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Predicting the Outcomes of Rhabdomyolysis A Good Starting Point

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Rhabdomyolysis is commonly encountered in the hospital; however, national estimates on the incidence of rhabdomyolysis are not available. While patients with highly elevated creatine phosphokinase (CPK) concentrations are generally closely monitored, it is often less clear how to best handle patients with moderate CPK elevations. Clinicians are usually fixated on these patients' (repeated) CPK measurements, yet it is likely that other relevant information can help stratify these patients by their likelihoods of experiencing unfavorable outcomes.

In this issue of *JAMA Internal Medicine*, McMahon and colleagues¹ present perhaps the largest study to date of patients hospitalized with clinically significant rhabdomyolysis. From the detailed data repository of 2 Harvard-affiliated teaching hospitals in Boston, Massachusetts, they identified from all primary admissions between January 1, 2000, and March 31, 2011, nearly 2400 patients who had at least 1 CPK level in excess of 5000 U/L; patients with myocardial infarction were excluded. This means that each hospital had approximately 10 patients per month with significant rhabdomyolysis, clearly not a rare event. The mean age of the study cohort was 50.4 years, 73.8% were men, and 27% were of nonwhite race. The patients were almost evenly split between primary surgical and medical services. The most common causes of rhabdomyolysis included trauma, immobilization, sepsis, and vascular and cardiac operations.

The primary outcome of interest was a composite of acute kidney injury requiring hemodialysis or hemofiltration, at least temporarily, and in-hospital mortality, which occurred in 19.0% of patients (8.0% required hemodialysis or hemofiltration, and 14.1% died). The primary analysis confirmed a counterintuitive but previously reported observation: no strong relationship exists between CPK and outcome—initial CPK levels predicted poor outcomes for patients with rhabdomyolysis no better than a coin flip (C statistic, 0.52). Prediction using peak CPK level was not much better (C statistic, 0.61).

Using data from 1 hospital, the researchers then developed a prediction tool for poor outcomes using commonly collected clinical data, including age, sex, origin of rhabdomyolysis, and laboratory parameters (initial creatinine, CPK, phosphate, calcium, and serum bicarbonate levels). The parsimonious regression model performed quite well, as did

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the simplified integer-based prediction tool derived from it (C statistic, 0.82 for both). The researchers then validated their prediction tool in the cohort of patients from the second hospital, where it performed just as well (C statistic, 0.83), which is remarkable.

This tool for the prediction of poor outcomes in patients with rhabdomyolysis has other attractive properties; it uses a limited set of variables that are routinely and inexpensively measured and readily available. Thus, it can be easily applied to patients in the emergency department, allowing physicians to prognosticate which patients are at high risk for poor outcomes early in their clinical course. For example, a man aged 71 years, admitted following a traumatic injury, with an initial creatinine concentration of 1.8 mg/dL (to convert to micromoles per liter, multiply by 88.4), CPK level of 10 000 U/L, phosphate concentration of 4.5 mg/dL, calcium concentration of 10.0 mg/dL (to convert to millimoles per liter, multiply by 0.25), and serum bicarbonate concentration of 18 mEq/L (to convert to millimoles per liter, multiply by 1.0), would carry a risk score of 10.5, which corresponds to a risk of dialysis or in-hospital mortality of 61.2%. This degree of risk may surprise some physicians, since the laboratory values are abnormal but not spectacularly so. Early risk estimation, especially if unintuitive, may improve outcomes for patients, particularly if supportive care such as aggressive fluid resuscitation can be started early. The early prediction of high risk will also allow physicians to seek timely subspecialty (nephrology) consultation, triage patients more quickly and appropriately to the highest level of care (such as the intensive care unit), and provide patients and their families with more accurate prognostic information. By contrast, on the lower end of the scale, the scoring system performed particularly well in that among the 488 patients with a score of 3 or less, only 4 (<1%) experienced in-hospital mortality or the need for hemodialysis, thus indicating that such patients may be discharged from the emergency department (dependent on other circumstances) and monitored closely as outpatients.

Prior literature on the incidence and outcomes of rhabdomyolysis is surprisingly sparse. Early literature focused on case reports and case series, primarily of crush victims in manmade and natural disasters.^{2,3} Generally, these reports featured high rates of patients with acute kidney injury requiring renal replacement therapy, as well as high mortality rates, but support the observation (never confirmed in any randomized clinical trials) that early and aggressive fluid resuscitation improved both kidney-related outcomes and all-cause mortality.

This novel research by McMahon and colleagues¹ adds a new prognostic tool to our clinical armamentarium. Their risk score may possibly take place among other trusted clinical risk scores such as the Wells criteria for pulmonary embolism,⁴ the Thrombolysis in Myocardial Infarction score for risk stratification in acute coronary syndrome,⁵ and the Laboratory Risk Indicator for Necrotizing Fasciitis score for suspected necrotizing fasciitis.⁶ To facilitate this kind of use, this new rhabdomyolysis risk score should be made available with an online calculator and must be familiar to hospitalists and emergency department physicians.

While the new McMahon rhabdomyolysis score has the potential to be an immediate classic, especially if validated in independent and diverse settings, it shares properties of risk calculators past that do not exploit the capabilities of modern-day electronic health records

systems. Nowadays, it is possible to embed code into these systems that calculates patient risk in real time from data continuously streaming into a patient's hospital record. Such an approach no longer requires parsimony and easy back-of-the-envelope calculability but can take into account almost unlimited information, including baseline, updated, and change parameters. Doing so, clinicians can be provided with real-time risk probabilities with an accuracy that may exceed the already impressive predictive capability of the McMahon score. If real-time prediction of rhabdomyolysis risk is the future, McMahon and colleagues will have provided crucial feasibility data and established an already excellent starting point for system-based practice that may improve the outcomes of patients with rhabdomyolysis and facilitate efficient resource use in their care.

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