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Emerging organ-assist technology in cardiac procurement: a viewpoint

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Cardiac failure is a major global killer.[1] Orthotopic heart transplantation is the resource-intensive surgical treatment of choice for end-stage cardiac failure.[2] Its main and worsening limitation is paucity of donors. This is a sobering reality that calls for donor organ stewardship and ultimately disruptive technological solutions in order to reduce the worldwide waiting lists for orthotopic heart transplantation. We have noted the increasing complexity of allocation and managing of finite resources in procurement (known as retrieval in the UK) of donor hearts. The three donation factors impacting on the outcomes of orthotopic heart transplantation are, in no particular order, donor age, donor cardiovascular history (especially stroke as the cause of death) and cold ischaemia time.[3] Most of the cadaveric donors have suffered brain death (Donor Brain Death [DBD]), whilst options on donors from cardiac death (Donor Cardiac Death [DCD]) have already been popularized in the last decade.[4]

With the aforementioned predicament in mind, we offer a viewpoint on an emerging relevant technology known as organ care systems (OCS). These have for some time been used to optimise the donation of abdominal organs, especially liver and kidney.[5] In liver procurement for example, the OCS scavenges harmful particles.[5]

It follows that the OCS concept could be applied to orthotopic heart transplantation.[6] At least two systems, one from a New England manufacturer in the US that is already in clinical use and another Swedish system with reported porcine success that is pending human application (Personal Communication), are currently being used in Europe.[6] The primary advertised advantage of an OCS is the almost

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complete removal of the aforementioned cold ischaemia time; the latter measured from application of the aortic cross clamp (in donation after brainstem death) or asystole (in donation after circulatory death) until *in situ* reperfusion of the donated heart. The input of pioneering cardiovascular perfusion practitioners has been pivotal so far in developing and managing the prototype apparatus.

The system from the New England manufacturer, the only clinically available system to date, enjoys investigatory device status in the UK and the rest of Europe.[6] There have been more than 200 runs from six UK cardiac procurement (retrieval) centres during the last two financial years, a figure that will be intensified henceforth as various funding avenues are being explored. The obvious aim is to obtain approval from The US Food & Drug Administration on the strength of favourable outcomes in the UK and Europe. The retail cost is considerable; tens of thousands of pounds per heart procured, exceeding roughly a tenth of that of the entire care bundle of an orthotopic heart transplant. The Swedish system is in the early stages of recruitment for a pilot study in humans and will not be discussed further.

The prototype OCS we use currently in the UK holds theoretical, scientific and clinical interest for perioperative physicians tasked with the care of the DBD donor from transferral from the intensive care unit until aortic cross clamping. We shall not, however, belabour the surgical considerations of the system from the New England manufacturer in this editorial. In brief, following cardiectomy, the donor heart is inspected for defects, in particular patent foramen ovale, and then directly inserted under aseptic conditions and without topical cooling into the specialized chamber by means of aortic cannulation and pulmonary artery venting. Electric cardioversion for asystolic hearts may be required, especially in the DCD, and the module incorporates various ingenious solutions for monitoring vital signs, metabolites and it can provide cardiac massage if required (see supplemental video of the cardiac OCS in operation).

Appropriate invasive haemodynamic monitoring (invasive arterial systemic blood pressure and pulmonary arterial pressure monitoring), dynamic assessment of volume status and responsiveness (combination of haemodynamic and echocardiographic parameters), thermoregulation and appropriate muscle relaxation are paramount in successful organ procurement. Apart from the standard cardiopulmonary and anaesthetic considerations during organ donation surgery, nuances of OCS management relevant to the anaesthetist and intensivist involved in cardiac OCS retrieval can be formalised into three broad metabolomic aspects: (i) maintenance of normoglycaemia (often requires insulin infusion); (ii) tight electrolyte (potassium and sodium in particular) control, and selection of the appropriate solution regimen; and (iii) permissive gravitational (siphoning) exsanguination of 1.0–1.5 l of donor blood through a single-stage right atrial cannula. For obvious reasons, the latter happens immediately before the cold ischaemia time, as loss of such volume may destabilize the donor.

Implementation of the aforementioned intraoperative strategies and a multidisciplinary perioperative approach (operating room and donor care practitioners, intensivists, perioperative physicians, retrieval surgeons) may have an effect on graft viability and ultimately determine the outcome of the organ recipient.

The New England manufacturers assert that their OCS negates the cold ischaemia time, in so much that the cold ischaemia time stops for the heart once it has been connected via the ascending aortic and pulmonary cannulation to the OCS.

Table 1. Key studies examining the effect of a cardiac organ care system (OCS) on patient-related outcomes.[7–13]

Reference	Study design	*n*	Intervention group (*n*)	Comparator (*n*)	Outcome measures	Results	Grade of evidence[a]
Yeter et al.[8] 2014	Observational (conference abstract – unclear whether prospective or retrospective)	21	OCS in extended donor criteria and transportation time ($n = 21$)	No controls	Not defined in the abstract	a) Median time of graft ex-vivo: 388 minb) Freedom from cardiac related death: 95% at 30 days and 6 months and 87% at 1 and 4 years	Low
Garcia Sáez et al.[9] 2015	Retrospective observational	30	OCS in continuous flow-LVAD patients ($n = 15$)	Cold storage ($n = 15$)	Not defined in the abstract	Better 30-day survival rates in the OCS group but not statistically significant	Low
Messer et al.[10] 2016	Prospective non-randomised	13	OCS in DCD donors ($n = 13$)	No controls	Primary graft dysfunction	No episodes of rejection (total, 1436 patient-days; range, 48–297)	Low
García Sáez et al.[11] 2016	Prospective observational	60	OCS in standard criteria donors ($n = 24$)	Extended criteria donors ($n = 36$) (at least 1 risk factor from the following: left ventricular ejection fraction <50%, left ventricular hypertrophy, interventricular septum in diastole > 14 mm, donor cardiac arrest, coronary artery disease, known cocaine abuse or circulatory death)	Not defined in the abstract	a) Transport time ≥2.5 h in 26 donors b) Increased requirement of ECMO support in the standard donor group 33% versus 11% ($P = 0.05$) c) 1-month, 1-year and 2-year survival were similar between the two groups	Low

(continued)

Table 1. Continued.

Reference	Study design	*n*	Intervention group (*n*)	Comparator (*n*)	Outcome measures	Results	Grade of evidence[a]
Esmailian et al.[12] 2016	Randomised controlled trial	38	OCS ($n = 19$)	Cold storage ($n = 19$)	a) 2-year survival, freedom from cardiac allograft vasculopathy b) any-treated rejection c) biopsy-proven cellular rejection d) biopsy-proven antibody-mediated rejection e) non-fatal major cardiac events	No significant between-group differences	Low JADAD score = 0[b]

[a]GRADE Working Group grades of evidence: [h]igh quality – further research is very unlikely to change our confidence in the estimate of effect; moderate quality – further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality – further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low quality – we are very uncertain about the estimate.[7]

[b]JADAD quality scoring system: total score (6) includes the quality of randomisation (a maximum of 2 points), the quality of blinding (a maximum of 2 points) and reporting withdrawals (a maximum of 1 point).[13]

LVAD, left ventricular assist device; DCD, donation after circulatory determined death; ECMO, extracorporeal membrane oxygenation.

There is a paucity of large-scale prospective studies examining the effect of cardiac OCS on patient-relevant outcomes (Table 1), and ultimately, donation stewardship.[7–13] Unfortunately, the included studies were either underpowered for their primary endpoint or had undefined outcomes.[7–13]

Summarising what a perioperative physician caring for a cardiac donor after brain death using cardiac OCS in a district general hospital should henceforth bear in mind, we note the importance of metabolomic management and most crucially, the vigilance around the exsanguination preclamping, because a volume loss may render the donor unstable.

It therefore remains unknown whether cardiac OCS in its present or future guises will confer a cost-effective benefit compared with cold storage preservation. Little has so far been asserted on the cost-effectiveness of expensive cardiac OCS for procurement. The assertion of minimising cold ischaemia time remains to be tested. The potential of cardiac OCS to expand cardiac donations, especially with regard to donations after cardiac death, would be most welcome.

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