Heart Failure Management

Objective: Describe recent advances

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I have the following financial relationships to disclose:

Consultant for: Abbott, Medtronic
Advisory Board: Abbott, Medtronic

I WILL be discussing off-label and investigational use of an ECG belt and the drugs: tafamadis & SGLT2i.

All $$$ donated to
Minneapolis Heart Institute Foundation
Outline

• Diagnostics

• Management
  – Readmissions
  – GDMT
  – EP devices
  – Advanced options

• What’s next
  – Valves
  – Amyloid
  – SGLT2i
  – HFpEF
Diagnostics

- Role of cardiac MRI
  - 16% of TAVR patients have ATTR-CA\textsuperscript{1}
  - Single-center study\textsuperscript{2} of 114 new HF of uncertain etiology:
    (a) 20% completely new dx
    (b) 48% changed clinical decision-making

- Radiolabeled plasma volume\textsuperscript{3}
  - Discrimination of risk of death or readmit <90d

\textsuperscript{1}Castaño A et al, Eur Heart J 2017.
\textsuperscript{3}Balderston JR et al, Am J Cardiol 2018.
Diagnostics

• Bone scintigraphy with technetium-labeling can detect myocardial ATTR\(^1\)
  – LR\(^+\): 7.0 [3.4-14.4]
  – LR\(^-\): 0.09 [0.06-0.14]
  – OR: 82 [43-153]

• Immune checkpoint inhibitors and cardiotoxicity\(^2\)

Are readmissions a sign of poor quality care?

*Figure 1. Comparison of Risk-Adjusted Hospital Readmission Rates and Mortality Rates 30 Days after an Index Admission for Heart Failure.*

The dashed lines indicate the upper and lower limits of the 95% confidence intervals, and the solid line indicates linear regression. Data are from the Centers for Medicare and Medicaid Services Hospital Compare public reporting database.¹  

WE OFFER 3 KINDS OF SERVICES
GOOD - RE-
ADMISSIONS - LOS
BUT YOU CAN PICK ONLY TWO
GOOD & CHEAP WON'T BE FAST
FAST & GOOD WON'T BE CHEAP
CHEAP & FAST WON'T BE GOOD
MORTALITY
CHAMPION trial

- 64 centers, 550 patients, NYHA III
- Wireless implantable hemodynamic monitor versus usual care
- 83 vs 120 admits for HR 0.7 (0.6-0.84, p<0.0001) with device

Implantable PA sensor in practice

- First consecutive 2000 implants with ≥ 6m F/U
- Older (69.7 vs 61.6 years)
- More women (40% vs 28%)
- More HFpEF (34% vs 22%)*


*EF only available in ~50% of 2000 patients*
Implantable PA Sensors and Cost

- US Medicare Claims Data of 1,114 patients with sensor implant
- 1020 HFH in 6m prior
- 381 HFH, 139 deaths, and 17 VAD/Tx in 6m after implant
- HR 0.55 [0.49-0.61]
- 6-month comprehensive HF cost reduction of $7,433/patient

Treatment of heart failure

- Congestion Management
- Neurohormonal Antagonists
- ICD ± CRT
- Advanced Options
Diuretics

• No long-term studies of diuretic therapy
• Meta-analysis showed reduced risk of death & worsening HF
• Other retrospective studies suggest increased mortality after chronic use of non-potassium sparing diuretics
• Consider referral if >2 mg/kg/day

Domanski M in JACC 2003
Domanski M in J Card Fail 2006
Ahmed A in Eur Heart J 2006
Eshaghian S in Am J Cardiol 2006
Practical tips on diuretics

• Fluid restriction
• Moderate restriction of daily salt intake ($\leq 2$ g)
• Avoid NSAIDs
• Institute & uptitrate ACEi, ARB, ARNI
• Give short-acting loop diuretic orally in several divided (and increasing) doses, bolus, or continuous IV administration
• Use sequential nephron blockade via combination loop diuretic and thiazide diuretic*
• Add aldosterone antagonist

GDMT

- Beta blockers
  - Carvedilol, Metoprolol succinate
  - Max titration
  - COPD rarely a contraindication
- Aldosterone antagonist
  - Switch to eplerenone if gynecomastia
- Vasodilators
  - A-HeFT trial for African-American patients
- Digoxin
  - No mortality benefit
- ACEi/ARB/ARNI
PARADIGM-HF

- Valsartan + neprilysin inhibitor sacubitril
- Significant improvement
- All subgroups (HF Hospitalization, CV Death) concordant


Clinical pearls: Hypotension, Diuresis, Do NOT overlap with ACEi

Electrical Therapy
ICD
CRT
Implantable electrical device therapy

• ICD (defibrillator)
  – LVEF ≤ 35% after >3 months of medical therapy
  – >90 days after revascularization
  – Reversible causes addressed
  – Life expectancy >1 year
  – Recent large WCD trial did not show benefit*

• Biventricular pacing (cardiac resynchronization)
  – LVEF ≤ 35%
  – NYHA II/III (some exceptions)
  – QRS > 150 ms (can consider some >120 ms)
  – LBBB, female, nonischemic favorable prognostic

ECG Belt for CRT Optimization?

Investigational

1. 17 anterior and 38 posterior torso electrodes record body surface potentials

2. The time at which electrical activation is first recorded is $t_0$

3. The time at which electrical activation is the steepest negative slope is measured

4. The time after $t_0$ at which a given electrode records activation is the local ventricular activation time (VAT)

5. Electrical heterogeneity is measured using the standard deviation of ventricular activation times (SDAT)

6. Isochronal body surface maps display the VAT data

Figure 1: Body surface mapping data interpretation schematic.

Bank A et al, HRS 2016
Patient Presentation

• 62 year old man, short of breath
• Presents to outside ED, collapses in triage
• Found to have saddle pulmonary embolism
• Treated with tPA
• Initially stabilizes, then deteriorates
• Epi 20, Levo 28, Neo 200, VPN 0.04
• BP 70/40, pH 6.8
• Transfers, VA-ECMO initiated
• Pulmonary thromboendarterectomy performed
Pubmed “ECMO”
LVAD outcomes continue to improve.

Mehra et al, NEJM 2018.

No. at Risk
Centrifugal-flow pump 190 161 141 122 111
Axial-flow pump 176 134 114 90 75

Hazard ratio, 0.46 (95% CI, 0.31–0.69)
P<0.001 by log-rank test

Months since Implantation
What’s next?

• HFpEF
• Valve
• Amyloid
• SGLT2i
“We are too much accustomed to attribute to a single cause that which is the product of several, and the majority of our controversies come from that.”
Phenotyping essential

• Need to match therapies with correct type
  – ALDO-HF (aldosterone receptor blockade tested early-stage without volume overload)
  – RELAX (tested PDE5i in patients with volume overload but not necessarily overt PH and RV dysfunction)
  – Ivabradine vs placebo in patients with exercise-induced elevations in LV filling pressures*
    • 61 patients randomized to ivabradine 5 mg bid or placebo for 7 days; significant improvement in exercise capacity (4.2±1.8 vs 5.7±1.9 METs, p=0.001)

• The 3 distinct groups had different:
  – Clinical characteristics
  – Cardiac structure/function
  – Invasive hemodynamics
  – Outcomes


**Exercise training**
- ACEi
- Ivabradine to slow HR?

**Volume overloaded**
- HFpEF
- Aldosterone antagonist
- Implantable PA pressure sensor
- Neprilisyn inhibition?

**Right heart failure**
- HFpEF
- Diuresis/ultrafiltration
- Midodrine for BP
- Address underlying causes of PH
- Pulmonary vasodilators?
Implantable PA sensor for HFpEF?

- PA pressure-guided therapy significantly reduced heart failure hospitalizations in HFpEF patients (EF > 40%)
- One of the few effective treatment strategy for this population of patients

IAS for HFpEF

Investigational

REDUCE LAP-HF trial
- 68 patients in phase 1 study, 21 centers
- Transcatheter interatrial shunt device (Corvia)
- EF >40%, Age >40, HFpEF symptoms despite therapy
- PCWP >15 at rest or >25 with exercise

- 52% had reduction of PCWP at rest, 58% reduction with exertion, and 39% met both
- REDUCE LAP II currently enrolling

Transcatheter MV Repair (COAPT)

- Moderate/Severe MR despite GDMT
- Randomized: Repair vs Not
- Efficacy: HF hospitalization within 24 months
- Safety: Freedom from device-related complications at 12 months
- 614 enrolled

Device Control

<table>
<thead>
<tr>
<th>Statistical Measure</th>
<th>Device</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAD/Tx</td>
<td>4.4%</td>
<td>9.5%</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.4%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Change KCCQ (12mo)</td>
<td>12.5</td>
<td>-3.6</td>
</tr>
<tr>
<td>Change 6mw (m, 12mo)</td>
<td>-2.2</td>
<td>-60</td>
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</tbody>
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Tafamidis for ATTR Amyloid

Multicenter, international, double-blind, placebo-controlled trial

- Randomly assigned 441 patients with ATTR amyloid to receive 80 mg/20 mg/placebo
- Lower all-cause mortality (29.5% vs 42.9%)
- Lower CV hosp (0.48/year vs 0.70/year)
- At month 30, lower rate of decline in 6MW
- Not yet available (as of late Sept ‘18)

Maurer MS et al, NEJM 2018.
Patient Population

1,299,915

SGLT2i?

Investigational for HF

Kosiborod M et al, presented at ACC 2017
https://www.acc.org/education-and-meetings/image-and-slide-gallery/media-detail?id=7f5d0c3c0a2343a3a04b16fc60a883fb
SGLT2i versus oral hypoglycemics

Heart Failure Hospitalizations

All-Cause Mortality

Kosaborod M et al, presented at ACC 2017
Thank you!

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