Development and validation of a prediction rule for early discharge of low-risk emergency department patients with potential ischemic chest pain

ABSTRACT

Objectives: Current guidelines emphasize that emergency department (ED) patients at low risk for potential ischemic chest pain cannot be discharged without extensive investigations or hospitalization to minimize the risk of missing acute coronary syndrome (ACS). We sought to derive and validate a prediction rule that permitted 20 to 30% of ED patients without ACS safely to be discharged within 2 hours without further provocative cardiac testing.

Methods: This prospective cohort study enrolled 1,669 chest pain patients in two blocks in 2000–2003 (development cohort) and 2006 (validation cohort). The primary outcome was 30-day ACS diagnosis. A recursive partitioning model incorporated reliable and predictive cardiac risk factors, pain characteristics, electrocardiographic findings, and cardiac biomarker results.

Results: In the derivation cohort, 165 of 763 patients (21.6%) had a 30-day ACS diagnosis. The derived prediction rule was 100.0% sensitive and 18.6% specific. In the validation cohort, 119 of 906 patients (13.1%) had ACS, and the prediction rule was 99.2% sensitive (95% CI 95.4–100.0) and 23.4% specific (95% CI 20.6–26.5). Patients have a very low ACS risk if arrival chest pain cannot be discharged without extensive investigations or hospitalization to minimize the risk of missing acute coronary syndrome (ACS). We sought to derive and validate a prediction rule that permitted 20 to 30% of ED patients without ACS safely to be discharged within 2 hours without further provocative cardiac testing.

Conclusion: The Vancouver Chest Pain Rule may identify a cohort of ED chest pain patients who can be safely discharged within 2 hours without provocative cardiac testing. Further validation across other centres with consistent application and comprehensive and uniform follow-up of all eligible and enrolled patients, in addition to measuring and reporting the accuracy of and comfort level with applying the rule and the clinical sensibility, should be completed prior to adoption and implementation.

RÉSUMÉ

Objectif: D’après les lignes directrices actuelles, on ne peut renvoyer du service des urgences (SU) les patients qui souffrent de douleurs thoraciques de nature probablement ischémique mais qui connaissent un faible risque de maladie cardiaque sans d’abord leur faire subir une exploration approfondie ou sans les hospitaliser afin de réduire le plus possible le risque de syndrome coronarien aigu (SCA) passé inaperçu. Aussi avons-nous tenté d’élaborer et de valider une règle prévisionnelle qui permettrait de renvoyer en toute sécurité de 20 à 30% des patients ne souffrant pas d’un SCA au cours des 2 heures suivant leur arrivée au SU, et ce, sans leur faire subir d’autres épreuves d’exploration cardiaque.

Méthode: Il s’agit d’une étude prospective de cohortes à laquelle ont participé 1,669 patients souffrant de douleurs thoraciques; deux groupes ont été formés: l’un, de 2000 à 2003 (cohorte d’élaboration); l’autre, en 2006 (cohorte de validation). Le principal critère d’évaluation était la pose d’un diagnostic de SCA au bout de 30 jours. Étaient incorporés dans un modèle de partitionnement récursif des facteurs de risque fiables et prévisionnels de maladie cardiaque, les caractéristiques de la douleur, les signes électrocardiographiques, et les valeurs des biomarqueurs cardiaques.

Résultats: Dans la cohorte d’élaboration, un diagnostic de SCA avait été posé au bout de 30 jours chez 165 patients sur 763 (21.6%); la règle prévisionnelle qui en avait découlé avait une sensibilité de 100.0% et une spécificité de 18.6%. Dans la cohorte de validation, un diagnostic de SCA avait été posé chez 119 patients sur 906 (13.1%); la règle prévisionnelle avait une sensibilité de 99.2% (IC à 95%: 95.4–100.0) et une spécificité de
Conclusions: La «regle de Vancouver» sur les douleurs thoraciques permet de cerner une cohorte de patients souffrant de douleurs thoraciques mais susceptibles d’etre renvoyes en toute securite au cours des 2 heures suivant leur arrivee au SU, sans leur faire subir des epurees d’exploration cardiaque. Toutefois, il faudrait proceder a une validation de la regle, avant son adoption et sa mise en oeuvre, dans d’autres centres hospitaliers, assortie d’une application uniforme de la ligne de conduite et d’un suivi general et homogene de tous les patients admissibles et inscrits; a cela s’ajouteraient une mesure de la precision de la regle et du degré de facilité de son application ainsi qu’une évaluation de sa sensibilité clinique.

Keywords: cardiology, outcomes, patient safety

Over 8 million patients present to US emergency departments (EDs) annually with potential ischemic chest pain,1 and these may account for 25% of hospital admissions.2 In Canada, estimates from Ontario (Dr. Michael Schull, Sunnybrook Hospital and the University of Toronto, personal communication, August 20, 2012) and Vancouver (Dr. Eric Grafstein, St. Paul’s Hospital and the University of British Columbia, personal communication, August 20, 2012) suggest over 600,000 annual ED visits. Between 2 and 5% of patients with acute coronary syndrome (ACS) may be discharged with an incorrect non-ACS diagnosis and no further follow-up,3,4 leading to adverse patient outcomes and medicolegal costs. As initial electrocardiogram (ECG) and biomarker results may lack sensitivity, further investigation is usually required. Although most patients are at low risk, many centres attempt to maximize diagnostic sensitivity by applying comprehensive rule-out protocols involving prolonged monitoring, serial cardiac investigations, provocative or invasive testing, and often admission to observation or coronary care units5–8; a recent study from Minnesota reported that nearly all chest pain patients were admitted to hospital.9

Prediction rules have been developed for ACS risk stratification,9–16 but few14–16 have been validated and none widely accepted. The 2007 American College of Cardiology/American Heart Association (ACC/AHA) guidelines,6 the 2005 AHA guidelines,7 and a recent AHA statement4 do not discuss early discharge of low-risk patients without additional testing. Rather, for any potential ACS patient, they recommend 6 to 12 hours of observation, serial ECG and biomarker testing, and additional confirmatory testing. This approach drives high resource use and increases ED crowding,17 potentially leading to substandard care and increased recurrent myocardial infarctions.18,19

A sensitive ACS prediction rule would help physicians identify low-risk patients who can be managed without extensive investigations. An acceptable rule could decrease lengths of stay and ED crowding, decrease patient anxiety, limit expensive or invasive testing, and preserve hospital resources for higher-risk patients.

Our objective was to (1) develop20 a clinical decision rule based on data available within 2 hours of arrival that would identify low-risk ED chest pain patients suitable for early discharge without further provocative cardiac testing and (2) validate this rule with a separate cohort of patients. Based on a previous Canadian survey of emergency physicians,21 the goal was for ACS sensitivity to exceed 98% while identifying the maximum number of low-risk patients who did not require hospitalization or prolonged testing.

MATERIALS AND METHODS

Study design and setting

St. Paul’s Hospital is a university-affiliated urban tertiary care centre with 60,000 annual ED visits during the study period. The derivation cohort was enrolled in two separate periods between June 29, 2000, and January 24, 2003. The prospective validation cohort enrolled patients between February 1, 2006, and September 29, 2006. Accepted methodology for clinical prediction rule development was followed.22,23

Patients

Consenting patients presenting to the ED with a chief complaint of anterior or lateral chest pain of a potential ischemic nature were eligible for enrolment. Patients typically received a Canadian Emergency Department
Information Systems (a standardized, validated form of triage complaints) designation of “chest pain, cardiac features” when they presented at the triage desk and were typically assigned a Canadian Triage and Acuity Scale (CTAS, a reliable and validated 5-point triage system) level 2 (urgent physician assessment) code. Patients were excluded if they were less than 25 years old; had a clear traumatic or radiologically evident alternate cause of chest pain; were previously enrolled within 30 days; or had a terminal illness, debilitating communication problem, or no telephone contact. The University of British Columbia and Providence Health Care Research Ethics Board approved this study.

Sample size

The sample size was calculated based on the following premises: (1) an ACS rate of ≈23% estimated for both the development and validation cohorts based on previous site data; (2) setting the lower goal of the 95% confidence interval for sensitivity at 95%; and (3) assuming that the true sensitivity of the rule is 0.98, around 187 ACS cases requiring an overall enrolment of 815 patients were required to exceed this lower bound of 95% probability.

Development cohort

Standard reporting guidelines for risk stratification of ED chest pain patients were followed. Procedures used to enrol the development cohort and derive the prediction rule are described in detail in a previous publication. Briefly, research assistants who were blinded to patient outcomes screened and enrolled consecutive patients from 7 am to 11 pm. As patients also underwent nonstandard investigations such as serum myoglobin, they consented to both new investigations and 30-day telephone follow-up. During the initial 2 hours of the ED stay, assistants recorded vital signs and ensured that serial ECGs and troponin T assays (Roche Elecsys, Hoffman LaRoche, Laval, QC; 99th percentile reference limit > 0.01 ng/mL, lower limit of detection 0.01 ng/mL, 10% coefficient of variation 0.03 ng/mL) were performed. Ninety-seven predictor variables were screened and recorded for each patient (Appendix 1). Interrater reliability was investigated by having a second emergency physician reviewer, who was blinded to the assessment of the first physician, assess a 10% convenient sample to generate kappa values.

ECG assessment

A single trained emergency physician blinded to both predictor variables and outcomes independently reviewed each ECG for rate, rhythm, and ischemic changes. These were defined as ST segment elevation > 2 mm in two consecutive precordial leads or > 1 mm in two consecutive inferior or lateral leads, or the following prespecified potential ischemic changes: any ST depression > 2 mm in V1 or V2 (denoting posterior infarction), ST depression > 0.5 mm in two contiguous leads, Q waves in two contiguous leads or T-wave inversion in two contiguous leads, left ventricular hypertrophy, paced rhythm, and left bundle branch block (LBBB). Interrater reliability was assured by having a second emergency physician reviewer, who was blinded to the assessment of the first physician, assess the first 20% of ECGs for an overall dichotomous determination of “ischemic features” or “no ischemic changes.”

Validation cohort

Assistants enrolled consecutive patients from 7 am to 11 pm. To maximize nighttime enrolment, patients who arrived after 11 pm but were discharged before 7 am were consented and enrolled postdischarge via telephone contact. Data collection was reduced to 53 potential predictor variables for each validation patient based on reliability and correlation measures from the derivation set (see Appendix 1).

Re-exploration of development cohort

A previously derived rule from the same cohort described in this article was 99.4% sensitive and 32.5% specific for ACS detection. However, this rule used the cardiac biomarker creatinine kinase–muscle/brain isomer (CK-MB) as a key decision point. Early in the rule validation phase, CK-MB fell out of favour, and our institution discontinued its availability, making validation impossible. A new rule was derived based on the same development cohort, incorporating the 53 predictor variables discussed above and troponin as the key biomarker instead of CK-MB.

30-day follow-up (both cohorts)

Research staff contacted patients via telephone to review medications and document physician or hospital visits.
that occurred within 30 days of the index ED visit. Test results (additional ECGs and troponin testing, provocative testing [exercise stress testing, radionuclide imaging, angiography]) were also recorded. If patient contact was unsuccessful, all records from hospital visits within the region were obtained to establish or refute a 30-day diagnosis of ACS. The following predefined adverse events (AEs) occurring within 30 days were identified: tachycardia or bradycardia requiring medical intervention; respiratory failure requiring assisted ventilations; pulmonary embolism; aortic dissection or aneurysm; new congestive heart failure requiring intravenous medications; hypotension requiring vasoactive agents or an intra-aortic balloon pump; chest compressions; percutaneous coronary intervention; or coronary artery bypass grafting. The enrolled patients were cross-checked with the provincial death registry to identify individuals who had died within 30 days.

**Outcome measures**

Emergency physician assessors who were blinded to all predictor variables used predetermined criteria (Table 1) to establish one of the following mutually exclusive 30-day diagnoses: acute myocardial infarction (AMI), unstable angina (UA), or no ACS. A 30-day diagnosis of ACS (AMI or UA) was the primary outcome. All potentially misclassified outcomes were independently reviewed by two cardiologists blinded to the initial classification, and discordant adjudications were resolved by the principal investigator (J.C.). Potentially misclassified outcomes were defined as (1) every death or ACS diagnosis without ECG changes or cardiac biomarker elevation, (2) patients not classified as ACS, but having a troponin elevation or ECGs indicative of ACS.

**Data analysis**

Data were collected on specially designed study forms and entered into an Oracle database (Oracle Corporation, Redwood City, CA). All potential predictors and 30-day outcomes were entered twice into the database for each case, and discrepancies were reviewed to ensure transcription accuracy in the final database. Descriptive summaries were produced using SAS (SAS Institute Inc., Cary, NC). The prediction rule was derived with the S-Plus (Insightful Corp, Seattle, WA) “rpart” recursive partitioning program. To maximize sensitivity, a 10:1 loss was specified for missed ACS patients compared to missed non-ACS patients. The eligibility criteria for a variable to be considered for inclusion in the rule were a univariate association with the outcome of \( p < 0.20 \) and adequate interrater reliability for subjective variables (e.g., elements from the history and physical examination) prespecified as a lower confidence boundary for the kappa coefficient of \( > 0.4 \). Eligible variables were entered into the recursive partitioning program, and multiple rules were derived. Investigators scrutinized each rule to determine clinical relevance, and the simplest rule with a sensitivity of at least 98% was chosen. Sensitivity, specificity, and predictive values were obtained for rule development but not confidence intervals (see above). Results obtained from the validation cohort were then placed into the rule, and sensitivity, specificity, and predictive values along with their confidence intervals were calculated.

**RESULTS**

Figure 1 graphically displays the 763 patients analyzed in the development cohort and 906 in the validation cohort. Although 73 patients were lost to follow-up, noncontact alternative sources verified that none had a 30-day regional ED visit or appeared on the provincial death registry. Two emergency physicians, blinded to predictors and outcomes, independently assessed 150 ECGs (19.7%) from the derivation cohort to obtain interrater reliability for “ischemic changes”; a kappa value of 0.83 was obtained.

Table 2 displays patient characteristics and outcomes for the derivation \( (n = 763) \) and validation \( (n = 906) \)
Figure 1. Study flow diagram. *Not assessed due to nighttime arrival. See Methods in the text. †Not enrolled in rule since troponin was not measured. See Limitations in the text.
cohorts. The derivation cohort had 77 patients with AMI (10.1%) and 88 patients with definite UA (11.5%), whereas the validation cohort had 39 patients with AMI (4.3%) and 80 patients (8.8%) with definite UA. There were 11 outcomes requiring adjudication, 6 in the derivation cohort and 5 in the validation cohort. The sample size was not achieved for either cohort due to a reduction in the ACS incidence rate (21.6% development cohort and 13.1% validation cohort), resulting in insufficient funding to enrol sufficient patients.

Variables used in the recursive partitioning algorithm are illustrated in Appendix 1; those selected for entry into the recursive partitioning algorithm are displayed with respective univariate statistics in Appendix 2. Interrater reliability measures (kappa) for clinically subjective variables were as follows: pain radiating to the neck, 0.68 (95% CI 0.54–0.83); pain radiating to the jaw, 0.81 (95% CI 0.69–0.93); pain radiating to the left arm, 0.79 (95% CI 0.67–0.91); and chest tenderness reproducing pain, 0.63 (95% CI 0.45–0.80).

Figure 2 is a clinical depiction of the Vancouver Chest Pain Rule. In the derivation cohort, the rule would have identified all 165 patients with a 30-day ACS diagnosis while permitting 111 of 598 patients without ACS to be discharged safely within 2 hours with no follow-up, for a sensitivity of 100% and a specificity of 18.6%. In the validation cohort, the rule would have identified 118 of 119 patients with ACS while allowing safe early discharge of 184 of 787 patients without ACS, for 99.2% (95% CI 95.4–100) sensitivity and 23.4% (95% CI 20.4–26.5) specificity. Table 3 illustrates rule performance for the derivation and validation cohorts, respectively, and decision trees are shown in Appendices 3 and 4.

The rule missed no ACS patients in the derivation cohort but missed one patient with UA in the validation cohort. He was a 48-year-old male with no history of ACS or nitrate use, and his nonradiating pain was not reproducible with pressure. Although the initial ECG and troponin were normal, subsequent troponin assays were not done as the patient was taken to the catheterization laboratory by Cardiology. The emergency physician referred him to Cardiology as he had documented prehospital hypotension. Angiography revealed a single 50% mid-left anterior descending coronary artery lesion; he was discharged uneventfully.

### Table 2. Population demographics and outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Derivation cohort (n = 763)</th>
<th>Validation cohort (n = 906)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>58 (14)</td>
<td>60 (15)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>473 (62.0)</td>
<td>555 (61.2)</td>
</tr>
<tr>
<td>Arrived by EMS, n (%)</td>
<td>238 (31.2)</td>
<td>280 (30.9)</td>
</tr>
<tr>
<td>Initial vital signs, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>81.2 (20.0)</td>
<td>80.2 (19.5)</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>144.1 (27)</td>
<td>143.2 (26.5)</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>18.8 (3.4)</td>
<td>18.6 (3.2)</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>128 (16.8)</td>
<td>147 (16.2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>293 (38.4)</td>
<td>386 (42.6)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>278 (36.4)</td>
<td>286 (31.5)</td>
</tr>
<tr>
<td>Cardiac, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous ACS</td>
<td>311 (40.8)</td>
<td>267 (29.4)</td>
</tr>
<tr>
<td>Abnormal initial ECG</td>
<td>229 (30.0)</td>
<td>268 (29.6)</td>
</tr>
<tr>
<td>30-day outcomes, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>77 (10.1)</td>
<td>39 (4.3)</td>
</tr>
<tr>
<td>Definite unstable angina</td>
<td>88 (11.6)</td>
<td>80 (8.8)</td>
</tr>
<tr>
<td>Possible unstable angina</td>
<td>29 (3.8)</td>
<td>21 (2.3)</td>
</tr>
<tr>
<td>No ACS but AE</td>
<td>32 (4.1)</td>
<td>23 (2.5)</td>
</tr>
<tr>
<td>No ACS, no AE</td>
<td>537 (69.8)</td>
<td>766 (84.5)</td>
</tr>
<tr>
<td>Death</td>
<td>9 (1.1)</td>
<td>5 (0.6)</td>
</tr>
</tbody>
</table>

ACS = acute coronary syndrome; AE = adverse event; AMI = acute myocardial infarction; BP = blood pressure; ECG = electrocardiogram; EMS = emergency medical services.
with a single stent. Although he may have met rule
criteria for early discharge (no sequential cardiac testing
was performed), he met study criteria for UA.

**DISCUSSION**

**Summary of major findings**

ED patients with acute ST elevation myocardial
infarction and those with obvious noncardiac causes
are often straightforward. In comparison, patients with
nonspecific symptoms and low cardiac risk pose a
significant diagnostic and cognitive burden on physi-
cians while consuming substantial hospital resources
and contributing to ED crowding. The Vancouver
Chest Pain Rule assists clinicians by identifying a subset
of chest pain patients (approximately one-fifth) who can
be safely discharged within 2 hours with no further
provocative cardiac testing while identifying more than
99% of patients who have ACS. If applied across
Canada, this could permit safe early discharge of up to
120,000 chest pain patients annually. Interestingly,
some traditional cardiac risk factors, including hyper-
tension, diabetes, and hyperlipidemia, were not included

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**Table 3. Rule performance for derivation and validation cohorts**

<table>
<thead>
<tr>
<th></th>
<th>Definite ACS</th>
<th>No definite ACS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Derivation cohort</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsuitable for early discharge</td>
<td>165</td>
<td>487</td>
<td>652</td>
</tr>
<tr>
<td>Suitable for early discharge</td>
<td>0</td>
<td>111</td>
<td>111</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
<td>598</td>
<td>763</td>
</tr>
<tr>
<td><strong>Validation cohort</strong>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsuitable for early discharge</td>
<td>118</td>
<td>603</td>
<td>721</td>
</tr>
<tr>
<td>Suitable for early discharge</td>
<td>1</td>
<td>184</td>
<td>185</td>
</tr>
<tr>
<td>Total</td>
<td>119</td>
<td>787</td>
<td>906</td>
</tr>
</tbody>
</table>

*ACS = acute coronary syndrome.
†The sensitivity was 99.2% (95% CI 95.4–100), and the specificity was 23.4% (95% CI 20.4–26.5). The positive predictive value was 16.4% (95% CI 13.8–19.2), and the negative predictive value was 99.5% (95% CI 96.6–100).
in the final model; neither was the duration or quality (i.e., stabbing, burning) of pain.

Comparison with other studies

Many efforts have been devoted to rapidly identifying chest pain patients at low clinical risk of ACS who are suitable for rapid discharge of patients. Guidelines developed by ACS–time-insensitive predictive instruments are structured toward disposition of low-risk patients, with only 21% of patients discharged home, but few at the 2-hour mark. The Erlanger protocol allows physicians to use objective criteria or clinical judgment to discharge or provocatively test patients at 2 hours from ED presentation but does not provide criteria to forego additional testing. Few studies have attempted to derive a clinical prediction rule to identify patients who can be safely discharged without further investigations, such as provocative testing or imaging. Bassan and colleagues developed a decision rule incorporating the clinical likelihood of ACS—patients selectively received investigations to confirm or refute the presence of disease, ensuring a varying “gold standard” for ACS diagnosis, whereas Fernandez Portales and colleagues had cardiologists enrol patients with a high clinical suspicion of ACS; hence, the resulting rule may have limited generalizability in an ED setting.

Several rules for identifying patients who can be rapidly and safely discharged have been prospectively validated. Marsan and colleagues developed and validated a sensitive algorithm that involves minimal investigations in patients age 24 to 39 years. Lyons and colleagues validated the thrombosis in myocardial infarction (TIMI) score in ED patients with a high likelihood of ACS, but this may be difficult to extrapolate to a general ED population. Several studies have attempted to use Global Registry of Acute Coronary Events (GRACE) or TIMI scores to predict ACS, but 3 to 4% of the low-risk patients had a 30-day ACS outcome, a risk that may be unacceptable to clinicians. Many rules are hampered by selection bias, a suboptimal methodological design, or low sensitivity. There has been no widely used clinical prediction rule for safe early discharge of such patients, and the few rules that have been validated permit risk stratification of selected patients but do not allow for minimal investigations or early discharge.

Than and colleagues developed a protocol to classify ED chest pain patients based on a combination of the TIMI score, ECG, and cardiac biomarkers. This promising strategy identified 9.8% of patients as low risk; this low-risk group had a 30-day AE rate of 0.9%. However, patients diagnosed with UA were included in the AE rate only if they were revascularized. Novel troponin assays appear to improve sensitivity for AMI diagnosis and accurately stratify mortality in ED patients, but their utility in diagnosing UA, ruling out ACS, or permitting safe and rapid discharge in low-risk patients has not been demonstrated.

This rule uses reliable clinical criteria and widely available tests to define a group of patients who can be safely discharged at 2 hours without further observation or investigation. Designated outcomes were obtained by predefined explicit criteria, and an a priori blinded adjudication process resolved controversial diagnoses. The rule identifies ACS patients in a logically stepwise process, with most patients recognized by an abnormal ECG or cardiac biomarker, some diagnosed by historical elements, and a few identified by pain characteristics and age.

LIMITATIONS

This rule was derived and validated in a single tertiary care centre, and performance may vary in other settings. Our physicians were not asked to assess or interpret the rule during the prospective validation phase or describe their comfort with it; as a result, their willingness and ability to successfully use the rule, as well as the clinical sensibility of the rule, was not measured. The development cohort was enrolled around 10 years ago, but outcome definitions (see Table 1) reflect the current guidelines of care (2007 ACC/AHA guidelines). In addition, although we classified patients with a new LBBB as having AMI, newer data indicate that this may not be the case. (One patient in the validation group had a new LBBB but had a complete circumflex artery occlusion and received a stent during angiography.). Although the ACS rate decreased between the derivation and validation cohorts, identical outcomes were used to minimize verification bias. Some very sick patients, or those transferred rapidly for a cardiac procedure, may not have been enrolled, although such patients are typically not a diagnostic conundrum. We enrolled patients presenting with chest pain; therefore, our findings cannot be extrapolated to those with atypical symptoms such as weakness, nausea, or dyspnea. In
particular, female patients, diabetics, and the elderly have been reported as having a higher percentage of alternate presenting complaints.\textsuperscript{16}

Patients who were discharged from the ED were not required to have follow-up marker assays or mandatory provocative cardiac testing, and only approximately 40\% of enrolled patients had these investigations. It is possible that we could have missed clinically silent ACS events or events for which patients did not seek medical care and thus did not receive additional testing or hospitalization. Our intensive patient follow-up was a reasonable proxy standard to capture clinically important outcomes. This rule cannot be endorsed for the detection of rare but potentially lethal causes of chest pain such as aortic dissection or pulmonary embolism.

A number of patients (n = 207) did not have sufficient data captured to participate in the validation cohort. Most often they were seen outside research assistant working hours and discharged with no cardiac biomarkers as emergency physicians were not mandated to obtain biomarkers or retain patients for at least 2 hours during the validation phase of the study. In comparison with those with data in the validation cohort, these patients were lower risk and younger (mean age 43 versus 60 years) with substantially lower rates of hypertension and hyperlipidemia than the overall cohort. None had previous ACS, and all had normal initial ECGs. All 207 patients were followed to 30 days: none died or suffered an ACS outcome or AE. Consequently, the exclusion of these patients did not falsely inflate rule sensitivity. Assuming that all would have had negative biomarkers, their inclusion would have increased specificity to 39.3\% and sensitivity closer to 100\%.

CONCLUSION

The Vancouver Chest Pain Rule identifies a cohort of ED chest pain patients who can be safely discharged within 2 hours without further provocative cardiac testing. Although use of this rule would preserve health care resources with maintaining high sensitivity for ACS detection, further prospective external validation is required across other centres with comprehensive and uniform follow-up of all eligible and enrolled patients. In addition, the comfort of emergency physicians with the rule and their ability to interpret it successfully require assessment.

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Competing interests: This study was funded by Canadian Institutes of Health Research grant MOP 33102 and the Heart and Stroke Foundation of British Columbia and Yukon.

REFERENCES

Safe 2 h discharge of chest pain patients


### Appendix 1. Candidate predictor variables collected for original derivation cohort

**Pain and associated symptom characteristics**
- Age*
- Gender*
- Was chest pain present on arrival?*
- Did 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
- Dyspnea
- 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 in centre 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 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?
- Within first 2 hours, did pain relieve and not return?
- Within first 2 hours, did pain continue?*
- Within first 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

### Appendix 1. Continued

- $S_3$ present
- $S_4$ present
- Carotid pulses equal with no bruit
- Radial pulses equal
- Physician palpation in area of maximum chest discomfort reproducing pain*
- Right arm systolic pressure
- Left arm systolic pressure
- Systolic pressure < 90 mm Hg in 2 hours*
- Bradycardia < 50 beats per minute in 2 hours*
- Tachycardia > 100 beats per minute in 2 hours*

**Risk factors**
- Regular smoker*
- History of diabetes*
- History of hypertension*
- History of hyperlipidemia*
- Parent or sibling with heart attack < 65 years
- Recreational substance use
- Alcohol use in past 24 hours
- Cocaine use in past 48 hours

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

**Laboratory markers**
- 0-hour troponin*
- 2-hour troponin*
- Difference in troponin at 0 and 2 hours*

**Cardiovascular history**
- Previous angina*
- Previous AMI*
- Previous cardiac arrest*
- Previous angiogram with lesion > 50%*
- Previous angiogram with lesion < 50%*
- Previous PCI*
- Previous peripheral vascular surgery
- Previous congestive heart failure*
- Previous CABG*
- Previous stroke*
- Previous TIA*
- Previous ventricular arrhythmias
- Previous atrial arrhythmias
- Previous unknown arrhythmias

**Medications**
- Previous ASA*
- Previous other antiplatelet agents*
- Previous ACEI*
- Previous digitalis*
- Previous beta-blocker*
Appendix 1. Continued

Previous warfarin*
Previous low-molecular-weight heparin*
Previous nitrates*
Previous lipid-lowering agents*
Previous antiarrhythmics*
Previous diuretics*
Previous other antihypertensives*

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; AE = adverse event; AMI = acute myocardial infarction; ASA = acetylsalicylic acid; CABG = coronary artery bypass grafting; ECG = electrocardiogram; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

*Variable included in validation cohort.

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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>ACS (%)</th>
<th>No ACS (%)</th>
<th>Odds ratio* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>165</td>
<td>598</td>
<td></td>
</tr>
<tr>
<td>Abnormal initial ECG†</td>
<td>57.6</td>
<td>22.6</td>
<td>4.7 (3.2–6.7)</td>
</tr>
<tr>
<td>Age ≥ 50 yr</td>
<td>96.4</td>
<td>72.2</td>
<td>12.8 (5.1–31.7)</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>35.8</td>
<td>21.0</td>
<td>2.1 (1.4–3.1)</td>
</tr>
<tr>
<td>Previous angina</td>
<td>53.9</td>
<td>31.0</td>
<td>2.6 (1.8–3.8)</td>
</tr>
<tr>
<td>Previous nitrate use</td>
<td>48.5</td>
<td>23.8</td>
<td>3.0 (2.1–4.4)</td>
</tr>
<tr>
<td>Previous AMI, angina, or nitrate use</td>
<td>66.7</td>
<td>40.6</td>
<td>2.9 (2.0–4.3)</td>
</tr>
<tr>
<td>Pain radiates to jaw</td>
<td>24.9</td>
<td>12.3</td>
<td>2.4 (1.5 – 3.7)</td>
</tr>
<tr>
<td>Pain radiates to neck</td>
<td>35.2</td>
<td>24.3</td>
<td>1.7 (1.1–2.5)</td>
</tr>
<tr>
<td>Pain radiates to left arm</td>
<td>57.0</td>
<td>43.4</td>
<td>1.7 (1.2–2.5)</td>
</tr>
<tr>
<td>No pain increase with inspiration</td>
<td>78.2</td>
<td>64.2</td>
<td>2.0 (1.3–3.1)</td>
</tr>
<tr>
<td>Palpitation does not reproduce pain</td>
<td>94.3</td>
<td>80.5</td>
<td>4.0 (2.0–9.3)</td>
</tr>
<tr>
<td>Pain radiates and does not increase with</td>
<td>48.4</td>
<td>25.6</td>
<td>2.7 (1.9–4.0)</td>
</tr>
<tr>
<td>inspiration or palpitation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin increase within first 2 hours</td>
<td>35.5</td>
<td>15.1</td>
<td>3.1 (2.0–4.7)</td>
</tr>
<tr>
<td>Ischemic ECG changes within first 2 hours</td>
<td>68.9</td>
<td>33.5</td>
<td>1.2 (0.4–2.9)</td>
</tr>
<tr>
<td>ST-T ECG changes within first 2 hours if initial ECG normal</td>
<td>42.9</td>
<td>20.7</td>
<td>2.9 (1.7–4.8)</td>
</tr>
</tbody>
</table>

ACS = acute coronary syndrome; AMI = acute myocardial infarction; ECG = electrocardiogram.

*Odds ratio > 1 indicates that the predictor is associated with an increased risk of ACS.
†A normal ECG is defined as no ST segment deviation and no T-wave inversion regardless of conditions such as left ventricular hypertrophy or left bundle branch block. T-wave flattening was not defined as abnormal.
Appendix 3. Decision tree for derivation cohort (n = 763). ACS = acute coronary syndrome; ECG = electrocardiogram.
Appendix 4. Decision tree for validation cohort (n = 906; 831 patients with complete data, 75 patients evaluable despite incomplete data). ACS = acute coronary syndrome; ECG = electrocardiogram.