It all starts early - The role of Primary Care

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DISCLOSURES

• NO FINANCIAL DISCLOSURES
Heart failure has devastating public health consequences in the US

<table>
<thead>
<tr>
<th>Heart Disease and Stroke Statistics—2020 Update</th>
</tr>
</thead>
</table>

- Based on data from NHANES 2013 to 2016, an estimated **6.2 million** Americans ≥20 years of age had HF.

- Projections show that the prevalence of HF will increase **46%** from **2012** to **2030**, resulting in >8 million people ≥18 years of age with HF.

- Additionally, the total percentage of the population with HF is predicted to increase from **2.42% in 2012** to **2.97% in 2030**.
<table>
<thead>
<tr>
<th>Stage A</th>
<th>Stage B</th>
<th>Stage C</th>
<th>Stage D</th>
</tr>
</thead>
<tbody>
<tr>
<td>At high risk for heart failure but without structural changes or symptoms</td>
<td>Structural heart disease but without signs or symptoms of heart failure</td>
<td>Structural heart disease with prior or current symptoms of heart failure</td>
<td>Refractory heart failure including specialized interventions</td>
</tr>
</tbody>
</table>

**NYHA Classes**

**Class I**
- No limitation in ordinary physical activity

**Class II**
- Slight limitation during ordinary activity

**Class III**
- Marked limitation in activity due to symptoms
- Symptoms even while at rest

**Class IV**
Transition to Advanced Heart Failure:
- Oral therapies failing
- A time for many major decisions
- Consider MCS and/or transplantation, if eligible
- Consider inversion of care plan to one dominated by a palliative approach, which may involve formal hospice

Advanced Heart Failure Mortality at 1 Year

Mortality expectation

- AIDS
- leukemia
- lung cancer
- Pancreatic CA
- End-stage heart failure with optimal medical management

Lee et al. JAMA 2003 290(19)
Impact of recurrent heart failure hospitalization on mortality
GOALS OF HEART FAILURE MANAGEMENT

- Improve symptoms and quality of life
  - Relieve circulatory congestion
  - Increase tissue perfusion

- Prolong life by slowing disease progression
  - Reduce vasoconstriction
  - Inhibit activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system
  - Inhibit progressive enlargement or remodeling of the left ventricle
Eras of Heart Failure Therapy

**PAST**
- Edema weight
- Exercise Tolerance

**PRESENT**
- Morbidity and mortality

**FUTURE**
- Heart Transplant

**Cardiorenal**
- Diuretics
- Digitalis

**Hemodynamic**
- Vasodilator
- Inotropes

**Neurohormonal**
- ACEI
- BB
- ARBs
- MRA
- HDZ/Nitrates

**Biomechanical**
- ICDs
- CRT
- LVAD
- Stem cells

**Personalized**
- Genomics
- Proteomics
- Epigenetics
- Xenotransplant
# MEDICAL THERAPY OF HEART FAILURE

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Medication</th>
<th>Population (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOLVD</td>
<td>1991-2</td>
<td>enalapril</td>
<td>N=6797</td>
</tr>
<tr>
<td>MERIT-HF</td>
<td>1999</td>
<td>metoprolol</td>
<td>N=3991</td>
</tr>
<tr>
<td>RALES</td>
<td>1999</td>
<td>spironolactone</td>
<td>N=1663</td>
</tr>
<tr>
<td>Val-HeFT</td>
<td>2001</td>
<td>valsartan</td>
<td>N=5010</td>
</tr>
<tr>
<td>COPERNICUS</td>
<td>2003</td>
<td>carvedilol</td>
<td>N=2289</td>
</tr>
<tr>
<td>CHARM-Alternative</td>
<td>2011</td>
<td>candesartan</td>
<td>N=2028</td>
</tr>
<tr>
<td>EMPHASIS-HF</td>
<td>2011</td>
<td>eplerenone</td>
<td>N=2737</td>
</tr>
<tr>
<td>PARADIGM-HF</td>
<td>2014</td>
<td>sacubitril/valsartan</td>
<td>N=8442</td>
</tr>
</tbody>
</table>
Drugs That Reduce Mortality in Heart Failure With Reduced Ejection Fraction

- Angiotensin receptor blocker
- ACE inhibitor
- Beta blocker
- Mineralocorticoid receptor antagonist

% Decrease in Mortality

- 0%
- 10%
- 20%
- 30%
- 40%
- Drugs that inhibit the renin-angiotensin system have modest effects on survival

Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF
MEDICAL THERAPY OF HEART FAILURE

Updates

2019 DAPA-HF

2019 DAPA-HF TRIAL
Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction
Randomized, parallel group, placebo-controlled trial

Objective: To evaluate dapagliflozin (a sodium-glucose cotransporter 2 [SGLT2] inhibitor) compared with placebo among patients with heart failure and a reduced ejection fraction (HFrEF).
Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies on All Cause Mortality

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>2 Year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>35.0%</td>
</tr>
<tr>
<td>ARNI (vs imputed placebo)</td>
<td>↓ 28%</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>↓ 35%</td>
</tr>
<tr>
<td>Aldosterone Ant</td>
<td>↓ 30%</td>
</tr>
<tr>
<td>SGLT2 inhibitor</td>
<td>↓ 17%</td>
</tr>
</tbody>
</table>

Cumulative risk reduction in mortality if all evidence-based medical therapies are used: Relative risk reduction 72.9%, Absolute risk reduction: 25.5%, NNT = 3.9

PROGRESSION OF HEART FAILURE

"STABLE HF"  CARDIOGENIC SHOCK

Transition to Advanced Heart Failure:
- Oral therapies failing
- A time for many major decisions
- Consider MCS and/or transplantation, if eligible
- Consider inversion of care plan to one dominated by a palliative approach, which may involve formal hospice

Advanced Heart Failure/Cardiogenic Shock

Clinical criteria

• Hypotension:
  • Systolic blood pressure (SBP) less than 90 mm Hg for at least 30 minutes or Need for supportive measures to maintain an SBP greater than or equal to 90 mm Hg
• End-organ hypo perfusion:
  • Cool extremities or
  • Urine output less than 30 mL/h and
  • Heart rate greater than 60 beats/min

Hemodynamic criteria

• Cardiac index less than or equal to 2.2 L/min/m² and
• Pulmonary capillary wedge pressure greater than or equal to 15 mm Hg
Management Pathways

Advanced Heart Failure

Palliative care/Hospice

Heart Transplant

Left Ventricular Assist Device Support

LVAD Destination Therapy (DT)

LVAD Bridge to Transplant (BTT)

Weeks
Years
Decade(s)
Survival
Life’s defining moment: Christiaan Barnard and the first human heart transplant

David K.C. Cooper, MD, PhD

From the Xenotransplantation Program, Department of Surgery, University of Alabama at Birmingham, Birmingham, Alabama, USA.
The prevalence of heart failure continues to grow, but the number of transplants has remained limited\textsuperscript{1,2}

\textbf{NUMBER OF HEART TRANSPLANTS REPORTED PER YEAR\textsuperscript{1}}

SURVIVAL WITH HEART TRANSPLANT

Year of transplant:
- 1982-1991 (N=21,478)
- 1992-2001 (N=40,077)
- 2002-2008 (N=26,039)
- 2009-6/2015 (N=26,164)

Median survival (years):
- 1982-1991 8.6
- 1992-2001 10.5
- 2002-2008 12.2
- 2009-2015 NA

All pair-wise comparisons significant at p < 0.05
Transplant Listing Candidacy

CONSIDERATIONS:

- Age: <70 years; not absolute
- Cancer free >5 years
- Obesity: BMI ≤35 kg/m²
- Severity of other medical comorbidities
  - Renal Function (Cr <1.8 mg/dL) or dual organ transplant....
  - Cirrhosis (cardiac or otherwise)
- Functional status
- Nutritional status
- Diabetes control (HgA₁C <7.5)
- COPD
Transplant Listing Candidacy

• Social:
  • No substance abuse: includes THC and ETOH (6 months tox free)
  • No tobacco abuse: 6 months free
  • Good family support system
• $$: can they afford meds???
• Adherence to medical follow-up

HIGHLY Selected Patients
Transplantation is considered the gold standard, but the supply of donor hearts is limited\(^1\),\(^2\)

At least \(\boxed{25,000}\) appropriate candidates for advanced therapies\(^1\)

\(\sim 3000\) heart transplants per year\(^2\)

Artificial Heart Keeping Man Alive

DOCTORS SAY PATIENT, 65, ‘LOOKS GOOD’

MECHANICAL HEART INSTALLED — Dr. Michael DeBakey, noted heart surgeon, gets ready to connect the mechanical heart to his patient, Marcel L. Delnyder, at Methodist Hospital in Houston today. Assisting surgeons are left unidentified.

APRIL 21, 1966
Ventricular Assist Device (VAD)

A mechanical circulatory device used to partially or completely replace the function of either the left ventricle (LVAD); the right ventricle (RVAD); or both ventricles (BiVAD)

**Long-Term VAD**
- **DURABLE**
- Implanted surgically with the intention of support for months to years

**Short-Term VAD**
- **Temporary**
- Utilized for urgent/emergent support over the course of days to weeks
Landmark events in the development of left ventricular assist devices

1932: DeBakey develops a roller pump
1953: Gibbon heart-lung machine successfully used during an atrial septal defect repair
1963: Liotta and Crawford implant the first LVAD
1967: Barnard performs the first heart transplant
1968: Shumway performs the first heart transplant in the United States
1969: Cooley implants the first artificial heart as a bridge to transplant
1984: DeVries implants the Jarvik7 artificial heart
1994: US FDA approves the LVAD as a bridge to transplant
2001: REMATCH trial results published
2010: US FDA approves the HeartMate III for destination therapy
2012: US FDA approves the HeartWare HVAD as a bridge to transplant
2014: Momentum 3 trial of the HeartMate III begins (currently enrolling patients)
2017: FDA Approves HMIII for BTT
Getting bigger by getting smaller

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Surgical</th>
<th>Minimally Invasive</th>
<th>Catheter Delivery System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow</td>
<td>10 L/min</td>
<td>7 L/min</td>
<td>3 L/min</td>
</tr>
<tr>
<td>Patient Class</td>
<td>Late Class IV</td>
<td>Class III &amp; IV</td>
<td>Class III</td>
</tr>
<tr>
<td>Treatable Popp.</td>
<td>100,000</td>
<td>360,000</td>
<td>1,000,000</td>
</tr>
<tr>
<td>Current status</td>
<td>IDE</td>
<td>Preclinical studies</td>
<td>Prototype and exploratory</td>
</tr>
</tbody>
</table>
LVAD Evolution

- Miniaturization
- Durability

Pulsatile Technology

1st Generation

Continuous Flow Technology
Axial Design

2nd Generation

Continuous Flow Technology
Centrifugal Design

3rd Generation

FDA Approved
BTT 2008
DT 2010

Bearings with stator

FDA Approved
BTT 1998
DT 2002

Bearings

Bearingless with magnetic levitation
Durable MCS

Bridge to Transplantation (BTT)
• Patient is approved and currently listed for transplant
• NYHA IV
• Failed maximized medical therapy

Destination Therapy (DT)
• Not a heart transplant candidate
• NYHA IV
• LVEF <25%
• Maximized medical therapy >45 of 60 days; IABP for 7 days; OR inotropic support for 14 days
• Functional limitation with a peak oxygen consumption of less than or equal to 14 ml/kg/min

http://www.cms.gov/medicare-coverage-database
REMATCH
Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure

- Randomized clinical trial
  - Optimal medical therapy vs pulsatile flow LVAD
- Nontransplant candidates (n = 129)
  - EF ≤ 25%
  - Peak VO2 < 12 mL/kg/min
  - Or continuous infusion inotropes
- FDA approval for XVE as destination therapy

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Why LVAD use has increased?

• Organ donor shortage with rising HF prevalence
• Improved survival on the transplant waiting list
• In selected patients (elderly, high risk transplants), LVAD is preferable to transplant to better utilize “limited resource” of donor organs
• Destination Therapy
Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633

Bridge to Transplant Listed and Destination Therapy by Era (n=12150)

<table>
<thead>
<tr>
<th>Device Strategy</th>
<th>% Survival post implant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>BTT (2008-2012)</td>
<td>1922</td>
</tr>
<tr>
<td>BTT (2013-2016)</td>
<td>2839</td>
</tr>
<tr>
<td>DT (2008-2012)</td>
<td>2317</td>
</tr>
<tr>
<td>DT (2013-2016)</td>
<td>5072</td>
</tr>
</tbody>
</table>

P(overall) < .0001
P(BTT v DT) 2006-2012< .0001
P(BTT v DT) 2013-2016< .0001
Home Inotropic support

- Palliative Care- comfort
- Bridge to decision/Therapy (MCS, Transplant)
When to Refer

Outpatients:
- ≥2 admissions for CHF in a year and LVEF <25%
- Abnormal labs: ↑Cr ↓NA
- Inability to titrate CHF Meds due to hypotension
- Escalating diuretic needs (>80 mg lasix QD) or need for primer
- >1 ICD discharge for VT in a year
When to Refer

**Inpatients:**

- End organ dysfunction:
- ↑ALT, ↑Bili, ↑Cr, ↑INR off warfarin
- Need for ventilator or balloon pump support
- Need for:
  - ≥ inotropes
  - Vasopressor
- Low EF and poor surgical candidate: LVEF ≤25% with CAD, dilated LV (LViDd >65 mm), RV dysfunction, or pulmonary HTN
**I NEED HELP**

- **I** – Inotropes
- **N** – NYHA IIIB/IV or Persistently elevated natriuretic peptide
- **E** – End Organ Dysfunction
- **E** – EF < 35%
- **D** – Defibrillator shocks
- **H** – Hospitalization > 1
- **E** – Edema despite escalating diuretics
- **L** – Low BP, High HR
- **P** – Prognostic medication, progressive intolerance or down-titration of GDMT
TRIGGERS FOR HF PATIENT REFERRAL TO HF PROGRAM (OR SPECIALIST)

- New onset HF
- Chronic HF with high risk features
- To assist with managing guideline directed medical therapy (GDMT)
- Persistently reduced LVEF (< 35%) despite GDMT for > 3 months
- Need 2nd opinion
- Annual review for established HF patients with advanced disease
- Participation in a clinical trial

10 Principles for Successful Treatment of Heart Failure

**How to implement GDMT...**

I. Initiate & Switch
   Treatment algorithm for guideline-directed medical therapy including novel therapies (Figure 2 and 3)

II. Titration
   Target doses of select guideline-directed heart failure therapy (Tables 1, 2, 3, 4, 5)
   Considerations for monitoring

**How to address challenges with...**

III. Referral
   Triggers for referral to HF specialist (Table 6)

IV. Care Coordination
   Essential skills for a HF team (Table 7)
   Infrastructure for team-based HF care (Table 8)

V. Adherence
   Causes of non-adherence (Table 9)
   Interventions for adherence (Table 10, 11)

VI. Specific Patient Cohorts
   Evidence based recommendations and assessment of risk for special cohorts:
   African Americans; older adults; frail (Table 12)

VII. Cost of Care
   Strategies to reduce cost (Table 13)
   Helpful information for completion of prior authorization forms (Table 14)

**How to manage...**

VIII. Increasing Complexity
   Ten pathophysiologic targets in HFrEF and treatments (Table 15)
   Ten principles and actions to guide optimal therapy

IX. Comorbidities
   Common cardiac and non-cardiac comorbidities with suggested actions (Table 16)

X. Palliative/Hospice Care
   Seven principles and actions to consider regarding palliative care

2017 ACCF/AHA Heart Failure Guidelines
Summary

• The management of heart failure is a dynamic process that requires frequent re-evaluation

• MCS and Transplant have shown to improve mortality rates AND quality of life

• EARLY Referral is the key!