Cardiothoracic London Anaesthesia Partnership

Anaesthesia for Heart Transplantation

Pre-operative assessment

Patients coming in from home will have been thoroughly worked up and may have even been called in previously for a potential transplant and been seen by an Anaesthetist. Patients in hospital who have been listed as "super-urgent" may not have had as holistic an assessment or their condition may have changed significantly. Heart transplants may be planned several hours in advance but due to the time-sensitive nature of the process it is wise to pre-assess these patients as soon as you are notified. The key areas to focus on *(with the rationale in brackets)* are:

- Aetiology/Indication *(restrictive cardiomyopathy may have additional challenges of size-matching compared to DCM, occasionally patients with congenital lesions are transplanted)*
- Presence of mechanical support device *(anticoagulation, bleeding, vasoplegia, length of time for sternotomy/bypass cannulation)*
- Presence of intracardiac thrombi *(anticoagulation, careful surgical handling of heart pre-bypass)*
- Previous sternotomy *(bleeding, length of time for sternotomy/bypass cannulation)*
- *Presence of implantable cardiac devices (ICD therapies need to be disabled pre-surgery)*
- Presence of pulmonary hypertension *(risk of death on induction, increased risk of RV failure)*
- Pulmonary vasodilator therapy *(must not discontinue prior to bypass)*
- Anticoagulants *(reversal plan, bleeding)*
- Renal impairment *(need for filtration), Hepatic impairment (higher risk, bleeding)*
- Discuss with Surgeon: Timing *(avoid prolongation of graft ischaemic time),* Cannulation strategy *(line placement, anticipation of problems),* Graft function *(risk of primary graft dysfunction)*

Don't forget the basics; airway assessment, fasting status, allergies, volume status, risk factors for oesophageal trauma, chronic pain issues, potential medication interactions and any recent changes in health (e.g. infections). Key investigations to review include; bloods including cross-matching, ECG, CXR/ CT chest, Echo, spirometry, right-heart catheter.

Consent should include the usual elements of cardiac surgery with added information regarding potential need for RRT, ECMO and a prolonged ICU stay for multi-organ failure.

Peri-operative management

Timing is critical to avoid unnecessary delays that may contribute to organ ischaemic time:

- The explanted heart should be accepted before inducing anaesthesia
- Stop IV UFH when patient sent for
- Allow 1 hr for anaesthesia setup, and 1 hr for pre-implantation surgery (2 hrs if re-sternotomy)
- Ensure native heart not excised until donor heart inspected
- Reverse Warfarin at time of explantation (Vit K + PCC)

Patients presenting for heart transplantation have end-stage heart failure and demonstrate some or all of the features below which you must be aware of:

- Significantly reduced physiological reserve
- Reduced sensitivity to vasoactive medication
- Pulmonary hypertension (pHTN) - defined by PASP >50 and PVR >3 (Wood units) or TPG >15. Patients responsive to pulmonary vasodilators will be on treatment (commonly a Milrinone infusion) that MUST be continued until full cardio-pulmonary bypass is established. Cessation of therapy can cause rapid and fatal RV failure during induction of anaesthesia. Patients unresponsive to therapy will have an LVAD. Significant disease may require a larger donor graft or a heart-lung transplant.
- LVAD dependance

Pre-induction preparation should include consideration of the following:

- Drawing up vasoactive infusions and "push-doses" of Noradrenaline and Adrenaline
- Ensure 4 units PRBCs + 4 units FFP and 2 Platelet pools available. Order PCC if patient on Warfarin
- Set up iNO (even if low risk of RV failure)
- Attach external defib pads, processed EEG and cerebral oximetry monitoring
- Continue vasoactive infusions, i.e. Milrinone
- Avoid/minimise sedation as much as possible (hypercapnia can precipitate severe RV failure)
- Insert a large bore peripheral line, A-line (recommend US if VAD present)

- Have a senior Surgeon and Perfusionist immediately available at induction (if LVAD present the LVAD Practitioner must be immediately available until device explanted)

Induction will be slow due to low cardiac output. Consideration of Etomidate or Ketamine for cardiovascular stability should be given. Have push-dose vasopressors to hand and avoid hypoxaemia and hypercarbia. Place central lines with pristine asepsis (imminent, severe immunosuppression) and use LIJ where possible (RIJ will be used multiple times for right-heart cath +/- cardiac biopsy in the future), insert a PAC but leave the tip of the catheter within the sheath until the donor heart has been grafted. Place the TOE probe very carefully in anticoagulated patients and avoid nasopharyngeal temp probes. Give the first dose of IV Methylprednisolone (0.5-1g).

In the operating room start antifibrinolytic therapy pre-bypass. This will usually be TXA but Aprotonin may be preferred for re-sternotomy. Antimicrobial therapy will usually follow elective cardiac surgery regimes but LVAD-related infections may require additional coverage. Cease ICD therapies. Treat LVAD low-flows with fluids +/- reducing pump speed in conjunction with the LVAD Practitioner. For re-sternotomies ensure 6 units of PRBCs + 6 units of FFP and 2-4 Platelet pools are available, and have 2 units of PRBCs immediately available prior to surgery. Be prepared for emergent bypass initiation, i.e “sucker bypass”. Consider filtration/diuresis to increase Hb concentration at each stage of the surgery. Pre-bypass TOE should focus on identifying intra-cardiac thrombi, aortic atheroma/calcification and pleural effusions. Note the surgical technique; Bi-atrial, or Bi-caval to help anticipate and identify post-operative complications.

After the left atrium and aorta are anastomosed a period of “reperfusion” (typically 1 hour) is undertaken to optimise graft function prior to attempting a bypass wean. A 2nd dose of Methylprednisolone is given at this point. The length of this period is proportional to the total ischaemic time of the graft. This period is crucial to improve the chance of successful separation from bypass. It requires optimisation of pacing, cardiovascular support and haemostasis. Optimisation strategies are based on institutional preferences rather than evidence. The following is an outline of my personal practice:

- Start low dose inotropes and iNO during reperfusion then titrate to function during bypass weaning
- Using multiple inotropes/vasopressors that work on different pathways can in theory minimise the doses required for therapeutic effect and therefore minimise side effects (which occur at higher doses)
- Pace DOO 50-60bpm during reperfusion and increase to 90-110bpm during bypass wean
- Float PAC once SVC and PA anastomosed
- Use TOE to guide de-airing, exclude intra-cardiac thrombi + shunts, assess biventricular function, check there is no SVC stenosis at the anastomosis site and that pulmonary vein flow is not impeded
- Treat arrhythmias in the conventional manner and consider extended reperfusion time if refractory
- Send TEG/ROTEM during reperfusion *(to guide blood product replacement after bypass weaned)*
- Consider reconstituted blood products *(to help minimise volume)*, consider desmopressin for patients with LVAD *(for acquired von Willebrand syndrome)*

Once successfully weaned from bypass and heparin is reversed repeat a TEG/ROTEM. Change pacing to DDD once chest closed and insert an NGT +/- vascath if RRT anticipated.

Problems to anticipate

- Low cardiac output (CO) - treat reversible causes: hypovolaemia, inadequate adrenergic stimulation, tamponade. More sinister causes to consider are myocardial injury during harvesting, acute rejection, sepsis, primary graft dysfunction
- Primary graft dysfunction - No reversible cause for low CO identified. Risk factors: Donor related: long ischaemic time (>4hrs), LVH, LV dysfunction, Age >60, DCD, size/sex mismatch, Recipient related: Age >60, LVAD, re-sternotomy, congenital heart disease, Procedure related: high volume blood transfusion. Mitigation involves prolonged reperfusion, iNO, judicious use of blood products (surgical haemostasis, reconstituted products) and a gradual weaning of inotropes post-op.
- RV failure - common, look for: RV dilatation, reduced free wall contractility, TR, leftward bowing of intra-atrial septum. Optimise preload, contractility and afterload. Dennervation leads to increased preload dependance. Assess preload by RV size and CVP response to volume administration. Increasing CVP >15mmHg unlikely to help. Maintain normoxia, normocarbia and normal pH. Avoid high ventilation pressures and hypotension.
- Vasoplegia - ~1/3 cases, hypotension despite adequate CO and preload. Risk factors: Pre-op ACEi, Aspirin or mechanical support, re-sternotomy, large BSA, thyroid disease, renal impairment, prolonged duration of bypass (>140 mins). Treat with Noradrenaline and Vasopressin. Consider placement of central

arterial line to guide response. Consider IV Methylene Blue (100mg/60 mins) +/- cytosorb filter if refractory. Continue post-op "shock-dose" steroids.

Failure to wean from bypass or marginal haemodynamics (MAP <65, CI <2, CVP >15) despite moderate to high dose inotropes should prompt initiation of mechanical support (VA-ECMO or temporary assist device). The evidence is in favour of early VA-ECMO use.

Critical care management
This is essentially a continuation of the post-bypass anaesthetic management outlined above. The goals are summarised below:
- Optimise haemodynamics *(PAC and echo guided, inotropic support is typically maintained for 48 hours)*
- Optimise fluid balance *(diuresis is initiated as early as possible, 40% develop AKI, 10-20% require RRT)*
- Provide adequate analgesia *(continue Fentanyl infusion and convert to Fentanyl PCA once extubated)*
- Aim for "early" tracheal extubation (<24 hrs)
- Provide timely antibiotic and immunosuppressant therapy

Always consider acute rejection in differentials for any deterioration e.g. new arrhythmia, pulmonary oedema. Avoid RIJ lines as right-heart cath and biopsy are performed weekly in the first month post-op. If managing patients for this procedure be prepared for RV free wall rupture and tamponade and follow the principles of anaesthesia for the patient with a heart transplant.

Anaesthesia for a patient with a heart transplant

Just as the end-stage heart failure patient has a constellation of disease characteristics, the post-transplant patient has several important physiological and pharmacological features to be aware of.

Physiologic attributes of the transplanted heart include:
- May see dual P-waves (from residual native atrial tissue, this can be confused with flutter)
- Efferent denervation - sympathetic stimulation and chronotropic responses to exercise, stress, and hypovolemia are not seen
- Blunting of baroreceptor responses (e.g. response to laryngoscopy)
- Afferent denervation - impedes vasoregulatory responses by means of the renin-angiotensin axis
- Perception of pain secondary to ischaemia (angina) is lost
- Restrictive pattern (high filling pressures) - results in an abrupt rise in LV filling pressures in response to fluid challenges
- Patients prone to pulmonary and systemic venous congestion
- Reduced exercise tolerance
- Altered response to exercise/stress
- Elevated pulmonary resistance
- Skeletal muscle atrophy from steroids + pre-transplant chronic oxygen debt

Common comorbodities that should be sought include:
- Hypertension
- Severe renal insufficiency
- Hyperlipidemia
- Diabetes
- Coronary allograph vasculopathy (CAV)

Chronic rejection and its treatment have a few important sequelae. Review records to note the incidence, timing, and nature of rejection as well its management. Multiple steroid courses may result in adrenal suppression. Humoral rejection is associated with CAV so have a high index of suspicion and assume all patients have a degree >1 yr post-transplant. They may warrant investigation via angio, stress echo or MPS.

Immunosuppressive medications must be continued peri-operatively and drug levels monitored regularly. They can mask infection due to lack of fever and leucocytosis. Patients will need a tailored peri-op antibiotic regime in consultation with a Microbiologist. Steroids may need conversion to IV and additional steroid coverage may be necessary depending on the dosage and extent of surgery being performed. Patients on Cyclosporine may need reduced dose of muscle relaxants. Nephrotoxic drugs should be avoided and alternatives used where possible. Tacrolimus and Cyclosporine may lower seizure threshold

Pre-op assessment and optimisation:
- Assess graft function, rejection status, CAV, functional status and end-organ involvement
- Be sensitive to the likelihood of subtle mental and psychiatric ailments
- Confirm CMV status (and communicate this to the blood bank)
- Leucodepleted and irradiated cells are required (to avoid graft versus host disease)
- Infective endocarditis prophylaxis is usually not necessary
- Manage any implantable cardiac devices as normal (interrogate, pause, external pads, re-initiate)

Peri-operative monitoring and management:
- The usual haemodynamic responses to light anaesthesia are lost - consider processed EEG monitoring
- Utilise a PAC +/- TOE if large fluid shifts are anticipated
- Adhere to strict aseptic precautions with procedures
- Maintain preload, sinus rhythm and avoid sudden changes in afterload
- Take care with NAB - patients may have thrombocytopenia and are more susceptible to infection
- Neostigmine is well known to cause bradycardia and even cardiac arrest when used for reversal - sugammadex is better

Post-operative care is often undertaken in a Level 2 monitored environment due to the higher risk of arrhythmias. Post-operative infection risk should be managed by removing intravascular catheters and drains as soon as possible. Higher than average post-operative VTE risk in this group should be managed by instituting thromboprophylaxis as soon as possible.

In summary, patients presenting for heart transplantation need careful anaesthetic management due to their severely depleted physiological reserve. A knowledge of the common complications and how to mitigate them will aid successful separation from bypass, or at the worst, help you to initiate mechanical support in a timely fashion to support those who cannot be weaned. Post-transplant patients need to be shown careful consideration of the consequences of their dennervation, transplant related comorbidities and the side effects and interactions of their immunosuppressant regimes.

This document is intended as an educational tool - always follow the policies, protocols and guidelines of your local institution

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