Direct procurement of donor heart with normothermic regional perfusion of abdominal organs

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Abstract:

Purpose: To evaluate if direct procurement of 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 utilized for a 41-year-old female following an irreversible brain injury. After meeting criteria for the organ donation, heart was retrieved and re-animated on ex-situ perfusion system while abdominal organs were perfused using 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.

Introduction:

Although utilization of hearts from donors after circulatory death (DCD) for transplantation is still in infancy and restricted to a very few centres in world, direct procurement and perfusion (DPP) using the organ care system (OCS) and thoraco-abdominal normo-thermic 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) following verification of donor death. This involves sternotomy, insertion of abdominal aorta and right atrial cannulas, clamping cranial branches of aortic arch and establishment of the satisfactory ECMO flow. The ECMO is weaned after re-animation of heart and its function is assessed by trans-oesophageal echocardiography (TOE) and pulmonary artery catheterisation before its procurement as in a brain-dead donor [3]. The DPP, on the other hand, involves sternotomy, immediate donor exsanguination via a cannula in right atrium, cardioplegia and procurement of the donor heart followed by preservation on ex-situ perfusion utilizing OCS [4].

The TA-NRP is not a standard of care for DCD in the UK 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 out the six retrieval zones in the country. In the present case, the abdominal retrieval team planned the TA-NRP; however, the DPP was institutional protocol of heart retrieval team. Given the super-urgent status of the heart recipient, 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 case, 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 years old female was admitted to Emergency Unit unconscious secondary to an intracranial haemorrhage from a ruptured cerebral aneurysm. She underwent decompression craniectomy and was treated in 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. Following discussion with her family it was decided to withdraw the life support and retrieve thoraco-abdominal 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 female with severe advanced heart failure due to 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 centres in the UK due to past history of tuberculosis and hilar lymphadenopathy. Liver and kidneys were accepted for suitable recipients.

Following withdrawal of life support (removal of endo-tracheal tube in this case) in donor, asystole was recorded in 10 minutes. Five minutes after asystole, she was

transferred into operation theatre, prepped for surgery and knife to skin was at 7 minutes after asystole. Chest and abdomen were opened simultaneously. The abdominal surgeons exposed 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 50000 IU of heparin in 1.5L of Hartmann's solution. A 1.3L of donor blood was sucked into a cell-saver chamber containing 500 mL of OCS proprietary priming solution and 60000 IU unfractionated heparin via a side-arm of the venous outflow circuit while descending thoracic aorta was clamped. The NRP was established 13 minutes after circulatory arrest with a flow of around 2.5L/min, satisfactory for abdominal organ perfusion. In the meantime, the thoracic team rapidly assessed 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 left atrium was opened for pulmonary return. A litre of cold cardioplegia (Custodial) mixed with 20000 UI heparin, 10000 UI erythropoitin and 50 mg glyceryl trinitrate was perfused via 14G needle inserted into ascending aorta at 16 minutes of asystole and topical cooling was achieved with ice slush poured into 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 x3) was carried out using 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 following which liver and kidneys were procured by the standard technique. The OCS donor heart perfusion was continued throughout transport of the organ to implantation centre, during which systematic organ assessment was carried out by visual and biochemical means. Left ventricular contractility was very poor in the beginning but improved moderately over first two hours of perfusion. A continuous absorption of lactate by donor myocardium was demonstrated by

decrease in overall OCS perfusate lactate levels along with consistently lower lactate levels in the venous blood compared to the arterial samples (Figure 1). Although visual left ventricular contractility was suboptimal compared to donor hearts retrieved by the DPP method without NRP combination in our experience, we decided to transplant this organ given the satisfactory lactate trend and super-urgent status of recipient. Despite re-do sternotomy, pre-operative mechanical circulatory assist and anti-coagulation for the same, cardio-pulmonary bypass (CPB) time and cross-clamp time were 149 and 58 min respectively. Following 74 minutes of re-perfusion, the CPB was weaned, chest was closed and the patient was transferred to ITU in stable hemodynamic condition on low dose adrenalin, nor-adrenalin and Milrinone. The ino-pressors were weaned on next day, patient was ex-tubated on day 2 and was discharged from the ITU on 10th day of the surgery. Five months following surgery the recipient is home and recent echocardiogram showed left ventricular ejection fraction of 74%. Liver and kidney implantation centres reported excellent outcomes for their recipients.

Comment:

Extension of the abdominal NRP to thoracic organs was proposed and successfully carried out in the UK by surgeons from Papworth hospital [3]. In this process, heart is re-animated on the TA-NRP and it is weaned off gradually as heart takes over cardiac output which is then functionally assessed with the help of TOE and pulmonary artery catheterisation. Warm phase dissection is carried out for both thoracic and abdominal organs before circulatory arrest, following which organ perfusion with plegia solutions and organ procurement is carried out. The OCS is utilized for further perfusion of donor heart and its transport to implanting centre. There remain ethical concerns around the TA-NRP for which clamping all aortic arch vessels, including the left subclavian artery, is necessary. Not only this can delay the beginning of TA-NRP but also it would not be enough to ensure absence of cerebral flow in case of an aberrant right subclavian artery coming from descending aorta. The donor heart following agonal time, cardiac arrest and observation

time, is volume-overloaded during TA-NRP and more so following ECMO weaning during assessment.

In DPP, the immediate cardioplegia delivery resuscitates arrested donor heart and hence, we believe the cardioplegia delivery time in the DPP is equivalent to reperfusion time in the TA-NRP. Mean time between donor arrest and cardioplegia in our experience (14 patients) of DPP was 10.7±2.75 compared to 12.7±2 minutes time between donor arrest and reperfusion in TA-NRP experience [2]. The DPP, thus decreased warm ischemia for donor heart by 2 minutes in comparison to TA-NRP technique. Also, rapid and immediate exsanguination of donor following sternotomy in the DPP protects the heart against volume overloading as in case of the TA-NRP. Although, the TA-NRP offers in situ functional assessment of donor heart, our team along with Sydney group follows DPP method that involves donor heart assessment in the OCS based on lactate trend and visual impression [1,5]. In addition, thorough echocardiogram is performed in the patients when they become potential DCD donor which rules out any structural and functional abnormality in the donor heart. The coronary arteries are visualised 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. The principal advantage of the DPP is rapid cardioplegia delivery and retrieval of donor heart from potentially hostile environment of necro-perfusion involving hypoxia, high concentration of lactic acid and procoagulant status. The DPP saves crucial 2 minutes of warm ischemia time, avoids complications related to ECMO implantation and possible cerebral perfusion contemplated in the TA-NRP. Table 1 briefly denotes benefits and disadvantages of these techniques.

Rapid retrieval of lungs in a DCD donor, in combination with abdominal NRP has been previously reported by Spanish and English teams [6,7]. Following establishment of the NRP through aorta and IVC in abdomen, the chest was opened, pneumoplegia was delivered via the pulmonary artery and lungs were retrieved after clamping SVC and IVC so

that abdominal NRP could be continued. In the present technique, we followed similar principals for retrieval of donor heart albeit with changes in donor blood management. The OCS Heart requires approximately 1.2L of donor blood in its prime to achieve adequate perfusate haematocrit. We fear evacuation of this blood in addition to blood loss during procurement of donor heart would not leave enough blood volume in 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 minimise potassium content in the circuit.

In the present case, donor lungs were not accepted for implantation due to suboptimal function. If accepted, antegrade pneumo-plegia can be delivered into main pulmonary artery via a cannula introduced into it following cardioplegia cannula. Once, heart is procured, the pneumo-plegia can be given retrogradely. Surgically, the azygos vein would have to be ligated prior lung retrieval, to avoid significant 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 hasten the lung procurement.

NRP for abdominal organ retrieval is carried out in France, Spain, Italy and the UK and early reports suggest superior post-transplant liver function compared to conventional super-rapid retrieval techniques. However; in terms of outcomes of DCD donor heart transplantation, both DPP and NRP methods have shown equivalence with DBD heart transplantation outcomes [8,9]. Experience with the DCD heart transplantation is still limited to double digit numbers and further studies are necessary to determine the superior method - till 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 case, 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 via IVC cannula before beginning the NRP. We recommend collection of the donor blood through a right atrial cannula by thoracic team to save this crucial time.

Conclusions:

Direct procurement of the donor heart in combination with abdominal NRP satisfying 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.

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Table 1: Comparison between DPP and NRP techniques

	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
Possibility of in-situ heart functional assessment	Yes	No	No
Reliance on heart ex situ assessment	No	Yes	Yes
Possibility of in-situ liver functional assessment	Yes	Yes	No
Requirement of agreement with lungs and abdominal organ teams	Yes	Yes	No
Length of DCD Heart/Lung retrieval	Long	Short	Short

(TA-NRP, Thoraco-abdominal normothermic regional perfusion; OCS, Organ care system; DPP, direct procurement and perfusion; ECMO, extracorporeal membrane oxygenation; DCD, donor after circulatory death)

Figure legends:

Figure 1: Lactate trend for the OCS Heart