Vasoactive-ventilation-renal score...a preliminary report

Tara Karamlou, MD

From Cardiovascular Research Institute, Phoenix Children's Hospital, Phoenix, Ariz.

Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication July 28, 2016; accepted for publication July 30, 2016; available ahead of print Sept 13, 2016.

Address for reprints: Tara Karamlou, MD, Phoenix Children's Hospital, 1919 E. Thomas Rd, Phoenix, AZ 85016

(E-mail: tkaramlou@phoenixchildrens.com).

J Thorac Cardiovasc Surg 2016;152:1430-1

0022-5223/\$36.00

Copyright © 2016 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2016.07.068>

The study by Scherer and colleagues¹ in this issue of the *Journal* investigates the predictive utility of the vasoactive-ventilation-renal (VVR) score regarding hospital length of stay (LOS). The present study is an extension of the authors' previous work on the VVR score,²⁻⁴ and the authors should be commended for their diligence in developing a useful clinical prediction algorithm that could contribute to higher quality care for patients undergoing congenital cardiac surgery. There are 2 questions to consider when evaluating the merit of the present study: (1) Are the data sufficiently novel, and (2) do the inferences reached by analyses of the data contribute important new knowledge to our field?

Let's examine the criteria for publication, as listed on the author submission guidelines for the *Journal Nature*.⁵ The criteria for publication of scientific papers (Articles and Letters) in *Nature* are that they report original scientific research (the main results and conclusions must not have been published or submitted elsewhere), are of outstanding scientific importance, and reach a conclusion of interest to an interdisciplinary readership.

Scherer and colleagues,¹ on the basis of the promising data from their initial retrospective studies,²⁻⁴ performed a prospective observational study of 164 patients undergoing cardiac surgery at their institution. In this study, the authors developed the score and showed that the VVR score was predictive of longer LOS. In the present study, the authors' main hypothesis was that the VVR score among a broader population (adult patients with congenital heart disease and those undergoing surgery with and without cardiopulmonary bypass) obtained at earlier, potentially more clinically useful time points would have greater discrimination for longer LOS than the vasoactive inotrope score (VIS) or serum lactate. On the basis of receiver operating characteristic curves and their corresponding c-statistics, the authors concluded that the VVR score at 12 hours (compared with other intervals, including 6, 24, and 28 hours) after intensive care unit admission is an equally robust predictor of prolonged hospital LOS and that it outperforms the predictive utility of the VIS, serum lactate, and other patient factors, such

Tara Karamlou, MD

Central Message

The article on the utility of the VVR score provides formative data that should be viewed as a preliminary step.

See Article page 1423.

as age, weight, and Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality categories.

To return to the question of whether the present study adequately satisfies widely accepted criteria for publication, let's deconstruct the rubric proposed in the article. First, Scherer and colleagues¹ assert novelty and importance because they have included a broader population, notably patients with adult congenital heart disease and those not requiring cardiopulmonary bypass, who were excluded in the initial study. From review of Table 1, the median age was 9.3 months (interquartile range, 2.6- 57.8 months), with a maximum age of 33 years. The authors do not disclose the number of adult patients included and report only 16 patients who underwent a systemic-to-pulmonary artery shunt or a pulmonary artery band. Therefore, is the claim that these data extend their previous work actually true?

Second, Scherer and colleagues¹ assert novelty and importance because of the varied time points investigated. Their analyses demonstrate that the VVR score at 12 hours has excellent discrimination (c-statistic is 0.93), but this is not significantly different than the discrimination of the score at the other investigated time points. Although it may be true that the provision of knowledge at 12 hours may be more helpful to direct clinical interventions than at 48 hours, it seems somewhat counterintuitive that waiting until 12 hours as opposed to acting within 6 hours would be

advantageous. This inconsistency is especially surprising given the authors' statement that "earlier prognostic data may increase the functionality of the VVR."¹ I would submit that the term "earlier," as used in this article, should be further qualified.

Third, the reader is informed that the VVR score outperforms the current VIS, the serum lactate, and several other important factors, such as patient age, weight, and Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality categories score. This is a somewhat unfair comparison. The VVR is a score composed of 3 components, one of which (serum creatinine) is related to patient age. Increasing the number of variables within a statistical regression model (unless they are prohibitively numerous or superfluous) will improve the predictive ability of the model. Therefore, it would be expected that the VVR score would improve model performance compared with a single variable model. Two interesting and potentially informative steps would be (1) to provide model performance using the individual components on the VVR score using t-statistics of the candidate parameters or by comparing likelihood ratio tests for a full versus the simplified models and (2) to provide additional information about the relationship between creatinine and age in the study population, which also may have elucidated whether VVR discrimination varies with patient age.

Finally, Scherer and colleagues¹ have failed to account for several important factors in their multivariable analysis, given the heterogeneity in patient age and complexity studied and the outcome metric LOS. A good example of the problems with using LOS in this varied population is postoperative feeding issues. Neonates, especially those within the higher complexity subgroups, may remain in the hospital until they "learn" to feed or obtain more

permanent feeding access with a surgical gastrostomy or nasogastric tube. Such concerns are unlikely to be needed in older children or adults and illustrate the need to explore interaction terms and variable relationships. Admittedly, however, it is reassuring that the final model had excellent predictive utility for prolonged hospital LOS.

Scherer and colleagues¹ systematic approach of directed prospective investigation based on promising retrospective data is excellent. The VVR score that they have developed and tested in this thoughtful manner may well become an important stratification tool for patients after congenital cardiac surgery. However, the single-institution data presented feel more like preliminary data that would fuel interest for a multi-institutional study, and therefore, I remain pessimistic that the present study fulfills the necessary criteria for a high-impact publication that will influence the clinical care for our patients...yet. Not unexpectedly, the authors state in their conclusions that a multi-institutional validation study would be the next step. I, for one, will await the final chapter...looking ahead only ruins the read.

References

1. Scherer B, Moser EAS, Brown JW, Rodefeld MD, Turrentine MW, Mastropietro CW, et al. Vasoactive-Ventilation-Renal Score Reliably Predicts Hospital Length-of-Stay after Surgery for Congenital Heart Disease. *J Thorac Cardiovasc Surg*. 2016;152:1423-9.e1.
2. Miletic KG, Spiering TJ, Delius RE, Walters HL III, Mastropietro CW. Use of a novel vasoactive-ventilation-renal score to predict outcomes after paediatric cardiac surgery. *Interact Cardiovasc Thorac Surg*. 2015;20:289-95.
3. Miletic KG, Delius RE, Walters HL III, Mastropietro CW. Prospective validation of a novel vasoactive-ventilation-renal score as a predictor of outcomes after pediatric cardiac surgery. *Ann Thorac Surg*. 2016;101:1558-63.
4. Gaies MG, Jeffries HE, Niebler RA, Pasquali SK, Donohue JE, Yu S, et al. Vasoactive-inotropic score is associated with outcome after infant cardiac surgery: an analysis from the Pediatric Cardiac Critical Care Consortium and Virtual PICU System Registries. *Pediatr Crit Care Med*. 2014;15:529-37.
5. Getting published in nature. Available at: www.nature.com. Accessed July 26, 2016.