We need better pediatric cardiac transplantation risk modeling

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Received for publication Oct 28, 2021; revisions received Dec 15, 2021; accepted for publication Dec 20, 2021; available ahead of print Jan 11, 2022.

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J Thorac Cardiovasc Surg 2022;164:2036-9
0022-5223/36.00
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It is our opinion that the United Network for Organ Sharing (UNOS) and the Scientific Registry of Transplant Recipients (SRTR) should undertake the task of improving risk modeling for the wide spectrum of patient complexity unique to pediatric cardiac transplantation. While some programs may disagree, it is our opinion that the risk associated with performing transplantation in children with dilated cardiomyopathy (DCM) with zero or 1 prior sternotomy is markedly different than the risk associated with children undergoing a fifth sternotomy for failed congenital heart disease (CHD), particularly those after the Fontan procedure. Major registry data indicate 1-year survival of 95% or higher in children with DCM compared with 80% to 90% for patients with CHD (patients with biventricular and single ventricular physiology combined).

We would respectfully put forward 2 alternative options to the current SRTR assessment: (1) retain the current data set and risk adjust and report only for patients with DCM; or (2) add more data elements to the data set to allow for better risk adjustment of the patients with more complex CHD. We offer a basis for this opinion.

The Reality of the Current Dataset and Model

The current UNOS dataset was implemented in 1994, at a time when patients with CHD and particularly patients who received the Fontan comprised a minority of cardiac transplant recipients. The dataset includes several relevant variables, but characterizes the congenital morphology in a binary manner as the presence or absence of CHD. Based on the variables required by UNOS data collection, the model does not include the form of CHD (eg, single-ventricle vs 2-ventricle anatomy), the specifics of prior interventions or palliations (eg, Fontan palliation), the number of prior sternotomies, the degree of sensitization (above the simple panel reactive antibody percentages without assessment of the severity of the associated titers), the number of required concomitant reconstructions at the time of transplantation, and many other potentially relevant variables. To be clear, we list these variables only to illustrate the lack of granularity in the current dataset. At this point, we recognize the challenges posed by the heterogeneity of the CHD population and do not claim to know exactly which new variables might be needed to improve the risk modeling.
We also emphasize that the UNOS/SRTR has not provided information about the accuracy of their models, specifically for pediatric organ transplantation, or evaluated their consistency with larger (and often more granular) registry data sets. In adults, a cohort with significantly greater homogeneity and better model performance, Wey and colleagues’ reported that SRTR-derived observed-to-expected (O/E) outcomes and tier rankings were not associated with outcomes after listing specifically for heart transplantation. It is difficult to imagine it would be better for a notably more heterogeneous pediatric population with approximately one-tenth of the number of patients from whom to derive a model.

An Informal View of Our Specialty
In 2018 and 2019, we conducted an informal survey (questions provided in Appendix E1) of pediatric transplant programs in the United States. Twenty-five programs representing the majority of well-established pediatric cardiac transplant programs in the United States completed and returned the survey. The brief summary of responses is as follows: (1) Over the most recent 4 years, 30% of programs performed more than 50 transplantations, and 22% of programs performed 15 to 30 transplantations; (2) 68% of programs indicated CHD comprised 50% to 75% of their volume; (3) 76% indicated that patients with single-ventricle physiology comprise more than 20% of their total transplant volume; (4) 6 programs indicated they had a recent UNOS report stating the probability that the hazard ratio for 1-year patient survival exceeding 1.2 was greater than 0.75 (a UNOS flag); and (5) 4 programs had lost designation as a center of excellence or been downgraded by a payer based on unfavorable O/E outcome reports. Most important, all programs indicated they view the current risk modeling as insufficient, even those that had not been flagged or had their payer standing impacted by a UNOS report. The majority thought there should be 2 separate risk models, 1 for CHD and 1 for cardiomyopathy, whereas a minority favored a single but improved risk model.

The Currently Proposed New Program Metrics
At the time of this writing, UNOS had just closed public opinion on new proposed program evaluation metrics. Those are as follows.

1. The waiting list mortality rate ratio describes the risk of death once candidates are listed but before they undergo transplantation. The waiting list mortality rate ratio estimates the program’s waiting list mortality relative to the national expectations.

2. The offer acceptance rate ratio indicates whether a program is more or less likely to accept offers than the national average. If the offer acceptance ratio is greater than 1.0, then the program tends to accept more offers than average; if the offer acceptance ratio is less than 1.0, then the program tends to accept fewer offers than average.

3. The 90-day graft survival hazard ratio provides an estimate whether the program has higher or lower than expected organ failure rates during the first 90 days after transplant compared with transplant outcomes for all US transplant programs. Organ failure numbers include organ failures, retransplantation, and patient deaths.

4. The 1-year graft survival conditional on 90-day graft survival hazard ratio provides an estimate of whether the program has higher or lower than expected graft failure rates during the first year after transplant.

We question the removal of 3-year survival and the reasons thereof; however, we offer no opinion on these metrics because that would be beyond our scope and purpose. To be clear, our focus is risk modeling and the traditional metrics. We include the new metrics in this opinion because any new metrics may also require additional data collection for accurate risk adjustment. Regardless of which metrics are chosen (if any), all (just as the currently used metrics) will remain vulnerable to inadequate risk adjustment because of insufficient data. Moreover, we suspect that some of the proposed metrics will require even more additional data elements to permit accurate risk modeling. Without accurate modeling, current and potentially new metrics could have marked unintended consequences in pediatric heart transplantation, specifically where differences in model accuracy between diagnostic groups may further deter listing of or transplantation in higher-risk patients.

Potential/Actual Consequences of Inaccurate Risk Modeling
Transplant programs in the United States are greatly impacted by the UNOS-reported (SRTR risk model calculated) O/E survival data (and any new metrics approved), because payers and accrediting entities rely on that data to make decisions about various center designations, in or out of insurance network plans, and willingness to negotiate on one-off contracts, among other critical access issues. Moreover, the bureaucratic burden to a UNOS-flagged program (and UNOS staff) can be immense. To be clear, we strongly support the mission of UNOS reporting and the scrutiny of program processes and outcomes, as well as ongoing improvement and maintaining performance standards. However, to fulfill that overall mission, it is critical that any risk modeling be accurate, meaningful, and consistent with real-life experience and understanding provided by experts in the field. Currently, this is not the case. For example, a program with patients who have undergone the Fontan, comprising 30% to 50% of overall annual volume achieving an 85% to 90% 1-year survival for those patients (a reasonable outcome for Fontan patients based on
registry data), will likely suffer the consequence of a “trig-
grering” O/E. At the same time, a program with transplant recipients predominantly with DCM may have a 95% to 100% 1-year survival and a “passing” O/E. The concern ex-
tends broadly because approximately half the programs in the United States perform 10 or fewer transplants per year, and 1 bad outcome can influence program evaluation.

Reporting inadequately adjusted outcomes, flagging, and the ensuing risk aversion not only impact programs but also can have a profound impact on patients and families. Examples include (1) being required by insurance to go to a program that does not have the expertise or infrastructure to provide the requisite care to high-risk pa-


tients; (2) being denied listing to preserve program metrics or due to evaluation at a program with inadequate experience; and (3) longer time on the wait list waiting for the “perfect” donor organ, resulting in higher risk of clinical deterioration and removal from the wait list. The latter may also affect the UNOS stated goal of efficient use of the greatest number of donor organs. Eliminating trans-

plants with high-risk donor or high-risk recipient status from the SRTR analysis might help reduce risk aversion, but this would require well-defined and validated criteria for a “high-risk” recipient.

Programs with experience and expertise in managing the entire spectrum of complexity face a mixed-message conundrum in their quest to be good stewards of limited donor organs while at the same time fulfilling the UNOS mission of directing organs to those patients with the greatest risk of death. Our specialty has promoted the survival of a significant and growing number of patients with complex CHD. Do we now simply apologize and deny them further lifesaving treatment?

What Can/Should We Do?

As a specialty, we continuously undertake initiatives to improve the overall care of the patients with more complex end-stage cardiac disease as they begin on the downward slope. Referral criteria for advanced therapies specific to the patient with complex CHD have recently been produced by a multi-site quality improvement learning network of pediatric programs (Advanced Cardiac Therapies Improving Outcomes Network), including specific recommendations for the Fontan patient. It is clear to those who practice in the field that there is a critical need to move away from the “adult ischemic”-based criteria to promote earlier referral. We could also do better at risk standardization and at least extend some effort to dialogue on what level of risk is acceptable for a competent program. We should continue our efforts to optimize mechanical circulatory sup-

port with the goal of eventually reaching a state of pro-
longed support and durable destination therapy that provides comparable length and quality of life to that pro-

vided by transplantation. There are certainly many other similar initiatives, and we as a community are dedicated to pursuing all means of prolonging and improving the lives of children with all forms of end-stage heart disease.

As a representative group of major pediatric heart transplant programs, we uniformly regard the current risk model as inadequate and believe it is time for the UNOS and our specialty to work collaboratively on developing better risk models. Even if the UNOS reported on only patients with DCM, either permanently or while developing more complete modeling for all diagnoses, accurate risk assessment for current metrics and CHD will require the addition of new data currently not collected by UNOS. We can only speculate that addition of new metrics could also require the addition of new data. We refrain from any claim that we currently have the answers. We acknowledge a host of challenges and the need for a plan addressing each chal-

lenge. In our opinion, the best path forward is an initial dia-

logue among our specialty (and its focused societies), UNOS, and SRTR to fully delineate the challenges, designate working groups to develop plans, enact those plans, and have representation within UNOS that can move the process forward. Will this be difficult? Yes. We acknowl-

edge this is not a trivial undertaking with significant implications for additional time, effort, and money. But it is eminently doable, and we owe it to our patients and our programs to strive together to meet the SRTR’s vision of providing “information that is accurate, clear, and timely” in support of our national organ transplantation systems.

Conflict of Interest Statement

R.K.W.: co-founder of OperVu, Inc (no relationship to content of this work). J.K.K.: DSMB, Xeltis (no relationship to content of this work). I.A.: consultant or proctor for Berlin Heart Inc, Medtronic Inc, Jarvik Inc, BiVACOR Inc, and Sony-Olympus Medical Solutions Inc. All other authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References


Key Words: pediatric cardiac transplantation, risk modeling
APPENDIX E1

This survey is being sent to pediatric heart transplant programs in the United States. We sincerely appreciate your participation. The purpose is to obtain information about public reporting of SRTR data and any potential impact on program status with respect to payors and various designations (eg, center of excellence) that may influence provision of care and patient referral. We recognize that accurate answers to certain questions will require an investment of time on your part. We thank you in advance for being willing to do so. The survey is designed so that we will not be able to identify individual programs. All information is and will be kept anonymous. We will analyze the composite information for any relevant findings.

All questions pertain only to pediatric patients (<18 years old at time of listing) and should include data based on transplantation occurring between January 1, 2012, and January 1, 2016.

1. For the 4-year period, your total number of pediatric heart transplants was
   a) <15
   b) 15-30
   c) 30-50
   d) >50

2. For the 4-year period, the percentage of patients undergoing transplantation at your program with DCM was
   a) <25%
   b) 25%-50%
   c) 50%-75%
   d) >75%

3. For the 4-year period, the percentage of patients undergoing transplantation at your program with CHD was
   a) <25%
   b) 25%-50%
   c) 50%-75%
   d) >75%

4. For the 4-year period, the percentage of patients undergoing transplantation with single-ventricle heart disease (any stage of palliation, denominator is total number of transplants regardless of etiology of heart disease) was
   a) <5%
   b) 5%-10%
   c) 10%-20%
   d) >20%

5. For the 4-year period, how many patients were referred to you and evaluated for transplantation after being declined listing at another program?
   a) <4
   b) 4-6
   c) 6-12
   d) >12

6. On your first SRTR report from 2016 for 1-year patient survival, was the probability that the hazard ratio exceeded 1.2 greater than 0.75?
   a) yes
   b) no

7. On your first SRTR report from 2016 for 1-year patient survival, was the O/E ratio
   a) <1
   b) 1-2
   c) 2-2.5
   d) >2.5

8. At any point in the past 10 years, has your center carried a center of excellence designation or other similar ranking (from any reimbursement entity, rating agency, or carrier)?
   a) yes
   b) no

9. At any point in the past 4 years, has your center lost a center of excellence designation or other similar ranking or been downgraded by any reimbursement entity, rating agency, or carrier?
   a) yes
   b) no

10. Your opinion regarding the current risk-adjustment model and SRTR pediatric heart transplant data reporting best fits which of the following responses? In answering this question, please assume an ideal situation in which change could be easily implemented.
    a) We are satisfied and think that nothing should be changed.
    b) We are dissatisfied and think that change is needed—report only based on DCM patients.
    c) We are dissatisfied and think that change is needed—creating a better risk model for all diagnoses and report based on all patients.
    d) We are dissatisfied and think that change is needed—create separate risk models for CHD and DCM and provide separate reports for each.