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EDITORIAL COMMENTARY

Acute kidney injury after Fontan completion: Risk factors and outcomes “The good, the bad, and the ugly”

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See related article on pages 190-7.

THE GOOD...

The article by Esch and colleagues¹ in this issue of the *Journal* is an excellent example of a hypothesis-driven investigation of the factors influencing a clinically important postoperative event, acute kidney injury (AKI), by harnessing the information provided by a unique iatrogenic condition—Fontan physiology, in essence, a “natural experiment” of sorts. Although the results of the study did not prove the original hypothesis, that elevated central venous pressure (evident after Fontan completion) was causal in the pathway of AKI, the data did uncover the

equally important finding that systemic hypotension-mediated reduction in renal perfusion pressure was likely the primary driver of post-Fontan AKI.

Recently described and validated definitions of renal dysfunction, including the modified Risk, Injury, Failure, Loss, End-stage renal disease (pRIFLE) score² and the Acute Kidney Injury Network (AKIN) criteria,³ have made understanding the incidence and impact of AKI more accurate and consistent within pediatric patients and have facilitated stratification into severity quartiles. By using these definitions, the prevalence of AKI has been estimated as high as 56%,² and therefore the present study investigates a common and important problem among pediatric patients after cardiac surgery. Esch and colleagues¹ described their population using both the pRIFLE and the AKIN criteria, and they also analyzed whether AKI prevalence or severity stratification would be altered with preferential selection of either criteria. This comparison lends credence to their results and strengthens their article.

Esch and colleagues¹ selected an ideally suited study population, considering that cyanosis, single ventricle

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physiology, and repeated exposures to cardiopulmonary bypass are consistent risk factors for the development of postoperative AKI. Moreover, leveraging the unique aspects of Fontan physiology as a model to determine whether renal venous congestion or reduced arterial perfusion predominantly mediates AKI is a testament to the authors' ingenuity and creativity in clinical research.

Last, the management strategies proposed by Esch and colleagues,¹ including decreasing afterload reduction and judiciously adding in vasoconstrictor agents to target renal perfusion pressure, because they were based on understanding a pathophysiologic process, might have broader applicability to other patients after congenital cardiac surgery. In fact, although not done in the present study, systematic analysis of particular components within the inotrope score, such as the dose of epinephrine or dopamine compared with the dose of milrinone, could provide a relatively facile method for the authors to test their newly generated hypotheses.

THE BAD...

Despite these strengths, there are several important limitations that should inform the reader. The first and ostensibly most critical is whether Esch and colleagues'¹ recommendation to increase the renal perfusion pressure is truly feasible among those patients at risk for moderate to severe AKI. Inspection of the postoperative profile among this subset indicates the existing provision of heightened levels of support, including higher inotrope scores and total fluid intake. These measures notwithstanding, these patients had lower cardiac index and lower urine output, indicating that patients at risk for AKI may be physiologically unable to maintain optimum hemodynamics despite higher levels of support. Whether achievement of prespecified targets of resuscitation is predominantly an indicator of physiologic reserve rather than evidence that such targets are inherently beneficial has been studied extensively among critically ill patients.⁴⁻⁶ Velhams and colleagues,⁴ in their prospective randomized trial of critically injured trauma patients, examined this exact question. Among 75 patients randomized to the "optimal" hemodynamic group or the control group, in which "normal" hemodynamics were accepted, only those in either group who could achieve "optimal" hemodynamics gained a survival advantage, regardless of the resuscitation technique. Moreover, only 19% of those in the control group who failed to achieve the prespecified hemodynamic targets died, compared with 50% in the "optimal" group who similarly failed to achieve the prespecified targets. These data suggest that attempts to optimize patients who do not possess the necessary physiologic reserve may actually be detrimental.⁴ Therefore, the real question is what criteria can be used to predict which patients will be able to respond to efforts to increase their renal perfusion pressure without compromising their overall clinical status? A group of patients in whom this question is particularly

consonant is those with important atrioventricular valvar regurgitation. Clearly, the strategies outlined by the authors⁴ could adversely affect atrioventricular valve (AVV) function and reduce cardiac output. In the present study,¹ although those who underwent AVV repair had reduced hospital length of stay when higher renal perfusion pressure was achieved, this does not address the questions of whether atrioventricular valvar regurgitation per se may alter the risk-benefit ratio of this strategy, whether AVV function among those undergoing AVV repair was negatively affected by this therapy, or whether the durability of AVV repair was compromised in the longer term.

Second, the study population was heterogeneous, composed of the spectrum of single ventricle physiology. Moreover, there are important breaches in "internal" consistency within the demographics, such as patients with systemic right ventricles having a higher prevalence of AKI, yet those patients with hypoplastic left heart syndrome (arguably the most severe morphologic form of systemic right ventricle) having a lower prevalence of AKI. Finally, although Esch and colleagues¹ described renal dysfunction using both AKIN and pRIFLE, their multivariable analysis of factors associated with AKI reverts back to a dichotomous "any AKI" outcome. Although this decision increases the statistical power of the study, it weakens the utility of identified predictor variables, especially considering the authors' other analysis demonstrating only moderate severe grades of AKI to be associated with their secondary end point. Clearly, clinical therapies often mandate discrete boundaries, but the use of a continuous metric of renal function, such as estimated glomerular filtration rate, could provide a more illuminating analysis and by avoiding arbitrary categorization, transcends the inevitable changes in such clinical boundaries over time.

AND THE UGLY...

Why is this study¹ interesting and what is the relevance to a surgical audience? Most (96%) of the patients had only mild or moderate AKI that resolved without identifiable sequelae at 1 year. The management outlined (for most pediatric cardiac surgeons) lies mainly in the purview of the cardiac intensive care physician, and it is doubtful that many surgeons are intensely interested in transient events without significant clinical residua. Moreover, the one modifiable "surgical" factor identified, minimizing exposure to cardiopulmonary bypass, is passé.

However, the importance of the present study¹ lies in its tremendous potential. Heightened attention to metrics that reduce resource use among the public, insurance providers, and hospital administrators demand similar attention and vigilance by congenital surgeons. The follow-up time of 1 year in the present study is insufficient to exclude possible longer-term implications of post-Fontan AKI. Watkins and colleagues⁷ have found postoperative AKI to be associated

with mortality at 4 years among pediatric patients who underwent cardiac surgery. Furthermore, given that 8% of the patients receiving the Fontan had enduring renal dysfunction, resolution of a higher-risk subset within this population may be possible with additional surveillance. Finally, as congenital surgeons push the envelope with single ventricle palliation and the fragility of those surviving Fontan completion and beyond increases, the relevance of Esch and colleagues'¹ findings and suggested management strategies will likewise undoubtedly increase.

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