Direct Procurement of Donor Heart With Normothermic Regional Perfusion of Abdominal Organs

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Purpose. **We wanted to evaluate if direct procurement of the heart is possible in combination with normothermic regional perfusion of abdominal organs in donors after circulatory death.**

Description. **A donation after circulatory death pathway was used for a 41-year-old woman after an irreversible brain injury. After meeting criteria for the organ donation, the heart was retrieved and re-animated on ex situ perfusion system, and abdominal organs were perfused with normothermic regional perfusion.**

Evaluation. **All the donated organs and their recipients had excellent short-term outcome.**

Conclusions. **We demonstrated a successful combination of direct procurement of the heart and normothermic regional perfusion of the abdominal organs.**

(Ann Thorac Surg 2019;108:597–600)

Technology

Although use of hearts from donors after circulatory death (DCDs) for transplantation is still in infancy and restricted to a few centers in the world, direct procurement and perfusion (DPP) with the use of the organ care system (OCS) and thoracoabdominal normothermic regional perfusion (TA-NRP) are the two established methods of heart procurement for this type of donation [1, 2]. The TA-NRP requires establishment of extracorporeal membrane oxygenation (ECMO) after verification of donor death. This involves sternotomy, insertion of abdominal aorta and right atrial cannulas, clamping cranial branches of the aortic arch, and establishment of the satisfactory ECMO flow. The ECMO is weaned after reanimation of the heart, and its function is assessed by transesophageal echocardiography and pulmonary artery catheterization before its procurement as in a brain-dead donor [3]. However, the DPP involves sternotomy, immediate donor exsanguination through a cannula in the right atrium, cardioplegia, and procurement of the donor heart, followed by preservation on ex situ perfusion with OCS [4].

The TA-NRP is not a standard of care for DCD in the United Kingdom, and the program is run by one retrieval team in the country at present, that is, currently only allowed to use this technique in one of the six retrieval zones in the country. In the present patient, the abdominal retrieval team planned the TA-NRP; however, the DPP was the institutional protocol of the heart retrieval team. Given the super urgent status of the heart recipient, the combined DPP and abdominal NRP approach was tailored. We demonstrate a technique that allows both the DPP and abdominal NRP without restarting the heart in situ.

Technique and Clinical Experience

In the present patient, our institutional DCD heart transplantation protocol related to the DPP and ex situ normothermic reperfusion with OCS was followed. This protocol had been previously reviewed by the UK Donation Ethics Committee, National Health Service Blood and Transplant, and by our hospital Clinical Practice Committee, and requisite approvals were gained in April 2015. A 41-year-old woman was admitted to the emergency unit unconscious, secondary to an intracranial

Accepted for publication Jan 23, 2019.

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0003-4975/$36.00
https://doi.org/10.1016/j.athoracsur.2019.01.087

hemorrhage from a ruptured cerebral aneurysm. She underwent decompression craniectomy and was treated in the intensive therapy unit (ITU) for 7 days; however, further maintenance of life support was deemed futile. Cough, gag, and pupillary responses were absent, but there were occasional spontaneous breathing efforts. After discussion with her family, it was decided to withdraw the life support and to retrieve thoracoabdominal organs if criteria for organ donation after circulatory death were met. Echocardiography showed good biventricular function with moderate left ventricular hypertrophy along with structurally normal valves. The heart was accepted for a 16-year-old girl with severe advanced heart failure because of dilated cardiomyopathy who was supported on a short-term left ventricular assist device during 29 days and registered on the UK national super urgent waiting list for heart transplantation. Lungs were declined by all the centers in the United Kingdom because of past history of tuberculosis and hilar lymphadenopathy. Liver and kidneys were accepted for suitable recipients.

After withdrawal of life support (removal of endotracheal tube in this patient) for the donor, asystole was recorded in 10 minutes. Five minutes after asystole, she was transferred into the operation theater and prepped for surgery, and knife to skin was at 7 minutes after asystole. Chest and abdomen were opened simultaneously. The abdominal surgeons exposed the right common iliac artery and vein, cannulated the vessels, and connected cannulas to an ECMO circuit incorporating Maquet Cardiohelp (Maquet, Rastatt, Germany) that had been primed with 4 units of washed red cells and 50,000 IU of heparin in 1.5 L of Hartmann's solution. Donor blood (1.3 L) was sucked into a cell-saver chamber that contained 500 mL of OCS proprietary priming solution and 60,000 IU of unfractionated heparin by a side arm of the venous outflow circuit while the descending thoracic aorta was clamped. The NRP was established 13 minutes after circulatory arrest with a flow of approximately 2.5 L/min, satisfactory for abdominal organ perfusion. In the meantime, the thoracic team rapidly assessed the heart for visible and palpable coronary artery disease. Once adequate donor blood was received into the cell saver, superior and inferior vena cavae (IVC) were clamped, the IVC was opened just distal to the clamp for venting, and the left atrium was opened for pulmonary return. A liter of cold cardioplegia (Custodial HTK solution, Sandor, Hyderabad, India) mixed with 20,000 IU of heparin, 10,000 IU of erythropoietin, and 50 mg of glyceryl trinitrate was perfused through a 14-gauge needle inserted into the ascending aorta at 16 minutes of asystole, and topical cooling was achieved with ice slush poured into the pericardium. The heart was procured, leaving the ascending aorta and caval clamps in situ to avoid any blood loss. The heart was implanted on the OCS with help of ascending aortic infusion and pulmonary artery drainage cannulae at 27 minutes of asystole. Cardioversion (10 Joules ×3) was performed with the use of internal paddles with successful conversion of ventricular fibrillation to sinus rhythm and later paced at 90 beats per minutes, using temporary pacing wires.

The abdominal NRP was continued for approximately 2 hours after which time the liver and kidneys were procured by the standard technique. The OCS donor heart perfusion was continued throughout transport of the organ to the implantation center, during which time the systematic organ assessment was performed by visual and biochemical means. Left ventricular contractility was poor in the beginning but improved moderately over the first 2 hours of perfusion. A continuous absorption of lactate by the donor myocardium was demonstrated by a decrease in overall OCS perfusate lactate levels along with consistently lower lactate levels in the venous blood compared with the arterial samples (Fig 1). Although visual left ventricular contractility was suboptimal compared with donor hearts retrieved by the DPP method without NRP combination in our experience, we

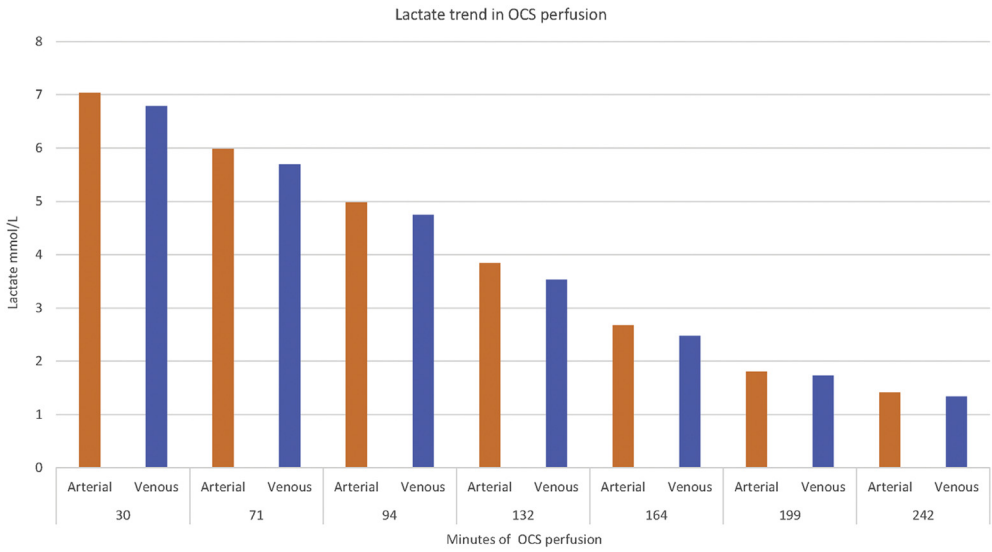

Fig 1. Lactate trend for the organ care system (OCS) heart.

decided to transplant this organ, given the satisfactory lactate trend and super urgent status of the recipient. Despite redo sternotomy, preoperative mechanical circulatory assist and anticoagulation for the same, cardiopulmonary bypass time and cross-clamp time were 149 and 58 minutes, respectively. After 74 minutes of reperfusion, the cardiopulmonary bypass was weaned, chest was closed, and the patient was transferred to the ITU in stable hemodynamic condition on low-dose adrenalin, noradrenalin, and Milrinone. The inopressive agents were weaned the next day, and the patient was extubated on day 2 and was discharged from the ITU on the 10th day after the surgery. Five months after surgery the recipient is home, and recent echocardiogram showed left ventricular ejection fraction of 74%. Liver and kidney implantation centers reported excellent outcomes for their recipients.

Comment

Extension of the abdominal NRP to thoracic organs was proposed and successfully performed in the United Kingdom by surgeons from Papworth Hospital [3]. In this process, the heart is reanimated on the TA-NRP, and it is weaned off gradually; as the heart takes over cardiac output, it is then functionally assessed with the help of transesophageal echocardiography and pulmonary artery catheterization. Warm phase dissection is performed for both thoracic and abdominal organs before circulatory arrest, after which time organ perfusion with plegia solutions and organ procurement is performed. The OCS is used for further perfusion of donor heart and its transport to the implanting center. There are important ethical concerns around the TA-NRP for which clamping all aortic arch vessels, including the left subclavian artery, is necessary. Not only can this delay the beginning of TA-NRP, but also it may not be enough to ensure absence of cerebral flow in case of an aberrant right subclavian artery or other unidentified collaterals coming from the descending aorta. The donor heart after agonal time, cardiac arrest, and observation time is volume-overloaded during TA-NRP and moreover after ECMO weaning during assessment.

In DPP, the immediate cardioplegia delivery protects the arrested donor heart during the short period needed to implant it into the OCS. Therefore, we do not see any beneficial effect of the reperfusion time during TA-NRP over ex vivo perfusion in the OCS. Mean time between donor arrest and cardioplegia in our experience (14 patients) of DPP was 10.7 $\pm$ 2.75 minutes compared with 12.7 $\pm$ 2 minutes between donor arrest and reperfusion in the TA-NRP experience [2]. The DPP, thus, decreased warm ischemia for the donor heart by 2 minutes in comparison with the TA-NRP technique, which may seem unimportant but in the context of agonal cardiac arrest may be crucial. In addition, the heart remains in the detrimental environment caused by the process of the donor's death. Rapid and immediate exsanguination of the donor after sternotomy in the DPP protects the heart against volume overloading as it occurs during TA-NRP. Although TA-NRP offers in situ functional assessment of the donor heart, our team along with the Sydney group follows a DPP protocol that involves metabolic donor heart assessment in the OCS based on lactate trend, coronary artery flow, aortic pressure, the level of vasodilator requirement, and inotropic support. Functional assessment is performed by visual inspection, and, if necessary, even coronary angiography can be performed when the heart is in the OCS [1, 5]. In our institutional experience, pathologic and anatomic examination of the rejected donor hearts has corroborated the diagnosis of non-macroscopically visible coronary artery disease, which was based on the adverse lactate trend in the OCS. In addition, a thorough echocardiogram is performed in the patients when they become a potential DCD, ruling out any structural and functional abnormality in the donor heart. The coronary arteries are visualized and palpated at the time of cardioplegia to rule out any major calcified plaques. Once perfused on the OCS, left ventricular contractility (empty beating) and lactate trend are crucial to detect any myocardial ischemia. Thus, the principal advantages of the DPP are rapid cardioplegia delivery and retrieval of the donor heart from the potentially hostile environment of necro-perfusion involving hypoxia, high concentration of lactic acid and procoagulant status, metabolic and functional assessment on the

Table 1. Comparison Between DPP and NRP Techniques

Variable	TA-NRP + OCS	Abdominal NRP + Heart DPP + OCS	Abdominal DPP + Heart DPP + OCS
Complexity of the procedure	+++	++	+
Requirement of additional blood	Yes	Yes	No
Requirement of ECMO	Yes	Yes	No
In situ heart functional assessment	Yes	No	No
Ex situ metabolic and functional assessment	Yes	Yes	Yes
In situ liver functional assessment	Yes	Yes	No
Requirement of agreement with lung and abdominal organ teams	Yes	Yes	No
Length of DCD heart/lung retrieval	Long	Short	Short

DCD = donor after circulatory death; DPP = direct procurement and perfusion; ECMO = extracorporeal membrane oxygenation; OCS = organ care system; TA-NRP = thoracoabdominal normothermic regional perfusion.

system, and the absence of philosophical and ethical concerns involving both a potential reperfusion of the donor's brain as well as the "resuscitation" of a heart in a diseased person who died of cardiac arrest. Furthermore, the DPP saves a crucial 2 minutes of warm ischemia time and avoids complications related to ECMO perfusion contemplated in the TA-NRP. Table 1 briefly denotes benefits and disadvantages of these techniques.

Rapid retrieval of lungs in a DCD, in combination with abdominal NRP has been previously reported by Spanish and English teams [6, 7]. After establishment of the NRP through aorta and IVC in the abdomen, the chest was opened, pneumo-plegia was delivered by the pulmonary artery, and lungs were retrieved after clamping the superior vena cava and IVC so that abdominal NRP could be continued. In the present technique, we followed similar principals for retrieval of the donor heart albeit with changes in donor blood management. The OCS heart requires approximately 1.2 L of donor blood in its prime to achieve adequate perfusate hematocrit. We fear evacuation of this blood in addition to blood loss during procurement of the donor heart would not leave enough blood volume in the donor to run the NRP. Therefore, the NRP reservoir was primed with donor-matched packed red cells before withdrawal of treatment; the packed cells were washed to minimize potassium content in the circuit.

In the present patient, donor lungs were not accepted for implantation because of suboptimal function. If accepted, antegrade pneumo-plegia can be delivered into the main pulmonary artery by a cannula introduced into it. Once the heart is procured, pneumo-plegia can be given retrogradely. Surgically, the azygos vein would have to be ligated before lung retrieval to avoid marked blood loss that would preclude continuation of abdominal NRP. This approach avoids exposure of donor lungs to in vitro circulation of ECMO and its inflammatory reaction and in addition accelerates the lung procurement.

NRP for abdominal organ retrieval is performed in France, Spain, Italy, and the United Kingdom, and early reports suggest superior liver function after transplantation compared with conventional super-rapid retrieval techniques. However; in terms of outcomes of DCD heart transplantation, both DPP and NRP methods have shown equivalence with heart transplantation outcomes with donation after brain death [8, 9]. Experience with the DCD heart transplantation is still limited to double digit numbers and further studies are necessary; until then the teams will be following their current methods of procurement. In this situation, it is essential to be able to combine the DPP with abdominal NRP.

In the present patient, we believe that the cardioplegia as well as the NRP were delayed by at least 2 minutes, as donor blood collection for the OCS heart was performed by IVC cannula before beginning the NRP. We recommend collection of the donor blood through a right atrial cannula by the thoracic team to save this crucial time.

In conclusion, direct procurement of the donor heart in combination with abdominal NRP to satisfy requirements of thoracic and abdominal retrieval teams is demonstrated. Teamwork, coordination, and planning, together with expertise with the thoracic and abdominal organ procurement procedures are essential for the successful outcome.

Disclosure and Freedom of Investigation

The authors are not funded by any source for the development of this technique and the tested technology is not purchased, borrowed, or donated to the study. Authors have full control of the design of the study, methods used, outcome parameters, analysis of data, and production of the written report. None of the authors have conflicts of interest. The project is not funded by any external source. All authors declare freedom of investigation.

The authors wish to acknowledge exceptional contribution of the reviewers that helped in the critical revisions of the manuscript, improving its quality and contents.

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