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Commentary: Intraoperative hemorrhage in Fontan transplantation—a common and potentially modifiable challenge?

Danielle S. Burstein, MD,[a]
Carol Wittlieb-Weber, MD,[a]
Katsumeda Maeda, MD, PhD,[b] and
Joseph Rossano, MD[a]

Danielle S. Burstein, MD, Carol Wittlieb-Weber, MD, Katsumeda Maeda, MD, PhD, and Joseph Rossano, MD

CENTRAL MESSAGE

Strategies to mitigate risk for intraoperative hemorrhage after heart transplantation in adults with failing Fontan are needed to potentially improve outcomes.

Heart transplantation for failing Fontan circulation in adult patients is increasingly being used in the growing population of adult congenital heart disease survivors.[1,2] Patients with Fontan circulation develop a multitude of consequences that ultimately lead to need for heart transplantation, including ventricular dysfunction, atrioventricular valve regurgitation, Fontan circuit failure, lymphatic failure, and extracardiac organ failure, all of which may have differing inherent risks for post-transplant outcomes.[3] This population has considerable risk for poor outcomes after transplantation, including multiple previous sternotomies, abnormal systemic and venous anatomy requiring complex reconstruction at the time of transplantation, high thoracic arterial and venous collateral burden, highly sensitized status, lymphatic disease, liver disease, and coagulopathy. All of these factors potentially contribute to the complex intraoperative and postoperative course that can result in significant perioperative bleeding. Cardoso and colleagues[4] describe a high rate of intraoperative bleeding that was associated with a significantly greater risk of death, with a 30-day mortality rate of 57% among patients with major intraoperative bleeding.

Survival of patients with Fontan circulation after heart transplantation has significantly improved in the current era, with a 1-year survival of 89% among children.[5] Post-transplant outcomes in adults with Fontan circulation are poorer compared with children, with reports of 1-year survival ranging from 65% to 80%.[6,7] The 30-day survival of 81% and 1-year survival of 71% after heart transplantation in this single-center contemporary cohort of adult patients with failing Fontan circulation is consistent with previous reports. Previous studies have identified primary graft failure necessitating extracorporeal membrane oxygenation support and bleeding occurring in approximately 16% of patients, which is nearly 5 times greater than adult noncongenital transplant recipients.[6] In the cohort by Cardoso and colleagues,[4] intraoperative bleeding was even greater at 23%, and 29% required extracorporeal membrane oxygenation support for primary graft dysfunction. Previously identified risk factors for post-transplant mortality in patients with Fontan circulation include pediatric age, shorter Fontan-transplant interval <10 years, low systemic ventricular ejection fraction, moderate-to-severe atrioventricular valve regurgitation, end-stage liver disease, and mechanical circulatory and ventilatory support.[5,8] However, Cardoso and colleagues[4] are the first to identify intraoperative hemorrhage as a significant risk factor for post-transplant death, with an odds ratio of 30 (95% confidence interval, 2.8-322), with those who experienced intraoperative hemorrhage having a dismal 30-day survival of

From the Divisions of [a]Cardiology, and [b]Cardiothoracic Surgery, Children's Hospital of Philadelphia, Philadelphia, Pa.

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Address for reprints: Joseph Rossano, MD, Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104 (E-mail: rossanoj@email.chop.edu or rossanoj@chop.edu).

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43%. This is a single-center study of a small cohort, so the generalizability of these findings to a broader adult Fontan transplant population needs to be validated.

Ongoing evaluations and interventions to improve outcomes after transplantation in patients with Fontan circulation are needed. Notably, in the cohort described by Cardoso and colleagues,[4] the majority of subjects with major intraoperative bleeding had preserved ventricular function (n = 6, 85.7%), the only significant difference in the pretransplant characteristics analyzed (Table 2), highlighting the need to better understand the risk of bleeding in the setting of Fontan circuit failure. It is particularly challenging to determine when the risk of bleeding would make a patient ineligible for transplant. More refined hepatic and hematologic evaluation strategies in patients with Fontan circulation could help risk-stratify patients who may benefit from combined heart–liver transplantation and mitigate hepatic dysfunction-related coagulopathy, which contributes to intraoperative bleeding risk. In addition, the identification of strategies to mitigate bleeding risk, including preoperative assessment of collateral burden and potential aortocollateral embolization, may influence this risk, although it has to be weighed against the risk of recurrent catheterization and embolization needed due to rapid redevelopment of collateral vessels during the waitlist period. There may be additional risk factors that may be modifiable based on underlying cause for Fontan failure that warrant further investigation.

References

1. Atz AM, Zak V, Mahony L, Uzark K, D'agincourt N, Goldberg DJ, et al. Longitudinal outcomes of patients with single ventricle after the Fontan procedure. *J Am Coll Cardiol*. 2017;69:2735-44.
2. Schilling C, Dalziel K, Nunn R, Du Plessis K, Shi WY, Celermajer D, et al. The Fontan epidemic: population projections from the Australia and New Zealand Fontan Registry. *Int J Cardiol*. 2016;219:14-9.
3. McCormick AD, Schumacher KR. Transplantation of the failing Fontan. *Transl Pediatr*. 2019;8:290-301.
4. Cardoso B, Kelecsenyi A, Smith J, Jansen K, De Rita F, Nassar MS, et al. Improving outcomes for transplantation in failing Fontan—what is the next target? *J Thorac Cardiovasc Surg Open*. 2021;8:565-73.
5. Simpson KE, Pruitt E, Kirklin JK, Naftel DC, Singh RK, Edens RE, et al. Fontan patient survival after pediatric heart transplantation has improved in the current era. *Ann Thorac Surg*. 2017;103:1315-20.
6. Hernandez GA, Lemor A, Clark D, Blumer V, Burstein D, Byrne R, et al. Heart transplantation and in-hospital outcomes in adult congenital heart disease patients with Fontan: a decade nationwide analysis from 2004 to 2014. *J Card Surg*. 2020;35:603-8.
7. Bhama JK, Shulman J, Bermudez CA, Bansal A, Ramani R, Teuteberg JJ, et al. Heart transplantation for adults with congenital heart disease: results in the modern era. *J Heart Lung Transplant*. 2013;32:499-504.
8. Berg CJ, Bauer BS, Hageman A, Aboulhosn JA, Reardon LC. Mortality risk stratification in Fontan patients who underwent heart transplantation. *Am J Cardiol*. 2017;119:1675-9.