EDITORIAL COMMENT

Risk Stratification in Unstable Angina: The Role of Clinical Prediction Models*

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CLINICAL SCENARIO

You are asked to see in your clinic a 49-year-old man with a two-day history of left-sided upper chest pain, which radiates to the jaw and is associated with mild shortness of breath. The pain occurred at rest, was rated as 8/10 in intensity, and lasted for approximately 1 h. The pain recurred the following day and lasted for 30 min. He is now pain-free at the time of his clinic visit. The patient took aspirin without relief; he did not have access to nitroglycerin. Past medical history is significant for hypertension, controlled on hydrochlorothiazide. Cholesterol is unknown. He has no history of coronary artery disease or other vascular disease. He smokes two packs of cigarettes per day (66 pack years). After a normal physical examination, electrocardiogram (ECG) was obtained and showed normal sinus rhythm (rate 78) with 0.5 mm of ST elevation in leads III and aVF. No prior ECG was available for comparison. Chest X-ray was negative for infiltrates, effusion, or pneumothorax.

You suspect that the patient has unstable angina and decide to admit the patient to a monitored bed to rule out myocardial infarction (MI). The patient minimizes his recent symptoms and asks for an explanation of the necessity for immediate hospitalization. You have reviewed various clinical prediction rules and guidelines for patients with symptoms of unstable angina in the medical literature, and you refer to these sources to better characterize the patient’s short-term risk of adverse outcomes, including nonfatal MI and death.

DISCUSSION

Prior efforts to stratify patients presenting with symptoms suspicious for an acute coronary syndrome (ACS), including unstable angina and MI, have concentrated upon the identification of high-risk clinical indicators and electrocardiographic (ECG) findings (1,2). Other attempts to improve the appropriateness of the triage of patients with suspected ACS have included the use of rapid determination of cardiac enzymes (3,4), cardiac troponin (5–7), two-dimensional echocardiography (8,9), thallium-201 scintigraphy (10), and Tc99m-sestamibi single-photon emission computed tomography (SPECT) scanning (11,12). Several of these methods have significant limitations, however.

Although serial cardiac enzymes show excellent sensitivity in the detection of acute MI, use of a single measurement to guide triage at the time of initial evaluation generally does not (except in the case where ischemic symptoms have been prolonged for at least 8 to 10 h) (13). Elevated troponin levels have been demonstrated to identify patients with unstable angina at increased risk of adverse cardiovascular events during follow-up (14–17); however, optimal triage and initial management of the large number of patients with marginally elevated (or indeterminate) troponin values remains uncertain, which argues against the indiscriminate use of this test in all patients with symptoms of possible ACS (18). The routine use of echocardiography and radionuclide imaging in the emergency department (ED) detection of ACS, while promising, depends upon the ready, around-the-clock availability of technical staff, expensive equipment, and/or radioisotopes, which is problematic at the majority of facilities without these resources. Both of these techniques may yield normal results in patients with small infarctions or small areas of at-risk myocardium (reducing sensitivity), and may present difficulties in differentiating between acute ischemia and old infarction in the ED (reducing specificity).

Related work has suggested the potential utility of critical pathways, accelerated diagnostic protocols, and chest pain observation units in reducing hospitalization for patients with possible unstable angina who are determined to be at low risk for acute cardiac complications (19–21). Indeed, the effective use of these strategies depends on the ability to recognize patients with possible ACS and to estimate the pretest probability of short-term adverse outcomes. For this purpose, risk stratification models, which are based on a combination of clinical and ECG findings, can be applied to predict short-term outcome in patients with unstable angina (22,23), and more generally in patients with symptoms suggestive of ACS (24–27).

In this issue of the Journal, Calvin et al. (28) present evidence to support the validity of a previously reported model originally developed to determine which factors of the Braunwald classification of unstable angina (29) predict the occurrence of in-hospital cardiac complications (22,30). In an analysis of 416 consecutively admitted patients diagnosed with unstable angina, the investigators compared the performance of two risk stratification models for unstable...
angina: 1) the modified Braunwald (RUSH) model, and 2) the Agency for Healthcare Research and Quality (AHRQ) risk model. Based on the RUSH model, predicted probabilities of complications were grouped into three categories: a priori low (<5%), intermediate (5% to 25%), and high risk (>25%). The difference in observed complications among risk groups was statistically significant when recurrent angina with ST depression, a secondary end point, was included in the composite outcome (4%, 9%, and 19% for low, intermediate, and high-risk groups, respectively). Agreement between observed and predicted complication rates was good at the low range of the probability scale (0% to 15%), but was poor at higher values. Possible explanations for this discrepancy are: 1) that the model was used to predict somewhat different outcomes compared to those examined in the original study (31) [In the original predictive model, major in-hospital cardiac complications were defined by the occurrence of death, MI after the first 24 h, congestive heart failure, ventricular tachycardia, or ventricular fibrillation. Recurrent ischemia with ST depression was not included in this definition]; 2) that the AHRQ guideline-based reminders, which were posted on each chart during the study period (32), may have resulted in improved care for high-risk patients. In this regard, the article by Calvin et al. (Table 3) indicates that patients at increased risk according to the RUSH model were more likely to receive IV nitroglycerin (with a trend toward increased use of IV heparin and surgery in these patients). More aggressive therapy may have lowered the observed rate of cardiac events (such as recurrent ischemia) for patients predicted to be at high risk.

The AHRQ guideline identified a smaller fraction of low-risk patients eligible for possible outpatient workup and performed less favorably in discriminating between patients at low versus intermediate to high risk of in-hospital cardiac complications. Indeed, the small fraction of patients identified as low risk by the AHRQ risk model has raised doubts regarding the clinical applicability of this model in patients with suspected unstable angina (33). Previous work, however, suggests that the AHRQ risk model does effectively identify patients at low risk of adverse outcomes over the short and long term (34–36). The unexpected results in the study by Calvin et al. may be attributable in part to selection factors.

First, the inclusion criteria limited the study sample to inpatients with several intermediate–high risk features of unstable angina. Second, use of the AHRQ guideline by emergency physicians in the initial evaluation of patients with suspected unstable angina may have affected triage decisions, leading to the ED discharge of patients classified as low risk according to the guideline; unfortunately, no information on whether the guideline was implemented in the ED is reported. Both of these factors would tend to reduce the proportion of guideline-identified low-risk patients in the study sample and to attenuate differences between guideline risk groups.

How do the two models compare in guiding the initial risk assessment of the patient in the above clinical scenario? Based on the RUSH model, our patient has a predicted probability of in-hospital cardiac complications of 6% (in the intermediate-risk range), given his age and history of not having received a beta-blocker (none of the other variables in the model apply). In contrast, the AHRQ risk model would also assign this patient to the intermediate-risk group (average observed risk of in-hospital complications, 9%), based on his history of prolonged rest angina (>20 min), which had resolved by the time of presentation. Although the two risk models include several common prognostic factors that are associated with cardiac complications in the literature, the AHRQ risk model captures additional clinical and ECG factors that are useful for risk stratification not only in patients with presumed unstable angina but also in the more heterogeneous spectrum of patients with symptoms suggestive of ACS. The performance of both models in a less selected population of patients presenting with symptoms suggestive of ACS in the ED, either alone or as part of a strategy including cardiac enzymes, exercise testing, and/or imaging, warrants further evaluation.

The risk model by Calvin et al. adds to a growing armamentarium of prediction rules that can help clinicians initially estimate the probability of short-term adverse outcomes in patients with suspected unstable angina. In addition, the investigators have performed a valuable service by raising new questions about a widely disseminated national guideline for unstable angina and the importance of confirming the validity of this and similar guidelines in target clinical settings. Few of these decision aids in isolation have been shown prospectively in large controlled trials to reduce the number of unnecessary critical care unit admissions for patients without ACS or to decrease the rate of inappropriate discharge of patients with confirmed ACS (37,38); even fewer have demonstrated the impact of implementing predictive models on clinical outcome.

Nonetheless, these tools have an emerging role at the “front-end” of clinical strategies for the initial triage and management of these patients, and they can anchor decisions regarding the need for additional observation in a chest-pain center, the use of accelerated protocols or cardiac imaging, and/or the administration of intensive medical treatment (heparin, antiplatelet agents, early revascularization). Clinicians should take advantage of validated risk stratification models and other decision aids in patients with suspected ACS, and they should use additional tests/procedures as indicated to revise initial estimates of the probability of adverse cardiac events.

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