

**HEART FAILURE AND TRANSPLANT MEDICINE
CORE COMPETENCY CURRICULUM
(ISHLT HFTX CCC)**

Heart Failure and Transplantation Council of ISHLT

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CONTENTS

1) INTRODUCTION AND OVERVIEW	3
2) HEART FAILURE	4
I. GENERAL CONCEPTS	4
II. EVALUATION OF THE PATIENT WITH HEART FAILURE	6
III. MANAGEMENT OF THE PATIENT WITH HEART FAILURE	6
IV. ACUTE HEART FAILURE EVALUATION AND MANAGEMENT	7
V. HEART FAILURE WITH PRESERVED EJECTION FRACTION	10
Selected references for Heart Failure	11
3) PULMONARY HYPERTENSION IN THE CONTEXT OF LEFT HEART FAILURE	14
Selected references for Pulmonary Hypertension	15
4) HEART TRANSPLANTATION	16
I. EVALUATION OF THE HEART TRANSPLANT CANDIDATE	16
II. EVALUATION AND MANAGEMENT OF THE POTENTIAL HEART DONOR	18
III. PERI-OPERATIVE MANAGEMENT OF THE TRANSPLANT RECIPIENT	19
IV. IMMUNOLOGIC CONCEPTS IN HEART TRANSPLANTATION	20
V. IMMUNOSUPPRESSION AND REJECTION	21
VI. LONG-TERM CARE OF HEART TRANSPLANT RECIPIENTS	23
Selected References for Heart Transplantation	24
5) MECHANICAL CIRCULATORY SUPPORT OVERVIEW	26
I. GENERAL CONCEPTS	26
II. COMPLICATIONS	27
Selected references for Mechanical Circulatory Support	29
6) HYPERLINKS AT A GLANCE	31

INTRODUCTION AND OVERVIEW

The International Society for Heart and Lung Transplantation recognizes the need for expert development and provides an integrated educational curriculum. The ISHLT Academy consists of multiple Core Competency Courses (CCC) and Master Class (MC) level postgraduate training opportunities.

The purpose of this Core Competency Document (CCD) is to provide a compendium of core competencies in the field of heart failure and heart transplant medicine (HF/TM). It serves as an outline with defined learning objectives and detailed contents listed for the subspecialty. It does not replace the didactic dimensions of textbooks, other specific educational materials. It represents the basis for actual learning activities. A variety of formats are offered at the ISHLT Academy days and the ISHLT Annual Meetings. In addition, individual professional study may be directed and facilitated with this ISHLT curriculum provided for HF/TM and the references and hyperlinks allow for further self-directed in depth study of specific topics.

The complexity of the subject implies an *evolving* document. We have limited the scope of this text to the specific area of interest for the ISHLT Heart Failure and Transplantation Council. We refer to other related subspecialties' separate CCD and courses. Feedback to the authors via ISHLT is much appreciated. We integrate and represent the educational interests of those who seek to develop and apply their professional expertise.

HEART FAILURE

I. GENERAL CONCEPTS

Learning Objectives

- Review the general concepts and definitions of heart failure
 - Understand the definition of the different types of heart failure
 - Discuss the major epidemiological problem of heart failure
 - Understand the stages of heart failure
 - Understand the economic impact of heart failure
 - Understand the pathophysiological mechanisms leading to LV dysfunction and heart failure
 - Review the potential etiologies of heart failure
 - Recognize important specific causes of heart failure
1. Definition of heart failure
 - a. Heart failure with reduced ejection fraction
 - b. Heart failure with preserved ejection fraction
 2. Epidemiology of heart failure
 - a. Incidence
 - b. Prevalence
 - c. Economic burden of heart failure
 - d. Hospitalizations
 - e. Mortality
 - f. Asymptomatic LV dysfunction
 - g. Risk factors for heart failure
 3. Classification
 - a. NYHA classification
 - b. AHA/ACC Staging of heart failure
 4. Pathophysiology
 - a. Cellular changes
 - b. Extracellular matrix and metalloproteinases
 - c. Hemodynamic alterations
 - i. Frank-Starling mechanism
 - ii. Pressure-volume loops
 - d. Neurohormal activation
 - i. RAAS system
 - ii. Adrenergic system
 - iii. Natriuretic peptides
 - iv. Other neurohormones
 5. Causes of heart failure
 - a. Ischemic cardiomyopathy
 - b. Dilated cardiomyopathies

- i. Idiopathic dilated cardiomyopathy
 - ii. Familial cardiomyopathies
 - iii. Special causes
 - 1. Wilson's disease
 - 2. Hemochromatosis / iron overload
 - 3. Sequela of viral myocarditis
 - 4. Sarcoidosis
- c. Restrictive cardiomyopathy
 - i. Amyloidosis
 - 1. TTR-related
 - a. Wild type (senile)
 - b. Familial forms (mutant transthyretin)
 - 2. AL amyloid
 - a. Light chain cardiomyopathy
 - ii. LSD cardiomyopathies
 - iii. Other causes of restrictive cardiomyopathy
 - iv. Non-specific or idiopathic restrictive cardiomyopathy
- d. Inflammation-induced cardiomyopathies
 - i. Myocarditis
 - ii. Acquired immunodeficiency syndrome
 - iii. Chagas' disease
 - iv. Hypersensitivity myocarditis
 - v. Other
- e. Toxic cardiomyopathies
 - i. Alcoholic cardiomyopathy
 - ii. Cocaine cardiomyopathy
 - iii. Chemotherapy-related
 - 1. Anthracycline-related
 - 2. Other agents
 - iv. Other
- f. Endocrine and metabolic
 - i. Diabetic cardiomyopathy
 - ii. Thyroid disease
 - iii. Acromegaly
 - iv. Obesity
 - v. Other
- g. Peripartum cardiomyopathy
- h. Valvular cardiomyopathy
- i. Sequelae of congenital heart disease with or without palliative procedures
 - j. Stress-induced (Takosubo) cardiomyopathy
- k. Other

II. EVALUATION OF THE PATIENT WITH HEART FAILURE

Learning Objectives

- Understand the general principles of evaluation of patients with heart failure
 - Recognize signs and symptoms of heart failure
 - Understand the importance of serial evaluation and risk stratification of the patient heart failure
 - Understand the indications for invasive evaluation in heart failure
1. Signs and symptoms
 - a. Low output
 - b. Congestion
 2. Evaluation techniques
 - a. Chest x-ray
 - b. Physical examination
 - c. EKG
 - d. Echocardiography
 - e. Ischemia evaluation
 - i. Coronary angiogram
 - ii. Myocardial perfusion imaging
 1. Ischemia evaluation
 2. Viability
 - f. Labs
 - i. Chemistry panel (Na, Cr, BUN, uric acid)BNP or Nt-Pro-BNP
 - ii. Other biomarkers
 - g. Device-based fluid monitoring via thoracic impedance
 - h. Direct hemodynamic measurement
 - i. Swan-Ganz catheter and right heart catheterization
 - i. Implantable hemodynamic monitors
 - j. Exercise testing
 - i. VO₂ max
 - ii. Six-minute walk test
 - k. Cardiac MRI
 - l. Cardiac endomyocardial biopsy

III. MANAGEMENT OF THE PATIENT WITH HEART FAILURE

Learning Objectives

- Understand the general principles of the management of patients with heart failure
 - Understand the indications for treatment with the various therapeutic modalities
 - Understand the mechanism of action of major therapeutic targets
 - Recognize failing therapy and need for advanced therapies
 - Understand the importance of minimizing renal dysfunction
 - Understand the importance of revascularization
 - Discuss future potential targets for management of patients with heart failure
1. General principles of treatment
 - a. Stage A to D
 2. Non-pharmacologic management
 - a. Sodium restriction
 - b. Fluid restriction

- c. Weight loss
- d. Activity and exercise
- e. Treatment of sleep disordered breathing
- 3. Pharmacological Treatment
 - a. Volume management
 - i. Diuretics
 - b. Digoxin
 - c. Neurohormonal blockers
 - i. RAAS blockers
 - 1. Angiotensin converting enzyme (ACE) inhibitors
 - 2. Angiotensin II-receptor blockers (ARB)
 - 3. Aldosterone receptor antagonists
 - ii. Beta-blockers
 - 1. Carvedilol
 - 2. Metoprolol Succinate
 - 3. Bisoprolol
 - 4. Nebivolol
 - iii. ARNI (Angiotensin Receptor/Nepriylsin Inhibitors)
 - 1. Entresto (Sacubritil/Valsartan)
 - iv. Vasodilators
 - 1. ISDN / Hydralazine fixed dose combination
 - 2. Nitrates
 - d. Ivabradine
 - e. Anticoagulation
 - f. Statins
 - g. Drugs under development
 - h. Inotropic agents
 - i. Bridge to advanced therapies
 - i. Palliative care
- 4. Device-based therapy
 - a. Implantable cardioverter defibrillator
 - b. Cardiac resynchronization therapy
- 5. Revascularization
 - a. High-risk percutaneous intervention
 - b. High-risk surgical intervention
- 6. Chronic Mechanical Circulatory Assist Devices (see MCS section)

IV. ACUTE HEART FAILURE EVALUATION AND MANAGEMENT

Learning Objectives

- Understand the definition of acute decompensated heart failure
- Understand the epidemiology of the syndrome
- Identify the etiologies and triggers of acute heart failure
- Understand the different targets of treatment of acute decompensated heart failure
- Understand the management options for acute heart failure
- Understand the indications for inotropic use or mechanical support

1. Definition
2. Epidemiology
3. Pathophysiology
 - a. Low output
 - b. Congestion and volume overload
 - c. Cardiorenal syndrome
 - i. Etiology
 - ii. Prognosis
4. Etiologies of acute heart failure syndromes
 - a. Acute coronary syndromes
 - b. Acute decompensated heart failure (not associated with ACS)
 - i. Dietary sodium load
 - ii. Associated infections / sepsis
 - iii. Progressive heart failure
 - iv. Arrhythmias
5. Evaluation techniques
 - a. Chest x-ray
 - b. Physical examination
 - c. EKG
 - d. Echocardiography
 - e. Labs
 - i. BNP or NT-Pro-BNP
 - ii. Chemistry panel (Na, Cr, BUN, uric acid)
 - f. Device-based fluid monitoring via thoracic impedance
6. Direct hemodynamic measurement
 - a. Right heart catheterization to guide therapy
 - b. Swan-Ganz catheter based monitoring /management
7. Management
 - a. Diuretics
 - i. Intermittent bolus
 - ii. Continuous infusion
 - b. Arginine vasopressin receptor antagonists
 - i. Tolvaptan
 - ii. Conivaptan
 - c. Vasodilator therapy
 - i. Nitrates
 - ii. Sodium nitroprusside
 - iii. Nesiritide
 - d. Inotropic agents
 - i. Dobutamine and dopamine
 - ii. Epinephrine and other adrenergic agents
 - iii. PDE-3 inhibitors (milrinone)
 - iv. Levosimendan
 - v. Other
 - e. Renal replacement therapies
 - i. Ultrafiltration
 - ii. Hemodialysis
 - f. Mechanical temporary support

- i. Intra-aortic balloon pump (IABP)
- ii. Percutaneous LVAD
 - 1. Tandem Heart
 - 2. Impella 2.5, CP and 5.0
 - 3. Other
- iii. Extra-corporeal membrane oxygenation (ECMO)

V. HEART FAILURE WITH PRESERVED EJECTION FRACTION

Learning Objectives

- Understand the definition of heart failure with preserved ejection fraction
- Understand the epidemiology of the syndrome
- Understand the different etiologies of heart failure with preserved ejection fraction
- Recognize signs and symptoms of heart failure with preserved ejection fraction
- Identify the etiologies and triggers of acute decompensation in heart failure with preserved ejection fraction
- Review the difference in management with heart failure with depressed ejection fraction
- Understand the different targets of treatment of heart failure with depressed ejection fraction
- Understand the management options for acute heart failure

1. Definition
2. Epidemiology
3. Incidence and prevalence
4. Pathophysiology
5. Morbidity and mortality
6. Etiologies of heart failure with preserved ejection fraction
 - a. Ischemia
 - b. Diabetes
 - c. Radiation
 - d. Infiltrative cardiomyopathies
 - e. Other
7. Diagnosis
 - a. EKG
 - b. Echocardiography
 - i. Diastolic function
 - ii. Ejection fraction
 - iii. Valvular function
 - c. Labs
 - i. BNP or NT-Pro-BNP
 - ii. Chemistry panel (Na, Cr, BUN, uric acid)
 - d. Direct hemodynamic measurement
 - i. Tau measurement
 - e. Right heart catheterization
 - f. Newer modalities to evaluate diastolic function
 - i. Cardiac MRI

- ii. Myocardial tissue Doppler
- iii. Other

8. Management

- a. Optimization of primary etiologic condition
- b. Management of ischemia
- c. Management of blood pressure
- d. Rate control if atrial fibrillation
- e. Diuretics
- f. ACE-inhibitors and angiotensin II receptor blockers
- g. Beta-blockers
- h. Aldosterone inhibitors
- i. Cardiomechs
- j. Other

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VI. PULMONARY HYPERTENSION IN THE CONTEXT OF LEFT HEART FAILURE

Note: The ISHLT Pulmonary Hypertension and Pulmonary Transplant Councils each have complete Core Competency Curriculum Documents which are more comprehensive than this subset.

Learning Objectives

- Understand the definition of pulmonary arterial hypertension
 - Understand the WHO classification of pulmonary hypertension
 - Understand the different etiologies of pulmonary hypertension in heart failure
 - Understand the prognosis and outcomes associated with pulmonary hypertension
 - Review the available management of pulmonary venous hypertension
 - Understand the mechanism of action of pulmonary vasodilators
 - Review the difference in management between pulmonary arterial hypertension and pulmonary hypertension associated with heart failure
 - Discuss the potential targets for management of pulmonary hypertension associated with heart failure
1. Definition
 2. Pathophysiology
 3. WHO classification
 - a. WHO class I (PAH)
 - i. Incidence and prevalence
 - ii. Associated conditions
 - iii. Prognosis
 - b. WHO class II (PVH) – (see 7 below)
 - c. WHO class III
 - i. Pulmonary hypertension out of proportion to lung disease
 - ii. When to manage
 - d. WHO class IV
 - i. Pulmonary thromboendarctectomy
 - e. WHO class V
 4. Pulmonary vasodilators
 - a. PDE-5 inhibitors
 - b. Endothelin receptor antagonists
 - c. Prostacyclin therapies
 - d. Tyrosine-kinase inhibitors
 - e. Soluble guanylate cyclase (sGC) stimulators
 - f. Other
 5. Principles of therapy
 - a. Single drug
 - b. Combination therapy
 - c. Parenteral therapy
 6. Invasive management
 - a. Atrial septostomy
 - b. Transplantation
 - i. Heart-lung transplantation
 - ii. Lung transplantation

7. Special considerations: pulmonary hypertension in heart failure
 - a. Incidence
 - b. Clinical implications
 - c. Diagnosis
 - d. Reactivity testing
 - e. Implications for transplantation
 - f. Management
 - i. Vasodilators
 - ii. Inotropes
 - iii. Mechanical circulatory support
 - iv. Heart-lung transplantation

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VII. HEART TRANSPLANTATION

I. EVALUATION OF THE HEART TRANSPLANT CANDIDATE

Learning Objectives

- Understand general and disease specific consideration for heart transplant
- Identify patients with advanced heart disease who might benefit from transplantation
- Understand the multi-disciplinary approach to the evaluation process and ongoing management
- Understand indications and contraindications for transplantation
- Understand the allocation system and waitlist management
- Understand the general immunological basis for transplantation, and risks associated with anti-HLA antibodies, elevated PRA and desensitization therapies

1) History of heart transplantation

2) Indications for Heart Transplantation

a) General Considerations

- i) End-Stage Heart Disease
- ii) Patients with ventricular assist devices
- iii) Hospitalized patients
- iv) Ambulatory patients
- v) Cardiopulmonary exercise testing
- vi) Right heart catheterization and hemodynamics
- vii) Heart Failure prognosis scores
- viii) Definition of Optimal Medical Management
- ix) Minimal or no co-morbid illness
- x) Substance abuse, including tobacco
- xi) Strong psychosocial support
- xii) Physiologic age considerations
- xiii) Previous or current malignancy
- xiv) Systemic disease
- xv) Body Mass Index (BMI) considerations
- xvi) Frailty

b) Special Populations

- i) Severe coronary disease with preserved ejection fraction
- ii) RV dysplasia
- iii) End-stage allograft vasculopathy
- iv) Recalcitrant ventricular arrhythmias
- v) Other

3) Evaluation of Transplant Candidate

- a) Transplant Cardiologist
- b) Cardiothoracic Surgeon
- c) Social Worker

- d) Psychiatrist/Psychologist
- e) Pre Transplant coordinator
- f) Financial coordinator
- g) Pharmacist
- h) Nutritionist
- i) Pre transplant education / Patient Support groups
- j) Testing
 - i) Echocardiography
 - ii) MUGA scan
 - iii) Cardiopulmonary exercise test (CPET)
 - iv) Right Heart Catheterization
 - v) Left heart catheterization or myocardial perfusion imaging
 - vi) Pulmonary function tests including ABG
 - vii) Renal function
 - viii) Malignancy screening
 - ix) Bone densitometry
 - x) Infectious serologies
 - xi) Toxicology screen including nicotine
 - xii) Blood typing and HLA
 - xiii) Plasma reactive antibodies (PRA) and single bead analysis
 - xiv) Other
- 4) Special Considerations: High Panel Reactive Antibody Screen
 - a) Assays to detect antibodies
 - i) Membrane-based (complement-dependent cytotoxicity) and solid phase assays (single antigen bead assay)
 - ii) Specification of antibodies
 - iii) Measure of strength
 - iv) Measure of function (including C1q assay)
 - b) Threshold for unacceptable antigens
 - i) Virtual crossmatch
 - ii) Prospective and retrospective crossmatch
 - c) When to desensitize
 - d) Desensitization strategies
- 5) Special Considerations: Combined organ transplantation
 - a) Combined heart-kidney transplant
 - i) General concepts
 - ii) Indications
 - iii) Management
 - iv) Outcomes
 - b) Combined heart-liver transplant
 - i) General concepts
 - ii) Indications

- iii) Management
 - iv) Outcomes
 - c) Combined heart-lung transplant
 - i) General concepts
 - ii) Indications
 - iii) Management
 - iv) Outcomes
- 6) Urgent Inpatient Evaluation
 - a) Mechanical ventilation
 - b) Inotrope dependency
 - c) Temporary assist devices
 - i) Percutaneous VAD
 - ii) Extracorporeal VAD
 - iii) ECMO
 - d) Durable assist devices
- 7) Allocation Systems
 - a) Concepts in donor allocation
 - b) Regional differences in allocation
 - i) United States
 - ii) Eurotransplant
 - iii) Australia
 - iv) Other countries

II. EVALUATION AND MANAGEMENT OF THE POTENTIAL HEART DONOR

Learning Objectives

- Understand the definition of brain death and the pathophysiology associated with it
- Understand the general principle of donor management
- Recognize acceptable donor and donor-recipient matching
- Understand the procurement methods to optimize allograft function

1) Donor Selection

- a) General Considerations
 - i) Evaluation of donor cardiac function
 - (1) LVH
 - (2) Hemodynamics
 - (3) Left heart catheterization
 - (4) Other
 - ii) Donors with potential drug toxicities
 - iii) Donors with pre-existing cardiac abnormalities

- iv) Donor-recipient size matching
- v) Other
- b) Management of donor heart
 - i) T4 infusions
 - ii) Vasoactive drugs
 - iii) Inotropic agents
- 2) Heart Procurement
 - a) Preparation and dissection (with and without lung procurement)
 - b) Cardioplegia
 - c) Recommendations on ischemic times
 - d) Transport requirements

III. PERI-OPERATIVE MANAGEMENT OF THE TRANSPLANT RECIPIENT

Learning Objectives

- Understand general consideration of donor-recipient matching
 - Discuss the hemodynamic monitoring required in stable and unstable patients
 - Understand the principles of post-transplant RV dysfunction and pulmonary hypertension, diagnosis and management
 - Understand the principles of primary graft dysfunction, diagnosis and management
 - Understand the importance of optimization of renal function in the early perioperative period
 - Understand the principles of infectious prophylaxis in the early perioperative period
- 1) Post-operative Monitoring
 - a) Invasive arterial pressure monitoring
 - b) Direct Measurement of right atrial or central venous pressure
 - c) Intermittent measurement of cardiac output (or mixed venous oxygen saturation)
 - d) Peri-operative vasoactive drug use
 - e) Peri-operative pacing and use of chronotropic agents
 - 2) Right Ventricular Dysfunction
 - a) Early diagnosis
 - b) Pulmonary vasodilators
 - c) Inotropic support
 - d) Mechanical support
 - 3) Primary graft dysfunction other than RV dysfunction
 - a) Preservation injury
 - b) Early diastolic dysfunction
 - c) Diagnosis
 - d) Management
 - 4) Optimization of Renal Function

- 5) Perioperative cardiac arrhythmias
- 6) Perioperative infectious prophylaxis
 - a) CMV
 - b) Fungal pathogens
 - c) Bacterial infections

IV. IMMUNOLOGIC CONCEPTS IN HEART TRANSPLANTATION

Learning Objectives

- Review the general concepts and definitions of basic immunology
- Understand the normal immune responses in a normal environment
- Understand the roles of lymphocytes responsible for immune responses in transplantation
- Understand the different types of rejection in heart transplantation
- Discuss the principles of treatment for the various types of rejection
- Discuss the principle of desensitization and the various possible combinations and protocols

- 1) Definitions
- 2) Normal immune responses
- 3) Immune response to allograft
 - a) Mechanisms of rejection
 - i) Acute and hyperacute rejection
 - ii) Chronic rejection
 - iii) Antibody-mediated rejection
- 4) Tolerance
- 5) Clinical Applications
 - a) ABO blood system
 - b) HLA
 - c) Methods to detect anti-HLA antibodies
 - i) Calculated PRA
 - ii) CDC
 - iii) Flow cytometry
 - iv) Solid phase assays
 - d) Non-HLA antigens
 - e) Desensitization protocols
 - i) Plasmapheresis and IVIG
 - ii) Rituxumab and bortezomib
 - iii) Cyclophosphamide and IVIG
 - iv) Eculizumab
 - v) Newer agents

V. IMMUNOSUPPRESSION AND REJECTION

Learning Objectives

- Discuss the principles of routine rejection surveillance in heart transplantation
- Review the role of noninvasive surveillance for rejection and allograft function
- Discuss the principles and possible complications of induction therapy
- Understand the principle of baseline immunosuppression in heart transplantation
- Discuss the various protocols available in heart transplantation
- Understand the importance of level monitoring for calcineurin inhibitors
- Discuss the side effects of each of the drug classes
- Discuss drug-drug interaction of the various immunosuppressants, especially calcineurin inhibitors
- Understand the difference between cellular and antibody-mediated rejection
- Understand the different approaches to the treatment of rejection

1) Rejection Surveillance

- a) Endomyocardial biopsy
- b) Noninvasive monitoring of acute allograft rejection
 - i) Molecular expression testing (Allomap)
 - (1) Cargo and Image
 - (2) Clinical Application
 - (3) When and how to use it
 - ii) ImmuKnow assay
- c) Donor specific antibodies
- d) Special staining on EMB for AMR
 - i) C3d and C4d
 - ii) CD68
 - iii) Other
 - e) Future
 - i) cfDNA
 - ii) micrRNA

2) Immunosuppression strategies

- a) Background and History
- b) Induction
 - i) Definition
 - ii) Risks and benefits
 - iii) Strategies
 - (1) IL-2 antagonists
 - (2) Anti-thymocyte antibodies (Thymoglobulin)
 - (3) Campath (anti-CD52)
- c) Maintenance regimens
 - i) CNI-based regimens
 - (1) Triple agent immunosuppression

- (2) Steroid withdrawal
 - (3) Tacrolimus-only regimen
 - (4) Comparison of various regimens
 - ii) Calcineurin inhibitors
 - (1) Mechanism of action
 - (2) Pharmacology
 - (3) Toxicity
 - (4) Interactions
 - iii) Anti-proliferative agents (mycophenolate mofetil and azathioprine)
 - (1) Mechanism of action
 - (2) Pharmacology
 - (3) Toxicity
 - (4) Interactions
 - iv) TOR Inhibitors
 - (1) Mechanism of action
 - (2) Pharmacology
 - (3) Toxicity
 - (4) Interactions
- 3) Rejection
- a) Acute cellular rejection
 - i) Diagnosis
 - ii) Asymptomatic rejection
 - iii) Management
 - (1) Augmentation of maintenance immunosuppression
 - (2) Steroid bolus
 - (3) Anti-thymocyte antibodies
 - iv) Recurrent or resistant cellular rejection
 - (1) Photopheresis
 - (2) Total lymphoid irradiation
 - (3) Other
 - b) Antibody-mediated rejection
 - i) Diagnosis
 - ii) Management
 - (1) Augmentation of maintenance immunosuppression
 - (2) Steroid bolus
 - (3) Plasmapheresis
 - (4) IVIG
 - (5) Rituxumab
 - (6) Bortezomib
 - (7) Eculizumab
 - (8) Newer agents
 - iii) Monitoring of future events

- (1) Donor-specific antibodies
- (2) Endomyocardial biopsy
- (3) AMR staining on endomyocardial biopsy
- (4) cfDNA and microRNA

VI. LONG-TERM CARE OF HEART TRANSPLANT RECIPIENTS

Learning Objectives

- Understand the general principles of long-term management of heart transplant recipient
 - Discuss the risks and benefits of minimization of immunosuppression in the long-term
 - Understand the general principles, prevention and treatment of cardiac allograft vasculopathy
 - Understand the importance of renal sparing regimen in heart transplantation
 - Understand the general principles behind post-transplant malignancies, incidence, prognosis and basics of treatment
 - Discuss the long-term complications of immunosuppression
 - Discuss the incidence and management on non-cardiac pathologies post-transplant, like hematologic disorders and other systemic disorders
- 1) Minimization of immunosuppression (details in prior section V)
 - 2) Infectious Disease
 - a) General principles
 - b) Risk factors
 - c) Prophylaxis
 - i) First year
 - ii) After first year
 - iii) Prophylaxis after cytolytic therapy
 - d) ImmuKnow assay
 - e) Principles of management
 - 3) Cardiac allograft vasculopathy
 - a) Possible etiologies
 - i) Immunological mediators (chronic rejection)
 - ii) Non-immunological risk factors
 - b) ISHLT nomenclature classification
 - c) Primary prevention
 - d) Definition
 - e) Screening
 - f) Management
 - i) Statins
 - ii) Revascularization strategies
 - iii) TOR inhibitors
 - iv) Re-transplantation
 - 4) Chronic kidney disease

- a) Incidence
- b) Management
- 5) Malignancy post-transplantation
 - a) Incidence
 - b) Risk factors
 - c) Minimization of immunosuppression
 - d) Post-transplant proliferative disorder (PTLD)
 - e) Principles of management
- 6) Hematologic disorders post-transplantation
- 7) Other co-morbidities post-transplantation
 - a) Diabetes
 - b) Hypertension
 - c) Bone disease
- 8) Return to work and quality of life post-heart transplantation
 - a) Depression and Mental health

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VIII. MECHANICAL CIRCULATORY SUPPORT OVERVIEW

Note: The ISHLT Mechanical Circulatory Support Council has a complete Core Competency Curriculum Document which are more comprehensive than this subset.

I. GENERAL CONCEPTS

Learning Objectives

- Understand the evolution of currently available commercial options for mechanical circulatory assist devices from earliest devices
- Understand the differences between pulsatile and continuous flow as well as axial versus centrifugal support devices
- Understand pathways for mechanical circulatory support including temporary support, long-term “destination” therapy, bridge to transplantation and bridge to decision
- Understand the studies that led to the approval of mechanical circulatory support for destination therapy
- Review published outcomes with currently approved durable mechanical circulatory support devices
- Understand the differences among the commercially available devices
- Understand the socio-economic burden of mechanical circulatory devices
- Review the timing to consider palliative care and hospice

1) Introduction

2) History of Mechanical Circulatory Support

3) Purposes for MCS

- a) Bridge to Transplant
- b) “Destination” Therapy
- c) Bridge to Decision

4) REMATCH trial: NEJM

- i) Established role for MCS vs medical therapy in stage D patients
 - (1) Limited durability of VAD
 - (2) Pulsatile flow
 - (3) No anticoagulation
 - (4) Drive line, drive line infections
 - (5) Stroke risk

5) Heartmate 2 BTT trial (Miller et al NEJM)

6) Heartmate 2 DT trial (Slaughter et al NEJM)

7) ADVANCE Trial (Heartware) (Aaronson, Circ)

8) ENDURANCE Trial (Heartware)

9) MOMENTUM (HM3 trial)

10) Current evaluation scale for MCS patients

- a) INTERMACS levels
- b) Risk scores

11) Currently available devices: Outcomes

- a) Second generation devices: Axial flow
 - i) Heartmate II
 - ii) Jarvik 2000
- b) Third generation devices: Centrifugal flow
 - i) Heartware

12) Quality of life with LVAD

- a) Supportive care
- b) Palliative care

II. COMPLICATIONS**Learning Objectives**

- Understand the etiology and causes of the common complications of mechanical circulatory support devices including modes of failure
- Understand the need for quick evaluation and management of catastrophic device complications
- Review the importance of driveline infection
- Understand the mechanism leading to RV failure after mechanical circulatory device
- Review the different approaches to the management of device complications
- Review strategies to manage patients with failed mechanical circulatory support devices
- Review the next generation of mechanical circulatory support devices

1) Device failure and complications

- a) Device thrombosis
 - 1) Symptoms
 - (1) Heart failure returns
 - (2) Volume overload
 - (3) Possibly alarms, maybe not
- b) Drive line failure / fracture
 - 1) Usually Alarms
 - 2) Circulatory collapse
- c) Aortic insufficiency
 - 1) Etiology
 - 2) Symptoms
 - 3) Management
 - (1) Medical
 - (2) Surgical AVR
 - (3) ? TAVR
- d) GI bleeding
 - 1) Etiology
 - (1) Von-Willebrand Factor
 - (2) Arterio-venous malformations
 - 2) Diagnosis
 - (1) Endoscopy
 - (2) Capsule
 - (3) ? bleeding scan etc
 - 3) Management
 - (1) Medical
 - (a) Octreotide
 - (b) Estrogens
 - (c) Electrocautery via endoscopy

- e) Early RV failure
 - 1) Medical treatment
 - (1) PDE-5 antagonist like sildenafil
 - (2) Nitric Oxide inhaled
 - (3) Epoprostenol inhaled
 - (4) Inotropes (Milrinone / dobutamine)
 - (5) Speed changes
 - (6) Temporary RV pacing at faster rates
 - (7) Diuresis / dialysis
 - 2) Device-based therapies
 - (1) Percutaneous RVAD
 - (2) Tandem
 - (3) Future Impella RP
 - (4) IABP
 - (5) Centrimag RVAD
 - (6) Thoratec PVAD
 - (7) Heartware RVAD
- f) Late RV failure
 - 1) Diagnosis
 - 2) Treatment
 - (1) Inotrope
 - (2) Diuresis
 - (3) Heartware RVAD
 - (4) Transplant
 - (5) Palliative care
- g) Drive Line infection
 - 1) Risk Factors
 - 2) Prevention- immobilization, internalization of drive line (using smooth portion not velour)
 - 3) Classification (ISHLT guidelines)
 - 4) Treatment
- h) CVA
 - 1) Incidence
 - 2) Treatment
 - 3) Differences between current devices?
- 2) When the pump has failed
 - a) Pump replacement for those who are candidates
 - b) The non-surgical candidate
 - 1) End of Life
 - 2) How do you die on MCS?
 - 3) Role of palliative care

III. PROSPECTS FOR THE FUTURE

Learning Objectives

- Review the next generation of mechanical circulatory support devices
- Review novel approaches to biventricular support that are not approved
- Discuss medical approaches that may complement mechanical support

- a) Smaller pumps
 - 1) Heartware MVAD
 - 2) Thoratec Heartmate X
 - 3) Circulite
- b) Wireless energy transfer- no more drive line
 - 1) Thoratec with Wi-Tricity
 - 2) Heartware with other technology
- c) Intermittent Aortic Valve opening
- d) Biventricular support
 - 1) Frazier's Thoratec Heartmate 2 BIVAD
 - 2) Heartware BIVAD's
 - 3) Better drivers for Total artificial heart
 - 4) Syncardia (Smaller ventricles)
 - 5) Carmat
- e) Adjunctive therapies
 - 1) Recovery protocols to allow device removal
 - 2) Stem cells at time of VAD placement?
 - 3) Gene therapy?

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HYPERLINKS AT A GLANCE

ACC / AHA Guidelines

2013 ACC/AHA Heart Failure Guidelines

<http://content.onlinejacc.org/article.aspx?doi=10.1016/j.jacc.2013.05.019>

Executive Summary 2013 ACC/AHA Heart Failure Guidelines

<http://content.onlinejacc.org/article.aspx?doi=10.1016/j.jacc.2013.05.020>

ACC/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy

<http://content.onlinejacc.org/article.aspx?articleid=1147838>

Executive Summary ACC/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy

<http://content.onlinejacc.org/article.aspx?articleid=1147858>

ISHLT Guidelines

2013 ISHLT Guidelines for Mechanical Circulatory Support

<http://download.journals.elsevierhealth.com/pdfs/journals/1053-2498/PIIS1053249812012946.pdf>

A 2010 Working Formulation for the Standardization of Definitions of Infections in Cardiothoracic Transplant Recipients.

<http://download.journals.elsevierhealth.com/pdfs/journals/1053-2498/PIIS1053249811007315.pdf>

Working Formulation for the Standardization of Definitions of Infections in Patients Using Ventricular Assist Devices.

<http://download.journals.elsevierhealth.com/pdfs/journals/1053-2498/PIIS1053249811007571.pdf>

The ISHLT Guidelines For The Care Of Heart Transplant Recipients

[http://www.jhltonline.org/article/S1053-2498\(10\)00358-X/abstract](http://www.jhltonline.org/article/S1053-2498(10)00358-X/abstract)

ACCF / AHA / ACP / HFSA / ISHLT 2010 Clinical Competence Statement on Management of Patients With Advanced Heart Failure and Cardiac Transplant

<http://content.onlinejacc.org/cgi/content/full/56/5/424>

ISHLT working formulation of a standardized nomenclature for cardiac allograft vasculopathy

[http://www.jhltonline.org/article/S1053-2498\(10\)00312-8/abstract](http://www.jhltonline.org/article/S1053-2498(10)00312-8/abstract)

Optimal Pharmacologic and Non-pharmacologic Management of Cardiac Transplant Candidates: Approaches to Be Considered Prior to Transplant Evaluation

<http://www.jhltonline.org/article/PIIS1053249806004578/fulltext>

Listing Criteria for Heart Transplantation

[http://www.jhltonline.org/article/S1053-2498\(06\)00460-8/fulltext](http://www.jhltonline.org/article/S1053-2498(06)00460-8/fulltext)

Heart Rhythm Considerations in Heart Transplant Candidates and Considerations for Ventricular Assist Devices

[http://www.jhltonline.org/article/S1053-2498\(06\)00457-8/fulltext](http://www.jhltonline.org/article/S1053-2498(06)00457-8/fulltext)

Other Professional Society Guidelines Documents**Heart Failure Society of America Heart Failure Practice Guideline**

http://www.heartfailureguideline.org/_assets/document/Guidelines.pdf

European Society of Cardiology Heart Failure Guideline <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/acute-chronic-heart-failure.aspx>

2009 ESC / ERS Guidelines on the Diagnosis and Treatment of Pulmonary Hypertension

<http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-PH-FT.pdf>