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CASE REPORT

WILEY

A Neonatal ABO non-compatible heart transplant from a circulatory-determined death donor using NRP/Cold storage

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Abstract

Background: Donation after Circulatory death is gaining worldwide acceptance. Most protocols regard their first cases to be performed with donor and recipient in the same institution. Few records of children or distant procurement have been published.

Methods: Our institution was offered a heart from a 3-day-old, 3.4-kg child, blood group A, suffering irreversible encephalopathy. Parents accepted withdrawal of life-sustaining therapy and agreed to donation. The donor hospital was located 340 km away. Concomitantly, a 2-month-old, 3.1 kg, blood group type B and with non-compaction ventricles was awaiting for the heart transplant in our unit.

Results: Thirty-seven minutes after withdrawal of life-sustaining therapy, the heart arrested. Five minutes afterwards, a sternotomy was performed. The supra-aortic vessels were clamped altogether. Aorta and right appendage were cannulated and connected to heart-lung machine. The innominate artery above the clamp was severed. The heart resumed spontaneous rhythm in less than 1 min. Ventilation was restored and extracorporeal circulation was maintained for 32 min. Upon cardiologic arrest, the graft was harvested as routinely. The heart was cold-stored and transported by plane to our Hospital. An orthotopic bicaval transplant was performed. Overall cold ischaemia was 245 min. Ten weeks later, the child was discharged home in good condition.

Conclusion: Donation in circulatory death could increase the pool in neonates. Extracorporeal circulation proves successful for procurement in neonates. Distant procurement plus cold storage for donation in circulatory death is feasible. Donation in circulatory death and ABO non-compatible strategies are complementary to each other.

KEYWORDS
ABO non-compatible, donor circulatory death, neonate, transplant

Abbreviations: BD, brain death; DCD, donation in circulatory death; OCS, organ care system; TA-NRP, thoraco-abdominal normothermic regional perfusion.

1 | INTRODUCTION

Donation after Circulatory Death (DCD) is gaining worldwide acceptance as an adjunct to brain death (BD) in transplant surgery.[1] Several techniques have been described to retrieve and preserve the DCD heart; cold static storage alone, Direct Procurement and Perfusion (DPP) using ex-situ heart perfusion, Thoraco-abdominal Normothermic Regional Perfusion (TA-NRP) followed by ex-situ heart perfusion (ESHP) and TA-NRP/cold storage, as displayed by groups in Australia,[2] Belgium,[3] Great Britain[4] and other countries. The first three cases[5] were performed in Denver (Colorado, USA) in 2008 (ultra-fast procurement, without in-situ graft evaluation), and since then few records of children have been published.[6]

Our Institution was offered a heart from a 3-day-old, 3.4-kg child, blood group A, suffering irreversible encephalopathy (EEG) as a result of neonatal asphyxia. Low flow in posterior cerebral arteries precluded brain-death donation. Parents accepted withdrawal of life-sustaining therapy (WLST) and agreed to donation. The donor Hospital was located 340 km away. Concomitantly, a two month-old, 3.1 kg, blood group type B and with non-compaction ventricles was awaiting HT in our neonatal unit. Parents were informed about this new strategy and risks of discarding the graft, if deemed unsuitable. We envisioned a great opportunity and considered a distant procurement of an ABO non-compatible DCD-HT.

2 | CASE REPORT

2.1 | Procurement

WLST was performed by the paediatric intensive care team in theatre, after parents´ farewell. Withdrawal consisted of extubation, stopping inotropes and comfort measures, which are routine practise end of life care measures in the neonatal intensive care unit. Prior to WLST, the donor was intubated and upon a Dobutamine infusion of 5 mcg/kg. As is our local protocol for all DCD donors, heparin was administered *ante mortem* (6 mg/kg). Seventeen minutes after WLST, mean blood pressure dropped below 30 mmHg. Twenty minutes later, the heart arrested.

Death was declared by the paediatric intensive care team 5 min following mechanical asystole. Routine sternotomy was performed. The supra-aortic vessels were clamped altogether ensuring no cerebral circulation (Figure 1). Purse-string sutures in the aorta and right appendage were placed, both cannulae inserted, fastened and connected to TA-NRP lines.

The time for reperfusion following skin incision was 7 min. Functional ischaemic time was 32 min (time from systolic <30 mmHg to reperfusion on TA-NRP), whilst overall warm ischaemia lasted for 49 (17+20+5+7) min (Figure 2).

Next step was a cut-down in the innominate artery above the clamp to reassure absence of brain perfusion due to the possibility of collateral flow. The heart resumed spontaneous rhythm in less than 1 min. Ventilation was restored and TA-NRP was maintained for 32 min. TA-NRP was weaned keeping the same inotropes as before WLST and the heart was assessed for 10 min. An epicardial echo revealed good biventricular function with a left ventricular ejection fraction of 65% upon cardioplegic arrest (500 ml HTK-Custodiol; Koehler Chemi, Alsbach-Haenlien, Germany), the graft was harvested as routinely. After retrieval, the heart was cold stored (CS) and transported by plane to our Hospital.

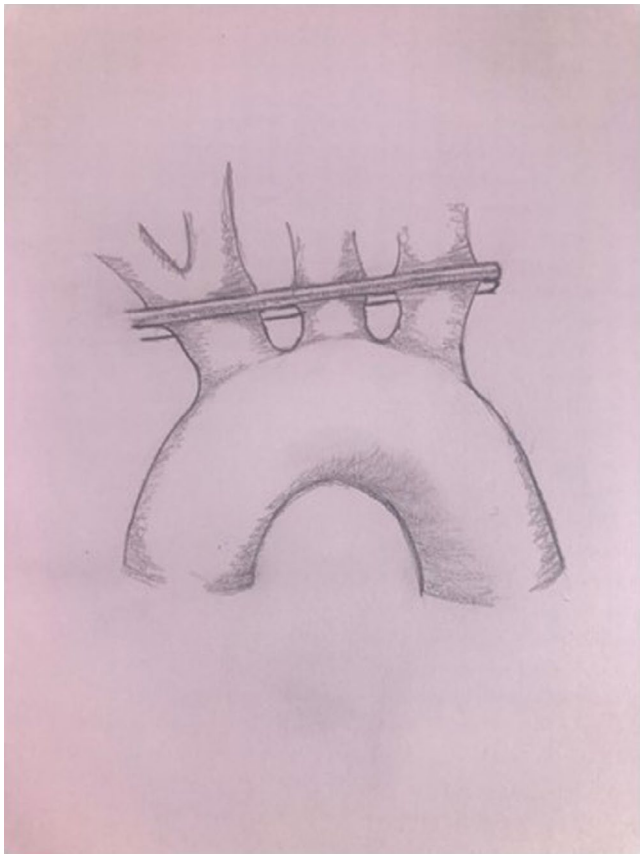

FIGURE 1 Exclusion of supra-aortic vessels (altogether) with a vascular clamp

2.2 | Transplant

The recipient was born with 1.9 kg and a non-compaction biventricular condition. Blood group was B. Her index age and weight at the time of transplantation were 2 months and 3.1 kg, respectively. Ejection fraction was lower than 20%. BNP >35 000 and emergent intubation-rushed transplant decision, assuming no conventional alternatives. An orthotopic bicaval transplant was performed. The five anastomosis were performed before clamp removal (65 min from box removal to clamp off). Isohemagglutinin titres proved negative in all four samples withdrawn in our ABO non-compatible protocol.[7] Sinus rhythm resumed spontaneously. Trans-oesophageal echocardiography showed good biventricular function. The patient was eventually handed over to the intensive care unit, on milrinone plus epinephrine low doses.

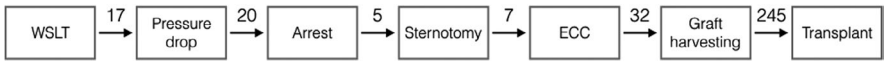

FIGURE 2 Display of key points since WSLT in the donor until clamp removal in the recipient. Stepwise time intervals (in min) is outlined

Overall cold ischaemia was 245 min. Ten days later, the thorax was revisited to drain a hematoma compressing the superior vena cava. The patient was extubated on day 21 after transplant and transferred to the ward on day 39. After ten weeks and no rejection episodes, the child was discharged home in good condition with corticosteroids, micofenolato and tacrolimus. Echo showed good biventricular function.

3 | DISCUSSION

A cluster of issues prompted us to carry out a neonatal DCD heart transplant using TA-NRP cold storage: shortage of neonatal donors, worsening of clinical situation, few chances of successful mechanical support, experience in ABO non-compatible heart transplant, ethical protocols approved both in donor and recipient centres, absence of OCS for patients under 50 kg. Distant procurement in this setting was considered an opportunity, rather than a hurdle, provided that reports of regular cold storage (CS) after DCD-HT had been published in Europe[3] and USA (Hoffman et al, JHLT, in press).

Graft evaluation is key in transplant surgery. Fast opening, like in the Colorado´s group report,[5] did not allow assessment until clamp removal on the recipient. We might have rejected the heart on the basis that the time from WLST to reperfusion was >30min. One of the benefits of TA-NRP is the confidence to see the heart beating with a functional assessment prior to retrieval. In-situ checking is affordable in NRP-ECMO, and ex-situ control can be performed in OCS. Efforts to keep the cold ischaemia as short as possible are the rule.

Regarding ethical implications of collateral flow, clamping of supra-aortic vessels (visual checking) plus severing them above the clamp to allow back-flow ensures no brain perfusion. Additional measures, like carotid doppler[8] or fontanelle ultrasonography in neonates may help.

Unlike other protocols for adult DCD-HT with ECMO, we suggest regular Extracorporeal Circulation through sternotomy for donors under 30 kg. *Pre-mortem* cannulation is avoided. TA-NRP can be instituted in less than 10 min.

ABO non-compatible HT programs[7] do not increase the number of donors, but take profit of the few available ones. The DCD-HT actually increases the number of donors. To our knowledge, this might be the first combined neonatal ABO non-compatible plus DCD-HT case in the world.

4 | CONCLUSIONS

In a nutshell, as a first case of DCD-HT, we had a donor neonate in a distant hospital; the graft was rescued on Extracorporeal Circulation and cold stored up to 4 h for transport, and implanted in an ABO non-compatible recipient. TA-NRP may allow many other centres in countries around the world to adopt paediatric DCD heart transplantation routinely.

ACKNOWLEDGEMENTS

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DATA AVAILABILITY STATEMENT

The data that support the findings in this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Domínguez-Gil B, Ascher N, Capron AM, et al. Expanding controlled donation after the circulatory determination of death: statement from an international collaborative. *Intensive Care Med*. 2021;47:265-281.
2. Dhital KK, Iyer A, Connellan M, et al. Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: a case series. *Lancet*. 2015;385:2585-2591.
3. Tchana-Sato V, Ledoux D, Detry O, et al. Successful clinical transplantation of hearts donated after circulatory death using normothermic regional perfusion. *J Heart Lung Transplant*. 2019;38:593-598.
4. Messer S, Page A, Colah S, et al. Human heart transplantation from donation after circulatory-determined death donors using normothermic regional perfusion and cold storage. *J Heart Lung Transplant*. 2018;37:865-869.
5. Boucek MM, Mashburn C, Dunn SM, et al. Pediatric heart transplantation after declaration of cardiocirculatory death. *N Engl J Med*. 2008;359:709-714.
6. Kleinmahon JA, Patel SS, Auerbach SR, et al. Hearts transplanted after circulatory death in children: analysis of the international society for heart and lung transplantation registry. *Pediatr Transplant*. 2017;21:13064.
7. Urschell S, West LJ. ABO-incompatible heart transplantation. *Curr Opin Pediatr*. 2016;28(5):613-619.
8. Manara A, Shemie SD, Large S, et al. Maintaining the permanence principle for death during in situ normothermic regional perfusion for donation after circulatory death organ recovery: A United Kingdom and Canadian proposal. *Am J Transplant*. 2020;20(8):2017-2025.

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