Advances in Heart Failure Therapy

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Disclosure

• Speakers bureau
  – None
• Funded research to our program
  – Medtronic, Guidant, ACORN, Resmed
  – Novartis, Fujiwara, Roche, celladon etc…
  – Thoratec
  – Heartware

Today’s Agenda

Background
  – We will be discussing SYSTOLIC heart failure: HFrEF
  – Evaluation for reversible causes
  – How to tell a patient is failing
• Chronic systolic heart failure
  – Current therapies
  – New Therapies
    • Medical
    • Device
    • Clinical trials
• Acute systolic heart failure
  – Current and new therapies
  – Heart transplant and mechanical circulatory support
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Etiology of Cardiomyopathy

- Abnormal loading conditions
  - Valvular disease
  - Hypertension
  - Shunts
- Toxins
  - Chemotherapeutics
  - Cohlbiurea metal
  - Alcohol
- Genetic
  - Familial
  - Muscular dystrophies
  - Mitochondrial disorders
  - Hypertrophic
  - ARVD
- Insults
  - Ischemia
  - Tachycardia
  - High PVC burden
  - Viral
  - Thyroid disease
- Unclear etiology
  - Peripartum
  - Idiopathic
  - HIV
- Infiltrative
  - Hemochromatosis
  - Sarcoidosis
  - Amyloid

Cardiomyopathy
evaluate for reversibility

- Alcohol intake?
  - In persons who consumed 70 g of ethanol (or the equivalent of 7 oz of whiskey, 20 oz of wine, or 72 oz of beer [ie, six 12-oz cans]) per day for 20 years, 36% had an abnormal ejection fraction.
- Tachycardia mediated
- Asynchrony
  - PVC-induced (≥ 10%)
  - BBB
  - RV pacing
- Ischemia
- Valvular disease
- Consider RV biopsy

**Cardiomyopathy**

**evaluate for reversibility**

- When to perform endomyocardial biopsy

Think about myocarditis with arrhythmias, + troponin

Gotsman & Keren: Fulminant lymphocytic myocarditis vs giant cell myocarditis. ESCARDIO.org Oct 2008

Yeglee N et al: Value of MRI in patients with a clinical suspicion of acute myocarditis. EUR RAD 2007;17:221

- Lymphocytic myocarditis
- Giant Cell Myocarditis

Kandolin R et al: Circ Arrhythm Electrophysiol 2011;4:303-309

Think Sarcoid with CHF, arrhythmias

**Cardiomyopathy**

**evaluate for reversibility**

- When to perform endomyocardial biopsy

Kandolin R et al. Circ Arrhythm Electrophysiol 2011;4:303-309

**Therapy For Chronic Systolic Heart Failure**

- Diminishing Returns with Vasodilators & Neurohormonal Antagonists in HF

- EVEREST: Tolvaptan vasopressin antagonist
- PreRELAX-AHF: Tolvaptan and vasopressin antagonist
- TRIDENT-1: Tolvaptan and vasopressin antagonist
- Tolvaptan: ADH antagonist
- Term: vasopressin receptor antagonist

And Hijacked from Dr. Ken Margulies and then further modified
**VASODILATOR THERAPY IN CHF**

*Highlights of Major Trials*

- **1986 - VHeFT I**: Survival benefit for Hydralazine plus Isosorbide in NYHA Class II - III CHF
- **1987 - CONSENSUS I**: Survival benefit for Lisinopril in NYHA Class IV CHF
- **1991 - SOLVD Treatment Trial**: Survival benefit for Lisinopril in NYHA Class II - III CHF
- **1991 - AHeFT II**: Better survival with Lisinopril than Hydralazine plus Isosorbide in NYHA II - III CHF
- **1992 - SOLVD Prevention Trial**: Reduced CHF progression and deaths with Lisinopril in NYHA Class I - II CHF
- **1992 - SAVE Study**: Better survival and reduced CHF and ischemic events with Captopril after myocardial infarction with LVD
- **2004 - AHeFT**: Survival benefit with BIDIL in AA who had NYHA III/IV symptoms despite ACE/BB

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**Early B-Blocker Trials Established:**

- The addition of
  - Metoprolol XL - MERIT HF (3991)
  - Bisoprolol - CIBIS II (2647)
  - Carvedilol - US Carvedilol (1094)
- To standard therapy (90% on ACE-I) in stable mild-moderate (II/III) CHF
  - Resulted in;
    - Decrease in mortality
    - Decrease in SCD and progressive heart failure
    - Improvement in NYHA functional class
    - Decrease in Hospitalizations

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**B-Blockers**

- **Sicker Patient NYHA III & IV**
- **When is earliest benefit seen?**
- **Does dose matter?**

- **CAPRICORN**
  - 1959 AMI
  - 23% reduc all c. mort
  - 26% reduc sudden d
  - 41% reduc non-fatal MI
  - Significantly less wd for SEs
  - In carvedilol group

- **MOCHA**
  - 345 mild-moderate HF
  - Significant linear response for dose related
  - Change in EF, hospitalizations & trend
  - mortality

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**Copernicus**

- 2289 Severe HF
- 35% reduc all c. mort
- 25% reduc death & hosp
- Significantly less wd for SEs
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Carvedilol Dose-Response Trial (MOCHA): Effect on Ejection Fraction and Morbidity

Changes in LVEF

Cardiovascular hospitalizations

Patients requiring diuretics, ACE inhibitors, a digoxin, follow-up duration 6 months; placebo (n=84), carvedilol (n=261).

Adapted from Bristow et al., 1996.

P<.01 vs placebo

ARBs

ELITE II

Lisinopril 30 mg QD vs Capoten 50 mg TID  
No differences in mortality, well tolerated  
Pitt et al. Lancet 2000;355:1582-1587

Val HeFT

Valsartan 160 mg BID vs placebo  
No difference in mortality  
Significant decrease in morbidity & mortality  
Cohn et al. NEJM 2001;345:1667-75

CHARM

Candesartan 24 mg QD vs Placebo all on ACE-I  
Significant decrease in CVd and HF admit  
McMurray The LANCET 2003:362:767

Aldosterone Inhibitors

RALES Trial

- 1663 NYHA III-IV  
- 25 mg Aldactone vs Placebo  
- 30% reduction in death  
  - Progressive HF  
  - SCD  
- 35% reduction in hospitalization  
- Significant improvement in NYHA functional class  
Pitt et al. NEJM 1999;341:709

EMPHASIS Trial:  
N=2737 with mild HF EF < 35%  
Improvement with Epleranone  
Zannad NEJM 2011;364:11

EPHESUS Trial

- 6632 pts 3-14 d after AMI EF < 40%  
  - AND sign of HF  
  - Or DM with or without sign of HF  
- 50 mgQD Eplerenone vs placebo  
- Significant reduction in:
  - Death 14 % v 17%  
  - CVd/hosp 27% v 30%  
  - SCD 4.9% vs 6%  
Pitt NEJM 2003;348:1309
Take Away Points

- **ACE-Inhibitors** are still first line therapy
- **ARBs** is as effective if ACE intolerant, the addition of ARB to ACE therapy may be done without harm, maybe some benefit, but close watch of potassium and renal function
- **Beta Blockers**: dose matters, try and achieve target doses, even at the cost of vasodilator dose
  - We are using **aldosterone inhibitors** earlier, they are becoming also part of the mainstay of therapy
    - Caveat: compliance, Scr < 2.5 and K < 5

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The Frequent Flyer

- Non Compliant
- Undereducated
- Undertreated
- The Truly Medically Refractory

- Solutions to Common Problems
- Inotropes
- MCS
- Transplant

- The keys:
  - Know WHO to intervene on
  - Know WHAT to intervene with

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Solutions to common problems: continued symptomatic LV dysfunction despite ACEI or ARB and beta-blockade

- add ARB if on ACEI
- Remember to add Aldactone
- Don’t forget about digoxin
- evaluate for CRT/ICD
- Disease management: food/volume diary
- consider hydralazine-nitrate
“Advances in Therapy for Heart Failure”
Joyce W. Wald, D.O.

Clinical Events During Double-Blind Period (MIRACLE)

Favors CRT  Favors Control

<table>
<thead>
<tr>
<th>Event</th>
<th>CRT (n=228)</th>
<th>Control (n=225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death—all cause</td>
<td>P=0.40</td>
<td></td>
</tr>
<tr>
<td>Death/HF hosp/ HF IV</td>
<td>P=0.53</td>
<td></td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>P=0.02</td>
<td></td>
</tr>
<tr>
<td>HF IV med</td>
<td>P&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Abraham W, et.al. NEJM 2002;346:1845-53

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This patient is slipping!!!!
Consider advanced therapies!!!!

- Intolerance of beta-blockers
- Intolerance of ACEi/ARBs
- Recurrent hospitalizations
- Need for inotropes
- Hyponatremia
- Progressive renal insufficiency
- Increasing diuretic need
- Living in a smaller and smaller space

Despite compliance with background therapy and diet
If you can't get a patient to be compliant, advanced therapies is NOT the answer

Despite compliance with background therapy and diet
If you can't get a patient to be compliant, advanced therapies is NOT the answer
Circulatory-renal limitations to ACEI use.

Kittleson et al. JACC 2003;41:2029

BNP Concentration for the Prediction of Clinical Events

Death or Heart Failure Hospitalization


The Prognostic Value of Maximal Oxygen Consumption

* p<0.005 for VO2 ≤ 14 vs > 14

Circulation 1991;83:778-786
Watch this patient carefully!!!!

- Historical data
  - Ischemic etiology
  - Low output signs & symptoms
- ECG findings
  - Atrial fibrillation
  - Electrical instability
- Biologic parameters
  - Low serum sodium at baseline
  - BNP > 250-430 pg/ml after therapy
- Hemodynamic parameters
  - EF < 20%
  - Further prognosticated with exercise testing
  - Restrictive pattern on echocardiogram
  - PCWP > 16 after therapy
  - CI < 2.2 at baseline
- Intolerance of beta-blockers
- Intolerance of ACEi/ARBs
- Recurrent hospitalizations
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What's new in Chronic HF Therapy?

- NECTAR-HF
  - Chronic vagal stimulation
- CUPID
  - Intracoronary infusion of SRCA 2a
- CONFIRM-HF
  - Iron therapy symptomatic anemic HF patients
- PARADIGM-HF
  - Angiotensin receptor-neprilysin inhibitor-LCZ696
- SHIFT
  - Ivabradine
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N=96 2:1 randomization
6 month follow up
Although no change in LV end syst diam
Significantly improved quality of life
Need larger trials

N=39 patients received IC adenovirus associated sarcoplasmic reticulum Ca2+ ATPase vs placebo
@ 3 years decrease in:
- MI
- Worsening HF
- HF-related hospitalization
- VAD/OHT/Death
Results carried out at 3 years

N=459, increase QOL, increased smwt, decreased symptoms and trend to increased time to first rehospitalization

Iron therapy for the treatment of iron deficiency in chronic heart failure: intravenous or oral?

N=459, increase QOL, increased smwt, decreased symptoms and trend to increased time to first rehospitalization
Advances in Therapy for Heart Failure
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The NEW ENGLAND JOURNAL of MEDICINE

N = 8442 NYHA II-IV HF EF < 40% LCZ696 200 mg BID vs enalapril 10 mg bid.

Await FDA approval & long term OC Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides to Balance Maladaptive Mechanisms in Heart Failure

Swedberg Lancet 2010;376:875

N=6558 Ivabradine 7.5 mg bid vs placebo (OMM)

Ivabradine selectively inhibits the sinus node thereby decreasing myocardial oxygen demand without effecting inotropy or blood pressure.

Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

Inclusion Criteria Background Tx

• > 18 years
• Class II to IV NYHA heart failure
• Ischaemic/non-ischaemic aetiology
• LV systolic dysfunction (EF ≤ 35%)
• Heart rate > 70 bpm
• Sinus rhythm
• Documented hospital admission for worsening heart failure < 12 months

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Main reasons for not prescribing beta-blocker, %

- COPD
- Hypotension
- Asthma
- Cardiac decomp.
- Fatigue

Main reasons for not achieving beta-blocker target dose, %

- Hypotension
- Fatigue
- Dyspnea
- Dizziness
- Bradycardia

Ivabradine
Placebo
n=344
n=341

COPD
37
32

Hypotension
17
20

Asthma
10
11

Cardiac decomp.
7
9

Fatigue
5
6

Bradycardia
6
6

Mean heart rate reduction

70% of patients on ivabradine 7.5 mg bid

Ivabradine
Placebo
n=2099
n=2126

Hypotension
44
45

Fatigue
32
32

Dyspnea
14
14

Dizziness
13
12

Bradycardia
6
6

Background beta-blocker treatment


Conclusion

Ivabradine significantly reduces major risks associated with heart failure (f/u up to 23 months):

- 18% reduction in CV death or hospital admission for worsening HF
- 26% reduction in death from heart failure
- 26% reduction in hospital admission for worsening heart failure

Benefits are apparent early (within 3 months), are consistent in predefined subgroups, and have been demonstrated on top of recommended therapy

Treatment is well tolerated

FDA

- On April 15, 2015 the FDA approved Ivabradine in the US
  - “To reduce the risk of heart failure hospitalization”
  - LVEF less than 35%
  - Heart rate above 70 on maximally tolerated beta blockade
- We await final labeling and launch of the drug

Take Away Points

Vagal nerve stimulation did not improve markers of remodeling, but did improve symptoms, more to come

- IV iron is beneficial in symptomatic HF patients, stay tuned for PO iron
- Intracoronary infusion of AAV1/SERCA2a in patients with advanced heart failure, positive signals of cardiovascular events which persist for years.
  - No safety concerns were noted during the 3-year follow-up.
  - Larger scale CUPID 2 was negative:
    - Correct carrier AAV1 vs AAV9
    - Correct molecule to effect cell function? S100A1

Take away points (cont’d)

- LCZ696: angiotensin-neprilysin inhibitor reveals significant reduction in cardiovascular event compared to ACE-I
  - Await FDA approval
- Ivabradine: SA node inhibitor leads to a significant reduction in morbidity and mortality in patients with systolic HF
  - Heart rate above 70 on maximally tolerated beta blockade
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Severe Heart Failure
Recognizing the “Walking Wounded”

• Underperfused
  – Walk in, drive in, fly in
  – Obvious
    • Malignant arrhythmias
    • Low BP
  – Less Obvious (3T’s)
    • End organ underperfusion despite a normal BP
      – Talk: lethargic, breathless at the end of a sentence
      – Touch: cool, pulses are low, lips/ears turn blue when they lay back for exam
      – Testing:
        • Lactate
        • Tbili/LFTs
        • Scr/BUN

NYHA

INTERMACS Registry: Patient Profiles

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The Right Time for VAD Implantation
Key to Survival After Mechanical Circulatory Support

Operative Risk
Death

Too Late
Futile Implants
1-Year Survival 6%

Successful Implants
1-Year Survival 53 – 94%

Worsening of nutritional state, end-organ and RH function
Deaths related to pt selection not device malfunction

Acute Decompensated heart failure vs SHOCK

• ADHF::: congestion, possibly low output, quickly responsive to medical intervention
  – Medical therapy
• SHOCK::: unstable hemodynamics, end organ underperfusion
  – Device therapy
  • Ischemic shock AMI
  • Hemodynamic shock
  • Arrhythmic shock

Goals of Therapy:
Chronic Versus Acute HF

Long-Term Goals
Ventricular Remodeling
Vascular Remodeling
Prevent CHF Progression And Death

Short-Term Goals
Increased PCWP
Decreased CO

Neurohormonal Antagonists
Hemodynamic Agents
Relief of Symptoms
Stabilization of Organ Function

PCWP = pulmonary capillary wedge pressure.
RELAX-AHF and Pre RELAX-AHF Trials

N=1395

Conclusion: decreased 180 day mortality, markers of end organ damage (e.g. troponins) and markers of decongestion (BNP) were improved in the seralaxin groups. Ongoing RELAX-AHF2: approximately 6800 patients.

More About Congestion

The CHAMPION Trial Abraham LANCET 2011

Protocol: if PAP pressures elevated:
1) increase diuretics
2) increase vasodilators

Target Pressures:
SPAP: 15-35
DPAP: 8-20
mPAP: 10-25

Congestion: what’s new with diuresis?

Combination of Loop Diuretics With Thiazide-Type Diuretics in Heart Failure

Ferreira EJIM 2014
**Neseritide**

- **V-MAC Trial** (48 pts)
  - Placebo v IV NTG vs Nes 0.01
  - Efficacies in lowering PCWP, PAP & sxs

- **Efficacy Trial** (27 pts, RIL)
  - Placebo v 0.015 Nes v 0.03 Nes [X 6 h]
  - No diuretics
  - Significant decrease in PCWP and symptoms and increase in UO

- **Comparative Trial** 305 pts
  - Standard TX 0.015 + Nes [up to 7 d]
  - Improvement in global clinical status similar to ST

- **PRECEDENT Study** 345 pts (RIL)
  - DB (5) v 0.015 Nes v 0.03 Nes
  - DB proarrythmic
  - Nes no increase in arrhythmias, heart rate, despite greater decrease in BP

- **Sackner-Bernstein** (meta-analysis)
  - Mortality (Circ 2005)
  - Renal failure (JAMA 2006)

- **E. Braunwald Panel’s Report**
  - June 13, 2005
  - Serum creatinine increase > 0.5 mg/dl (VMAC)
    - Control 7% (5 days) 21% (30 days)
    - Neseritide 8% (5 days) 28% (30 days)
  - Mortality
    - Completed trials; trend increase in 30 d mortality
    - Approximately 1.3 HR, 30% increase
    - Confidence intervals around this ratio are wide
  - No increase in 180 day mortality

**Neseritide**

- **Braunwald Panel conclusions**
  - Conduct a large (several thousand subjects) trial of clinical outcomes to assess further benefits and risks of neseritide, compared to standard therapy in acute, decompensated heart failure and severe dyspnea

  - Current use
    - In hospital
    - Acutely decompensated Heart Failure
    - Dyspnea at rest
  - And should not be used
    - to replace diuretics
    - or as outpatient

- **ASCEND Trial**
  - N=7141 ADHF
  - Neseritide had no effect on renal function
  - Out to 30 days
  - Change in renal function is associated with 30 day mortality or HF rehospitalization

*Van Deursen CIRC 2014 130-958*
**Mechanical Fluid Removal**

Testani Sem in Dialysis 2014;27(3):231

**Inotropic Therapy**

in Patients With ADHF

- Routine use not indicated in short- or long-term setting (despite low EF)
- Rather, inotropes should only be used in patients with:
  - Cardiogenic shock ie: signs of end organ underperfusion
  - Decompensated patients refractory to diuretics
  - Short-term bridge to definitive treatment such as revascularization or cardiac transplantation
  - To optimize vasodilator therapy or add BB therapy


**Inotropes**

Digiom: improved QOL
DB: beta agonist
Milrinone: PDE inhibitor

Hasenfuss & Teerlink EHJ 2011
Heart Failure Studies

- **Human Heart Tissue Protocol (Kenneth Margulies, MD)**
  - To study heart tissue specimens in human heart failure. All patients listed for transplant or VAD are asked to participate.
  - As well as non-failing hearts that are not suitable for heart transplant:
    - 3 types of hearts:
      - Failed (evaluated at time of OHT)
      -Failed but rested (after LVAD support)
      - Non-failing heart
  - Dr. Margulies has assembled the largest biorepositories of human heart samples in the world

- **Samples**
  - Processed for study
  - With clinical data
  - Banked for future study

**Human Heart Tissue Protocol Findings**

- **Cellular Characteristics**
  - Potential for recovery
    - Tissue in end stage
      - SRCA depleted
    - After a period of rest
      - Some functional recovery at cellular level
      - But never to normal
  - Despite this, does NOT translate to clinical recovery
  - Features that fail to improve sufficiently with LVAD support alone suggest a role for therapeutic adjuvants:
    - Excess fibrosis \(\rightarrow\) Ang II and aldosterone antagonists
    - Too much decrease in LV Mass \(\rightarrow\) Clenbuterol
    - Residual insulin resistance \(\rightarrow\) GLP-1 agonist

Heart Failure Studies

- **observations**
  - Failed myocyte
    - Down regulation of B receptors
    - Deplete of SRCA 2a
  - **Recovery Plan**
    - Promoting growth of new cells?
    - Improving function of existing cells?
    - VAD as a platform

K Margulies, Biorepository, University of Pennsylvania
**Recovery**

- **Study Protocol**
  - De novo
    - Gene therapy
    - Stem cell therapy
  - LVAD platform
    - Clenbuterol
    - Stem cell
    - OMM
- **Planned**
  - Short duration of HF
  - Reversible insult
- **Surprise**
  - De novo

**CUPID Study**

**STOP-HF Study**

**CUPID Study**

**STOP-HF Study**

**Gene therapy**

**JY, RM, WG, JC**

**Stem cell therapy**

**NK, IV, RM, WG, JC**

**OMM**

**RESTAGE-HF**

**Clenbuterol**

**JB: VO2 43, 2 ½ y**

**Stem cell**

**NK, JY, RM, WG, JC**

**OMM**

**RESTAGE-HF**

**Planned**

- Short duration of HF
- Reversible insult

**Surprise**

**CHF**

**Joconde**

**OHT**

**VAD**

**Research**

**Hospice**

**Vasodilator Therapy**

**Ace-inhibitors & H/I**

**B-Blockers**

**ARBs**

**Research**

**Hospice**

**Inotropes**

**CHF**

**Devices**

**Heart Transplant Evaluation**

Evaluation process designed to answer the following:

- From a cardiac standpoint will patient feel better and/or live longer with transplant compared to other treatment options?
- Are there co-morbidities (medical, psych, social, financial) that make transplant unacceptably risky?
**Advanced Surgical Therapies:**
Heart Transplant or VAD Therapy

- Are they sick enough for Transplant/VAD?
  - Inotropes
  - Poor cardiac reserve
  - VO2 < 14
  - Despite OMM
  - Limitations are only Cardiac
  - Intractable arrhythmias

- Any other organs that limit life span?
  - Cancer
  - Diabetes
  - Lung disease
  - Pulmonary HTN
  - Liver disease
  - Renal disease

- Are they healthy enough to undergo surgery?
  - Malnourished
  - Too deconditioned
  - Liver failure
  - Do they have Social Support?

Relative age cut off for heart transplant is 65 yo
Age cut off for Heart Lung is 55 yo
Age cut off for heart liver or heart kidney is 60 yo

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**Heart Transplant vs LVAD/DT**
How to Choose?

- Are they sick enough for Transplant/VAD?
  - Inotropes
  - Poor cardiac reserve
  - VO2 < 14
  - Despite OMM
  - Limitations are only Cardiac
  - Intractable arrhythmias

- Age over 65
  - Concern for worsening co morbidities with immunosuppression
  - DM
  - Need to test compliance
    - recent smoking
    - recent non compliance
  - Need to test social support
  - Malignancy < 5 years (treated)

**BTT:** bridge to transplant  **DT:** destination therapy  **BTD:** bridge to decision  **BTI:** intent

---

**Limited Donor Pool**
How to Choose a Device?

- When to think about needing a device
  - End organ perfusion that is not improving despite medical hemodynamic therapy
    - Intropes
    - Hypotension
  - Ischemia with a large territory at risk
  - Hemodynamically unstable arrhythmia

- Temporary devices
  - Crash and burn
  - Unknown
  - Reversible insult

- More permanent devices
  - BTT, DT, Recovery

Temporary Devices

- IABP
- Tandem heart
- Impella 2.5, CP 5.0
- ECMO
- Centrimag

Future Temporary Devices

- Impella
  - 2.5 (current)
  - 3.5 (CP)
  - 5.0 (surgically placed)
  - RP (right sided support)
- Tandem heart
  - PROTEK duo (via RIJ: RA→PA)
Acute Myocardial Infarction & Shock

- 302 patients
  - Shock 2nd LV dysfunction
  - Complicating AMI
- Randomized
  - Revascularization (w/i 6 h)
  - Medical therapy

- Recommended
  - IABP
  - Lytics

6 mos mortality

Hochman SHOCK Trial JAMA 2006

Shock with Acute MI

Cheng EJH 2009

Permanent Mechanical Circulatory Support

1990's

2000

2010 and Beyond
Survival with DT by Preoperative Risk
Destination Therapy Registry 2002-2005, n=208

- Low: 94% (N=21)
- Medium: 74% (N=127)
- High: 31% (N=22)
- Very High: 8% (N=38)

Survival with DT by Preoperative Risk

Survival with DT by Preoperative Risk

Future Devices

Future Devices

Future Devices
Curves of downshifting risk.


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**Take away points**

**Congestion** is a target of therapy as well as a marker of outcome

- If patient remains congested despite OMM, they are at high risk for poor outcome w/o aggressive intervention
- IV diuretics: Continuous infusion is no better than bolus, but also not harmful
- Combination diuretics are safe but RQ close monitoring of labs
- Mechanical unloading (UF) may have earlier decongestion, but no definite improvement in outcomes (conflicting results)

**Inotropes** should not be used routinely for ADHF, however in select patients:

- End organ under perfusion during ADHF refractory to standard therapy (vasodilators, diuresis)
- Bridge to advanced therapy to maintain end organ function
- Exciting new molecules to help improve myocardial performance without the cost of increasing mortality

**Take away points (cont’d)**

**Neseritide** is safe and effective for decongestion, renal perfusion and optimization of hemodynamics—when used correctly

- Must be able to recognize the **walking wounded**
- Outcomes are better, no matter the therapy, if patients are recognized and referred early for advanced therapy
- The survival for **SHOCK** is still poor
  - Even contemporary data shows a 30 d mortality of 46%
  - **Temporary devices** for the acutely ill with MOF: impella and tandem heart have proven hemodynamically superior to IABP, however in small trials, this has not translated to improved 30 day mortality.
Conclusions

Chronic heart failure

- Ambulatory patients on medical therapy
  - BB therapy is important and dose matters
  - Aldosterone inhibitors are becoming a mainstay of therapy
  - Consider iron for symptomatic HF pts who are iron deficient
  - Ivabradine (if HR > 70 despite OMM) improved outcomes
    - FDA approval, await launch and
  - LCZ696: angiotensin neprilysin inhibitor: await FDA approval
  - Targeting congestion is important to patient outcomes
    - cardiomems PA monitoring
  - Target recovery: besides aggressive medical therapy,
    - cell therapy, gene therapy, mechanical support

- Acute decompensated heart failure
  - IV diuresis bolus = continuous, high dose better
  - Neseritide is safe but should be used selectively
  - Seralaxin may have a benefit RELAX-AHF 2 is underway

Conclusions (cont’d)

Advanced heart failure

- End organ under perfusion or severe symptoms despite maximal therapy
- Acutely ill, refractory to medical therapy
  - Temporary devices
    - IABP
    - Impella 2.5, CP, 5.0
    - Tandem heart, RP
    - ECMO
  - Permanent Platforms: better outcome with earlier tx
    - Heart transplant
    - Durable VADs (Mechanical Circulatory Support)
      - IDM II
      - Heart ware
      - with exciting new, smaller devices on the horizon

THANK YOU!!