UCSF Anesthesia Resident Pearls
Orthotopic Heart Transplant

1. Background

- Cardiac transplantation can improve quality of life and survival in patients with severe heart failure
- In North America, transplants from January 2012 to June 2017, patient survival at one year was 90 percent, while 5-year survival, conditional on survival to one year, was 86.9 percent, respectively. For patients who survive the first year, survival is 50 percent at 13 years.

2. Causes of heart failure

- Non-ischemic Cardiomyopathies: It has overtaken ischemic heart disease as the number 1 indication.
  - Dilated cardiomyopathy
  - Idiopathic cardiomyopathy
  - Peripartum cardiomyopathy
  - Doxorubicin-induced cardiomyopathy
  - Substance abuse
- Ischemic heart disease
- Restrictive cardiomyopathy (infiltrative, connective tissue diseases)
- Congenital cardiomyopathy
- Hypertensive heart disease
- Primary valvular heart disease

3. Indications

- Persistent New York Heart Association functional class III-IV HF symptoms refractory to maximal medical therapy (left ventricular ejection fraction <20%; peak VO2 <12 mL/kg/min)
- Cardiogenic shock requiring either continuous intravenous inotropic support or circulatory support with a device such an intra-aortic balloon pump, ventricular assist device or total artificial heart.
- Intractable or severe anginal symptoms in patients with CAD not amenable to (or in spite of maximized) percutaneous or surgical revascularization or severe transplant coronary artery disease.
- Intractable life-threatening arrhythmias unresponsive to medical therapy, catheter ablation, surgery, and/or cardiac implantable electronic device (CIED).
- Congenital heart disease with New York Heart Association functional class III-IV HF not amenable to palliative or corrective surgery.

4. **Contraindications** (major, some criteria vary by center)

- Life expectancy <2 years due to illness despite heart transplant
- Severe symptomatic cerebrovascular diseases
- Psychosocial issues: psychosocial instability, ongoing history of substance abuse, or inability to comply with complex medical regimen and follow up care.
- Systemic lupus erythematosus or sarcoidosis that has multi-system involvement and currently active.
- Any systemic process with a high probability of recurrence in the graft heart
- Severe, nonreversible pulmonary hypertension (consider combined heart-lung transplant)
- Irreversible renal or hepatic dysfunction (consider concurrent kidney or liver transplant)
- Malignancy (at risk for second malignancy)
- Active systemic infection, including HIV/AIDS (CDC definition of CD4 count <200 cells/mm3)
- Obesity (BMI > 35 kg/m2)
- Advanced age (rarely ≥70 years old)

5. Day of Surgery Pre-op Assessment

- Review available studies including 12-lead ECG, Holter monitor, echocardiography, stress test, and right/left heart cardiac catheterization.
- Determine the presence and setting of any cardiac implantable electronic device (CIED) such as a pacemaker or defibrillator, including the magnet response if known. Consider an EP consult/interrogation or company 24-hour hotline if suspect the patient may be pacemaker dependent.
- Recent deteriorations in cardiac or functional status.
- Current level of cardiovascular support needed (PO drugs, continuous inotrope infusion, **mechanical assist devices such as IABP, LVAD, RVAD, TAH, or ECLS).**
- Assess pulmonary function via physical exam and chest X-ray.
- Any anatomical (vascular) pathology such as IJ thrombosis or persistent left SVC.
- Recent laboratory test to assess renal and hepatic function, which may be affected by low cardiac output or right heart failure.
- Most recent or ongoing **anticoagulation/anti-platelet therapy and/or evidence of coagulopathy.**
- NPO status (may need RSI if full stomach, severe GERD, or 1st generation VAD).
- Review any past anesthetic record.

6. Preoperative Preparation

- **Machine check/airway equipment**, including **inhaled nitric oxide (iNO)** circuit.

- **Monitoring** equipment
  - Pulse oximeters x2
  - Triple transducer: A-line, CVP, PA
  - Cerebral Oximeters x2
  - EEG entropy
  - TEE
  - Edwards Oximetric/CCO PA catheter and cables
  - Temperature

- **Bolus medications**
  - Induction agents: midazolam, fentanyl, ±propofol/etomidate/ketamine, NMBDs
  - Vasoconstrictors/inotropes
  - Nitroglycerin (20 mcg/mL)
  - Calcium
  - Full dose heparin (400 unit/kg)

- **Infusions**: remember that there is a down regulation of beta receptors in most transplant candidates that may cause a decreased responsiveness to beta agonists
  - Norepinephrine (mcg/kg/min)
  - Epinephrine (mcg/kg/min)
  - Dobutamine (mcg/kg/min)
  - Vasopressin (Units/min or units/hr)
  - Milrinone (mcg/kg/min) – longer half-life and hypotension, please discuss with surgeon
  - *Insulin (units/hr)
  - Propofol

- **Antifibrinolytics** (Just one)
  - Aminocarpoic acid (10 g bolus over 30 minutes, 2 g/hr infusion)

- **Antibiotics**
  - Check with attending for the latest protocol: Cefazolin 2g/Vancomycin 1g/Cefepime 2g IV

- **Immunosuppression**
  - Methylprednisolone 500mg.
  - Any additional antimicrobial or induction regimen to be confirmed by the transplant surgeon during time out.

- **Blood Products** (make sure they are checked by RN):
  - PRBC (4 units) and FFP (4 units): required prior to sternotomy, more if repeat sternotomy.
  - Platelet (2 units) and cryoprecipitate (20 units): prior to weaning from bypass.

* Denotes items requiring pharmacy orders (Don't forget 5% Albumin)

7. Pre-induction Access

- Usually one PIV
- Radial arterial line
- Discuss with attending the need for central venous access prior to induction.
  - Preop PICC line or central line is useful for induction, but it will need to be removed to reduce CLABSI. It is not uncommon to find IJ thrombus at the site of recently removed central line. And the patient may have had numerous catheterization in the past with IJ stenosis. Scan the neck bilaterally with ultrasound first prior to prepping and drape.
- **9Fr 2-Lumen Introducer (MAC) with CCO PAC**

8. **Induction** (after confirmation of the donor organ)

- **Goal**: Smooth induction of anesthesia and secure of airway with minimal hemodynamic perturbation.
  - Discuss plan with your attending. Examples:
    - Etomidate
    - High dose opiate
    - Balance IV and inhaled induction

- Considerations to **co-morbidities**
  - Severely depressed cardiovascular function and ongoing inotropic and/or mechanical support
  - Risk of malignant (ventricular) arrhythmias: history of VT, previous sternotomy (Don't forget pre-induction defib patches)
  - COPD and other lung diseases
  - Pulmonary hypertension and RV dysfunction
  - Potential full stomach/difficult airway
  - Renal/hepatic dysfunction and their effects on pharmacokinetics

- **Hemodynamic instability** is common during induction
  - Any preop MCS devices such as LVAD, ECLS or IABP should be continued.
  - Any preop inotropes such as dobutamine or milrinone should be continued or titrated.
  - Ultimately, any persistent hypotension can lead to emergent cannulation and CPB

9. Procedure Summary/Special anesthetic management

- **CVC/PAC** if not placed pre-induction
  - PAC should be locked at 20-25 cm, to be "floated" before weaning from CPB
  - Turn off the CVP (blue) transducer to prevent leakage of the saline into the PAC sheath

- **Prior to sternotomy**:
  - Start antibiotics (may consider starting vancomycin earlier, e.g. during line placement).
  - Start the comprehensive TEE exam. In addition to the basics, pay special attention to the degree of atherosclerotic disease in the aorta, intracardiac thrombus (LV apex, LAA), any unusual cardiac anatomy (e.g. a dilated coronary sinus suggestive of persistent left SVC), and VAD flow.
  - A sterile draped magnet should be placed over the ICD (if applicable) to prevent interference from electro-cautery.

- **Pre-CPB**
  - Maintenance with an inhaled halogenated anesthetic, usually isoflurane. Although it may cause further myocardial depression and hypotension, it provides some protection against intra-operative awareness and can induce cardiac pre-conditioning. Also, isoflurane is used during CPB.
  - Continue/adjust inotrope(s) and/or vasopressor(s) as needed
  - Provide analgesia with opiates, either bolus during periods of stimulation or constant infusion
  - Ensure muscle relaxation as needed

- **Dissection**: **median sternotomy and pericardiotomy** are performed
  - The dissection can be time consuming as the patient often has had previous sternotomy/cardiac surgery, e.g. CABG, valve surgery, device implantation, previous transplant (>2 hr vs. <1h in an un-operated chest). **The possibility of injuring previous coronary bypass graft, RV, great vessels and VAD cannula/drive line during the repeat sternotomy and pericardiotomy is significant.**
  - The urgency to finish the dissection and cannulation before the donor organ arrives is felt by both the surgical and the anesthesia teams.
  - The need for blood products such as PRBC in the room is an absolute.
  - Be aware that the patient may have an acquired heparin resistance, either due to current illness, recent or ongoing heparin treatment. FFP or antithrombin may be necessary before adequate ACT is achieved.
  - At UCSF, IVC is typically cannulated via a groin cut-down and the femoral vein.
  - Once ascending aorta and bicaval venous cannulation are obtained, CPB is initiated and the aorta is cross clamped.

- **On CPB** (usually normothermic at UCSF)
  - **Cardiectomy**: The recipient heart is removed, usually this includes much of the RA. Only the stumps of SVC and IVC (bicaval technique) and a single left atrial cuff.
  - Ideally, the recipient cardiectomy is completed just before arrival of the cardiac allograft to minimize the organ ischemic time (goal ≤6 hr)
  - Any lead from preexisting CIED will be cut with the distal tip(s) removed with the recipient heart.
  - The **left atrial anastomosis** is always performed first. This is usually followed by the **anastomoses of the pulmonary artery and the aorta**. This will allow the reperfusion of the donor heart (after de-airing the LV and the aorta) to occur on CPB support before finishing the rest of the anastomoses and therefore shortening the warm ischemic time.
  - **Methylprednisolone (500mg)** is given during aortic anastomosis, prior to the release of aortic cross clamp and reperfusion.
  - The donor heart usually begins to beat spontaneously once the clamp is released, but may require defibrillation. Epicardial pacing wires are always placed in case pacing is needed.

  - **The anastomosis of IVC and SVC are performed last (bicaval technique).** This is slightly more time consuming than the standard ("biatrial") technique in which a part of the graft RA is excised in order to complete the anastomosis. "Bicaval" technique has been shown to result in lower RA pressure, less tricuspid regurgitation and higher likelihood of sinus rhythm in the graft heart.

- **Weaning from bypass**
  - Zero the pressure transducers.
  - It is routine to provide chronotropic support for the denervated heart in the form of **epicardial pacing (usually >100BPM)** and/or inotropes (epinephrine or dobutamine). UCSF surgeons prefer **dobutamine as the first line agent at 5 mcg/kg/min**, started after unclamping.
  - The graft heart is denervated (no direct sympathetic, parasympathetic, or sensory innervation) so it lacks swift heart rate responses to baroreceptor or volume status changes.
  - The length of organ reperfusion is dictated by the transplant surgeon (typically 1/5 of total ischemic time) but may be longer due to evidence of graft dysfunction, most commonly RV failure. Information from TEE, CVP and PAC are used to assess RV function.
  - There is an opportunity to **"float" the PAC into the pulmonary artery.**
  - At UCSF, **iNO (20 ppm) is routinely initiated** during weaning for this reason (remember to increase the fresh gas flow to match minute ventilation to avoid rebreathing and NO2 buildup).
  - Switch to **TIVA with propofol** to conserve vapor and reduce greenhouse gas.
  - Significant vasoplegia can be present, further compounded by the use of ino-dilators such as dobutamine or milrinone. This frequently requires high dose **norepinephrine and/or vasopressin** infusion to maintain acceptable MAP.
  - Frequent ABGs are drawn to track the degree of metabolic acidosis, which can be due to hypoperfusion on CPB, graft reperfusion, low cardiac output, or high dose vasoconstrictors.

- **Post-CPB and Hemostasis:** Hemostasis is achieved with **the reversal of heparin with protamine**, transfusion of blood products to replace factor/platelet deficiency, and surgical control.
  - During this period, the heart is frequently lifted, compressed and otherwise manhandled, so frequent swings in hemodynamics are common. Try to avoid any prolonged periods with MAP below 50-60mmHg. The BP fluctuation can be temporized with boluses of vasoconstrictors and calcium, but the surgeons should be reminded.
  - Again, the graft heart, due to ischemia and reperfusion, may have significant diastolic dysfunction and can be very sensitive to its preload. TEE and CVP are used and the anesthesiologist and the surgeon will have to work closely to find the optimal balance.
  - **Surgeons pay close attention to CVP** using it as a surrogate for RV preload. Rise in CVP may suggest worsening RV function. For this reason, you may consider using a non-CVP port to give medication, as injection into and flushing the CVP port can cause delay and confusion.

- **Chest closure**: There is a risk of RV compression during sternum approximation causing significant dysfunction and hemodynamic change. Rarely, it will require keeping the chest open, ECMO or even RVAD.
  - Any CIED will be removed from its pocket and skin closed.

10. Transfusion Goals

- Hematocrit on CPB and thereafter should be discussed during time out with the surgeon and the perfusionist. The latter can perform ultrafiltration on CPB to hemo-concentrate.

- Hemostasis and coagulopathy after CPB
  - **Platelet dysfunction** (quantitative/qualitative) is the most common cause of NON-SURGICAL bleeding post-CPB.
  - **Hyperfibrinolysis** is also common despite routine anti-fibrinolytic use.

- Ideally, the treatment of non-surgical, microvascular bleeding should be guided by objective, laboratory data such as thromboelastography.
  - Most common request by the UCSF surgeons are **platelet (2 units) and cryoprecipitate (20 units)** after the protamine administration.
  - PCC and/or FFP for factor deficiency
  - Factor VIIa is the last resort, but remember to replace any platelet/factor deficiency first. The typical dose is 1mg before reassess hemostasis.

11. ICU transport

- Have a transport bag ready and emergency medications in line.
- **Respiratory therapist** will provide the modified transport ventilator equipped with iNO.
- Low dose propofol is usually used for sedation during transport.

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