Banner University Medicine

Growing Challenges in Heart Transplantation

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Growing Challenges in Heart Transplantation

General Challenges

- Number of transplants performed
- Eligibility criteria
- UNOS waitlisting criteria

Patient Related Challenges

- Surgical techniques
  - Orthotopic vs Heterotopic transplantation
  - Biatrial vs Bicaval anastomosis
- Chronic immunosuppression
- Early complications
  - Primary graft dysfunction
  - Acute right ventricular failure
  - Conduction abnormalities
  - Other common post-operative complications
- Late complications
  - Chronic allograft vasculopathy
  - Infection
  - Malignancy
  - Chronic kidney disease
  - Other steroid related complications

COVID-19 Related Challenges

- The influence of COVID-19
  - Donor offers
  - Donor testing
  - Actively listed patients
  - Immediate posttransplant management
  - Ambulatory posttransplant management
  - Transplant patients with COVID-19 patients

Growing Challenges in Heart Transplantation
Number of transplants performed

- Total transplants performed: 3,209 – Adult 2,764 (2016)
- Increase in number of waitlisted patients
  - 57% increase between 2005 - 2016
- Waitlist mortality decreasing
  - 14.6 deaths/100 waitlist years (2015) ➢ 9.7 deaths/100 waitlist years (2016)
- Reduction in number of transplant
  - 27.8% reduction between 2005 - 2016
- Growth in high-risk transplant
  - >65-year-old recipients
  - Highest UNOS status
- Posttransplant survival remains the same at approximately 10.7 years
  - 84.5% 1-year
  - 72.5% 5-year

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Eligibility Criteria

Indications

- Cardiogenic shock requiring intravenous inotropes (dobutamine, milrinone, etc.)
- Refractory cardiogenic shock requiring IABP or LVAD
- Peak VO2 <10 mL/kg/min
- NYHA III or IV despite maximal medical or resynchronization therapy
- Recurrent life-threatening left ventricular arrhythmias despite use of ICD, antiarrhythmic therapy, or catheter-based ablation
- End-stage congenital heart failure without evidence of pulmonary hypertension
- Refractory angina without potential medical or surgical therapeutic options

Absolute Contraindications

- Irreversible liver disease
- Irreversible pulmonary parenchymal disease (or FEV1 <1 L/min)
- Irreversible pulmonary artery hypertension (PASP >60 mmHg, PVR >5 Wood units despite use of vasodilators)
- Clinically severe symptomatic cerebrovascular disease
- History of solid organ or hematologic malignancy
- Severe irreversible multisystem disease process

Relative Contraindications

- Age >70 years
- Severe obesity (BMI >35 kg/m2) or cachexia
- Diabetes with end organ damage other than non-proliferative retinopathy or persistent poor glycemic control (HbA1c >7.5% or 58 mmol/mol) despite best effort
- Irreversible renal dysfunction (GFR <30 mL/min/1.73 m2)
- Severe peripheral vascular disease
- Severe cerebrovascular disease
- Severe osteoporosis

Relative Contraindications

- Acute pulmonary embolism (within 6 to 8 weeks)
- Active infection (excluding LVAD-related infections)
- Psychological instability
- Substance abuse within 6 months (alcohol, cocaine, opioids, tobacco products)
- Lack of social support or sufficient resources to permit ongoing access to immunosuppressive medication and frequent medical follow-up
- Inability to comply with drug therapy on multiple occasions

Circulation. 2009 Apr 14;119(14):1977-2016.

Circulation. 2010 Jul 13;122(2):173-183.

Growing Challenges in Heart Transplantation
Panel Reactive Antibodies (PRA)

- <10% vs >10%
- High risk population
- Non-HLA antibodies

Growing Challenges in Heart Transplantation
Non-HLA Antibodies

Non-HLA Antibody	Class	Clinical Outcome
Major histocompatibility Class I chain A (MICA)	MHC class-1 related chain A genes	↑AMR
Angiotensin II type 1 receptor antibody (AT_1R)	G-protein coupled receptor	↑CAV ↑AMR ↑ACR
Endothelin-1 type A receptor antibody (ETAR)	G-protein coupled receptor	↑CAV
Vimentin	Cytoskeletal protein	↑CAV
Cardiac myosin	Cytoskeletal protein	↑CAV ↑AMR
Polyreactive antibodies	Natural occurring antibodies	↑AMR

ACR=acute cellular rejection; AMR=antibody mediated rejection; CAV=cardiac allograft vasculopathy; MHC=major histocompatibility complex

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UNOS waiting list criteria

Status 1 & 2

Status 1

- Venoarterial extracorporeal membrane oxygenation
- Nondischargeable, surgically implanted, nonendovascular biventricular support device
- Mechanical circulatory support with life-threatening ventricular arrhythmias

Status 2

- Nondischargeable, surgically implanted, nonendovascular left ventricular assist device
- Intraaortic balloon pump
- Ventricular tachycardia or ventricular fibrillation
- Mechanical circulatory support with device malfunction/mechanical failure
- Total artificial heart, biventricular assist device, right ventricular assist device, or
- ventricular assist device for single ventricular patients
- Percutaneous endovascular mechanical circulatory support device

Status 3

Status 3

- Dischargeable left ventricular assist device for up to 30 days
- Multiple inotropes or single high-dose inotropes with continuous hemodynamic monitoring
- Venoarterial extracorporeal membrane oxygenation after 7 days; percutaneous endovascular circulatory device or intraaortic balloon pump after 14 days
- Nondischargeable, surgically implanted, nonendovascular left ventricular assist device after 14 days
- Mechanical circulatory support with device infection
- Mechanical circulatory support with hemolysis
- Mechanical circulatory support with pump thrombosis
- Mechanical circulatory support with right heart failure
- Mechanical circulatory support with mucosal bleeding
- Mechanical circulatory support with aortic insufficiency

Status 4

Status 4

- Stable left ventricular assist device candidates not using 30-day discretionary period
- Inotropes with hemodynamic monitoring
- Retransplant
- Diagnosis of congenital heart disease
- Diagnosis of ischemic heart disease with intractable angina
- Diagnosis of hypertrophic cardiomyopathy
- Diagnosis of restrictive cardiomyopathy
- Diagnosis of amyloidosis
- Status

Status 5, 6 & 7

Status 5a

- Combined organ transplants

Status 6

- All remaining active candidates

Status 7

- Inactive/not transplantable

[a]Status 5 candidates may ascend to higher acuity status if indicated based on cardiac status

United Network of Organ Sharing

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Donor Offer

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Donor Offers	Obtain COVID-19-Focused travel and social history	Risk for infection
	Exclude donors at increased risk of other disease transmission (e.g., HIV, HBV, HCV)	Role of donor contact tracing
	Exclude marginal donors (e.g., LVH, mild LV dysfunction)	

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Donor Testing

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Donor testing	Confirm availability and rapid turnaround of PCR assay	Universal vs. targeted testing
	Obtain at least 2 sets to increase sensitivity and specificity	Need for chest CT to exclude viral pneumonia
		Window period of infection

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Actively Listed Patients

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Actively listed patients	Ensure COVID-19–free hospital location	Separate consent for potential COVID-19–positive donors
	Nurses who treat patients with COVID-19 should not be assigned to patients awaiting transplant	Temporary inactivation of stable outpatients (UNOS status 4–6)
	PCR assay to exclude hospital-acquired infection	Lower threshold for implantation of LVAD as BTT
	Telephone or mail communication regarding expected delays and changes in institutional Policies	Need to reduce overall program transplant activity

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Immediate Posttransplant Management

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Immediate posttransplant	Assign to negative pressure ventilation room with airborne isolation	Need to alter threshold for induction therapy
	Nurses who treat patients with COVID-19 should not be assigned to posttransplant patients	
	Limit staff contact and outside visitors	

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Ambulatory Posttransplant Management

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Ambulatory posttransplant management	Patient/family hygiene including frequent handwashing and social distancing	Threshold for urgent, in-person visit vs. routine telemedicine
	Ensure that patients with symptoms concerning for rejection receive prompt testing and diagnosis	Need for self-quarantine
	Delay elective testing, including echocardiography, RHC, and endomyocardial biopsy	Implications of delaying endomyocardial biopsies and noninvasive elective testing
	Laboratory work at a local laboratory or using home services rather than at the hospital to minimize exposure	Novel methods for rejection surveillance
		Vaccine development

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Transplant Patients with COVID-19

Area of interest	Recommendations/Considerations	Gaps in Knowledge
Transplant patients with COVID-19 infection	Consider reduced-dose CNI and holding MMF/ azathioprine	Role of IL-6 depletion (e.g., tocilizumab) for cytokine-release syndrome
	Rule out coinfection (bacterial, fungal)	
	Monitor time course of viremia	Effectiveness of remdesivir in shortening time to recovery
	Monitor for drug-drug interactions	
	Continue statins (unless elevated LFTs, CK) and ACE inhibitors/ARBs (unless acute kidney injury or hypotension)	Monitoring for allograft dysfunction (cardiac biomarkers, point-of-care ultrasound)

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