Finding the Holy Grail Is Not a Short-Term Project

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Clinical decision instruments exist for a myriad of disease states as they present to the emergency department (ED), including cervical spine imaging rules,[1,2] instruments that estimate the risk of venous thromboembolism,[3] and the mortality risk associated with pneumonia,[4] to name a few. As the second most common reason to visit an ED,[5] chest pain has been the target of decades of clinical decision instrument research efforts.

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Given that less than a quarter of these patients are suffering from an acute coronary syndrome,[6] multiple groups have attempted to derive a highly sensitive decision instrument that identifies essentially all the patients with an acute coronary syndrome, while at the same time facilitating the safe, early discharge of a cohort of low-risk patients.[7–10] Emergency physicians have identified 1% as the maximum miss rate that would acceptable to them in order to actually use such a tool in the clinical setting.[11,12] A tool that has a sensitivity with a lower confidence interval of 99%, but still has a high enough specificity to identify a substantial proportion of chest pain patients for ED discharge would be the holy grail of clinical decision instruments.

Early instruments had poor clinical uptake because of unacceptably low sensitivity: these include the Goldman Risk score, acute cardiac ischemia time–insensitive predictive instrument (ACI-TIPI), the Thrombolysis in Myocardial Infarction (TIMI) risk score, and Global Registry of Acute Coronary Events (GRACE).[13–16] More recently, the North American Chest Pain Rule, the Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins (ADAPT) study, and the HEART (History, Electrocardiogram, Age, Risk factors, Troponin) Pathway, among others, have incorporated conventional troponins into their clinical decision instruments.[7,8,10]

The North American Chest Pain Rule demonstrated a sensitivity of 100% (95% confidence interval, 97.2–100) in the derivation phase, and allowed for the early discharge of 18% of patients. Although the sensitivity remained high in subsequent validation studies, the proportion of patients eligible for early discharge dropped to 11%.[17] The Asia-Pacific Evaluation of Chest pain Trial (ASPECT) study[12] also had high sensitivity, but only 10% were identified for early discharge, although the subsequent ADAPT tool[10] identified 20% for discharge. The latter tool has been validated using high-sensitivity troponins, and maintained the high sensitivity while identifying >20% of patients for early ED discharge.[18] The HEART score has evolved into the HEART Pathway, which showed 100% sensitivity using 2 sets of conventional troponins, although it had a lower confidence interval of 72%.[8] An external validation study of the HEART Pathway had a miss rate of 1.7% (95% confidence interval, 1.0–2.9); lowering the low-risk score cutoff from 3 to 2 resulted in a miss rate 1.1%.[19] It is clear that researchers are getting closer to a clinically acceptable tool for the safe early disposition of patients with chest pain from ED , but no instrument seems ready for prime-time yet.

In this issue of *Circulation: Cardiovascular Quality and Outcomes*, Mahler et al[20] assessed objective cardiac testing in ED patients with chest pain up to 30 days after the ED visit, using a rigorously conducted randomized control trial. Patients were randomized to the HEART Pathway (where a HEART score of ≤3 was used to define low risk) or standard of care. In addition to objective cardiac testing, the authors compared time spent in the ED and hospital, the proportion of patients who achieved early ED discharge (discharge without objective cardiac testing), and major adverse cardiac events (MACE) at 30 days. The study found a substantial reduction in objective cardiac testing up to 30 days after the ED visit among the HEART Pathway patients, relative to controls. In addition, patients in the HEART pathway arm had substantially shorter times in the ED and hospital than control patients, and more were discharged early from the ED (21% increase in early discharge compared with controls, compared with 8% more using the ADAPT tool[21]).

There was no difference in MACE at 30 days; however, it is important to note that the study was not powered to find a difference in MACE. Although one might look to the previously published, observational HEART studies (that showed high sensitivities for MACE) to confirm the safety of this approach, post-ED diagnostic testing and interventions that occur in observational studies may have decreased the rate of 30-day MACE. In other words, more episodes of MACE might have occurred if further testing had not been performed. In addition, although the authors present this as a real-world test of the HEART Pathway, the clinicians in this RCT were alerted if they had miscalculated the patient's HEART score (underestimated it), which may also have led to underestimation of MACE. These issues will need to be addressed prior to clinical use of the HEART Pathway.

A similar RCT has been conducted for the ADAPT tool[21]: that study included comparable outcomes, with the exception

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of objective cardiac testing up to 30 days after the ED visit. The authors of the ADAPT studies have made it clear that patients discharged using their accelerated diagnostic protocol still require further nonurgent follow-up investigations.[10,18] This is because of the aforementioned limitation of observational studies, where subsequent investigations and treatments may have lowered the frequency of MACE. In comparison, the study by Mahler et al[20] takes the goal of getting low-risk chest pain patients out of the ED and hospital one step further, by assessing *both* inpatient and outpatient objective cardiac testing up to 30 days after the ED visit, with the aim of reducing it as well (in comparison, in the ADAPT study all patients received objective cardiac testing within 72 hours of ED discharge).[21]

Clinically, the leap of faith required for this outcome measure is sizeable. Even in Canada, where physicians are far less likely to request objective testing before ED discharge,[7,9] we suspect that removing the safeguard of subsequent outpatient objective cardiac testing on patients with a reasonable presentation for acute coronary syndrome is not likely to gain widespread traction. In one Canadian study, this is how 17% of the acute coronary syndromes were identified.[9]

Therefore, although the study by Mahler et al[20] showed a decrease in objective cardiac testing up to 30 days after ED discharge, the key question to ask is whether that is a good thing. The American College of Cardiology/American Heart Association recommends that patients deemed low risk in the ED setting should undergo objective cardiac testing, either in hospital, in an ED observation unit, or in the early period after ED discharge.[22] However, there are no studies with long-term outcomes to substantiate, or disprove, this one-size-fits-all approach. Most emergency physicians are aware that there is a high rate of false positives associated with objective testing of low-risk patients, and would like to avoid sending such patients for testing, consistent with the Choosing Wisely campaign.[23] Specifically, what they want to reduce is *inappropriate* objective cardiac testing in low-risk chest pain patients, as opposed to reducing outpatient cardiac testing overall.

A valuable finding in the study by Mahler et al[20] was that a substantial minority (29%) of discharged low-risk patients in the HEART Pathway arm received subsequent objective cardiac testing within 30 days anyway. The rate of testing would probably have been higher had follow-up been longer than 30 days, raising the question of whether the HEART Pathway simply delays objective testing as opposed to forgoing it. The family physicians and outpatient specialists who took over the care of these patients after ED discharge apparently did not feel comfortable trusting in the decision instrument's recommendations; this finding highlights the need to engage the practitioners who are tasked with the long-term care of these patients, to effectively implement such a decision instrument in clinical care. Finally, it would be interesting to incorporate the patient's perspective on the risks and benefits associated with the decision instrument's recommendations, as well as on a care pathway approach that focuses on what the patient does not have, as opposed to what is causing their chest pain.

The study by Mahler et al[20] is to be applauded for highlighting the understudied nature of the American College of Cardiology/American Heart Association guideline recommendations for objective cardiac testing. We look forward to future studies by this group that are powered to determine the short- and long-term effect of the HEART Pathway on outcomes of ED chest pain patients. Successful clinical implementation of a highly sensitive tool that can facilitate the safe early discharge of more ED chest pain patients would be a tremendous gain for healthcare systems around the world, and defining a group of patients who do not need outpatient objective cardiac testing after ED discharge would be a further coup.

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