Cardiac Transplant

Patients who have undergone cardiac transplantation have a denervated heart, and are at risk for dysrhythmias, rejection & transplant coronary arteriopathy, renal dysfunction, hypertension & malignancy.

ANESTHETIC CONSIDERATIONS:

- Physiology of the transplanted heart
  - Denervated heart
    - Preload dependent
    - Decreased response to indirect sympathomimetics
    - No vagal influence
  - Prone to dysrhythmias (pacemaker in 20%)
- Allograft function
  - Rejection
  - Cardiac transplant coronary arteriopathy (CAD common within 1 year)
  - Immunosuppressive therapy (strict aseptic tech.; increased risk of infection, stress dose of steroids)
  - IE prophylaxis only if valvulopathy
- Side Effects of Immunosuppressive Medications
  - Renal dysfunction
  - HTN in 90%
  - Malignancy
  - Hepatobiliary and pancreatic dysfunction
  - Coagulopathy
  - Bone marrow suppression

ANESTHETIC GOALS:

- Hemodynamic Goals
  - Preload: **maintain**, as transplanted heart increases CO by increasing SV (Frank-Starling mech)
  - Afterload: maintain
  - Rate: maintain
  - Rhythm: maintain NSR
  - Contractility: maintain

HISTORY & PHYSICAL

- Functional status, can still ask about angina (absence has no clinical significance)
- Any evidence of rejection? (CHF & dysrhythmias are late signs, most recent biopsy results for early)
- Heart transplant history (meds, pacemaker, related complications—end organ disease)
- Any evidence of infection?
- Focused exam: airway, cardiopulmonary with special attention to rule out CHF, infections, PPM/ICD function

INVESTIGATIONS

- **Labs** (as indicated by history, might include the following)
  - ↓ K, Mg (diuretics and risk of dysrhythmias)
  - ↑ Cr (anti-rejection drugs and CHF)
  - ↑ LFTs (anti-rejection drugs) ↑ coagulation studies (liver dysfunction from drugs)
  - ↓ platelets, WBC, Hb (anti-rejection drugs or sepsis)
  - ↑ glucose (steroids, DM)
- **Imaging**
  - EKG (RAD, incomplete RBBB, two P waves (native P unrelated to QRS), Q waves / other signs of ischemia)
  - CXR : failure?
  - Echo to assess LV function; Dobutamine Stress Echo for CAD as EST limited by HR response
  - Cardiac cath with biopsy results to R/O early rejection
    - MIBI not useful d/t diffuseness of disease
  - Consider U/S neck veins prior to cannulation to ensure patency

OPTIMIZATION

- Optimize LV function - ensure adequate preload, no rejection
- Optimize end-organ dysfunction: HTN, DM, Renal dysfunction
- Transplant physician to guide peri-operative transplant medications; stress dose steroids?
- Preoperative antibiotics for prophylaxis against local / systemic infection (patient specific)

ANESTHETIC OPTIONS

- General Anesthesia
  - Frequently preferred as changes in preload and afterload may be more predictable
  - Caution with renally excreted medication and avoid nephrotoxins
  - Assess anesthetic depth with BP not HR
  - Cyclosporine and tacrolimus lower seizure threshold (avoid hyperventilation)
- Regional Anesthesia
  - Ensure coagulation studies okay (many immunosuppressants cause thrombocytopenia)

- Maintain ventricular filling pressures and maintain pressure with direct acting agents
  - May have impaired response to hypotension with neuraxial tech

ANESTHETIC SETUP

- **Drugs**
  - When hepatic and renal function are normal, there is no contraindication to any anesthetic drug
  - Despite reports of cyclosporine-induced enhanced neuromuscular blockade, doses remain same
  - Vasoactive drugs: recall that direct acting agents are most useful
    - Also, **glucagon** may be useful for it's inotropic +/- chronotropic effects (increases cAMP in heart resulting in increased Ca available for depolarization)

Drug	Actions	HR	BP
Atropine	Indirect	-	-
Digoxin	Direct	↓	-
Dopamine	Both	↑	↑
Epinephrine	Direct	↑	↑
Edrophonium	Indirect	-	-
Ephedrine	Both	-/↑	-/↑
Fentanyl	Indirect	-	-
Isoproterenol	Direct	↑	-/↑
Neostigmine	Both	-/↓	-
Norepinephrine	Direct	↑	↑
Pancuronium	Indirect	-	-
Phenylephrine	Direct	-	↑
Verapamil	Direct	↓	↓

- **Equipment**
  - Standard CAS monitors + 5 lead EKG, crash cart
  - Consider art line, CVP based on surgery (realizing potential risk of infection), TEE
  - PNS, glucometer

MANAGEMENT OF ANESTHESIA

- **Induction:** aseptic technique (EtOH swabs to injection ports), hemodynamically neutral induction (especially etomidate)
- **Maintenance:** minimize cardiac depression
- **Emergence:** note that neostigmine will usually not decrease HR and glycopyrrolate / atropine will not increase HR but still required for peripheral anti-muscarinic effects

CARDIAC TRANSPLANT

- Strict aseptic technique placing lines: art line, large bore IV, ± PAC (with ability to read Svo2)
- Inotropes readily available prior to induction (Dobutamine, dopamine, epinephrine, norepinephrine, isoproterenol, milrinone, vasopressin, phenylephrine are all options)
  - Consider instituting or increasing dose before induction
- Have surgeons, perfusionists, and 4 units PRBC immediately available with FFP, PLT and cryo
- Presence of an LVAD or prior sternotomy increases the length and the risks associated with the procedure
- TEE if no contraindications

DISPOSITION & MONITORING

- Ensure patient continues on regular schedule of anti-rejection medications
- Consider consultation w/ transplantation team to ensure optimal drug levels

PREGNANCY IN PATIENTS WITH CARDIAC TRANSPLANT

- Women post-transplant without complications can undergo a relatively normal pregnancy and delivery
- Anti-rejection drugs have no adverse effects on fetal and neonatal outcome
- Since preload dependent, slow titration of epidural helps to prevent hypotension
- If hypotension occurs, treat with small doses of phenylephrine

PATHOPHYSIOLOGY

- Cardiac transplantation is indicated for viral or ischemic cardiomyopathy; 6000 listed/year
  - LVADs can support patients to bridge to transplant
  - In patients with CHF, VO2 >10mL/kg/min have better 1 yr survival with medical therapy than with transplantation
  - Patients listed should have NYHA Class III or IV failure despite optimal therapy, and without surgical options (revascularization and/or valve repair)
    - Contraindications:
      - Pulmonary HTN [severe and irreversible; transpulmonary gradient >12 mmHg (mean PA pressure - PCWP); pulmonary arteriolar resistance >2.5 Wood units high risk RV failure]
      - Significant atherosclerosis—high periop risk of atheroembolic phenomenon
      - Significant non-cardiac disease, ie. FEV1 <50% predicted despite optimal management for CHF are at increased risk for ventilatory failure and infections
  - Current survival rates 90% at 1 yr, 80% at 5yrs
- 20-25% of cardiac tx recipients will require general surgery in the two years following transplant
- Normal heart:
  - Autonomic innervation:
    - PNS → vagus (decreased HR)—heart normally has chronic vagal tone
    - SNS → C5-T6, via stellate (R side chronotropy, L side inotropy)

        - $beta_1$ receptors (increased inotropy, dromotropy, chronotropy, lusitropy)
        - $alpha_1$ receptors (increased inotropy, minor)
    - Response to exercise: ↑ CO initially by ↑ HR
- Denervated heart:
    - Ventricular function slightly reduced but contractile reserve normal, Frank-Starling mechanism intact, LV wall thickness normal, but diastolic relaxation abnormal; preload dependence for increased SV
    - Altered pharmacokinetics—
        - direct acting agents will have most effect (though ephedrine may have a blunted effect)
        - vagally mediated responses will not be present
        - upregulation of receptors on heart will result in increased responses to β effects of epinephrine/norepinephrine
        - **isoproterenol** is the primary chronotropic agent
    - Lacks sympathetic, parasympathetic, or sensory innervation
        - Loss of vagal tone results in higher than normal resting heart rate (vagolytics ineffective)
        - Blunted and delayed HR responses to laryngoscopy, surgical stimuli
        - HR responses dependent on circulating catecholamines
    - Unable to respond to acute hypovolemia or hypotension b/c no immediate ↑HR; **preload dependent** to ↑CO
    - Initially no afferent pain pathway for ischemia (no angina) – unpredictable efferent sympathetic reinervation may develop within 12 months, anginal symptoms not consistent
    - Response to exercise: ↑ CO initially due to ↑ SV with ↑ venous return; catecholamine release will cause a delayed ↑HR and contractility
- Dysrhythmias
    - Bradyarrhythmia (1st degree AV block) occur in 20%—prolonged donor ischemia
        - Pacemaker
        - Isoproterenol effective to increase HR
    - Late onset of atrial dysrhythmias are indicative of allograft CAD or acute rejection
    - RBBB and 1° heart block is common in transplanted hearts
    - Ventricular arrhythmias uncommon unless advanced allograft CAD present
- Rejection and Anti-rejection medications (see table)
    - Causes progressive deterioration of cardiac function and is the main cause of late mortality in heart transplant patients
        - Most rejections occur within the first 3 months of transplant w/ peak at 4 to 6 weeks

STEROIDS	• Stress dosing may be required • Glucose intolerance • Cushingoid habitus may make intubation difficult • Skeletal demineralization, aseptic necrosis of the hip
AZATHIOPRINE	• ↓ NDMR doses • Anemia, thrombocytopenia and marrow aplasia
CYCLOSPORINE, TACROLIMUS	• Cyclosporine induced systemic HTN (resistant to medical tx) • Cyclosporine induced nephrotoxicity • Hepatotoxicity • Neurotoxicity • Diabetes
MYCOPHENOLATE MOFETIL	• Bone marrow supp. (anemia, thrombocytopenia, leukopenia) • CMV, sepsis • N & V, diarrhea • Dizziness, headache
ANTILYMPHOCYTE GLOBULIN AND OKT3	• Leucopenia, thrombocytopenia
RAPAMYCINS (SIROLIMUS, EVEROLIMUS)	• Wound dehiscence • Thrombocytopenia, leucopenia • Acne, skin rash • GI tract ulcers (esp with PO formulations)

- Infection: should be ruled out pre-op as can be a significant cause of morbidity and mortality
    - Strict aseptic technique should be followed and minimize invasive procedures
- Coronary artery disease
    - At 3 yrs, 30% of pts have multivessel coronary stenoses, 50% at 5 yrs
- Cancer: long term immunosuppression ↑ risk, especially of lymphoproliferative (EBV) & cutaneous

REFERENCES

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