PEDIATRIC HEART TRANSPLANTATION

Surgical Specialty:	Cardiac Surgery
Authors:	Bridget Pearce, M.D. University of Michigan, Ann Arbor, MI

Background:

- **General Considerations**
  - A heart transplant is needed when a patient has end-stage failure refractory to medical therapy.
  - Oxygen delivery is inadequate to meet the demands of the body.
  - Pediatric indications include congenital heart disease, cardiomyopathies, cardiac neoplasms, and re-transplantation.
  - The most common indication for infants is CHD and for older pediatric patients, cardiomyopathy.[1]

- **Patient Considerations**

  Selection of Pediatric Heart Transplantation Candidates, AHA Guidelines:[2]

  1. Progressive *deterioration of ventricular function* and functional status despite optimal medical therapy,
  2. *Growth failure* secondary to severe congestive heart failure unresponsive to conventional medical treatment
  3. *Malignant dysrhythmias or survival of cardiac arrest*, unresponsive to conventional medical treatment or implantable cardioverter defibrillator
  4. Need for ongoing intravenous *inotropic* support
  5. Unacceptably *poor quality of life*
  6. Progressive *pulmonary hypertension* that would preclude heart transplantation later

  The use of assist devices like extracorporeal membrane oxygenator (ECMO) and left ventricular assist devices (LVADs) are being utilized with increased frequency as a bridge.[3]

Anesthetic Planning:

Preoperative Assessment and Planning

- Assessment of comorbidities for optimal anesthetic management.
  - Note that some comorbid conditions may improve with heart transplant, e.g. hepatic or renal impairment primarily due to cardiac disease.
- A detailed review of cardiac anatomy with specific attention to stenoses of vascular access sites

- Timing
    - The surgical team is dispatched to harvest the donor heart and OR start time for the recipient is based on the estimated time of arrival (ETA) of the new organ.
    - The goal is to minimize ischemic time of the donor heart.
    - Delays in procurement include travel time, donor patient preparation, and coordination with other surgical services.
    - Direct faculty-to-faculty communication between anesthesia and cardiac surgery helps mitigate timing errors.
    - The recipient may have had prior cardiac operations and the resultant longer surgical entry for cannulation than first-time operation needs to be factored in for OR start time.
- Re-do operations pose a higher risk for inadvertent vascular injury during sternal entry and require emergent transition to bypass.
    - A well-defined plan for emergent cannulation of femoral or neck vessels with the surgeon and perfusionist before starting is prudent.
- Additional Labs and Tests
    - Lab Studies
        - Complete Blood Count including Platelet Count
        - Comprehensive Metabolic Panel
        - Coagulation studies if the patient is taking anticoagulants
    - Chest Radiograph
    - Electrocardiogram
        - If the patient has a pacemaker or automatic implantable cardioverter defibrillator (AICD), contact their electrophysiologist to determine the need for reprogramming.
            - Have a magnet in the OR in case an asynchronous mode is needed.
    - Echocardiogram
    - Cardiac catheterization data
    - CT scan may be obtained to determine the distance of great vessels or conduit to the sternum.
        - If tissue is adherent to the sternum, entry via the chest is high risk, and femoral cannulation for Cardiopulmonary Bypass (CPB) may be done.

Specific Room Set-Up Requirements

- Monitors
    - Standard monitors with 5 lead ECG
    - Temperature monitors
        - Head - nasal or esophageal
        - Body - bladder with older patients, or rectal with neonates and infants
    - Invasive monitors include arterial line and central venous catheter
        - Placed preop or intraop depending on age and cognitive status of the patient
    - Foley placed after induction
    - Transesophageal Echo (TEE)
    - Cerebral near-infrared spectroscopy (NIRS).
    - Somatic NIRS
        - Depending on institutional practice
    - Processed electroencephalogram (EEG)
        - Depending on institutional practice
- Additional Equipment
    - Ultrasound for vascular access

- Cutaneous defibrillator pads if performing a re-do sternotomy or the patient is at high risk for dysrhythmias
- Rapid transfuser if performing a re-do sternotomy

Intraoperative Considerations:

Induction and Maintenance

- Inhalation induction if age appropriate and no venous access
- IV induction
    - Ketamine, etomidate, or propofol.
        - Dose according to cardiac pathophysiology
    - Non-Depolarizing Muscle relaxant
    - Opioid
    - Benzodiazepine
- If the patient is not supported with a VAD or ECMO, decompensation during induction may require emergent bypass.

Airway

- Endotracheal or nasotracheal intubation with preparation for advanced airway management if indicated

Drugs

- **Emergency** medications include
    - Succinylcholine 2 mg/kg
    - Atropine 20 mcg/kg
    - Epinephrine 10 mcg/mL solution, dosed at 10 mcg/kg
- Bolus medications
    - Epinephrine 1 mcg/mL, dosed according to inotropic and chronotropic needs
    - Calcium chloride 10 – 20 mg/kg or calcium gluconate 20-30 mg/kg
        - Used to treat hypocalcemia from dilution or chelation with blood products
    - Heparin, age and weight-based dosing
        - Institution-dependent, example:
            - 0-6 months 600 U/kg
            - > 6 months – 6 years 400 U/kg
            - > 6 years 300 U/kg
        - Note: If the patient has been anticoagulated, therapeutic anticoagulation for CPB may require a higher heparin dose
    - Protamine for heparin reversal at end of bypass run.
        - Dosing is 1 mg – 1.3 mg protamine for every 100 IU of heparin.
    - Antiemetics if extubation is to be attempted
        - Dexamethasone 0.1 mg/kg up to 4 mg
        - Ondansetron 0.1 mg/g up to 4 mg
    - IV acetaminophen
- Continuous infusions
    - Analgesics options:
        - Fentanyl 1-5 mcg/kg/hr
        - Morphine 10-40 mcg/kg/hr
    - Sedatives options:
        - Dexmedetomidine 0.3 – 1 mcg/kg/hr
        - Midazolam 0.5 mcg/kg/min – 2 mcg/kg/min (ask Mo)
    - Vasoactives:

                - Epinephrine 0.02 mcg/kg/min – 0.1 mcg/kg/min
                - Norepinephrine 0.02 mcg/kg/min – 0.1 mcg/kg/min
                - Milrinone loading dose of 50 mcg/kg, infusion of 0.3-0.7 mcg/kg/min
        - Antifibrinolytics:
                - Tranexamic acid or aminocaproic acid are given and are institution, age and weight-based
                - Tranexamic acid dosing (example)
                        - Patients > 12 months to 18 yo and < 70 kg, 8-4 rule
                                - Give 8 mg/kg bolus and infuse at 4 mg/kg/hr with normal renal function
                                        - Maximum 1 gram bolus
                                        - No CPB load
                        - Patients < 12 months 10-10-4-4 rule
                                - Bolus 10 mg/kg and infuse at 10 mg/kg/hr
                                - 4 mg/kg given to perfusionist to bolus CPB circuit
                                - When bypass commences, decrease infusion to 4 mg/kg/hr
                - Aminocaproic Acid (example)
                        - For patients > 18 yo or > 60 kg
                        - Bolus: 75 mg/kg, max 5 gm
                        - Pump load: 75 mg/kg, max 5 gm
                        - Infusion: 1 gram/hour, max 5 gm

Blood product availability

- Packed RBCs, from 1-4 Units.
    - To minimize allo-sensitization, irradiated products may be used.
- Whole blood if available
- Fresh frozen plasma and cryoprecipitate are often indicated for neonates and younger infants
- The overlying principle with the use of blood products is that it is age, size, and institution-dependent.

Positioning

- Supine, head turned toward left to expose the right neck and RIJ anatomy for emergent access for CPB.

Hemodynamic and Physiologic Goals

- Maintain cardiac output and end-organ perfusion
- Specific cardiovascular goals are a function of the pathophysiology
    - Examples:
        - With dilated cardiomyopathy and poor ventricular function, avoid negative inotropes
        - With hypertrophic cardiomyopathy, negative inotropic agents may be needed to maintain cardiac output
        - With diastolic dysfunction, avoid fluid overload and pulmonary edema
        - With failed Fontan, maintain euvolemia to optimize cardiac output

<u>Pre-Cardiopulmonary Bypass</u>

- Immunosuppressive steroids are given intra-operatively and timing should be discussed with the surgeons
- Autologous blood removed from the patient if appropriate (see below)

Cardiopulmonary Bypass

- Communication with the perfusionist with the goal of optimizing organ perfusion by maintaining mean arterial pressure, urine output, and NIRS as indices of organ perfusion during bypass
- Deviations in blood pressure, oliguria, or decreases in cerebral oximetry may require intervention by the anesthesiologist or the perfusionist to maintain optimal organ perfusion and oxygen delivery

Post-Cardiopulmonary Bypass Considerations

- Heparin is reversed with protamine, dosing is 1 – 1.3 mg protamine per 100 Units of heparin.
  - Adequacy confirmed with activated clotting time measurement.
- Optimize blood pressure:
  - Avoid hypertension which puts the patient at risk for surgical bleeding
  - Avoid hypotension and inadequate end-organ perfusion
  - Vasoactive support may be needed to achieve blood pressure goals, either vasopressors or vasodilators
- Inhaled nitric oxide to decrease pulmonary vascular resistance (PVR), RV support and mitigate ischemic reperfusion injury and acute rejection.[4]
- Diastolic dysfunction may occur in the immediate post-CPB period and the patient may be sensitive to minor changes in filling pressures
- Isoproterenol or pacing for bradyarrhythmias.
- Cardiac function may be poor post-CPB and ECMO may be required with the hopeful expectation of graft function recovery.

Management of Hemostasis

- Begins prior to bypass with the administration of antifibrinolytics and removal of autologous blood to preserve the patient’s platelets and clotting factors.
- Either tranexamic acid or aminocaproic acid, as discussed above.
  - Aprotinin is currently not available in the U.S.
- In order to decrease the need for blood products, some institutions phlebotomize autologous blood prior to bypass, store it in CPD anticoagulant, then and return it, filtered, to the patient post-bypass.[5]
- Point-of-care testing with viscoeleastography tests like thromboelastography (TEG) or rotational thromboelastometry (ROTEM) can be utilized to guide blood product usage.[6]
  - Pre-bypass, TEG or ROTEM can help identify patients with a baseline coagulopathy or residual chemical anticoagulation.
  - Post-bypass, TEG or ROTEM aid in assessing the adequacy of clot formation by identifying deficiencies of platelets, fibrinogen, and coagulation factors.
- Blood product administration and pharmacologic interventions may be used to treat coagulopathies.[7]
  - Blood product administration may include:
    1. Fresh frozen plasma
       - Given pre-bypass for reversal of Warfarin or for those with antithrombin III deficiency
       - Can be added to bypass prime for neonates and infants
       - Given post-bypass if factor-deficient, as evidenced by elevated clotting time
    2. Platelets:
       - Infused pre-bypass if the patient is severely thrombocytopenic

    - Administered post-bypass to treat quantitative and qualitative platelet deficiency
  3. Cryoprecipitate can be used to treat fibrinogen deficiency
- Pharmacologic interventions:
  1. Prothrombin complex concentrate (PCC) for post-bypass management of coagulopathy
  2. Fibrinogen concentrate for post-bypass
  3. Factor VIIa – some institutions prefer the use of this agent instead of PCC.

Of note, giving **both** PCC and FVII to the patient may put them at risk for catastrophic thrombosis.

SPECIAL CONSIDERATIONS FOR HEART TRANSPLANT PATIENTS

Timing of induction

- The goal is to minimize donor heart ischemia time
- The heart transplant recipient OR time is based on the ETA of the donor heart by the harvest team
- Delays with harvest or travel can result in multiple revisions of recipient OR start time.
- *Consider direct communication with faculty cardiac surgeon to avoid inaccurate information*.

ABO incompatible (ABOi) transplantation

- Efforts to increase pediatric heart transplants include using blood group antibody incompatibility.[8]
  - Eligibility is institution-dependent, but up to 1 to 2 years of age
  - Perfusionists have detailed protocols regarding pump prime and exchange transfusions for ABOi cases.
  - Anesthesia protocol is typically the same regardless of histocompatibility status but discussion with the perfusion and surgery team is advised to outline potential alteration of standard practice

Ventricular Assist Device Patients

- Patients may have a ventricular assist device (VAD) as a bridge to transplant
- Routine non-invasive blood pressure measurement may not be accurate in these patients. The recommendation is that patients with continuous flow VAD have blood pressure measured with an arterial line or Doppler.
- Anticoagulation with LVADs may be with heparin or bivalirudin, a thrombin inhibitor.
- Discussion about when to stop the anticoagulation is paramount. Bivalirudin has a half-life of 25 minutes and delays in the retrieval of the donor heart may occur.
- Closed-loop communication with surgeons about when to discontinue the bivalirudin anticoagulant is important to avoid thrombosis of the VAD circuit.

Fontan transplantation and vasoplegia

- A failed Fontan patient is at risk for postoperative vasoplegia which is defined as low systemic vascular resistance with normal cardiac output.
  - The etiology is multifactorial and includes previous operations, aspirin, and ACEI use, long bypass times with exposure of blood to foreign surfaces of the CPB circuitry, and altered endothelial glycocalyx.[9]

- High levels of circulating inflammatory mediators including 0_2 free radicals, endothelins, nitric oxide, and cytokines lead to systemic vasodilation and hypotension refractory to catecholamines.
- Treatment options include
    - Vasopressin 0.0003-0.0012 mcg/kg/min
    - Methylene blue 2 mg/kg bolus and 0.1-1 mg/kg/hr if needed
    - Angiotensin II 20 – 80 ng/kg/min

Postoperative Management

- Patients may be extubated at the end of the procedure or remain intubated and sedated
- To avoid right heart failure which may account for half of pediatric OHT deaths, protective strategies include decreasing PVR with iNO, higher Fi02, and afterload reduction with milrinone
- Primary graft dysfunction may occur in the immediate postop period and is defined as significantly depressed left ventricular function (EF <40%), a need for higher inotropic or ECMO support.
    - Etiologies may be:
        - Donor - age, size, and cause of death
        - Recipient – PVR, comorbidities/organ dysfunction
        - Procedural variables – long ischemic time, small volume centers
        - Lack of parasympathetic innervation and no baroreceptor reflex leaves the recipient without a compensatory response to hypotension and/or hypovolemia.
            - Patients may need exogenous chronotropic support with isoproterenol or epicardial pacing to maintain heart rate and cardiac output

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Reviewed by:

Reviewer #1: Chinedu Otu, M.D., Texas Children's Hospital

Reviewer #2: Destiny Chau, M.D., Arkansas Children's Hospital

Reviewer #3: Amanda Redding, MD, Medical University of South Carolina

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