OPEN

Successful Heart-Liver Transplant Using Dual-organ Normothermic Perfusion in a Patient With Fontan Failure

Isaac S. Alderete, BS,[1] Qimeng Gao, MD, MHS,[1] Abigail Benkert, MD,[2] Katherine Sun, MD,[3] Riley Kahan, MBS,[1] Kannan Samy, MD,[1] Vincenzo Villani, MD,[1] Joseph W. Turek, MD, PhD,[2] Deepak Vikraman, MD,[1] Carmelo A. Milano, MD,[2] Michael W. Manning, MD, PhD,[3] and Andrew S. Barbas, MD[1]

Advances in surgical technique and multidisciplinary management have improved long-term survival for patients born with single ventricle physiology. However, patients who have undergone Fontan completion remain at risk for long-term comorbidities associated with the complex hemodynamic changes following the procedure, including Fontan failure and Fontan-associated liver disease.[1] Combined heart-liver transplantation (CHLT) is a rare but lifesaving procedure that has been described in the setting of heart and liver failure secondary to Fontan failure.[2] As long-term survival continues to improve for Fontan patients, the incidence of Fontan-associated liver disease will increase. Thus, improving CHLT outcomes and access to both organs is a strong priority.

Here, we describe a successful CHLT for a patient with chronic ventricular dysfunction and Fontan-associated liver disease. The key innovation in this case was the use of normothermic machine perfusion (NMP) to preserve both the heart and liver grafts. This approach extended the preservation time for the liver while also mitigating the risk of ischemic injury and reducing the time pressure constraints on the heart transplant team. Notably, this stands in contrast to traditional static cold storage (SCS), where metabolic activity is reduced through hypothermia, but the extended cold ischemic time can lead to increased vulnerability to reperfusion injury.

CASE DESCRIPTION

Our patient is a 45-y-old woman with a history of congenital double inlet left ventricle with L-looped ventricles and L-malposition of the great arteries who underwent atriopulmonary Fontan with oversewn tricuspid and pulmonary valves as an infant. Additional comorbidities include atrial flutter requiring multiple cardioversions, severe junctional bradycardia for which she received an atrial transvenous pacemaker, chronic ventricular dysfunction, and known liver disease secondary to cardiac cirrhosis. She was admitted to our institution following a presentation to the emergency department with new-onset ventricular tachycardia requiring electrical cardioversion. Inpatient workup revealed an ejection fraction of 18%. She had biopsy-proven cirrhosis 8 y before the presentation, and her liver function has deteriorated over the years. Given her worsened ventricular function, Fontan physiology, recurrent ventricular arrhythmias, and known liver cirrhosis in the setting of cardiac disease, she underwent multidisciplinary transplant evaluation and was deemed a suitable candidate for combined orthotopic heart-liver transplantation. The patient was listed as status 2 for a heart transplant and placed on the liver transplant waitlist.

Two weeks after placement on the waitlist, a suitable heart and liver became available from a young, standard criteria donor after brain death. Procurement teams traveled to the donor hospital and placed both organs on the Transmedics Organ Care System (OCS) devices. The recipient underwent redo sternotomy and was placed on cardiopulmonary bypass. After the arrival of the donor heart, implantation of the graft occurred in standard manner. The graft functioned well on the OCS device and it was preserved for a total of 253 min. The patient was successfully weaned and decannulated from cardiopulmonary bypass with good allograft function. To provide support for liver transplantation, venoarterial extracorporeal membrane oxygenation was initiated via femoral venous and central aortic cannulation.

The total liver preservation time was 660 min, including 556 min on the OCS device. The liver met goal flow rates

Received 14 September 2023. Revision received 26 October 2023.
Accepted 4 November 2023.

[1] Department of Surgery, Duke University Medical Center, Durham, NC.
[2] Division of Cardiovascular and Thoracic Surgery, Duke University Medical Center, Durham, NC.
[3] Department of Anesthesiology, Duke University Medical Center, Durham, NC.

I.S.A. participated in conception and study design, analysis, and interpretation of data, drafting and critical revision of the article, and final approval of the version to be published. Q.G., A.B., K.S., R.K., and A.S.B. participated in conception and study design, interpretation of data, critical revision of the article, and final approval of the version to be published. K.S., V.V., J.W.T., D.V., C.A.M., and M.W.M. participated in interpretation of data, critical revision of the article, and final approval of the version to be published.

Correspondence: Andrew S. Barbas, MD, Department of Surgery, Duke University Medical Center, BOX 3512, Durham, NC 27710. (andrew.barbas@duke.edu).

The authors declare no funding or conflicts of interest.

ISSN: 2373-8731
DOI: 10.1097/TXD.0000000000001573

for the portal vein and hepatic artery throughout the course of NMP. Metabolic function was evidenced by robust bile production and clearance of perfusate lactate. The liver was implanted via the standard caval interposition technique. Warm ischemic time (implant time) was 39 min. No reperfusion syndrome was noted on portal vein reperfusion. After the completion of the arterial anastomoses and biliary reconstruction, the abdomen was then closed, and the patient was then turned back over to the cardiac surgery team for decannulation of venoarterial extracorporeal membrane oxygenation and chest closure. The estimated blood loss for the liver transplant was 1.3 L. She was extubated on postoperative day 1 and was discharged home on day 13. Her immediate postoperative course was notable for acute kidney injury with a peak creatinine level of 5.1 mg/dL that improved down to 2.5 mg/dL without the need for dialysis or renal replacement therapy. On 1-y follow-up, the patient recovered well without any need for hepatobiliary intervention or signs of graft rejection in either organ. Notably, the patient developed tricuspid regurgitation several months following transplantation, for which she had a valve replacement but continues to recover well.

DISCUSSION

This is the first reported CHLT for Fontan failure using NMP to preserve both organs. Perioperative mortality rates for cardiac transplantation are approximately 15% to 25%, higher for Fontan patients compared with other types of heart failure.[1] Several factors make cardiac transplantation for Fontan failure difficult: (1) the physiology of Fontan failure makes these patients less hemodynamically stable; (2) patients require redo sternotomy and have complex cardiac anatomy; and (3) additionally, the presence of the comorbid liver disease has the potential to prevent successful cardiac transplantation in these patients.[1,2] These surgical challenges prolong the total preservation time of both the heart and the liver grafts and increase the pressure on both transplant teams to move quickly.

NMP has emerged in the past decade as a superior alternative to SCS.[3-5] Bral et al[3] demonstrated comparable liver transplant outcomes between cohorts of NMP and SCS, despite significantly longer preservation time in the NMP cohort (786 versus 235 min). Furthermore, they noted that the extended preservation time allowed for better operating room logistics, which is particularly valuable in CHLT given the high level of coordination needed for success. Our experience further validates this, as NMP minimized the deleterious effects of increased preservation time and cold ischemia while also allowing our heart transplant team to operate without time pressure constraints. Moreover, no hemodynamic instability was noted on liver reperfusion, which is particularly important for tenuous patients undergoing complex combined procedures. Although there is 1 case in the literature of multiorgan transplant using OCS for liver preservation, normothermic regional perfusion was used for perfusion of the heart, making this the first case in which NMP was used for both organs.[6]

Another challenge in CHLT is finding a pair of suitable organs for transplantation.[2] Because heart transplant takes priority in CHLT, there is generally prolonged cold ischemia time associated with the liver graft. As a result, a liver graft of excellent quality is usually needed. In addition to increasing total preservation time, NMP has the added benefit of allowing the transplant team to evaluate and use marginal allografts that may otherwise not be transplanted without compromising results. While our patient received a liver from a standard criteria donor, the PROTECT trial in 2022 demonstrated comparable transplant outcomes between the NMP and SCS cohorts despite using a significantly higher number of livers donated following circulatory death in the NMP cohort.[5] Therefore, the widespread utilization of MP may allow for the utilization of marginal allografts, increasing the donor pool for CHLT and other multiorgan transplants. Additionally, if it is deemed at the time of operation that the liver should not be transplanted, preservation via NMP allows time for reallocation of the liver to the backup recipient.

In conclusion, this case successfully demonstrates the use of NMP in CHLT. Although this case focuses on CHLT, we believe that the observed benefits could be applied to other types of multiorgan transplantation, as machine preservation minimizes the ischemic injury of the organs, reduces the time pressure constraints on the first transplant team, and may expand the donor pool by using marginal allografts.

REFERENCES

1. Mauchley DC, Mitchell MB. Transplantation in the Fontan patient. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2015;18:7–16.
2. D'Souza BA, Fuller S, Gleason LP, et al. Single-center outcomes of combined heart and liver transplantation in the failing Fontan. *Clin Transplant*. 2017;31:e12892.
3. Bral M, Gala-Lopez B, Bigam D, et al. Preliminary single-center Canadian experience of human normothermic ex vivo liver perfusion: results of a clinical trial. *Am J Transplant*. 2017;17:1071–1080.
4. Markmann JF, Abouljoud MS, Ghobrial RM, et al. Impact of portable normothermic blood-based machine perfusion on outcomes of liver transplant: the OCS liver PROTECT randomized clinical trial. *JAMA Surg*. 2022;157:189–198.
5. Nasralla D, Coussios CC, Mergental H, et al; Consortium for Organ Preservation in Europe. A randomized trial of normothermic preservation in liver transplantation. *Nature*. 2018;557:50–56.
6. Brubaker AL, Urey MA, Taj R, et al. Heart-liver-kidney transplantation for AL amyloidosis using normothermic recovery and storage from a donor following circulatory death: short-term outcome in a first-in-world experience. *Am J Transplant*. 2023;23:291–293.