Journal of the American Heart Association

EDITORIAL

Why Haven't We Seen This Before? The Importance of Reporting Experience to Improve Access and Equity

Kurt R. Schumacher, MD, MS

Recently, our team was asked to evaluate a unique patient for pediatric heart transplant. She was a 5-month-old female patient with trisomy 21 and a tetralogy of Fallot–type atrioventricular septal defect status post complete surgical repair 2 months earlier. The surgery was complicated complete heart block and pacemaker dependence, but she recovered uneventfully and was discharged home after several weeks. After 3 weeks at home, she presented to the emergency department with lethargy and was found to be in cardiogenic shock. Her echocardiogram demonstrated a severely dilated left ventricle and severely depressed biventricular function. She required support with venoarterial extracorporeal membrane oxygenation. After 4 days, she was able to be weaned from mechanical circulatory support, but her systolic function demonstrated no signs of recovery despite aggressive medical management, prompting referral for heart transplant evaluation. While perhaps an unusual case given the specific congenital heart disease lesion, none of the patient's cardiac course was particularly impactful in terms of our team's decision making on transplant candidacy. However, her Down syndrome made her extremely unique as a heart transplant candidate at our center. We had never been asked to consider transplant in a patient with trisomy 21 before. We were completely ignorant of the ramifications of Down syndrome on transplant outcomes. Was the increased risk of pulmonary vascular disease present in these patients a risk for long-term graft function and survival?[1] Given the increased incidence of leukemia in individuals with Down syndrome, was the risk of posttransplant lymphoproliferative disorder higher than normal?[2] Did trisomy 21–associated immunologic dysfunction predispose to posttransplant infection?[3] At the time, the medical literature was unhelpful. Without any further available knowledge to be gained on trisomy 21's impact on posttransplant outcomes and having deemed the infant to be a candidate for transplant, we proceeded. After a few months, she was transplanted and had an uneventful perioperative course. Now, more than a year later, she is thriving. However, her success has raised more significant questions. At our large program, why had we never been consulted on a child with Down syndrome before despite the high incidence of cardiac disease in this population? Was the necessity of transplant a rare occurrence in this group of individuals, or was the lack of transplants in patients with Down syndrome suggestive of a more concerning problem in health equity?

See Article by Godown et al.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Godown and colleagues[4] provide the information we sought when considering our patient's candidacy. Although essentially a case series, the authors go to great lengths to establish that

Key Words: Editorials ■ Down syndrome ■ health disparities ■ heart transplantation ■ outcomes

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

Correspondence to: Kurt R. Schumacher, MD, MS, Congenital Heart Center, C.S. Mott Children's Hospital, University of Michigan, 1540 E Hospital Dr, Ann Arbor, MI 48109. Email: kurts@med.umich.edu

For Disclosures, see page 2.

JAHA is available at: www.ahajournals.org/journal/jaha

based on the available data, heart transplant outcomes in patients with Down syndrome are not different from those in patients without Down syndrome. Despite most cases having congenital heart disease, a risk factor for decreased posttransplant survival, all 23 patients who underwent transplant survived to hospital discharge. Of that cohort, 20 patients remain alive, with a median follow-up of 2.8 years. This survival was similar to the general population without Down syndrome in the Organ Procurement and Transplantation Network database. Furthermore, freedom from rejection and malignancy was not different than in patients without Down syndrome. Infections occurred but in a minority of patients. The authors rightfully concluded that Down syndrome in and of itself should not be considered a contraindication to heart transplant. Although limited in case numbers, the data still strongly suggest that transplant in individuals with Down syndrome is feasible and may be considered in otherwise reasonable candidates. This type of report, even with limited cases, is extremely important. When faced with uncertainty about outcomes, it is sometimes hard to choose to actively move forward with an advanced therapy. This report should instill confidence that moving forward with heart transplant in individuals with trisomy 21 is possible.

However, the data also raise more significant concerns about access and equity for this population. Patients with Down syndrome have a congenital heart disease incidence as high as 44%.[5] They also have an increased risk of leukemia compared with the general population, raising the potential for anthracycline-induced cardiomyopathy.[2,6] These associations with Down syndrome suggest the possibility of an increased incidence of heart failure compared with the general population. In contrast, among 17 experienced pediatric heart transplant centers, only 28 total patients with trisomy 21 had been listed for transplant. Why? There is no clear answer as a contemporary study examining the incidence and outcomes of heart failure in patients with Down syndrome has not been published. Trisomy 21 affects 1 of 800 births worldwide,[6] with an estimated 200 000 individuals living in the United States today. It is possible that the relative rarity of the syndrome means that even a high relative incidence of heart failure in this population leads to low absolute cases. Alternatively, it may be that heart failure is a regular occurrence in these individuals, but rather than escalate to advanced care requiring a high level of medicalization, such as heart transplant, parents and families elect to pursue other pathways, such as medical management only or comfort care. On the basis of the experiences I have had caring for patients with Down syndrome in other venues, including the cardiac intensive care unit, I find it unlikely that parents would routinely choose against pursuing live-saving therapy for their child (acknowledging the limitations of my own experience and risks of generalization). It is also possible that providers are less vigilant in seeking heart failure symptoms or more symptom tolerant than they would be in patients without Down syndrome, leading to lack of perceived need for advanced heart failure referral. Perhaps heart failure is recognized, but the referral to an advanced heart failure or transplant provider is not made. A lack of referral could stem from a personal bias that it is not in the patient's best interest or a lack of understanding that advanced therapies, including heart transplant, are possible with favorable outcomes. Finally, it may be that heart transplant programs themselves have used trisomy 21 as justification for not offering transplant. Each of these potentials, poor heart failure vigilance, nonreferral, or declining heart transplant based on the presence of trisomy 21, would all represent an inappropriate limitation in access and lack of health equity for patients with Down syndrome who have heart failure. The results of Godown and coauthors make it clear, heart transplant can be a consideration in these individuals. If health inequities are causing inappropriate limitations of Down syndrome patient access to therapies, I sincerely hope that this report improves future access to care for all patients who could benefit. Data, information, and formal experience are meaningful in changing practices; publishing case series of other rare diseases could also lead to improved health equity.

ARTICLE INFORMATION

Affiliation

Congenital Heart Center, C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI.

Disclosures

None.

REFERENCES

1. Bush D, Galambos C, Dunbar ID. Pulmonary hypertension in children with Down syndrome. *Pediatr Pulmonol*. 2021;56:621–629. doi: 10.1002/ppul.24687
2. Taub JW, Berman JN, Hitzler JK, Sorrell AD, Lacayo NJ, Mast K, Head D, Raimondi S, Hirsch B, Ge Y, et al. Improved outcomes for myeloid leukemia of Down syndrome: a report from the Children's Oncology Group AAML0431 trial. *Blood*. 2017;129:3304–3313. doi: 10.1182/blood-2017-01-764324
3. Verstegen RHJ, Chang KJJ, Kusters MAA. Clinical implications of immune-mediated diseases in children with Down syndrome. *Pediatr Allergy Immunol*. 2020;31:117–123. doi: 10.1111/pai.13133
4. Godown J, Fountain D, Bansal N, Ameduri R, Anderson S, Beasley G, Burstein D, Knecht K, Molina K, Pye S, et al. Heart transplantation in children with Down syndrome. *J Am Heart Assoc*. 2022;11:e024883. doi: 10.1161/JAHA.121.024883
5. Freeman SB, Taft LF, Dooley KJ, Allran K, Sherman SL, Hassold TJ, Khoury MJ, Saker DM. Population-based study of congenital heart defects in Down syndrome. *Am J Med Genet*. 1998;80:213–217. doi: 10.1002/(SICI)1096-8628(19981116)80:3<213:AID-AJMG6>3.0.CO;2-8
6. Bull MJ. Down syndrome. *N Engl J Med*. 2020;382:2344–2353. doi: 10.1056/NEJMra1706537