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EDITORIAL COMMENT

Beyond Technical Success of Fetal Aortic Valvuloplasty*

Lindsay R. Freud, MD

Fetal aortic valvuloplasty (FAV) for severe aortic stenosis with evolving hypoplastic left heart syndrome has advanced considerably since it was first described over 30 years ago.[1] In the 2000s, the experience was revitalized in North America by the teams at Boston Children's Hospital and Brigham and Women's Hospital. The program in Boston has remained a leader in FAV and, admirably, continues to report and refine their experience with patient selection, technical adaptations, and outcomes.

In this issue of *JACC: Advances,* the Boston group reports their technical success and serious adverse events in an impressive number of FAV procedures performed at their center over 20 years (n = 165).[2] The key findings, which expand upon their prior work in FAV,[3] demonstrate that greater left ventricular (LV) size by long axis dimension z-score and higher ejection fraction were predictors of technical success, while earlier gestational age, smaller LV size by 5/6 area-length calculated volume, and increased procedure time were associated with serious adverse events. These findings continue to highlight not only the importance of LV size but also the importance of LV health, ie, ejection fraction, for a technically successful outcome. More advanced gestational age and decreased procedure time likely render the fetus more "resilient" to LV puncture and the hemodynamic sequelae of FAV.

As candidacy for FAV[4] and improved technical success with less adverse events point to a larger, healthier LV at a more advanced gestational age, it behooves us to ask the question of what we are trying to achieve for this patient population. FAV is performed for fetuses with severe aortic stenosis and distinct physiologic features suggestive of evolution to hypoplastic left heart syndrome to prevent further adverse LV remodeling, mitigate left heart growth arrest, and, ultimately, permit a biventricular outcome after birth. Waiting too late for FAV may be a missed opportunity to avoid a single-ventricle outcome. On the other hand, if fetuses need to have a larger, healthier LV for technical success and features suggestive of a salvageable LV, ie, generating significant pressure,[4] do they need the procedure? Where does the line become drawn where fetuses may be "good" technical candidates but do not necessarily require FAV for a biventricular outcome after birth? Or perhaps the better question is—when? At what timepoint would the LV not be expected to re-model or growth arrest be mitigated?

Moreover, among fetuses with technically successful interventions who are live-born, approximately half will have biventricular circulation at experienced centers.[4-6] This is an amazing feat over the past 20 years, which has been heralded by the Boston group, but why do only half respond? These are questions that arise from this work and others. Technical success cannot be divorced from an understanding of the postnatal outcomes achieved.

If we restrict the conversation to technical aspects, then it would be informative to understand maternal, as well as fetal, factors that influence procedural outcome. Body mass index, for example, may affect technical success and whether FAV is offered. While the procedure appears to be performed with limited maternal morbidity and no known mortality,[7,8] there

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From the Division of Cardiology, Department of Paediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.
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is a paucity of data regarding maternal candidacy, safety, and tolerability in the literature.

The Boston group also highlighted their procedural learning curve. They were able to achieve a higher rate of technical success and shorter procedure times in the most recent era, 2010 to 2020, as compared to the earlier era, 2000 to 2009, which is noteworthy. However, the rates of serious adverse events and fetal demise were not significantly lower. The overall serious adverse event rate was 41%, and the fetal demise rate was 8%. How one perceives these risks depends on the frame of reference of the expectant parent(s). Management of hypoplastic left heart syndrome has improved, but morbidity and mortality remain high. A biventricular outcome likely offers improved long-term outcomes, but the upfront cost is steep. Where the favorable risk-benefit ratio falls is up to the expectant parent(s), guided by their values and the information they receive. This is where the art of fetal counseling takes center stage.

During counseling for FAV, the procedural outcomes reported in this issue are valuable to share. However, center outcomes are known to be variable, particularly when volumes are lower. In a report from the International Fetal Cardiac Intervention Registry in 2020,[9] 108 FAV procedures were performed across 15 fetal interventional centers (not including Boston) from 2002 to 2018. Center-specific outcomes were not reported, but these numbers would suggest that, on average, 7 to 8 cases were performed per center. The serious adverse event rate was only slightly higher at 48% in the context of a broader definition, but the fetal demise rate was almost 18% (19/108)—more than double that reported by the Boston group.

These disparate outcomes raise several issues. First, center-specific outcomes, including rates of technical success and serious adverse events, need to be transparent to expectant parent(s) during counseling. They should also be benchmarked to the outcomes reported in this issue. One decision-making model has suggested that for fetal demise rates greater than approximately 12%, the risks of the FAV may outweigh the benefits.[10] All centers that offer FAV should periodically review their fetal demise rates with this threshold in mind. To that end, there should be national, or even multinational, regionalization of fetal cardiac intervention to provide the best possible fetal and maternal outcomes. While regionalization has occurred in some parts of the world (ie, all fetal cardiac interventions in Canada are performed at the Hospital for Sick Children and Mount Sinai Hospital in Toronto), it should be formalized. The recent recommendations for centers performing congenital heart surgery in the United States may serve as a foundational framework.[11]

For better or worse, fetal aortic stenosis with evolving hypoplastic left heart syndrome is relatively rare. Among those with the condition, ideal fetal and maternal candidates for intervention are even less common. This poses challenges not only for centers to gain technical expertise but for all of us in the field to rigorously evaluate FAV postnatal outcomes. Calls for a randomized-controlled trial have been hampered by concerns regarding cost and time given the rarity of the disease, as well as by questions of equipoise. Our solution as a diverse community will require research methodology that is thoughtfully crafted and, like FAV, innovative and unconventional.

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ADDRESS FOR CORRESPONDENCE: Dr Lindsay Freud, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada. E-mail: lindsay.freud@sickkids.ca.

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