A Clinical Prediction Rule for Early Discharge of Patients With Chest Pain

Jim Christenson, MD
Grant Innes, MD
Douglas McKnight, MD
Christopher R. Thompson, MD
Hubert Wong, PhD
Eugenia Yu, MSc
Barb Boychuk, BSc
Eric Grafstein, MD
Frances Rosenberg, MD, PhD
Kenneth Gin, MD
Aslam Anis, PhD
Joel Singer, PhD

From the University of British Columbia (Christenson, Innes, McKnight, Thompson, Wong, Yu, Boychuk, Grafstein, Rosenberg, Gin, Anis, Singer); St. Paul’s Hospital (Christenson, Innes, Thompson, Boychuk, Grafstein, Rosenberg); Vancouver Hospital (McKnight, Gin); and the Center for Health Evaluation and Outcome Sciences (Christenson, Innes, Grafstein, Wong, Yu, Anis, Singer) Vancouver, British Columbia, Canada.

Study objective: Current risk stratification tools do not identify very-low-risk patients who can be safely discharged without prolonged emergency department (ED) observation, expensive rule-out protocols, or provocative testing. We seek to develop a clinical prediction rule applicable within 2 hours of ED arrival that would miss fewer than 2% of acute coronary syndrome patients and allow discharge within 2 to 3 hours for at least 30% of patients without acute coronary syndrome.

Methods: This prospective, cohort study enrolled consenting eligible subjects at least 25 years old at a single site. At 30 days, investigators assigned a diagnosis of acute coronary syndrome or no acute coronary syndrome according to predefined explicit definitions. A recursive partitioning model included risk factors, pain characteristics, physical and ECG findings, and cardiac marker results.

Results: Of 769 patients studied, 77 (10.0%) had acute myocardial infarction and 88 (11.4%) definite unstable angina. We derived a clinical prediction rule that was 98.8% sensitive and 32.5% specific. Patients have very low risk of acute coronary syndrome if they have a normal initial ECG, no previous ischemic chest pain, and age younger than 40 years. In addition, patients at least 40 years old and with a normal ECG result, no previous ischemic chest pain, and low-risk pain characteristics have very low risk if they have an initial creatine kinase-MB (CK-MB) less than 3.0 $\mu$g/L or an initial CK-MB greater than or equal to 3.0 $\mu$g/L but no ECG or serum-marker increase at 2 hours.

Conclusion: The Vancouver Chest Pain Rule for early discharge defines a group of patients who can be safely discharged after a brief evaluation in the ED. Prospective validation is needed. [Ann Emerg Med. 2006;47:1-10.]

INTRODUCTION

Background

Approximately 15% to 25% of patients who present to emergency departments (EDs) with undifferentiated chest pain prove to have acute coronary syndrome within 30 days. US data suggest that 2.1% of patients with acute myocardial infarction and 2.3% of patients with unstable angina are initially misdiagnosed, whereas a recent Canadian study identified 11 of 241 (4.6%) missed cases of acute myocardial infarction and 10 of 157 (6.4%) cases of missed unstable angina. Chest pain units reduce the rate of missed myocardial infarction but do so in part by including very-low-risk patients in extensive rule-out myocardial infarction protocols.

Many investigators have developed chest pain risk stratification tools. Goldman et al developed a clinical/ECG algorithm that identified patients with less than 7% risk of acute chest pain as very-low-risk patients and safely discharged them from the ED. However, such algorithms may not be applicable to all EDs or settings.
myocardial infarction. Limkakeng et al subsequently found that 4.9% of patients who had low-risk Goldman criteria and a negative initial troponin I assay result experienced death, acute myocardial infarction, or revascularization within 30 days. Pozen et al developed a 7-item predictive equation that reduced coronary care unit admissions but not inappropriate discharges. Selker et al modified this to create the acute cardiac ischemia time-insensitive predictive instrument (ACI-TIP1), which defined low risk as less than 10% chance of acute coronary syndrome. The Erlanger protocol is an intense 2-hour assessment that includes serial ECGs and creatine kinase-MB (CK-MB) and troponin measurements, but it does not define a subset of patients who can forgo nuclear stress testing. The American Heart Association/Agency for Health Care Policy and Research guidelines suggest early discharge only for patients with “evidence” of an alternate diagnosis. Unfortunately, few patients clearly fall into this category. Our own study of patients with chest pain who were eligible for discharge after 2 hours of presentation. This study did not prospectively evaluate this rule.

Not surprisingly, this study found that patients younger than 40 years and with normal initial ECG results and no previous ischemic chest pain were at very low risk of acute coronary syndrome. Additionally, patients older than 40 years had low-risk if they had a normal ECG result, no previous ischemic chest pain, low risk chest pain characteristics, and an initial creatine kinase-MB (CK-MB) less than 3.0 ug/L or an initial CK-MB greater than 3.0 ug/L but without an increase or ECG changes within 2 hours.

This derivation study should not change clinical practice because it has not yet been validated. It does, however, provide support for the general belief that young patients with a normal ECG result and no cardiac risk factors are at very low risk of an adverse cardiovascular event.

Editor’s Capsule Summary

What is already known on this topic
Although several algorithms and computer programs have been developed for emergency department (ED) patients with potential acute coronary syndrome, none has achieved sufficient accuracy to allow safe and rapid discharge of ED chest pain patients.

What question this study addressed
This study developed a clinical decision rule to identify low-risk ED chest pain patients who can be safely discharged within 2 hours of presentation. This study did not prospectively evaluate this rule.

What this study adds to our knowledge
Not surprisingly, this study found that patients younger than 40 years and with normal initial ECG results and no previous ischemic chest pain were at very low risk of acute coronary syndrome. Additionally, patients older than 40 years had low-risk if they had a normal ECG result, no previous ischemic chest pain, low risk chest pain characteristics, and an initial creatine kinase-MB (CK-MB) less than 3.0 ug/L or an initial CK-MB greater than 3.0 ug/L but without an increase or ECG changes within 2 hours.

How this might change clinical practice
This derivation study should not change clinical practice because it has not yet been validated. It does, however, provide support for the general belief that young patients with a normal ECG result and no cardiac risk factors are at very low risk of an adverse cardiovascular event.

Importance
Clinical prediction rules are decisionmaking tools for clinicians that contain elements of the medical history, physical examination, and simple diagnostic tests. An objective clinical prediction rule to identify very-low-risk patients with chest pain who can be safely discharged without prolonged ED observation, expensive rule-out protocols, or provocative testing is needed. Such a rule would help reduce emergency crowding, minimize patient inconvenience, and improve cost-effectiveness of acute coronary syndrome diagnostic testing.

Goals of This Investigation
Our specific objective was to develop a clinical prediction rule that would improve on current practice by identifying patients with chest pain who are safe for discharge after 2 hours of ED evaluation. The rule will miss fewer than 2% of acute coronary syndrome patients and allow discharge within 2 to 3 hours of at least 30% of patients without acute coronary syndrome.

MATERIALS AND METHODS

Study Design
Using established methodology for clinical prediction rules, this prospective cohort study was conducted in 2 separate periods between June 29, 2000, and January 24, 2003, when research assistants were funded.

Setting and Selection of Participants
Patients presenting to St. Paul’s Hospital, an urban tertiary care ED, with a primary complaint of anterior or lateral chest pain were eligible for the study. Research assistants obtained informed consent and enrolled eligible patients between 7 AM and 10 PM 7 days per week. Patients were excluded if they were younger than 25 years, had a clear traumatic or radiologically evident cause, were enrolled in the study in the previous 30 days, had a terminal noncardiac illness, had severe communication problems, were without a fixed address in the province of British Columbia, or were without available telephone contact. The Providence Health Care Research Ethics Board approved the study protocol.

Data Collection and Processing
This report conforms to the published standard reporting guidelines for studies evaluating risk stratification of ED patients with potential acute coronary syndromes, although they were developed before this publication. A total of 123 potential predictor variables were screened (Figure 1). During the first 2 hours of the index visit, research assistants documented vital signs every 30 minutes, initiated ST-segment monitoring, and ensured that serial ECGs (0, 1, and 2 hours) were performed. Cardiac markers at 0 and 2 hours were evaluated on several platforms: creatine phosphokinase (Access,
**Pain and Associated Symptom Characteristics**

- Age*
- Sex
- Chest pain present on arrival?
- Chest pain continue at rest?
- Number of episodes in previous 24 hours*
- Number of episodes in previous week*
- Maximum duration of previous episode
- Diaphoresis
- Weakness
- Shortness of breath
- Nausea
- Vomiting
- Palpitations
- Syncope
- Dizziness/lightheadedness
- Radiation to left arm/shoulder*
- Radiation to right arm/shoulder*
- Radiation to back
- Radiation to neck*
- Radiation to jaw*
- Radiation to abdomen
- Radiation to lower limb
- Pain center of chest*
- Pain in left lateral chest
- Pain in right anterior chest
- Pain in right lateral chest
- Most prominent character of pain*
- Heavy chest discomfort
- Maximum discomfort level*
- Pain diagnosed in past as AMI*
- Pain diagnosed in past as angina*
- Pain diagnosed in past as either AMI or angina
- Pain worse with deep breaths*
- Pain worse with movement
- Pain worse in different positions
- Did pain improve within 5 minutes of nitroglycerin?*
- Did pain improve within 5 minutes of oxygen?
- Did pain improve within 5 minutes of liquid antacid?
- During 2 hours, did pain relieve and not return?*
- During 2 hours, did pain continue?*
- During 2 hours, did pain come and go?

**Physical Examination**

- Chest clear
- Crackles at bases
- Crackles to scapulae
- Wheezes
- Heart sounds normal
- Systolic murmur
- Diastolic murmur
- S3
- S4
- Carotid pulses equal with no bruit
- Radial pulses equal
- Chest tenderness reproducing pain*
- Right arm systolic pressure, left arm systolic pressure
- Systolic pressure <90 mm Hg in 2 hours
- Bradycardia <50 beats/min in 2 hours*
- Tachycardia >100 beats/min in 2 hours
- Jugular venous pressure*

**Risk Factors**

- Regular smoker
- Hx diabetes*
- Hx hypertension*

**ECG Findings**

- First ECG result normal*
- First ECG with only T-wave flattening*
- Aggregate of ECGs no ischemic changes*
- 2h ST segment monitoring (any ST elevation or ST depression)*

**Laboratory Markers**

- 0h CPK (Standard)*
- 2h CPK (Standard)*
- Difference in CPK (2 h–0 h) (Standard)*
- 0h Tn I or T (Standard)*
- 2h Tn I or T (Standard)*
- Difference in Tn I or T (2 h–0 h) (Standard)*
- 0h CRP
- 0h CK-MB (Biosite)*
- 2h CK-MB*
- Difference in CK-MB (2 h–0 hour) (Biosite)*
- 0h Tnl (Biosite)*
- 2h Tnl (Biosite)*
- Difference in Tnl (2 h–0 h) (Biosite)*
- 0h Myoglobin (Biosite)*
- 2h Myoglobin (Biosite)*
- Difference in myoglobin (2 h–0 h) (Biosite)*

**Cardiovascular History**

- Previous angina*
- Previous MI*
- Previous cardiac arrest
- Previous angiogram yes and previous lesion >50%*
- Previous angiogram and no lesion >50%
- Previous PCI*
- Previous peripheral vascular surgery
- Previous CAGB*
- Previous CVA
- Previous TIA
- Previous ventricular arrhythmia
- Previous atrial arrhythmia
- Previous unknown arrhythmia

**Medications**

- Previous ASA*
- Previous other antiplatelets
- Previous calcium-channel blockers
- Previous ACE inhibitor
- Previous digitals
- Previous β-blocker
- Previous Coumadin
- Previous low-molecular-weight heparin
- Previous nitrates*
- Previous lipid-lowering agents
- Previous antiarrhythmics
- Previous diuretics*
- Previous antihypertensives

**Figure 1.** List of all predictors collected for possible inclusion in the prediction rule. Those meeting criteria for inclusion in the model are identified with an asterisk.

AMI, Acute myocardial infarction; Hx, history; MI, myocardial infarction; PCI, percutaneous coronary intervention; CAGB, coronary artery bypass graft; CVA, cerebrovascular accident; TIA, transient ischemic attack; ASA, acetylsalicylic acid; ACE, angiotensin-converting enzyme.
Mortality with no acute coronary syndrome

% with CK-MB
% With chest pressure reproducing pain 16.6
% With pain increasing with a deep breath 32.8
% With pain radiating to left arm, jaw, or neck 59.0
% With pain similar to past MI or angina 27.0
% With abnormal initial ECG result 30.1
% With past angina 35.9
% With past MI 24.2

Mortality with no acute coronary syndrome or adverse event (%)

N (all patients) 165 604
First ECG result not normal 57.6% 22.6% 4.65 3.2–6.7
Age ≥40 y 99.4% 87.9% 22.55 3.8–908.0
Previous MI 35.8% 21.0% 2.09 1.4–3.1
Previous angina 53.9% 31.0% 2.61 1.8–3.8
Previous nitrate use 48.5% 23.8% 3.01 2.1–4.4
Previous angina, MI, or nitrate use 66.7% 40.6% 2.93 2.0–4.3

Table 2. Univariate predictive statistics for predictors used in the rule.

Predictor | Acute Coronary Syndrome | No Acute Coronary Syndrome | Odds Ratio* | 95% CI for Odds Ratio
--- | --- | --- | --- | ---
N (all patients) | 165 | 604 | | |
First ECG result not normal | 57.6% | 22.6% | 4.65 | 3.2–6.7
Age ≥40 y | 99.4% | 87.9% | 22.55 | 3.8–908.0
Previous MI | 35.8% | 21.0% | 2.09 | 1.4–3.1
Previous angina | 53.9% | 31.0% | 2.61 | 1.8–3.8
Previous nitrate use | 48.5% | 23.8% | 3.01 | 2.1–4.4
Previous angina, MI, or nitrate use | 66.7% | 40.6% | 2.93 | 2.0–4.3

<Table 1. Baseline characteristics and outcomes of patient cohort (n=769).>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y±SD)</td>
<td>58±14</td>
</tr>
<tr>
<td>Age range, y</td>
<td>25–93</td>
</tr>
<tr>
<td>% Male</td>
<td>62.0</td>
</tr>
<tr>
<td>% With diabetes</td>
<td>16.6</td>
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<tr>
<td>% Smokers</td>
<td>30.4</td>
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<tr>
<td>% With hypertension</td>
<td>38.2</td>
</tr>
<tr>
<td>% With hyperlipidemia</td>
<td>36.2</td>
</tr>
<tr>
<td>Median time from symptom onset to arrival in minutes (quartiles)</td>
<td>104 (52.5, 262)</td>
</tr>
<tr>
<td>Mean systolic BP on arrival (mm Hg±SD)</td>
<td>142±27</td>
</tr>
<tr>
<td>Mean pulse rate on arrival (beats/min±SD)</td>
<td>81±20</td>
</tr>
<tr>
<td>Mean respiratory rate on arrival (breaths/min±SD)</td>
<td>19±3</td>
</tr>
<tr>
<td>% With past MI</td>
<td>24.2</td>
</tr>
<tr>
<td>% With past angina</td>
<td>35.9</td>
</tr>
<tr>
<td>% With abnormal initial ECG result</td>
<td>30.1</td>
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<td>% With pain radiating to left arm, jaw, or neck</td>
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<tr>
<td>% With pain increasing with a deep breath</td>
<td>32.8</td>
</tr>
<tr>
<td>% With chest pressure reproducing pain</td>
<td>16.6</td>
</tr>
<tr>
<td>% With CK-MB &lt;3.0 μg/L on arrival</td>
<td>63.5</td>
</tr>
<tr>
<td>% With any increase in Tn during 2 hours</td>
<td>19.5</td>
</tr>
<tr>
<td>% With any increase in CK-MB during 2 hours</td>
<td>41.8</td>
</tr>
</tbody>
</table>

30-Day outcomes (%)

Definite AMI | 77 (10.0) |
Definite unstable angina | 88 (11.4) |
Possible unstable angina | 29 (3.7) |
AE but no acute coronary syndrome | 32 (4.2) |
No acute coronary syndrome or adverse event | 543 (70.6) |
Overall 30-day mortality | 9 (1.2) |
Mortality with AMI (%) | 5 (6.5) |
Mortality with definite unstable angina (%) | 1 (1.0) |
Mortality with possible unstable angina (%) | 0 |
Mortality with no acute coronary syndrome but an adverse event (%) | 2 (2.6) |
Mortality with no acute coronary syndrome and no adverse event (%) | 1 (0.2) |

Beckman Coulter, Mississauga, Ontario, Canada), troponin I (Access and Biosite Triage, San Diego, CA), troponin T (Roche Elecsys, Hoffman LaRoche, LaValle, Quebec, Canada), myoglobin (Biosite Triage), and CK-MB (Biosite Triage). Serum markers ordered by research protocol but not for clinical purposes were unavailable to clinicians. They acquired chest pain characteristics, patient risk factors, and medical history independently of clinicians and recorded physical findings determined by emergency physicians, provisional emergency diagnosis, admission and discharge times, consultations, cardiac medications administered, other cardiac investigations, hospital discharge diagnoses, and predefined adverse events.

Adverse events included death, tachycardia requiring intervention, bradycardia requiring intervention, assisted ventilations, proven pulmonary thromboembolism, proven aortic aneurysm or dissection, new congestive heart failure requiring intravenous therapy, hypotension requiring intervention, chest compressions, percutaneous intervention, and coronary artery bypass grafting.

Interobserver reliability was estimated by having a second emergency physician blindly evaluate 95 patients. At 30 days, research staff telephoned patients to review current medications, physician visits, and hospital visits. Reports of all diagnostic tests performed during the 30 days in any setting were obtained, and relevant physicians were contacted for confirmation of any new diagnoses. In cases in which patient contact was lost, other city hospital records were reviewed to...
identify hospital visits, procedures, and new diagnoses, and the study list was cross-referenced against the British Columbia Death Registry.

**Outcome Measures**

Investigators used predefined explicit criteria to assign a 30-day outcome diagnosis of acute myocardial infarction, definite unstable angina, possible unstable angina, or no acute coronary syndrome. The primary outcome was definite acute coronary syndrome (acute myocardial infarction or definite unstable angina). The diagnosis of acute myocardial infarction required any one of the following: (1) a CK-MB increase definite for acute myocardial infarction based on the specific hospital criteria or troponin I level greater than or equal to 1.0 μg/L; (2) a troponin I increase (>0.1 μg/L but ≤1.0 μg/L) with dynamic ECG changes consistent with ischemia, a coronary angiogram with greater than 70% lesion, a positive stress test result (radionuclide scan, echocardiogram, or ECG), or urgent revascularization; (3) ECG evolution consistent with acute myocardial infarction; (4) fibrinolytic therapy or primary angioplasty and a clinical diagnosis of acute myocardial infarction; or (5) death with no other definite cause found in pre- or postmortem investigation. The diagnosis of definite unstable angina required rest pain greater than or equal to 20 minutes and at least 1 of the following related to the presenting symptoms: (1) troponin increase 0.1 to 0.99 μg/L but no other acute myocardial infarction criteria, (2) dynamic ECG changes consistent with ischemia in 2 contiguous leads (dynamic ST depression >0.5 mm or dynamic deep T-wave inversion) but no persistent ST elevation, (3) a coronary angiogram with greater than 70% lesion plus hospital admission for acute coronary syndrome, or (4) a positive stress test result (radionuclide scan, echo, or ECG stress test) plus admission for acute coronary syndrome.

If a diagnosis could not be assigned or if an investigator assigned a diagnosis of “no acute coronary syndrome” despite objective criteria (eg, positive troponin assay result), or if an investigator assigned a diagnosis of “definite unstable angina” based on only a positive troponin assay result, 2 cardiologist coinvestigators independently reviewed all clinical data and assigned an adjudicated outcome diagnosis. If necessary, final diagnosis was based on agreement of any 2 adjudicators and the principal investigator. If all 3 disagreed, the final outcome was the most significant diagnosis.

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**Figure 2.** Decision tree.
Investigators reviewed all ECGs in a structured format to identify T-wave flattening, T-inversion in 2 contiguous leads, ST depression (≥0.05 mV) in 2 contiguous leads, ST-elevation (≥0.1 mV in limb leads or ≥0.2 mV in precordial leads), and the presence of left bundle-branch block, paced rhythm, or left ventricular hypertrophy. In addition, investigators blinded to final outcome reviewed all ECGs for each patient and recorded their impression of the likelihood of ischemia. Evaluation of all available ECGs was used for outcome determination.

Evaluation of ECGs up to 2 hours was used as predictors in the rule.

**Primary Data Analysis**

Data were collected on specific study data forms and entered into an Oracle database (Oracle Corporation, Redwood City, CA, USA). Proportions, medians, means, and SDs were calculated and multiple clinical prediction rules were derived using the S-Plus (Insightful Corp., Seattle, WA) “rpart” recursive partitioning module. The algorithm was run using all of the default options except that a 10:1 loss was specified for missed acute coronary syndrome patients versus missed non-acute coronary syndrome patients. This higher penalty on missed acute coronary syndrome patients encouraged the algorithm to choose splits that maximized sensitivity and so reduce the complexity of the model. Cut points for continuous predictors were chosen initially by the algorithm and then rounded to convenient values by the investigators, and the patients were reclassified based on rounded values. Predictor variables were allowed in the model if they were univariately associated with the primary outcome (\(P<.2\)). In addition, variables subjected to interpretation (medical history and physical examination findings) were included if they were reliable (lower bound of confidence [95%] was at least 0.4 for the reliability measure; prevalence and bias adjusted \(k\) coefficient for dichotomous variables and intraclass correlation coefficient for continuous variables).

Investigators reviewed each derived rule for clinical relevance. Nodes with small numbers of patients were reaggregated and recursive partitioning was reinstated to simplify the branch points. This modification, although not previously described, makes clinical sense and reduces the chance of selecting a nonoptimal splitting variable when partitioning groups with smaller sample sizes. The simplest, most specific prediction rule that met the goal of sensitivity greater than 98% was chosen.

We do not report confidence intervals (CI) around the sensitivity and specificity values, because these values arise as a consequence of the rule development process, not as an evaluation of a fixed rule. Specifically, the sampling variability in the estimated sensitivity cannot be assessed because different
samples lead to different rules (all of which are forced to satisfy the "at least 98% sensitive" criterion). Meaningful CIs will be obtained in the validation phase.

The sample size of 800 patients was chosen so that equal numbers would be used in rule development and in subsequent rule validation. In the validation phase, the aim is to confirm that the sensitivity of the rule exceeds current practice (ie, to obtain a lower bound on the 95% CI for sensitivity of acute coronary syndrome detection that is no less than 0.95). Assuming that the true sensitivity is of the rule is 0.98, roughly 187 positive cases (800 patients in total) are needed to achieve this lower bound with 90% probability.

RESULTS

We enrolled 819 patients and subsequently excluded 50 patients from analysis, 31 who met exclusion criteria and 19 who were lost to follow-up. Of the 19 lost to follow-up, 14 were known to be alive at subsequent hospital visits, and the other 5 did not appear in the provincial death registry. Table 1 summarizes baseline characteristics and outcomes for the 769 patients analyzed showing 30-day diagnosis was acute myocardial infarction in 77 (10.0%) and definite unstable angina in 88 (11.4%). Documented adverse events related or unrelated to acute coronary syndrome included tachycardia (35), bradycardia (14), assisted ventilations (4), proven pulmonary thromboembolism (5), proven thoracic aortic aneurysm or dissection (0), new congestive heart failure requiring intravenous therapy (12), hypotension requiring intervention (9), and chest compressions (2). Eighty-three patients had percutaneous intervention and 31 had coronary artery bypass grafting within 30 days.

Of the 123 possible predictor variables screened, 48 were retained for entry into the recursive partitioning algorithm. Table 2 lists the variables selected for the rule by diagnostic groups with respective univariate statistics and P values. These variables include a normal ECG result (which could include T-wave flattening but no ST deviation or T-wave inversion), age, previous ischemic pain, 3 pain descriptors, 1 physical finding, and both CK-MB and troponin results. Reliability measures (95% CI) for clinical subjective variables were pain radiates to neck, 0.68 (95% CI 0.54 to 0.83); pain radiates to jaw, 0.81 (95% CI 0.69 to 0.93); pain radiates to left arm, 0.79 (95% CI 0.67 to 0.91); and chest tenderness reproduces pain, 0.63 (95% CI 0.45 to 0.80).

Table 2. Diagnostic accuracy of the rule.*

<table>
<thead>
<tr>
<th></th>
<th>Definite Acute Coronary Syndrome</th>
<th>No Definite Acute Coronary Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsuitable for early discharge</td>
<td>163</td>
<td>408</td>
</tr>
<tr>
<td>Meet rule criteria for early discharge</td>
<td>2</td>
<td>196</td>
</tr>
<tr>
<td></td>
<td>165</td>
<td>604</td>
</tr>
</tbody>
</table>

*Sensitivity 98.8%; specificity 32.5%; positive predictive value 28.5%; negative predictive value 99.0%

allows the early discharge process to be divided into 2 sequential stages.

The 2 missed patients were subsequently diagnosed with unstable angina. A 66-year-old woman was diagnosed 8 days later by outpatient nuclide stress testing, with no subsequent admission or adverse event. The other was a 52-year-old patient with a clear history of new and accelerating angina before rest pain who was treated medically for a single critical lesion not amenable to intervention. During validation, we will clarify the definition of past angina to include a recent history of typical angina of effort whether diagnosed or not.

LIMITATIONS

Although we used accepted and validated methodology,15 the Vancouver Chest Pain Prediction Rule was developed in 1 cohort of patients in a single center. We are currently beginning validation of the rule, and it will subsequently require evaluation of implementation in multiple centers. Our criterion standard for definite acute coronary syndrome was not based on mandated investigations but on a careful evaluation of all tests and visits during 30 days. It is possible that we missed some patients with silent events. The cohort was collected during day and evening hours and will require validation in patients presenting at all hours of the day. The rule is modestly complex and may be difficult to remember, which could limit its use by clinicians. However, the rule is largely intuitive, and simple memory aids (eg, pocket cards or PDA algorithms) will enhance implementation once the rule is validated. It is important to note that although our focus was on identifying patients with very low risk of acute coronary syndrome, no patients were missed with pulmonary embolism or aortic dissection. Suspicion of other life-threatening conditions requires appropriate, independent investigations. In retrospect, this rule development should have included patients 24 hours per day. Ideally, the study would be strengthened by mandating initial and 30-day imaging studies to improve the criterion standard of acute coronary syndrome. The cost implications of the Vancouver Chest Pain Rule are not yet known.

DISCUSSION

Patients who present to the ED with chest pain fall into 3 categories: those with objective ischemia who need admission...
and treatment, those with a clear noncardiac cause, and those who require a diagnostic process to rule out acute coronary syndrome and other life-threatening conditions. The Vancouver Chest Pain Rule identifies 32.5% of patients who do not have acute coronary syndrome using information available in the first 2 hours of the ED visit. These very-low-risk patients are identified with minimal error, in fact including only 1.2% of those who do have unstable angina or acute myocardial infarction. This information can be integrated into the decision framework of the emergency physician who continually evaluates patients for safe and appropriate disposition.

This prediction rule is different from previous risk stratification tools. In 1988, Goldman et al6 developed a clinical/ECG algorithm that identified patients with less than 7% risk of acute myocardial infarction. This was not designed to detect patients with unstable angina and it did not improve disposition decisions relative to experienced clinician judgment alone. Limkakeng et al27 later reported that 4.9% of patients with low-risk Goldman criteria and a negative initial troponin I level experienced death, acute myocardial infarction, and revascularization within 30 days. Lee et al19 and Goldman et al20 subsequently developed a strategy to identify patients unlikely to have acute myocardial infarction and criteria to identify patients who need coronary care unit admission. These criteria required 12 to 24 hours of observation and did not facilitate early ED disposition decisions.21 Pozen et al8 developed and tested a predictive equation using 7 clinical and ECG variables. After application of this instrument, inappropriate coronary care unit admissions fell from 24% to 17%, but the 3% inappropriate discharge rate was unchanged. Selker et al10-12 modified the Pozen et al8 equation and linked it to ECG findings, creating an electronic tool called the ACI-TIPI. This tool increased the rate of appropriate discharges by unsupervised residents but did not change the performance of attending physicians. Of note, ACI-TIPI defines low risk as less than 10% chance of acute myocardial infarction or unstable angina, and few clinicians will discharge patients with this level of risk.22

In 1992, Baxt23 and Baxt and Skora24 “trained” neural networks to recognize acute myocardial infarction and, in 1993, Jonshu et al25 developed a sensitive computer-derived algorithm. Doyle et al26 studied 9 algorithms but found none that improved clinical decision making. The recently described Thrombolysis in Myocardial Infarction (TIMI) Risk score27 is an excellent stratification tool but was derived from studies of patients with objective evidence of acute coronary syndrome and has not been validated in undifferentiated ED patients with chest discomfort. The Erlanger protocol28 is an intense 2-hour assessment that includes serial ECGs, 2 CK-MB and troponin measurements, clinical judgment, and nuclear stress testing. It is the most detailed published protocol designed to facilitate early discharge but requires nuclear imaging to increase sensitivity from 80% to 99%. None of the above stratification tools help clinicians identify patients who are safe to discharge after a brief ED evaluation.

Recent American College of Cardiology/American Heart Association14 guidelines recommend that all patients with a compatible history have serial marker testing until 9 hours after symptom onset, followed by provocative testing. Applying this guideline in the ED, where most patients have ill-defined chest discomfort, could greatly increase diagnostic and ED bed utilization without a corresponding improvement in patient outcomes. The ED/AHCRP guidelines and the Toronto Heart Centre ACS Guidelines29 recommend excluding patients with discomfort because of other causes from the diagnostic pathway, but neither suggests a process for identifying these patients.

The Vancouver Chest Pain Rule is unique in its ability to identify very-low-risk patients who are suitable for early discharge. It is also unique in that it identifies patients in a clinically logical stepwise process with a minimum of investigations. First, age, initial history, and ECG findings identified 56 of 198 patients who ultimately meet rule criteria. A further 121 patients were identified based on initial CK-MB and low-risk pain characteristics. The last 21 patients were identified by the absence of changes in the ECG or serum markers during 2 hours. If disposition according to the rule was implemented in this stepwise manner, ED lengths of stay and investigational costs could be reduced substantially in many settings.

Some would argue that the age criteria might result in missing younger patients with myocardial infarction, but age is in fact a powerful predictor, and the low-risk group younger than 40 years is also defined by a near-normal ECG and the absence of past myocardial infarction or angina. Marsan et al30 recently studied 1032 patients younger than 40 years and presenting with chest pain and found that those with no cardiac history and either no cardiac risk factors or a normal ECG result had less than 0.5% 30-day risk of acute coronary syndrome.

We found that CK-MB at a low threshold was consistently a better discriminator than any level of troponin, surprising because many studies suggest troponin is the superior marker. Our findings are not unique, and at least 1 other investigator has reported that CK-MB was more predictive of acute coronary syndrome than troponin early in the patient’s presentation.31 Laboratory technicians used the Triage (Biosite) point-of-care device, and we attribute the greater discriminatory power of CK-MB over troponin to its better analytic performance within the normal range. The reported 99th percentile for troponin on the Triage point-of-care device is actually the detection limit (0.19 μg/L), whereas the 95th percentile for CK-MB (usual cutoff) is well above the detection limit (0.75 μg/L). de Winter et al32 determined that an increase in CK-MBmass greater than 2 μg/L represents the critical difference between 2 results for the detection of myocardial damage. We hypothesize that it is the absence of a critical increase over baseline value (median 1.5 μg/L) that underlies the discriminatory power of a CK-MB level less than 3 μg/L. In comparison, present troponin methods do not permit the detection of a change within the normal range.
An early discharge strategy such as the one developed here defines patients safe for early discharge and reduces the number who require more definitive testing but also defines the companion group of patients who are not clearly “safe” and require further investigations. To maximize diagnostic efficiency, a more prolonged “chest pain unit” rule-out strategy should be applied to patients without objective ischemia who do not meet early discharge criteria.

In summary, the Vancouver Chest Pain Rule defines a group of chest pain patients who can be safely discharged from the ED in the first few hours after arrival. If validated in an independent cohort, it will improve the process of diagnostic decisionmaking in patients presenting with chest pain.

The authors are grateful for the support and data supplied by the physicians and nurses at St. Paul’s Hospital, Vancouver, Canada, and for the dedication of Patti Lawson, BA, and Courtney Barker.

Supervising editor: Judd E. Hollander, MD

Author contributions: DM, HR, EY, EG, FR, AA, and JS helped design the study, analyzed the data, and reviewed the manuscript. BB helped design the study, collected data, and reviewed the manuscript. JMC, GI, and CRT conceived and designed the study, collected data, and wrote the manuscript. BB helped design the study, collected data, and wrote the manuscript. JMC takes responsibility for the paper as a whole.

Funding and support: Canadian Institutes of Health research grant MOP 53102 and Heart and Stroke Foundation of British Columbia and Yukon Grant. Materials for analysis of some laboratory testing were donated by Biosite.

Publication dates: Received for publication March 17, 2005. Revision received June 13, 2005. Accepted for publication July 13, 2005. Available online October 19, 2005.

Reprints not available from the authors.

Address for correspondence: Jim Christenson, MD, Department of Emergency Medicine, St. Paul’s Hospital, 1081 Burrard Street, Vancouver, British Columbia V6Z 1Y6, Canada; 604-806-8985, fax 604-806-8798; E-mail jimchris@interchange.ubc.ca.

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Clinical Prediction Rule for Early Discharge of Chest Pain Patients

Christenson et al


