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Commentary: Solving the Cassandra complex: Improving actionability of predictions

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“...he does not know the sufferings that await him...”
—Cassandra of Troy (Euripides)

Discussions of predictions in medicine often evoke the thought of Cassandra, who in Greek mythology was sister of Paris of Troy. She was cursed with the ability to prophesize the future but for those prophesies to be ignored.

Patients undergoing cardiac surgery experience are at increased risk of postoperative pulmonary complications (PPCs).¹ These are associated with increased morbidity, mortality, hospital length of stay, and costs.²⁻⁴ Currently, there exist several risk-stratification instruments that use preoperative measurements to predict cardiac surgery patients' postoperative mortality.⁵ In this issue of the *Journal*, Khanna and colleagues⁶ present their novel and independently validated nomogram to risk-stratify cardiac surgery patients for PPCs. This is a strong study with the use of robust statistical methodology. Incorporating 13 preoperative, 10 intraoperative, and 2 postoperative variables, it demonstrated excellent discrimination for PPCs among 17,433 patients undergoing cardiac and vascular surgery.⁶ This model and the nomogram derived therefrom certainly offer a distinct advantage over risk-stratification tools that are based solely on preoperative

CENTRAL MESSAGE

A novel and independently validated nomogram predicts risk of postoperative pulmonary complications in cardiac surgery patients. Its intra- and postoperative clinical utility remains to be seen.

variables. Simply put, patients without preoperative predictors still experience PPCs. This is due to invariable interaction between patient baseline risk and the multitude of potential intraoperative and postoperative insults—factors not typically accounted for. However, this issue drives at the heart of the challenges in interpreting and using the results of this study. An intimately related issue is that of the distinction between discrimination and prediction, perhaps an issue that may be dismissed as esoteric by clinicians but is critical to understanding how we should view and use the evidence generated by Khanna and colleagues.⁶

The inclusion of intraoperative and especially postoperative variables certainly improves the ability of the model to discriminate between those who developed PPCs and those who did not. However, inclusion of such variables also limits the ability of the model to predict development of PPCs because the knowledge and incorporation of such “predictive” variables occurs too late and too close temporally to the development of PPCs (ie, the outcome), so late in fact that it would be infeasible to act on such predictions. Much like Cassandra and those poor souls who failed to heed her prophesies, it puts us in a situation of delayed foreknowledge that is impotent and without any capacity to avoid certain calamity. What, if any, adjustments can be made to a patient's care in the preoperative period if nearly one half of the variables used for prediction derive from the intra- or postoperative period? The authors address this by describing the

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“optimal approach”: identify high-risk patients using the nomogram in an “incremental manner” throughout the perioperative period.⁶ Certainly, using intraoperative events to immediately stratify patients for postoperative care could be feasible. Depending on the type of procedure and use of intra-aortic balloon pump, among other variables identified by the authors,⁶ a patient could be targeted specifically for intensive care, step-down, or short-stay units. This would allow them to receive care most suitable to their needs as well as facilitate better resource allocation for hospitals. Nevertheless, the nomogram’s utility is still further undermined by the incorporation of postoperative variables. Little can currently be done to ameliorate the impact of immediate postoperative events once they occur. That being said, this is not all doom and gloom. Although real-time adaptive prediction is not yet a reality, studies like this one by Khanna and colleagues⁶ foreshadow an exciting future that is made possible with growing technological capacity for real-time patient monitoring and explosions in computational power of analytic systems coupled with advances in machine learning. It is conceivable that real-time collection of data can generate risk-prediction on an ongoing basis and flag high-risk patients in real-time, such that clinicians can intervene successfully even when the predictor is temporally close to the outcome.⁷

Returning from the future to the present: given the remaining one half of predictor variables are derived from the preoperative environment, what can be done for those patients identified as high risk preoperatively? The authors allude to “preemptive measures” that could then be implemented but do not go so far as to endorse specific measures.⁶ The most apparent interventions would be around improving the modifiable risk factors themselves (such as smoking, hypertension, diabetes, and ejection fraction).⁶ In addition to optimizing lifestyle and medical management, these risk factors could be targeted using interventions such as respiratory physiotherapy and prehabilitation.^{8,9} To improve patient adherence to these risk-reduction strategies, preoperative acute pain management consults could also be incorporated. Ultimately, these interventions could all be integrated under formal enhanced recovery protocols for select patients,¹⁰ which have been shown to reduce PPCs in a variety of surgical populations.¹¹

Overall, the authors offer a novel instrument to identify patients undergoing cardiac surgery who are at risk for

PPCs by using a combination of perioperative variables. The rigorous study methodology and the instrument’s application in a large dataset help to substantiate its internal validity. The major limitation is that the true capacity for prediction is lower than suggested by the conclusions and the abstract of this study. However, there are 2 important facts that inform how the reader should interpret this limitation. First and foremost, the truth is that even with omission of the intraoperative and postoperative variables, the model by Khanna and colleagues is robust and has excellent discrimination and prediction, better than most reported in the literature. Second, the inability to act on intraoperative and postoperative risk factors is not immutable just because we lack the capacity today. It will be possible with advances in technology and computation; we just have to be paying attention, as Khanna and colleagues have.

At the end of the day, the curse of Cassandra was not that she was wrong but that those around her failed to listen to her. We would all do well to avoid such a fate.

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