

# Failure is a Chance to Begin Again:

## Advanced Heart Failure Therapies

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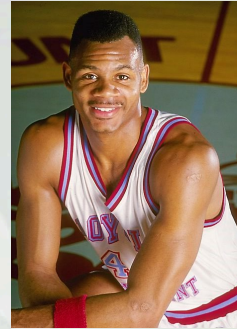
## Disclosures

- I have no relevant relationships with ineligible companies to disclose within the past 24 months. (Note: Ineligible companies are defined as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)

# Educational Objectives

- Identify markers of advanced heart failure through the application of the ACC, "I NEED HELP" tool and the Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) patient profile
- Recognize the indications and contraindications for advanced heart failure therapies
- Describe the basic function and limitations of Left Ventricular Assist Device (LVAD) therapy
- Describe the basic function and limitations of heart transplantation therapy
- Define when to refer a patient, as advanced heart failure markers are present

# What Does Heart Failure Look Like?



# Heart Failure(HF) By The Numbers

- The lifetime risk of developing HF is **20% for Americans  $\geq 40$  years of age**
- In the United States, HF prevalence increased from 5.7 million to 6.5 million in Americans patient  $\geq 20$  years old
- Projections show prevalence will **increase by 46% from 2012 to 2030** resulting in more than 8 million people 18 yrs and older with HF
- 1 in 5 Americans will be  $>65$  years of age by 2050 and because HF prevalence is highest in this group, the number of Americans with HF is expected to significantly worsen in the future.
- The absolute mortality rates for HF remain approximately 50% within 5 years of diagnosis**



# Let's All Speak the Same Language!

## Classification of Heart Failure: ACC/AHA Stage vs NYHA Class

ACC/AHA Heart Failure Stage	NYHA Functional Class
A. At risk for heart failure but without structural heart disease or symptoms	None
B. Structural heart disease but without heart failure	I. Asymptomatic
C. Structural heart disease with prior or current heart failure symptoms	II. Symptomatic with moderate exertion III. Symptomatic with minimal exertion
D. Refractory heart failure requiring specialized interventions	IV. Symptomatic at rest

- Remember that Stages and Classes of Heart Failure are not the same.
- Think of Stages as the Objective data; only moves forward.
- Think of the Class as the Subjective data; moves forward and backwards

Hunt SA et al. *Circulation*. 2001;104:2996-3007.

Farrell MH et al. *JAMA*. 2002;287:890-897.

# Markers of Advanced Heart Failure Therapies

- Unfortunately, many patients still go undiagnosed or unreferred for too long which means they miss the “window’ for help.
- If you are unsure if your patient is “sick enough” or “needs cardiology”, screen with these tools:
  - “I NEED HELP” tool
  - Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) Profile



# “ I NEED HELP”

## Markers of Advanced Heart Failure

<b>I</b>	<u>I</u> notropes	Previous or ongoing
<b>N</b>	<u>N</u> YHA class/ <u>N</u> atriuretic peptides	NYHA III/IV or high NT-pBNP
<b>E</b>	<u>E</u> nd-organ dysfunction	Worsening renal/liver function
<b>E</b>	<u>E</u> jection fraction	EF <20%
<b>D</b>	<u>D</u> efibrillator shocks	Appropriate shocks
<b>H</b>	<u>H</u> ospitalizations	≥1 HF hospitalizations in 12 months
<b>E</b>	<u>E</u> dema/ <u>E</u> scalating diuretics	Persistent overload, diuretic resistance
<b>L</b>	<u>L</u> ow blood pressure	<90mmHg
<b>P</b>	<u>P</u> rognostic medication	Inability to titrate (or decrease) GDMT



# Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) Profile

INTERMACS Profile scoring is a useful tool in ambulatory and inpatient setting for classifying Advanced Heart Failure Progression

INTERMACS 1 is the sickest, INTERMACS 7 is the “Healthiest”

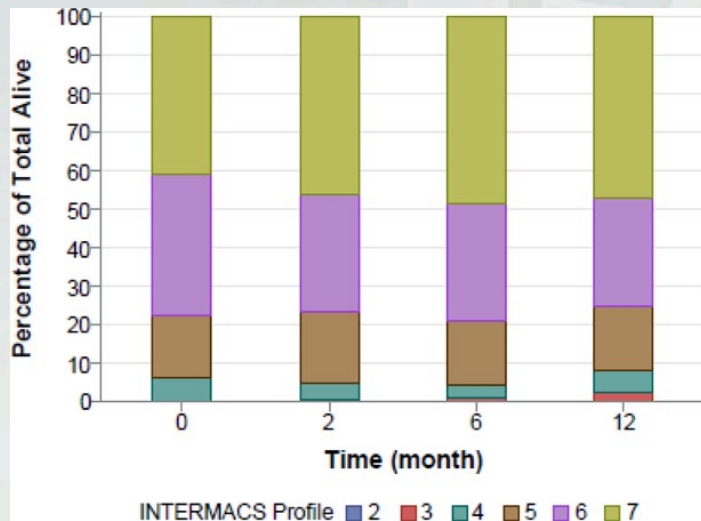


Table 4: INTERMACS Profiles

Profiles	Brief Description	Details
INTERMACS 1	Critical cardiogenic shock (Crash and burn)	Life-threatening hypotension despite rapidly escalating inotropic support.
INTERMACS 2	Progressive decline (Sliding fast on inotropes)	Declining function despite intravenous inotropic support.
INTERMACS 3	Stable but inotrope dependent (Dependent stability)	Stable on continuous intravenous inotropic support.
INTERMACS 4	Resting symptoms on oral therapy at home	Patient experiences daily symptoms of congestion at rest or during activities of daily living.
INTERMACS 5	Exertion intolerant	Patient is comfortable at rest and with activities of daily living but unable to engage in any other activity.
INTERMACS 6	Exertion limited (Walking wounded)	Patient has fatigue after the first few minutes of any meaningful activity.
INTERMACS 7	Advanced NYHA class III (Placeholder)	Patients living comfortably with meaningful activity limited to mild physical exertion.

*INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; NYHA = New York Heart Association. Adapted from: Stevenson LW, et al.<sup>25</sup>*

Birati E et al; *Cardiac Failure Review* 2015;1(1):25–30

Kittleson MM. INTERMACS profiles and outcomes of ambulatory advanced heart failure patients: A report from the REVIVAL Registry. *J Heart Lung Transplant*. 2020 Jan;39(1):16-26.

## Consider this Case....

55 yo male with h/o HTN and DM2 admitted to the hospital with an NSTEMI. In speaking to you he relays that over the last few months he has been “slowing down” and that he can’t “keep up with his kids.” He tells you he thought he had an URI and has seen his PCP twice over the last 6 weeks and has been told he had a viral URI and then was giving a course of abx just “to be safe.” He relays this did not help his URI symptoms. He came to the hospital after feeling “really short of breath.”

On Presentation, BP 107/72 mmHg, HR 115, RR 20, SpO2 95% of RA

Labs: BNP 420, Troponin-HS 12, Cr 1.4 (baseline 0.8)

CXR: “b/l pulmonary congestions with no consolidation or effusions noted. Correlate clinically”

Echo: EF 25%, LVEDD 8.2 cm, Severe Aortic Regurgitation

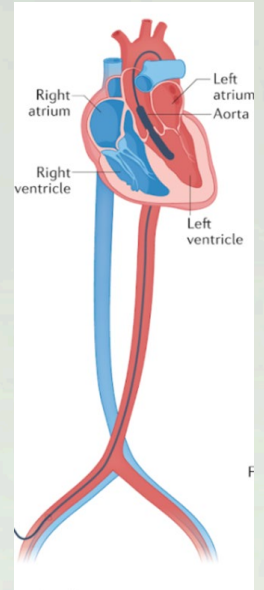
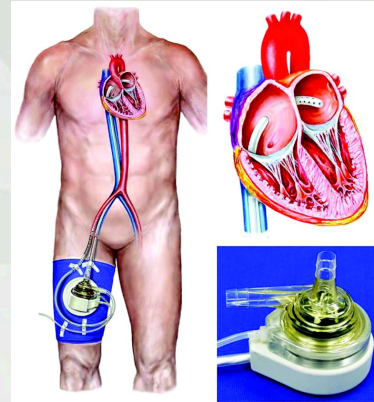
What is his INTERMACS Profile?

# What Are Advanced Heart Failure Therapies?

- Advanced Heart Failure Therapies can be options for treatment in patients with heart failure that have Stage D, NYHA Class IIIB-IV heart failure and have 1 of the following:
  1. Failure to Respond to optimal medical therapy
  2. Short-term Support device dependent for 7 days
  3. Inotrope-dependent for at least 14 days
  4. Intolerant of ACE/ARB/ARNI or Beta-Blocker Therapy
  
- Advanced Heart Failure Therapies Include:
  1. Heart Transplant
  2. Left Ventricular Assist Device (LVAD)
    - BTT (Bridge to Transplant)
    - DT (Destination Therapy)

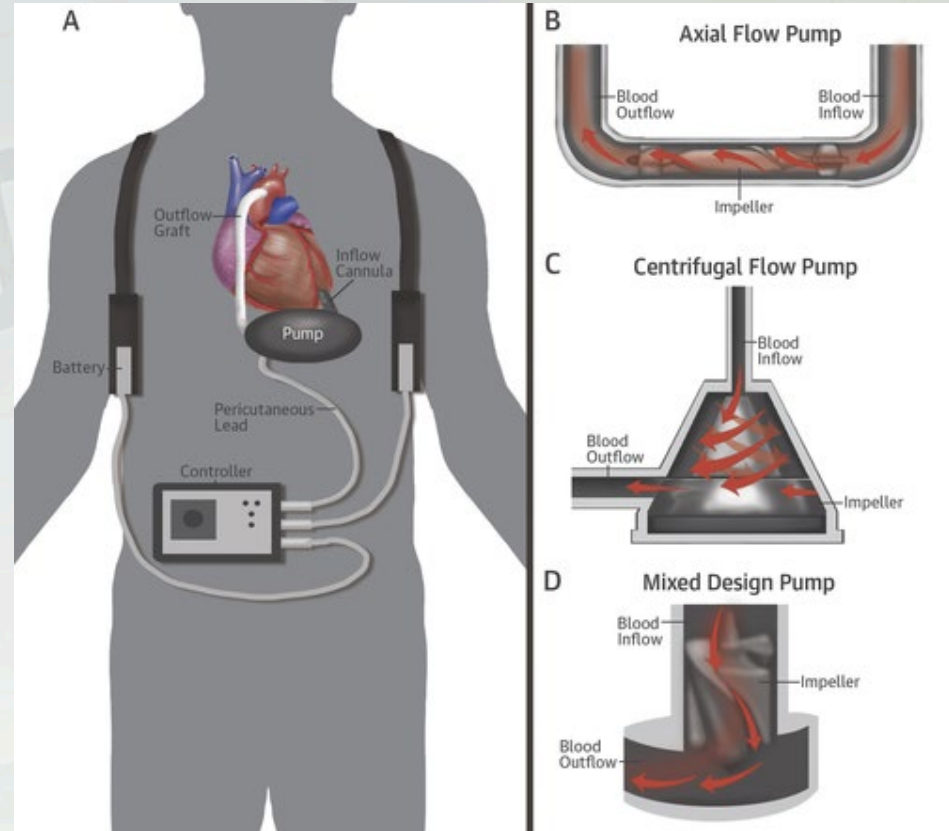
# Mechanical Circulatory Support (MCS) Devices

- MCS devices are designed to augment cardiac output and offload the heart.
- MCS support is best used in the **RIGHT** patient at the **RIGHT** time for the **RIGHT** reasons.
- Two different “buckets” of MCS support
  - **Temporary Support Devices**
    - Intra-Aortic Ballon Pumps (IABP)
    - Temporary Surgical Ventricular Assist Device (VAD)
    - Percutaneous VAD
    - Microaxial VAD
    - Extracorporeal Membrane Oxygenation (ECMO)
  - **Implantable (Long-Term) Support Devices**
    - **Left Ventricular Assist Device (LVAD)**  
 \*\*\*Most common and focus of our talk today\*\*\*
    - Bi-Ventricular Assist Device (BiVAD)
    - Total Artificial Heart (TAH)



# Left Ventricular Assist Device (LVAD) Basics

- Two Types of Continuous Flow LVADS
  - Axial Flow
    - Becoming less common as newer generation devices are Centrifugal
  - Centrifugal Flow



# LVAD 101

- **Continuous Flow = No Pulsatility= No Pulse**
  - Will most likely not be able to palpate peripheral pulses
  - Most likely unable to obtain SBP/DBP
  - Most reliable/accurate measurement is by Doppler-> MAP
- **Components of the LVAD**
  - Pump- “the motor”
  - Inflow graft
  - Outflow graft
  - Driveline- “the power cord”
  - Controller- “the brains”
  - Batteries – “the power”
- **Power**
  - Electricity dependent. Must be on batteries or wall power
- **Medications**
  - Will be anticoagulated with ASA\*\*\* and Warfarin\*\*\*

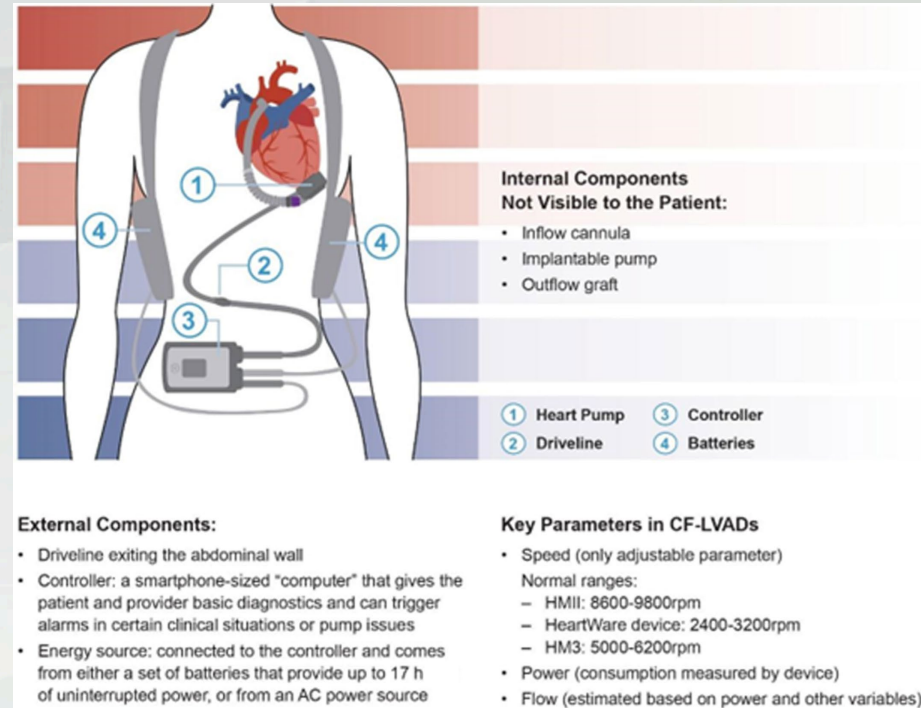


Image Source: Chaudry SP, et al. *JAHA* 2022; 11:e027251



# Should an LVAD Patient still receive Guideline-Directed Medical Therapies for Heart Failure?

- Remember the device is supporting the Left Ventricle. The rest of the heart still must play in the game
- All Patients still get per the ACC/AHA Clinical Practice Guidelines:
  - Beta-Blocker
  - ARNI/ACE/ARB
  - Aldosterone Antagonist
  - SGLT II Inhibitor
  - Diuretics as needed

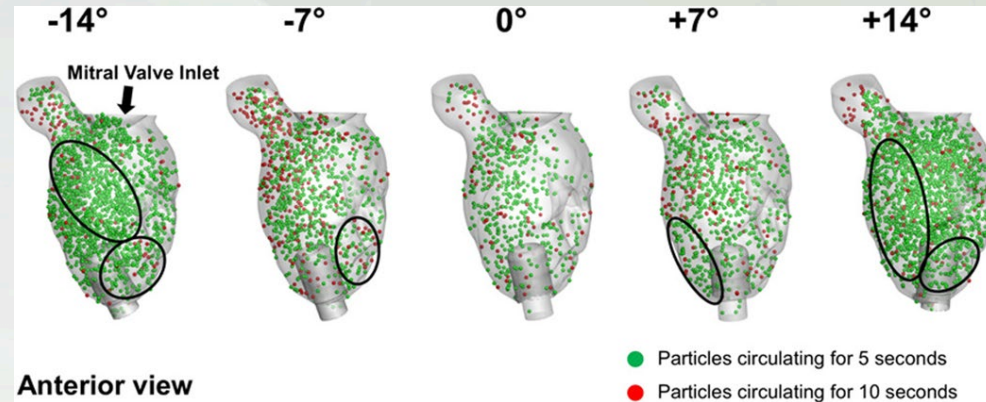
**Don't Fear the LVAD!**

**These patients have a safety net that your non-LVAD patient don't have!!!**



# LVAD Complications

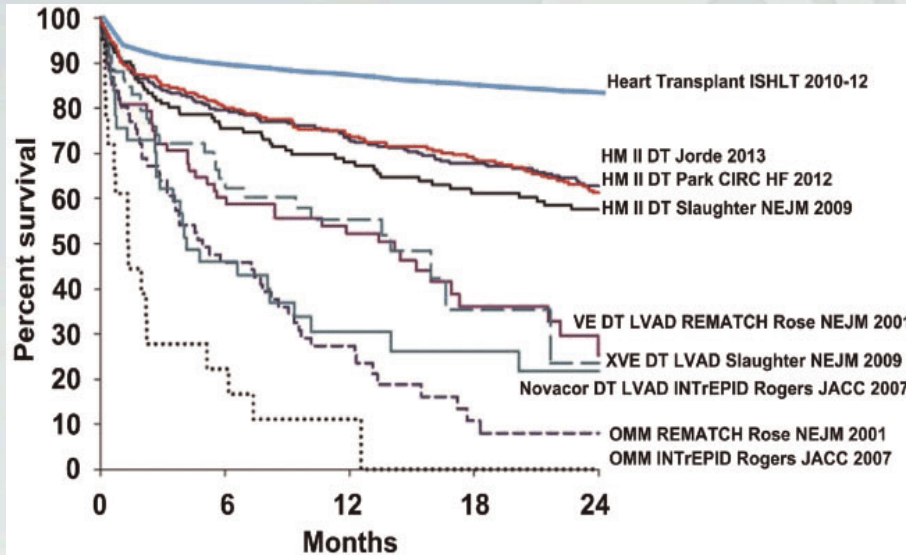
- **Bleeding**
  - Supratherapeutic INR
  - AV Malformations
- **CVA**
  - Subtherapeutic INR
- **Driveline Infection**
  - Driveline changes
  - Exposure to water
- **Pump Thrombosis**
- **Pump Malposition**
  - Angulation of the inflow cannula of >7 degrees from the apical axis is a risk factor
- **Driveline Fracture**
  - Unsecured driveline



Venkat Keshav Chivukula. Circulation: Heart Failure. Left Ventricular Assist Device Inflow Cannula Angle and Thrombosis Risk, Volume: 11, Issue: 4, DOI: (10.1161/CIRCHEARTFAILURE.117.004325)

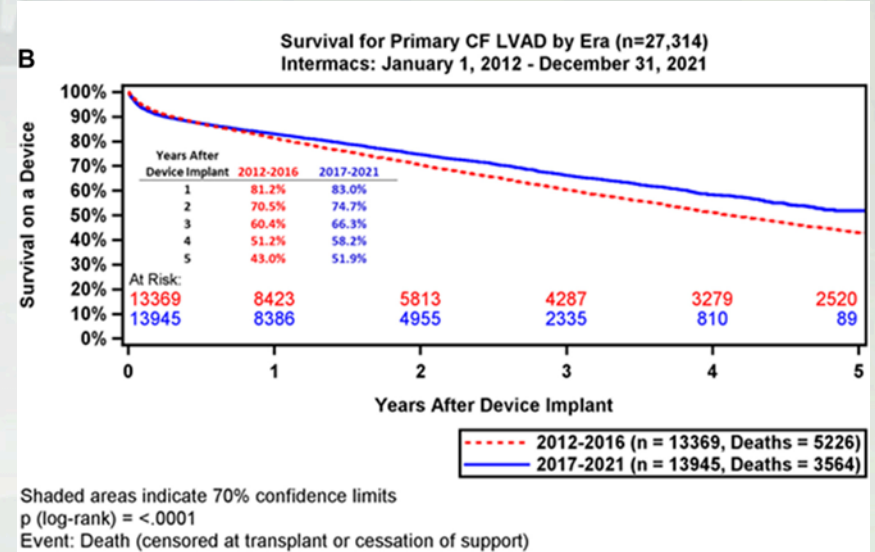
# LVAD Treatment outcomes in Stage D HF/EF Patients

- At the Start....



Huchs, M et al. *Eur Assoc.CTS* 2019; 55:i38-i48.

- Now....



*The Annals of Thoracic Surgery* 2023 115311-327DOI:  
(10.1016/j.athoracsur.2022.11.023)

# Heart Transplantation Basics

- **Waitlist Status- Think of a Sports Team!**
  - Status 1 through Status 7
  - Status 1 is the highest, 7 is the lowest
- **Organ Offer is based on Blood Type, Status, Time on the List, Height, Weight, and PRA (Panel Reactive Antibody)**
  - PRA score is expressed as a percentage between 0%-99% which represents the proportion of the population a person has pre-existing antibodies too. This is important in regards to rejection.
  - Any person, regardless of sex, gender, age, race, ethnicity can be a donor!
- **Donors are legally brain dead for a variety of causes (CVA, Closed Head Injury, Hypoxic Brain Injury, Drug overdose) OR can be DCD donors**
- **Increased Risk Donors- IV Drug Users, Incarcerated Persons, Hemophiliac, Prostitution History, High-Risk Sexual Activity, and Exposure to HIV**
  - Statistically NO difference in outcomes from these donors. Only increased monitoring

# ISHLT 2019 Cumulative Data-

## Adult Heart Transplants Donor and Recipient Characteristics

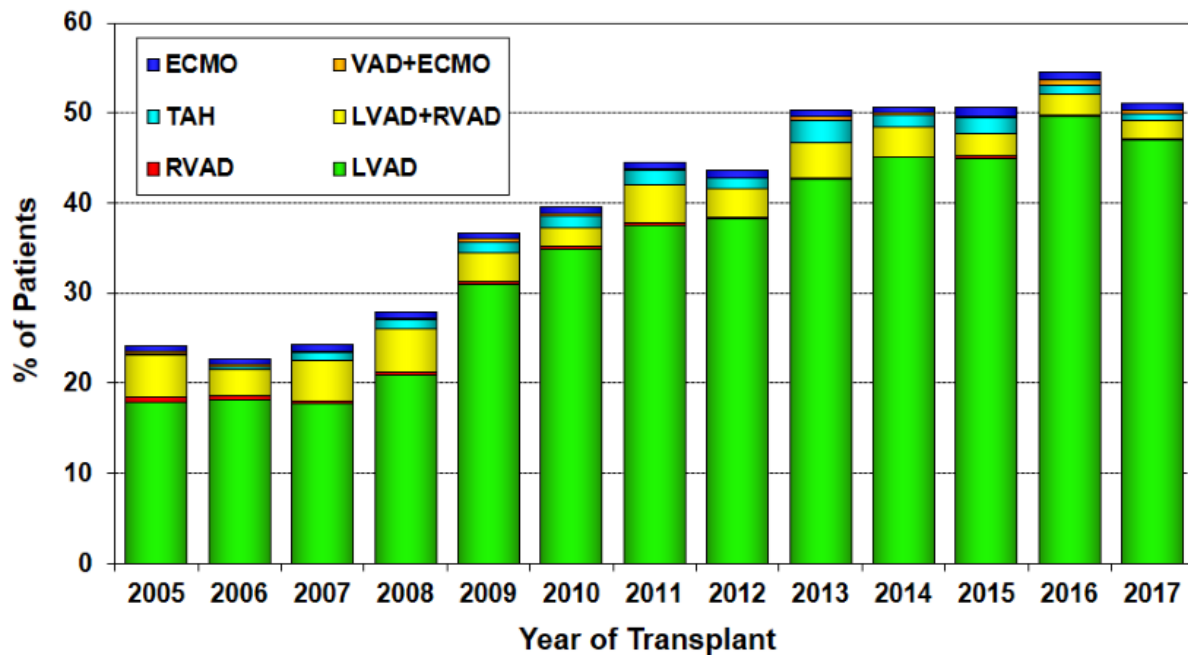
	1992-2000 (N = 37,794)	2001-2009 (N = 33,625)	2010-6/2018 (N = 36,883)	pvalue
Recipient age (years)	54.0 (28.0 - 65.0)	54.0 (25.0 - 66.0)	55.0 (25.0 - 68.0)	<0.0001
Donor age (years)	31.0 (15.0 - 54.0)	34.0 (16.0 - 56.0)	35.0 (17.0 - 58.0)	<0.0001
Donor and recipient age difference (years)	-19.0 (-44.0 - 7.0)	-17.0 (-43.0 - 11.0)	-16.0 (-43.0 - 13.0)	<0.0001
Recipient weight (kg)	75.3 (53.0 - 102.0)	78.0 (53.5 - 107.0)	80.1 (54.0 - 109.8)	<0.0001
Recipient height (cm)	173.0 (157.0 - 188.0)	174.0 (157.5 - 188.0)	174.0 (157.0 - 188.0)	0.0042
Recipient BMI	25.0 (19.0 - 32.5)	25.7 (19.3 - 34.0)	26.5 (19.5 - 34.9)	<0.0001
Donor weight (kg)	74.8 (52.0 - 102.1) <sup>1</sup>	77.6 (55.0 - 110.0)	80.0 (57.0 - 115.2)	<0.0001
Donor height (cm)	175.0 (157.0 - 188.0) <sup>1</sup>	175.3 (159.0 - 190.0)	175.0 (157.5 - 188.0)	<0.0001
Donor BMI	24.2 (18.8 - 32.8) <sup>1</sup>	25.1 (19.6 - 35.2)	26.0 (19.9 - 37.5)	<0.0001

Continuous factors are expressed as median (5<sup>th</sup> – 95<sup>th</sup> percentiles)



## Adult Heart Transplants

### % of Patients Bridged with Mechanical Circulatory Support\* by Year and Device Type



\* LVAD, RVAD, TAH, ECMO

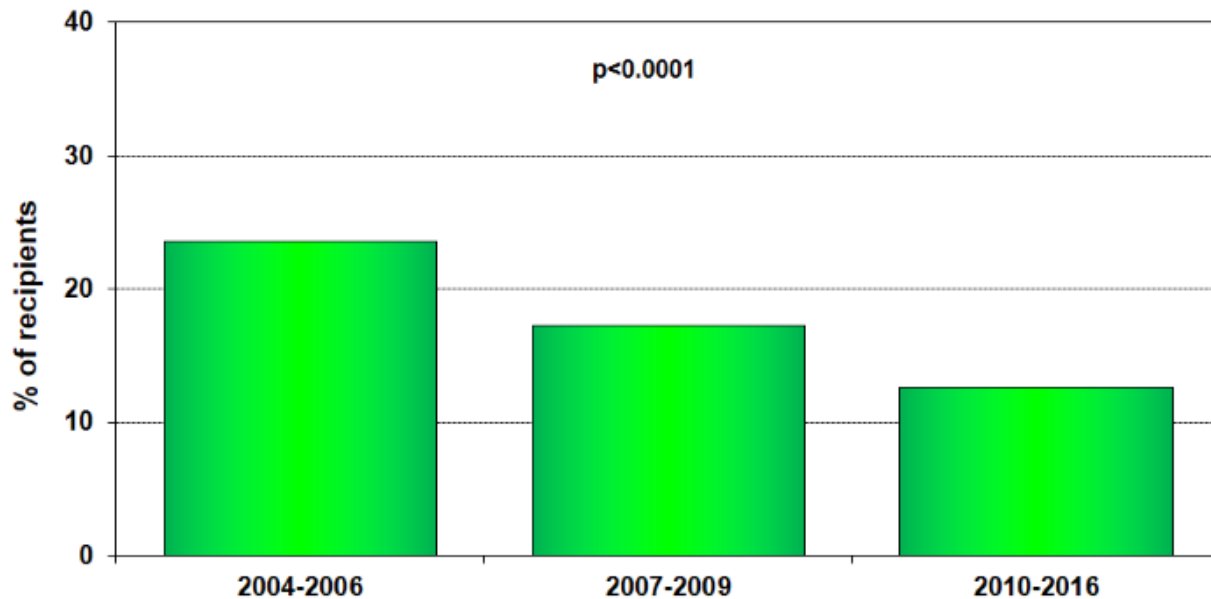


# Complications (ISHLT DATA)

- Rejection
  - Acute Cellular Rejection
  - Antibody Mediated Rejection
- Malignancy (
- Cardiac Allograft Vasculopathy
- Other
  - Leukopenia
  - Tremors
  - Renal Insufficiency
  - Recurrent Infection
  - Osteoporosis
  - Tricuspid Valve Insufficiency
  - Emotional Distress\*

## Adult Heart Transplants

% of Recipients Experiencing Treated Rejection Between Transplant Discharge and 1-Year Follow-Up by Transplant Era



Analysis is limited to patients who were alive at the time of the follow-up.

Treated rejection = Recipient was reported to (1) have at least one acute rejection episode that was treated with an anti-rejection agent; or (2) have been hospitalized for rejection.

## Adult Heart Transplants

### Cumulative Morbidity Rates in Survivors within 1, 5 and 10 Years Post Transplant (Transplants: January 1995 – June 2017)

Outcome	Within <u>1 Year</u>	Total N with <u>known response</u>	Within <u>5 Years</u>	Total N with <u>known response</u>	Within <u>10 Years</u>	Total N with <u>known response</u>
<b>Severe Renal Dysfunction<sup>1</sup></b>	<b>6.7%</b>	<b>(N=39,544)</b>	<b>15.7%</b>	<b>(N=22,462)</b>	<b>22.3%</b>	<b>(N=9,195)</b>
<i>Creatinine &gt; 2.5 mg/dl</i>	5.1%		12.2%		14.3%	
<i>Chronic Dialysis</i>	1.5%		2.9%		6.0%	
<i>Renal Transplant</i>	0.1%		0.6%		2.0%	
<b>Diabetes<sup>2</sup></b>	<b>20.0%</b>	<b>(N=39,834)</b>	<b>33.8%</b>	<b>(N=22,720)</b>	-	
<b>Cardiac Allograft Vasculopathy</b>	<b>7.7%</b>	<b>(N=36,774)</b>	<b>29.0%</b>	<b>(N=17,392)</b>	<b>46.8%</b>	<b>(N=5,962)</b>

<sup>1</sup> Severe renal dysfunction = Creatinine > 2.5 mg/dl (221 µmol/L), dialysis, or renal transplant

<sup>2</sup> Data are not available 10 years post-transplant.

## Adult Heart Transplants

### Post Transplant Malignancy (Transplants: January 1995 – June 2017) Cumulative Morbidity Rates in Survivors

Malignancy/Type		1-Year Survivors	5-Year Survivors	10-Year Survivors
No Malignancy		38,866 (94.9%)	20,974 (84%)	8,466 (72.3%)
Malignancy (all types combined)		2,068 (5.1%)	3,997 (16%)	3,238 (27.7%)
<i>Malignancy Type*</i>	<i>Skin</i>	695 (1.7%)	2,395 (9.6%)	2,166 (18.5%)
	<i>Lymphoma</i>	190 (0.5%)	262 (1%)	200 (1.7%)
	<i>Other</i>	1,148 (2.8%)	1,562 (6.3%)	1,192 (10.2%)
	<i>Type Not Reported</i>	35 (0.1%)	28 (0.1%)	16 (0.1%)

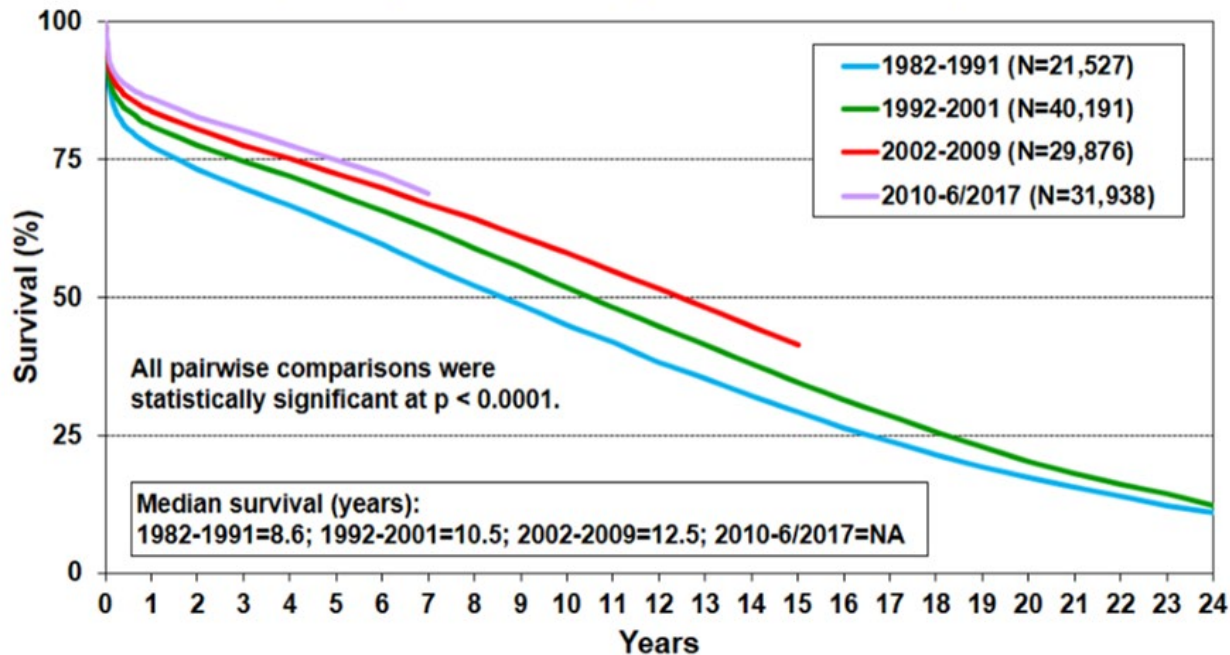
“Other” includes: prostate (8,18,9), adenocarcinoma (5, 2, 1), lung (6, 4, 1), bladder (2, 2, 0), Kaposi’s sarcoma (0, 1, 0), breast (1, 3, 1), cervical (2, 3, 2), colon (0,3, 2), and renal (2, 4, 1). Numbers in parentheses are those reported within 1 year, 5 years and 10 years, respectively.

\* Recipients may have experienced more than one type of malignancy so the sum of individual malignancy types may be greater than the total number with malignancy.

## Treatment and Outcomes

- Lifestyle considerations: infection prophylaxis, open water, fresh fruits and vegetables from buffets, live virus vaccines, gardening/mowing
- All patients go on ASA 81 mg, Calcium supplementation, and Statin therapy
- All patients will be on life-long immunosuppression
- In the first year, typically a 3-drug approach is used:
  - Tacrolimus, Mycophenolate Mofetil, and Prednisone
- Most common regimen for long-term immunosuppression is:
  - Tacrolimus and Mycophenolate Mofetil

## Adult Heart Transplants Kaplan-Meier Survival by Era (Transplants: January 1982 – June 2017)





# Work up for Advanced Heart Failure Therapies

## This requires a Multi-Disciplinary Approach with all parties having a voice!

Cardiac Surgery  
Advanced Heart Failure\*  
Palliative Medicine\*  
Social Work  
Nutritional Consult  
Behavioral Health\*  
Dental Clearance

## Labs:

CBC/BMP/Liver Profile/ Coags/ Lipids/ HgA1C/ UA/Urine Culture/ Drug Screen/ Nicotine/ Cotinine/ TSH/ Hepatitis Panel/ HIV/ Iron Studies/ PSA/ Pregnancy test/ Pre- Albumin/ Albumin/ ABO type and Screen

## Imaging/ Testing:

CXR/ EKG/ Echocardiogram/ Right Heart Cath/ Left Heart Cath/ Pulmonary Function Test/ Cardiopulmonary Exercise Test/ Carotid Ultrasound/ LE Duplex Ultrasound/ Abdominal Ultrasound/ Colonoscopy

**Based on results of testing, other consults and further work-up may be indicated.**

**Decision to offer therapy is made after multi-disciplinary meeting to discuss patient.**

**Destination Therapy**

**Bridge to Transplant**

**Transplant listing**

# Contraindications to LVAD

- BMI > 45 kg/m<sup>2</sup>- LVAD\*
- Active Pregnancy
- Irreversible Multi-Organ Failure
- Active, ongoing infection
- Liver Cirrhosis
- Severe Renal Dysfunction
  - Requiring chronic maintenance HD, or Serum Cr > 3.0
- COPD and/or Restrictive Lung Disease
  - FEV1 <1.5 L or < 50% of predicted
  - FVC < 50% of predicted
  - DLCO adj. < 50% of predicted
- Fixed Pulmonary Hypertension
  - PVR > 8 Woods unit despite optimal medical therapy
- RV Failure
- Significant Septal Hypertrophy
- PE or CVA within 90 days
- Inability to tolerate anticoagulation
- Coagulopathy
- Cardiac Cachexia BMI <21kg/m<sup>2</sup> (M) / <19 kg/m<sup>2</sup> (F)
- Ongoing Substance Abuse
- Active Psychiatric Instability/ Irreversible Cognitive Impairment
- Unsafe Living Environment/ Lack of Social Support

# Contraindications to Heart Transplant

- BMI > 35 kg/m<sup>2</sup>-
- Active Pregnancy
- Irreversible Multi-Organ Failure\*\*
- Active, ongoing infection other than Driveline Infection
- Liver Cirrhosis\*\*
- Severe Renal Dysfunction
  - Requiring chronic maintenance HD, or Serum Cr > 3.0
- COPD and/or Restrictive Lung Disease\*\*
  - FEV1 < 1.5 L or < 50% of predicted
  - FVC < 50% of predicted
  - DLCO adj. < 50% of predicted
- Fixed Pulmonary Hypertension
  - PVR > 8 Woods unit despite optimal medical therapy
- PE or CVA within 90 days
- Coagulopathy
- Cardiac Cachexia BMI < 21 kg/m<sup>2</sup> (M) / < 19 kg/m<sup>2</sup> (F)
- Ongoing Substance Abuse
- Active Psychiatric Instability/ Irreversible Cognitive Impairment
- Unsafe Living Environment/ Lack of Social Support

## Key Take Aways

- Refer early and refer often!
- Look for the window.
- Advanced Heart Failure therapies can be beneficial for the **right** patient at the **right** time for the **right** reasons.
- Advanced Heart Failure Therapies are not a cure but can offer improvement in quality of life and quantity of life.

# Resources for Clinicians

## 1. LVAD Center locator-

- [Find a Clinic for HeartMate 3 LVAD Therapy | Abbott \(cardiovascular.abbott\)](#)
- Also can be requested from CMS
- All centers must be accredited to provide services through CMS and JACHO

## 2. Transplant Center locator-

- [Transplant Centers \(srtr.org\)](#)
- 149 active adult heart transplant centers in the USA
- All centers must be accredited to provide services through CMS and JACHO

# Resources for Patients

## 1. Heart Failure Resources

- [Patient Resources for Providers | HFSA](#)
- [Patient Hub | HFSA](#)

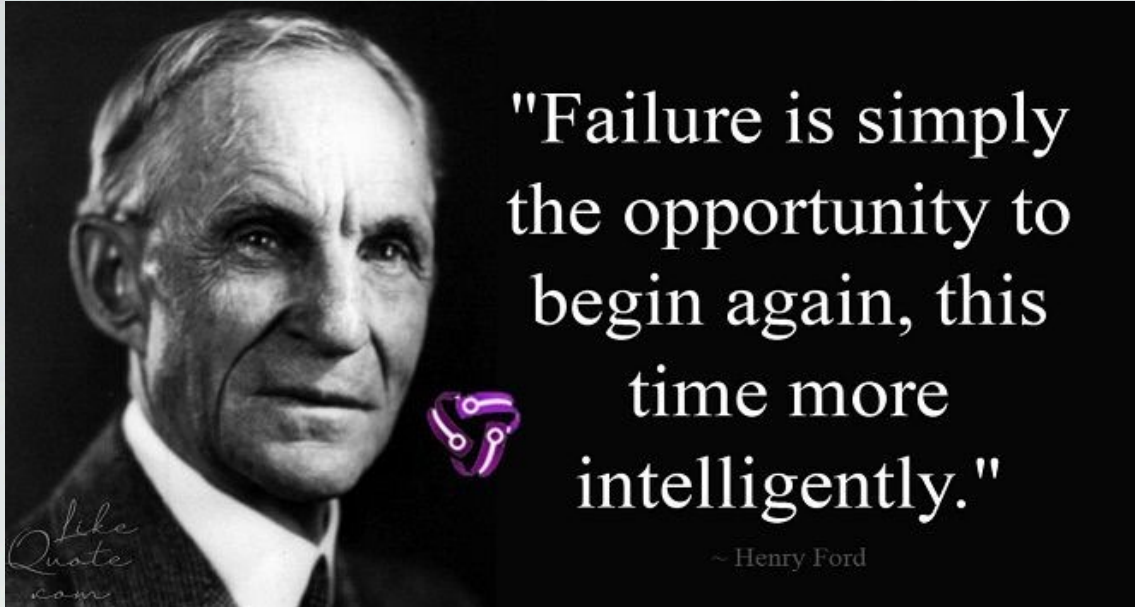
## 2. LVAD Resources

- [Patients and Caregivers | Abbott \(cardiovascular.abbott\)](#)
- [Learn about LVADs | MyLVAD](#)

## 3. Heart Transplant Resources

- [Patient Resources | ISHLT](#)





Thank you!

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