

Cardiothoracic Organ Perfusion Protocol

Date: Thursday 10th December 2015
Time: 11am – 3pm
Venue: Rooms on Regents Park, 27 Sussex Place, Regent's Park,
London NW1 4RG

Teleconference number (for those only participating in one agenda item): 020 772 6389 Pin: 9978

Attendees:

- § Steven Tsui (Cardiothoracic Advisory Group) – Joint Chair
- § Rutger Ploeg (National Clinical Lead for Organ Retrieval) – Joint Chair
- § CT NORS Team Leads and Transplant Programme Clinical Director, or their nominated representatives:
 - Diana Garcia Saez (Harefield)
 - Majid Mukadam (Birmingham)
 - Nawwar Al-Attar (Glasgow)
 - Stephen Clark (Newcastle)
 - Rajamiyer Venkateswaran (Manchester)
 - Marius Berman (Cambridge – NORS Team Lead)
 - [Shah]
- § Gabriel Oniscu (Research, Innovation and Novel Technologies Advisory Group) [Note – by teleconference only from 1.15pm]
- § Debbie McGuckin (NHSBT Commissioning)
- § Ade Bakare (NHSBT Procurement)
- § Claire Williment (NHSBT Head of Transplant Development)

For agenda item 5:

- § Olive McGowan (NHSBT Assistant Director for Education and Governance)
- § John Dark (National Clinical Lead for Governance)
- § Paul Murphy (National Clinical Lead for Organ Donation)

Aim of meeting: To discuss and agree a UK protocol for cardiothoracic organ perfusion.

Introduction

Heart and Lung preservation documentation included some inconsistencies. The aim of the meeting was to review available evidence and agree a UK protocol for CT organ perfusion.

Cost for T3 is increasing and need to review evidence base for the use of T3 and agree protocol.

State of the Art – Hearts

The group was given a presentation regarding the use of medication during management of DBD donor by Rajamiyer Venkateswaran. Key points included: strong evidence for the use of vasopressin and steroids.

- § Approx. 85% of donors are T3 deficient.
- § If administer T3, need to do this 6 – 8 hours prior to retrieval in order to be potentially effective.
- § Published evidence suggests little impact on donors.
- § Discussed:
 - No benefit for the use of T3 in donors. Focus attention on early donor management.
 - To (dis)prove effect in marginal heart donors, a national randomised controlled trial of around 200 donors would be required. Possible primary end point of conversion rate of anatomically useable hearts. Secondary endpoints could include changes in donor haemodynamics .

AGREED:

- § There is no evidence that the use of T3 will help with the optimisation of cardiac donors. It should be removed from the donor care bundle utilised by SN-ODs and CLODs. Use of T3 in selected cardiac donors at the discretion of the retrieval team is permitted but not mandated.

ACTION: DMcG to confirm costing for T3.

The group was given a presentation by Nawwar Al-Attar regarding heart preservation. Key points included:

- § Scout project has positively impacted on CT donation.
- § Scotland had developed a secure system for sharing and storing echocardiograms real-time.
- § In Scotland, the IVC is clamped in the pericardium and the abdominal team vent in the abdomen. Likewise for Manchester and Cambridge.
- § Many different cardiac preservation solutions currently in use amongst UNOS transplant centres.
- § In UK, only two solutions are used:
 - Sterile Concentrate for Cardioplegia Infusion (Martindale Pharmaceuticals) - one 20 ml ampoule diluted with 1 litre of Ringer's solution provides equivalent constituents to Plegivex. Pressure and volume are left at the discretion of the retrieval team.
 - Modified Bretschneider cardioplegia HTK solution (Custodiol) (only used by Harefield)
- § No randomised control trials, but Cannata study compared solutions (HTK, Celsior and Custodiol) and found no difference in outcomes .
- § Limited evidence that UoW solution may have more long-term benefit in comparison to Celsior.
- § Warm perfusion shows potential for longer perfusion times and increase organ utilisation in comparison to cold perfusion particularly in VAD explant patients.
- § Somah Normothermic Storage study being developed, which is designed to allow near normo-thermic perfusion. Currently developmental, not available on the market.

DISCUSSION:

Discussion about venting by dividing the upper IVC in the pericardium as practiced by some continental European teams vs. venting in the abdomen by using a special drain introduced in the distal IVC. Some evidence that venting in to abdominal IVC has negative impact on abdominal organs (liver: relative outflow-block at hepatic vein level). Possible stasis for kidneys with hampered outflow from renal veins. Agreement that both venting options are possible and lead surgeons of CT and abdominal team should discuss and agree prior to retrieval operation.

The need to reconstitute Sterile Concentrate for Cardioplegia Infusion. However, it was agreed that this is not a complex task and should be well within the competency of a transplant practitioner role. Some units ask their pharmacy to provide this service.

Whilst there is no evidence for the benefit of any single solution, there is a need to eliminate any human risk factors by reducing the need for extra intervention or reconstitution..

ACTION: D McG to contact the suppliers [Martindale?] to determine whether it is possible to have ready-mixed bags and if so, the cost implications.

AGREED:

§ No change to current practice regarding where to vent.

§ Hearts:

- Solution: Sterile Concentrate for Cardioplegia Infusion diluted in 1 Ringers solution should be used for national shared CT organs.
- Volume:
 - § For donors between 30-70 Kg, provide 1 litre of reconstituted Cardioplegia solution.
 - § Donors >70 Kg, use 1.5 L.
 - § At the discretion of the recipient surgeon request, it is possible to change the standard dose dependent on logistics and/ or donor physiology.
- Pressure: To be confirmed.
- Medication: 30,000 units heparin IV
- Packing
 - § Inner bag: Saline 2 L.
 - § 2nd bag: Saline 2 L.
 - § outer bag: Saline 2 L.

ACTION: S Tsui and N Al Attar to undertake root pressure measurements using 9F DLP cannulae.

State of the Art – Lungs

Lung preservation: A presentation was provided by Stephen Clark regarding lung preservation. Key points included:

- § Prostaglandin E1 demonstrated some benefit, but there is no consensus regarding dosage and timing of administration.

§ Retrograde flush irrigates pulmonary and bronchial circulation and limits effect of pulmonary arterial vasoconstriction.

§ Lungs are better inflated when stored.

ACTION: S Tsui to provide Papworth Perfadex guideline as a basis for discussion/adoption in the national protocol

The Papworth guidelines regarding the use of Perfadex are provided at Annex A.

§ Advised:

- Prostaglandin (Flolan 10ml) into PA
- No role for methylprednisolone
- Possibly review trials of Celsior to replace Perfadex
- Exogenous surfactant can be considered

DISCUSSION:

Perfadex comes in 2 bag sizes, with inequitable price differences: cost per litre for 1L bags << 2.8L bags.

AGREED:

§ Solution: Perfadex

§ Volume: 50 - 75ml/Kg.

§ Temperature: DBD and DCD: 1st litre at room temperature. The rest cold.

§ Use of heparin and prostacycline:

- in DBD donors, systemic heparinisation by the anaesthetists and then 10ml Flolan injected slowly into pulmonary artery prior to cross-clamping.
- For DCD donors, heparinisation into the PA by retrieval surgeon directly followed by 10ml of Flolan.

§ Technique: 24 French straight cannulae with pneumoplegia bag 25cm above the donor.

§ Oxygenation: limit to FiO₂ of 50%.

§ Lung inflation (airway pressure): 15 – 20 cmH₂O Packing

§ Inner bag: Saline 2 L.

§ 2nd bag: Saline 2 L.

§ outer bag: Saline 2 L.

Use standard organ boxes.

State of the Art: Abdominal Normothermic Regional Perfusion (NRP)

In DCD Maastricht Category 3 (withdrawal of support) currently plans are going ahead to implement NRP. Abdominal retrieval teams isolate abdominal compartment from CT compartment and legs and use the donor's blood. Cannulation of the abdominal aorta; use double-balloon for abdominal aorta or cross-clamp below the diaphragm or in the thoracic cavity and then start the pump which is maintained for 2 hours. Assessment every 30 mins including blood gases etc. Gabriel Oniscu revealed that this approach has supported an increase in donation to almost 60% and 20% reduction of ischaemic/ biliary damage. Increased utilisation in pancreas. 5-6% increase in kidneys, with outcomes being comparable with living donors.

Spanish experience with DCD elected a dual approach with 2 pumps – one for CT and another for abdominal – and to allow variation in perfusion approaches.

Haemostasis is crucial, especially in the chest when lungs are retrieved – a small number of instances where there has been excessive bleeding in the chest following immediate lung removal. Alternative approach is to leave donor lungs in-situ until the end of NRP.

Donor is cannulated as for any abdominal retrieval. Cannulate abdominal vessels, with intra-aortic balloon occlusion at level of diaphragm. There is a 3-stage IVC cannulae approach is used, to allow the liver to be well drained.

Average of 16 minutes from asystole to start NRP.

Issue regarding potential for sudden heavy blood loss in the thorax after immediate lung excision during NRP, which risks the loss of potentially transplantable abdominal organs.

Process of lung removal must be haemostatic in order to have successful NRP.

AGREED:

- § For DCD donors requiring NRP, offer CT retrieval surgeons two options:
 - Immediate lung retrieval with meticulous haemostasis **OR**
 - Delayed lung retrieval until the end of NRP. This requires clamping of the donor arch vessels (to prevent restoration of donor cerebral circulation) and decompression of the donor heart (vent insertion and Y to venous line of NRP circuit if required)
- § Agreement between local teams regarding who will cannulate, but perfusion will not commence until neck and head vessels have been clamped.
- § The approach for NRP must be tailored to the experience of those present. Options are:
 - § Experienced CT retrieval surgeon will remove lungs immediately and achieve haemostasis.
 - § Less experienced CT retrieval surgeons
 - NRP cannulation in the thorax and cross clamp the arch vessels or
 - Cross clamp the arch vessels and let the abdominal team cannulate the abdominal vessels to establish NRP

The revised paper 'DCD Donors on NRP', reflecting the above 3 options for NRP approach, based on experience of the surgeon, is attached at Annex B.

Reducing Ischaemia Time of Donor Heart

The average time from donor aortic cross clamp to donor organ in box for DBD heart only is 14 minutes versus DBD heart (with lungs) 23 minutes. Therefore, if the donor heart was excised and bagged before pneumoplegia is commenced, we could potential save 9 minutes of ischaemic time for the donor heart when lungs are also retrieved. This could be achieved by using

two Foley catheters into the right and left pulmonary arteries for pneumoplegia delivery after the heart has been excised.

Glasgow, Newcastle and Papworth are in favour. Manchester is concerned

AGREED:

- § Option to either stay with current practice or alternatively undertake above technique, where the heart is removed and bagged and then lungs removed. This will be left at the discretion of the CT retrieval surgeon
- § Training video should be provided and made available to retrieval teams.

ACTION: S Tsui to circulate slides.

Next steps for CT Perfusion Protocol

1. C Williment to send draft on to S Tsui and R Ploeg for comment.
2. C Williment to circulate to attendees for comments from their Unit.
3. D McGuckin to add in costings.
4. R Ploeg to share with NRG for approval.
5. S Tsui to share with CTAG for comment.

Incidences relating to DCD lung retrieval

There is confusion amongst the organ donation staff members and retrieval teams regarding what and when it is permissible to inflate and ventilate the lungs in DCD donors. There has been an incident where a heart was re-started following premature re-inflation of the lungs. The NORS standards and Lung DCD retrieval protocol requires clarification. These led to the development of a Safety Briefing document and proposed revision to the NORS standards.

ADVICE FROM GROUP:

- § Safety document: A single recruitment manoeuvre should be undertaken, but this may be a staged delivery of a certain volume of gas through manipulation of the air-pressure-release valve.
- § If DCD lung only, follow protocol as set out in the safety briefing document:
 - *“At a point no earlier than 10 minutes after the onset of irreversible asystole, the lungs should be re-inflated with single vital capacity breath.”* This manoeuvre may be repeated if required.
 - *“Cyclical lung ventilation must not be instituted automatically at this stage and can only begin once lung perfusion has commenced*
- § Add in to notes section: If the arch vessels are to be clamped, for instance to support normothermic regional perfusion, then lung recruitment and ventilation can begin as soon as the cerebral circulation has been so isolated. Draft amendment to NORS standard: amend para 4 to say ‘The cardiothoracic team must facilitate the abdominal team...’ Also, include requirement regarding if DCD hearts are being retrieved as well as lungs.

ACTION: O McG to re-circulate revised drafts by 11 December 2015.

ACTION: C Williment, S Tsui and R Ploeg to revise NORS protocol.

Annex A

PERFADEX**Guideline for use**

- Shelf life of 3 years at pH 5.5.
- Store at < 30° C
- DO NOT add any drugs or buffering agents to the Perfadex bags until it is finally confirmed that lungs are being retrieved.
- Once the Perfadex container is opened and additives have been added the solution must be kept cold and used within 24 hours.

Donor size and required volume of Perfadex

Donor Wt (Kg)	Antegrade Vol (L)	Retrograde Vol (L)	Total Vol (L)	Number of 1L bags required
30-40	1.0	1.0	2.0 (50-67 ml/kg)	2
41-60	2.0	1.0	3.0 (50-73 ml/kg)	3
61-80	3.0	1.0	4.0 (50-67 ml/kg)	4
81-100	4.0	1.0	5.0 (50-62 ml/kg)	5
101-120	5.0	1.0	6.0 (50-59 ml/kg)	6
121-140	6.0	1.0	7.0 (50-58 ml/kg)	7

- Will need up to 7 of 1L bags per retrieval
- Keep enough at 4° C for 3 retrieval, i.e. 3 x 6 of 1.0L bags

Additives (see table below)

- Prior to administration, the pH needs to be buffered upwards to 7.4 by the addition of THAM/TRIS (Tromethamine) for all bags
- Calcium chloride is also required
 - Calcium chloride 0.5 ml for each 1.0 L bag
 - THAM 1.6 ml for each 1.0 L bag
- The first two 1.0L Perfadex bags should also contain Prostacyclin and GTN - 500 mcg Prostacyclin and 25 mg of GTN diluted in 50 mL of supplied diluent, divided equally between the first two bags.

- The Perfadex bags must be labeled either
 - a) "With ALL drugs" or
 - b) "With Ca⁺⁺ & THAM only"
- Drugs should be added to the bags individually. Give the bag a good shake
- Return Perfadex bags 2-7 in the ice-box after adding drugs until required

	Bag 1	Bag 2	Bag 3	Bag 4	Bag 5	Bag 6	Bag 7
Temperature	Room	Cold	Cold	Cold	Cold	Cold	Cold
Prostacyclin	Yes	Yes	-	-	-	-	-
GTN	Yes	Yes	-	-	-	-	-
Calcium Chloride	Yes	Yes	Yes	Yes	Yes	Yes	Yes
THAM	Yes	Yes	Yes	Yes	Yes	Yes	Yes

PERFADEX DELIVERY

- It is delivered from a height of about 25 cm above donor
- If monitor delivery pressure via infusion line used for prostacyclin bolus, aim for a pressure of 25 mmHg
- Preservation solution is delivered in two phases, antegrade followed by retrograde.
- The same antegrade cannula is removed from the PA and placed into each pulmonary vein in turn.
- The retrograde phase consists of delivering 250 mls of Perfadex into each pulmonary vein. This is done by pinching the cannula between the fingers so as to prevent the pneumoplegia from leaking back into the left atrium.
- Prior to the retrograde flush, the heart is excised and the pulmonary trunk transected just before its bifurcation

Steven Tsui
December 2015

Annex B

DRAFT ADDENDUM TO DCD LUNG RETRIEVAL PROTOCOL

For DCD donors to be placed on NRP, BEFORE treatment withdrawal, the cardiothoracic and abdominal NORS teams must discuss the following 2 questions and agree on which approach is to be adopted:

- 1) At which point will the donor lungs be retrieved?
 - a. Immediate donor lung retrieval with meticulous haemostasis
 - b. Delayed donor lung retrieval until the end of NRP

If the answer to Q1 is (b).

- 2) Which NORS team will perform cannulation for NRP?
 - a. Cardiothoracic NORS team
 - b. Abdominal NORS team

If the decision was to leave the lungs in situ and delay lung retrieval until the end of NRP, there would be perfusion of the lung via the bronchial arteries, predominantly from the descending thoracic aorta. The heart could either be made to eject or the left heart could be vented to keep the left atrial pressure low. This should maintain viability of the donor lungs until the abdominal organs are ready to be retrieved, and obviate difficulties with haemostasis in the chest after early lung removal.

After cardiac arrest:

- The time of death must be noted.
- On arrival in the operating theatre, the donor should be re-intubated with a cuffed endo-tracheal tube; this may be preceded by a rigid bronchoscopy, depending on the skills available. Intra-abdominal manipulation may cause aspiration, so early protection of the airway is important.
- Simultaneously, the chest is rapidly opened.
- Heparin (20,000 units in 10ml) is injected into the main pulmonary artery and Heparin (20,000 units in 10ml) is injected into the right atrium.
- The aortic arch vessels are cross clamped.
- The arterial and venous systems are cannulated (either CT or abdominal NORS team as agreed) and NRP is commenced
- If cardiac contractility cannot be restored, a vent is inserted into the left ventricle and Y to the venous tubing of the NRP circuit. A purse-string suture may be required on the LV vent site to prevent blood loss.
- Thorough airway toilet should be performed as soon as possible.
- Atelectatic lung may be recruited with a single breath, perhaps 30-40mmHg pressure for 40 seconds, ideally using the anaesthetic machine (after a minimum of 10 minutes from donor asystole or when aortic arch vessels have been clamped).
- CPAP should be maintained at 5 cm H₂O and continuous O₂, once again ideally with the theatre anaesthetic machine.
- Cyclical ventilation can commence AFTER the aortic arch vessels have been cross clamped
- The lungs are examined for collapse, consolidation, mass lesions and pleural adhesions. If there is a suspicion of airways disease, the degree of collapse when the lungs are disconnected should be noted.
- When the abdominal organ dissection is complete and NRP is to be terminated, the pulmonary artery is cannulated. During the first 30 min-1 hour of NRP the amount of dissection varied but in general was limited to allow organs to recover. The "standard" duration of NRP was two hours (although the "optimal" duration is still to be determined. Would you be happy with two hours of NRP prior to PA cannulation?
- Pneumoplegia administration and lung retrieval can then proceed as for DBD lung retrieval

Steven Tsui

22 December 2015

Deleted: August