myocardial infarction, because increases in creatine kinase MB activity were included as one criterion for the diagnosis of definite acute myocardial infarction. This study corroborates earlier reports that increases in cardiac troponin T may be found in patients with unstable angina at rest in whom creatine kinase MB level is not elevated. Consequently, the specificity of cardiac troponin T is lower than that of creatine kinase MB when standard myocardial infarction criteria are used for definite diagnosis as it was done in our study. However, myocardial damage is likely in these patients, because unstable angina continuously ranges from no myocardial damage to non-Q-wave myocardial infarction. In addition, patients with myocarditis or cardiomyopathy and increased markers tested only false-positive in respect of the diagnosis “myocardial infarction” and not regarding the more comprehensive diagnosis “myocardial damage.” The latter was very likely in these patients, and markers are released after myocardial damage regardless of the underlying cause.

We recognize some limitations of this study. Patients were not enrolled consecutively, which decreases to some extent the generalizability of our study results to the typical population presenting to the emergency department. Creatine kinase MB isomeric ratio gained particular interest as an early marker for acute myocardial infarction during recent years, but creatine kinase isomers were not measured in this study. However, this is only a minor limitation, because recently it has been demonstrated that the early sensitivities of creatine kinase MB isomeric ratio and creatine kinase MB mass are equal. In future studies, the use of creatine kinase MB mass for the early diagnosis of myocardial infarction will also have to be evaluated against echocardiography and myocardial scintigraphy.

We found that after 3 h from the onset of chest pain, creatine kinase MB mass concentrations more accurately predicted myocardial infarction than the ECG. Nevertheless, physicians should give priority to recording an ECG regardless of the moment of entry in the emergency department. In patients with positive diagnostic ECGs, it is unacceptable to delay reperfusion therapy only because of waiting for the creatine kinase MB mass test result and additionally the ECG is the basis for the differential diagnosis of Q-wave and non-Q-wave myocardial infarction. However, as mentioned above, new assays for creatine kinase MB mass will provide results very rapidly and only a few minutes later than the time period needed for recording and interpretation of the ECG. But even then, our algorithm will be more important to confirm a suspected myocardial infarction rapidly than for the first selection of possible candidates for thrombolytic therapy, because the therapeutic consequences of early diagnosis of acute myocardial infarction in patients with nondiagnostic presenting ECG are not yet clearly delineated. There is currently no information regarding biochemical guidelines for commencing thrombolytic therapy or giving thrombolytic therapy to patients with ST-T changes alone. Therefore, at present, the decision for or against fibrinolysis is usually made clinically and electrocardiographically and will only in rare instances rely on the demonstration of increased myocardial markers. The accuracy of the ECG was superior to creatine kinase, creatine kinase MB mass and activity, myoglobin, and cardiac troponin T during the 0 to 3-h period after the onset of chest pain, which makes it unlikely that these biochemical markers will play a major role for the decision regarding reperfusion therapy in the future as well. Serum markers and diagnostic strategies that are also based on myocardial marker measurement, such as the presented decision tree, are, however, important to confirm a suspected myocardial infarction, may decide the diagnosis in difficult cases, and may be also useful for more rapid and accurate triaging of chest pain patients, for which there is an increasing demand.

In summary, the decision tree obtained is based on only the presenting ECG recording and the myocardial marker levels of the initial blood sample that was drawn immediately after emergency department admission. Nevertheless, this algorithm could accurately (90% correctly classified patients) separate the patients with acute myocardial infarction from the others, and, therefore, it could be a valuable diagnostic aid to emergency department physicians for confirming a suspected myocardial infarction rapidly.

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