The role of transesophageal echocardiography in guiding heart donation after circulatory death

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Keywords

Thoraco-abdominal normothermic regional perfusion (TA-NRP), donation after circulatory death (DCD), heart transplantation, transoesophageal echocardiography (TOE), heart donation.

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Data statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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List of abbreviations:

DCD	Donation after Circulatory Death
TA-NRP	Thoraco-Abdominal Normothermic Regional Perfusion
TOE	Transoesophageal Echocardiography
WLST	Withdrawal of Life Sustaining Therapy
OR	Operating Room
V-A-ECMO	Veno-Arterial Extracorporeal Membrane Oxygenation
PA	Pulmonary Artery
TAPSE	Tricuspid Annular Plane Systolic Excursion
RV	Right Ventricle
LV	Left Ventricle
RWMA	Regional Wall Motion Abnormality
SCS	Static Cold Storage
ICU	Intensive Care Unit
OCS	Organ Care System
TTE	Transthoracic Echocardiography
LVOT VTI	Left Ventricular Outflow Tract Velocity Time Integral
PAP	Pulmonary Artery Pressure
CO	Cardiac Output

ABSTRACT

Heart donation after circulatory death (DCD) can significantly expand the heart donor pool, helping to overcome the problem of organ shortage and the increase in waiting list mortality and morbidity. To improve the outcome of DCD heart transplantation, thoraco-abdominal normothermic regional perfusion (TA-NRP) can be performed by selectively restoring circulation followed by in vivo functional heart assessment. Here, we report on the use of periprocedural transoesophageal echocardiography (TOE) as a minimally invasive cardiac assessment tool during different stages of a DCD heart procurement procedure using TA-

NRP. We conclude that TOE is a valuable method to assess the donor heart for transplantation eligibility before and after withdrawal of life-sustaining therapy and during subsequent TA-NRP.

Keywords

Thoraco-abdominal normothermic regional perfusion (TA-NRP), donation after circulatory death (DCD), heart transplantation, transoesophageal echocardiography (TOE), heart donation.

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INTRODUCTION

Organ transplantation remains the definitive treatment for several end-stage organ dysfunctions including heart failure. Unfortunately, organ shortage deprives thousands of patients from the benefits of receiving a new organ and the number of patients actively on an organ waiting list is only rising as is the waiting list morbidity and mortality. Organ donation after circulatory death (DCD) has significantly contributed to extend the organ donor pool worldwide, particularly for lungs, kidneys and livers. Despite the fact that the first successfully transplanted heart was retrieved using a DCD procedure, heart donation has long been excluded from the DCD program; mainly due to important concerns about the

deleterious consequences of the inevitable warm ischemia occurring after withdrawal of life sustaining therapy (WLST) and subsequent cardiac arrest on cardiac graft quality.[1]

Recently, DCD heart transplantation revived in several teams around the world. In particular, the team from Papworth (UK) reported the results of heart transplantations performed with organs retrieved from DCD donors using either thoraco-abdominal normothermic regional perfusion (TA-NRP) followed by *ex situ* normothermic machine perfusion or direct procurement followed by *ex situ* normothermic machine perfusion.[2,3] Following the Papworth publication in 2017 [2], two Belgian centers (CHU Liège and UZ Leuven) developed in parallel their own TA-NRP protocols. The details of these protocols and outcome of the first cases of DCD heart transplantation in Belgium have already been published.[4,5,6]

We wish to describe our clinical protocol with the use of transoesophageal echocardiography (TOE) to guide heart evaluation and procurement during the different stages of the TA-NRP procedure in heart donation after circulatory death.

METHODS

Both Belgian centers (CHU Liège and UZ Leuven) developed their own unique TA-NRP protocols in parallel.[4,5,6] These clinical protocols were both approved by the local ethics committee and conform to Belgian law. When a possible DCD donor was reported to the transplant coordination team, the necessary examinations were performed and recipients were matched through Eurotransplant (Leiden, The Netherlands).[7] Both Belgian TA-NRP protocols [4,5,6] differ from the Papworth protocol [2,3] since premortem interventions are not prohibited by Belgian law, provided that they do not directly cause patient discomfort or harm. Withdrawal of life sustaining therapy (WLST) is therefore performed in the operating room (OR) to avoid any delay caused by transportation during the five-minute no touch period after circulatory arrest. This also allows premortem administration of heparin and guidewire (UZ Leuven protocol) or cannula (CHU Liège protocol) insertion into the femoral vessels. After declaration of death and femoral cannulation, venous drainage is initiated, while simultaneous sternotomy and clamping of the supra-aortic vessels is performed.

Thoraco-abdominal normothermic regional perfusion (TA-NRP) is started through peripheral veno-arterial extracorporeal membrane oxygenation (V-A-ECMO) in order to perfuse and oxygenate the thoraco-abdominal organs. Shortly after reperfusion onset, the heart regains its function. In the Papworth protocol premortem heparinization, cannulation or insertion of guidewires are not allowed. Also, in their protocol the TOE probe is inserted after declaration of death.[2,3] In both the Papworth and CHU Liège protocol the TOE probe is used together with a pulmonary artery (PA) catheter to assess heart function. On the contrary, in UZ Leuven, only TOE assessment is performed. In both the UZ Leuven and CHU Liège protocol, the TOE probe (UZ Leuven: Philips CVx3D system, transducer X8-2t, Philips Healthcare, Brussels, Belgium; or GE Vivid S6 system, transducer 6Tc, GE Healthcare, Diegem, Belgium; CHU Liège: Philips EPIQ 7C system, transducer X8-2t, Philips Healthcare, Brussels, Belgium) is inserted before WLST and TOE is considered as the cornerstone of donor heart functional assessment during all stages of the procedure. TOE assessment was always performed by a skilled cardiologist (UZ Leuven) or a specialized anesthesiologist (CHU Liège), in close communication with the anesthesiologists, the organ procurement team, and the perfusionist. Since the procedure needs to move on quickly over the various phases, we limit ourselves mainly to transgastric assessment with 4- and 3-chamber views at the long axis and basic measurements during the TOE study: tricuspid annular plane systolic excursion (TAPSE) to assess the right ventricular (RV) function (next to eye-balling of the RV), left ventricular (LV) function (eye-balling and regional wall motion abnormalities), LV and RV cavity dimensions and changes in valvular insufficiencies using color and doppler assessment. The final functional assessment before acceptance of the donor heart is performed 30 minutes after weaning of the V-A-ECMO support. It includes color doppler examination of the four heart valves and of both right and left ventricular function. On the left side, our main criteria for acceptance include the absence of severe regional wall motion abnormality (RWMA), significant ventricular dilatation and/or significant increase in mitral valve regurgitation as compared to the pre-WLST assessments, plus a residual ejection fraction (eyeballing) of >50%. On the right side we search for any significant

change in tricuspid regurgitation, change in pulmonary artery pressures or change in right ventricular function (tricuspid annular plane systolic excursion (TAPSE) and S' wave) as compared to the pre-WLST assessment. Using continuous TOE assessment of the donor heart during the procedure, circulatory arrest after WLST is visualized, but this is not used as confirmation for circulatory arrest. Logistical and financial considerations led both Belgian centers to opt for the use of TA-NRP with peripheral V-A-ECMO followed by organ storage using static cold storage (SCS).[4,5,6]

RESULTS

To date, eight successful DCD heart transplantations were performed at UZ Leuven, three of them with distant procurement at CHU Liège. One potential DCD heart donor was rejected after premortem assessment by heart catheterization because of a 50% stenosis at the circumflex artery, which made it a marginal donor heart, and there was at that moment no matching recipient on the high urgency transplant waiting list within the Eurotransplant area. All selected DCD donors proceeded to circulatory arrest within 30 minutes after WLST, followed by successful organ procurement. All donor hearts were accepted following final functional evaluation and successfully transplanted.

Following data are expressed as median (min-max). The donor age was 43 years old (12-60), there were six male and two female donors. The cause of WLST was post anoxemic brain damage in six cases, and devastating traumatic brain injury in two cases. TOE assessment of LV end-diastolic diameters, LV ejection fraction and TAPSE did not show any relevant changes of these parameters between pre-WLST assessment and during the final evaluation of the graft.

The thirty-day survival was 100% in all eight recipients, with a median left ventricular ejection fraction after thirty days of 60% (55-60). Median ICU stay was 7.22 days (2.12-8.76) and the median mechanical ventilation time was 1.26 days (0.61-2.58). None of the recipients needed postoperative mechanical circulatory support. Vasoactive-inotropic support post transplantation included: three recipients received at least one day of inhaled nitric oxide,

five recipients received noradrenalin infusion for more than two days, five recipients received dobutamine infusion for more than one day. Three patients required postoperative implantation of a pacemaker, because of atrial-ventricular block. Five recipients have already reached the milestone of one-year post transplantation and all recipients are currently doing well. Other donor organs that were successfully transplanted from the five DCD procedures at UZ Leuven consisted of five livers, three pairs of kidneys, and two pairs of lungs.

DISCUSSION

Eligibility assessment of the donor heart for transplantation following its reperfusion is currently a critical step in the DCD heart procurement procedure. In case of thoraco-abdominal normothermic regional perfusion (TA-NRP) followed by static cold storage (SCS), assessment of the beating heart after selective reperfusion in the donor's thoraco-abdominal cavity is limited to visual inspection, transoesophageal echocardiography (TOE) and *in vivo* hemodynamic monitoring using a pulmonary artery (PA) catheter. However, our experience showed that TOE assessment during the entire procedure was a useful tool in assessing the eligibility of the heart for donation after reperfusion and regaining its function. This is reflected by our excellent survival rate of 100% with good graft function. As a result, the team of CHU Liège has recently decided to abandon the systematic use of the PA catheter.

TOE assessment is valuable at different time points during the DCD heart procurement procedure, as summarized in Figure 1 and 2. Before WLST, TOE nicely complements the results of the initial echocardiography (most commonly transthoracic) performed when the patient is considered as a potential heart donor and which determines the eligibility for heart donation. During the DCD procedure itself, it can help to confirm the positioning of the femoral guidewires and venous cannula for the VA-ECMO. Finally, assessment of the heart during the TA-NRP phase will ultimately result in acceptance or rejection of the DCD heart for transplantation. Indeed, comparing various pre-WLST and post reperfusion echo parameters (as summarized in Figure 2) can provide the team with important information concerning the possible negative impact of the DCD procedure on organ performance.

TOE also plays a pivotal role in the assessment of dynamic changes during (e.g. afterload effects of the V-A-ECMO, left ventricular dilatation, valve insufficiencies) and after weaning from V-A-ECMO. Indeed, changes in preload and afterload by increasing or decreasing the pump support could result in improvement or worsening of the cardiac and/or valvular function. Therefore, the echo-operator should continuously be in close communication with the organ recovery and perfusion team. Ultimately, the heart stays in secure follow-up by live TOE until 30 minutes after weaning off the V-A-ECMO-support. This allows visualization of late-onset dysfunction before organ procurement.

When local law and the ethical committee allow premortem interventions, continuous TOE assessment can be extremely valuable during DCD heart procurement using TA-NRP. We described the Belgian DCD heart procurement protocols using TA-NRP and a small case series of eight successful DCD heart transplantations. Future research is necessary to define TA-NRP specific acceptance criteria and cutoffs based on TOE comparison.

CONCLUSION

Live TOE follow-up of the heart during the different stages of a heart donation after circulatory death (DCD) procedure using thoraco-abdominal normothermic regional perfusion (TA-NRP) opens a novel, low-invasive and interesting field overarching cardiovascular imaging and cardiac transplantation surgery. In a next stage, prospective multicenter trials could help us in identifying valuable echo parameter cutoffs for organ acceptance in relation to preserved graft function after transplantation.

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DISCLOSURES

CV does not report any conflicts of interest.

REFERENCES

1. White CW, Messer SJ, Large SR, Conway J, Kim DH, Kutsogiannis DJ, et al. Transplantation of hearts donated after circulatory death. Fron Cardiovasc Med. 2018;5:8.
2. Messer S, Page A, Axell R, et al. Outcome after heart transplantation from donation after circulatory-determined death donors. J. Hear. Lung Transplant. 2017;12:1311–8.
3. Messer S, Cernic S, Page A, Berman M, Kaul P, Colah S et al. A 5-year single-center early experience of heart transplantation from donation after circulatory-determined death donors. J Heart Lung Transplant. 2020;39(12):1463-1475.
4. Tchana-Sato V, Ledoux D, Detry O, et al. Successful clinical transplantation of hearts donated after circulatory death using normothermic regional perfusion. J. Hear. Lung Transplant. 2019;6:593–8.
5. Tchana-Sato V, Ledoux D, Vandendriessche K, et al. First report of a successful pediatric heart transplantation from donation after circulatory death with distant procurement using normothermic regional perfusion and cold storage. J. Hear. Lung Transplant. 2019;10:1112–5.
6. Vandendriessche K, Tchana-Sato V, Ledoux D, Degezelle K, Rex S, Neyrinck A, et al. Transplantation of donor hearts after circulatory death using normothermic regional perfusion and cold storage preservation. Eur J Cardiothorac Surg 2021;00:1-7.
7. Eurotransplant. Eurotransplant manual – Chapter 6 ET Thoracic Allocation System (EThAS) [Internet]. Smith J [updated 2022; cited 2022 Jun 10]. Available from: https://www.eurotransplant.org/wp-content/uploads/2022/04/H6-EThAS-April-19-2022.pdf

FIGURE LEGENDS

Figure 1 – Schematic overview of the UZ Leuven TA-NRP protocol for DCD heart procurement. TOE is performed during the premortem stage and for continuous imaging of the heart after declaration of death. TOE: transoesophageal echocardiography, WLST: withdrawal of life sustaining therapy, DCD: donation after circulatory death, TA-NRP: thoraco-abdominal normothermic regional perfusion.

Figure 2 - Schematic overview for TOE guided heart donation procedure after circulatory death. Pre-donation assessment (blue) resides in the intensive care unit whilst phases in green reside in the operating room. TOE is used to reassess the pre-donation findings and to compare pre-WLST findings to cardiac physiology after reperfusion in order to proceed to organ acceptance. TTE: transthoracic echocardiography; TOE: transoesophageal echocardiography; WLST: withdrawal of life-supporting therapy; NRP: normothermic regional perfusion; RWMA: regional wall motion abnormalities; LV: left ventricle; RV: right ventricle; LVOT VTI: Left ventricular outflow tract velocity time integral; TAPSE: Tricuspid annular plane systolic excursion; PAP: Pulmonary Artery Pressure; CO: cardiac output

.**Figure 1**

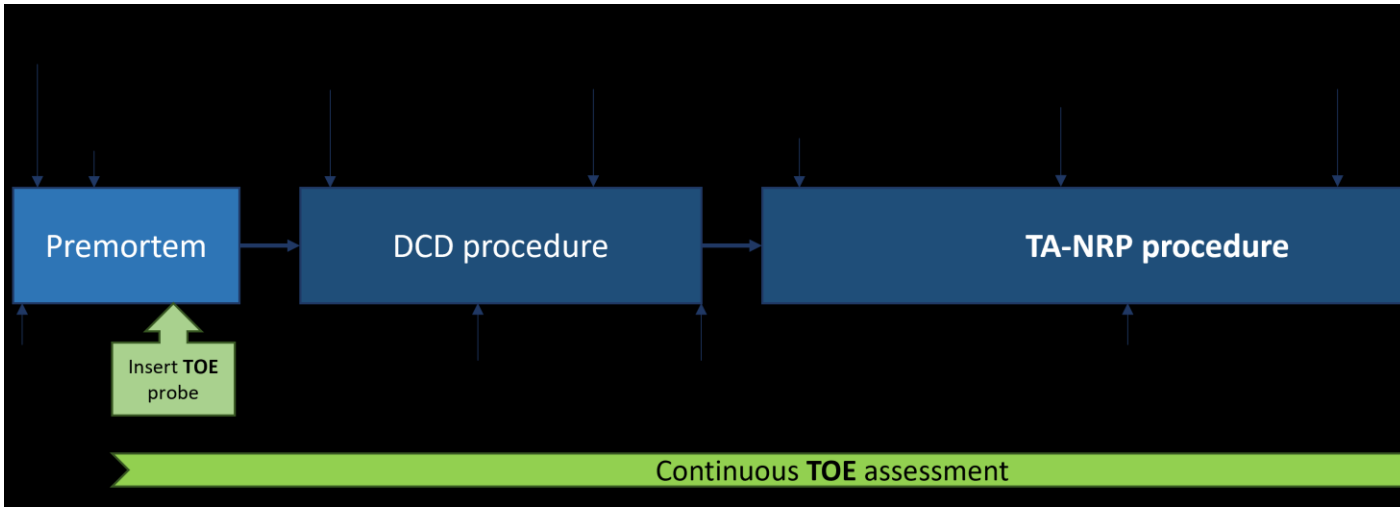

Figure 2