Integrating Heart Failure and Structural Cardiology

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Disclosure Information

Peter Eckman, MD

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.

All $$$ donated to
Minneapolis Heart Institute Foundation
77 year old man with exertional dyspnea

- Prior CAB, Parox AF (flutter ablation ‘13), HFP EF
- Sleeps a lot, can only walk 10-20 feet (>1 mile 6 months ago)
- Aortic stenosis – moderate vs severe?
- PFTs reassuring, OSA on CPAP (religiously)
- BP 132/60, HR 51
- Meds: Amlodipine 5, HCTZ 25, Losartan 100, Metoprolol 50 bid, ASA/Warfarin/Rosuvastatin
- Labs: Na 140, BUN 28, Cr 1.2, Hgb 12.8

77 year old man with exertional dyspnea

- Echo: LVEF 45-50%, grade 3 diastolic filling, elevated E/e;
- RV size normal, mild dysfunction
- Ao AVA 0.82, mean gradient 12, peak 2.2 m/s, DI 0.21
- Angiography: patent grafts
- AoV moderate stenosis
- RHC:
  - Baseline SBP 160 and PCWP 17
  - Arm exercise: SBP to 180 and PCWP to 27
HFpEF Management Framework

- Consider uncommon etiologies (constriction, restrictive disease, amyloid, etc)
- Phenotype (exercise-induced, PH, volume overload)
- Address pertinent comorbidities
  - CAD
  - Atrial fibrillation
  - Sleep disordered breathing
  - Anemia
  - Deconditioning/obesity
- Congestion management, including CardioMEMS, consider spironolactone
- Role of nitrates (NEAT-HFpEF found worse exercise)
- Consider clinical trials

CardioMEMS in HFrEF/HFpEF

Adamson PB et al, Circ Heart Failure 2014.
HFpEF

- Hallmark is effort intolerance
- Profound/brisk increase in LA pressure during exercise
- Lutembacher syndrome (1916)
  - Combination of mitral stenosis and secundum ASD
  - Originally described 1750 by Johann Friedrich Meckel, Sr.

HF Cardiologist on Valves

- Very common in HF patients (LV/RV/BiV)
- Outcomes with surgery in low LVEF poor
- Not infrequent to see patient who had MV surgery ~6-12 months ago who now needs a VAD/Transplant
- Meds will often make it better
  - Decongest, vasodilate, treat HF
- Spend more time on:
  - BB, ACEI/ARB/ARNI, AA, ICD, CRT, etc

Medical Management of TR

• Preload
  – Can be hard to optimize volume status – what is goal? How to measure with pulsatile JVP?
• Afterload
  – Pulmonary vasodilators expensive and off-label
• Contractility
  – Digoxin?
• Consider addressing anatomy/mechanical

Outcomes of Isolated TR

• 353 patients with isolated TR
• Age 70, 33% male, EF 63%, all with RVSP <50, no other valve disease >mild, no pacer/ICD wires
• Severe by ERO ≥ 40 mm²
• Difficult to study due to confounders, PH, left-sided disease
• Independent or surrogate?
• Hard to assess, define severe TR
• Limited indications for isolated surgery, timing??

Topilsky Y et al JACC: Cardiovasc Imag 2014
Survival by EROA in TR

Topilsky Y et al JACC: Cardiovasc Imag 2014

No difference if AF/SR
No difference if symptoms/not

TR associated with increase mortality independent of RVP and RV failure

- Systematic review of 70 studies with 32,601 patients
- Mean follow-up 3.2±2.1 years
- Mod/sev associated with mortality risk 1.95 [1.75-2.17]

TR in HFrEF – Long Term Outcomes

- 3,943 patients
- All with LVEF <35%
- Age 69±14, 74% male
- Median follow-up:
  - 8.1 years
- Excluded:
  - AS/AI > Moderate
  - Mitral stenosis
  - Valve replaced

<table>
<thead>
<tr>
<th>Severity</th>
<th>%</th>
<th>Median Survival (y)</th>
</tr>
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<tbody>
<tr>
<td>Non-signif</td>
<td>70%</td>
<td>4.9</td>
</tr>
<tr>
<td>Moderate</td>
<td>24%</td>
<td>2.3</td>
</tr>
<tr>
<td>Severe</td>
<td>6%</td>
<td>1.6</td>
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</tbody>
</table>

Timing of surgical referral for ITVR

- All ITVS in France 2013-2014 (84 repair 157 replacements)
- 61±16 years old, 53% women, 10% CAD, 26% CHF, 20% endocarditis, 10% renal failure
- In-hospital mortality 10%
- Major complications 19% (death, dialysis, MV with ECMO)
- Hospitalization 26±40 days
- *Do transcatheter options change timing?*


The 2 times to fix the tricuspid valve

Too early

Too late
Address TR with Left-sided surgery?

Meta-analysis: 15 studies, 2840 patients

Cardiac Death

- 2000-2010: 1,294 with mod/sev MR
- Median age 77, 42% with LVEF <50%
- Mean EROA (available in n=822) 0.25 cm²
- 51% CV death with RR 2.23 [2.06-2.41]
- 64% with HF at 5 years
- Surgery in 15% (75% repairs) but only 5% of those with LVEF <50%
- Only ~25% with class I surgical indications had surgery

Survival after isolated mod/sev MR


Management/Outcomes of mod/sev FMR with severe HFrEF

- Mod/Severe FMR and severe HFrEF (EF ≤30% or LVEF >55 mm)
- 1,441 patients, median follow-up 4.7 years
- Median age 64, 39% women
- Therapy:
  - Medical therapy 75%
  - PCI 8%
  - CAB 6%
  - CAB/MV 7%
  - MV surgery alone 4%
  - Repair 143/151

Samad Z et al Eur Heart J 2015

**ACC/AHA Guidelines**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
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<tr>
<td>Medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR (stage D) and LVEF less than 60% in whom surgery is not contemplated</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Vasodilator therapy is not indicated for normotensive asymptomatic patients with chronic primary MR (stages B and C1) and normal systolic LV function</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
</tbody>
</table>
Does medical therapy alter FMR?

- Extent of FMR at baseline and 50 months in 163 consecutive HFrEF patients
  - 31% with severe MR at baseline, 38% of those improved to nonsevere
  - 18% nonsevere developed severe despite GDMT
- Sustained severe FMR or worsening FMR had OR 2.5 [CI 1.5-4.3] for major AE’s
- LBBB and diabetes predictive of deterioration of MR
Evolution of MR in HFrEF

- 249 patients with HFrEF
- 19% had progression of MR
- Progression predicted mortality
  - Uni: HR 2.33 [1.34-4.08], p=0.003
  - Multi: HR 2.48 [1.40-4.39], p=0.002
- Regression of MR was NOT associated with benefit


Valsartan/sacubitril and FMR

- 118 HF with FMR randomized to valsartan/sacubitril vs valsartan
- Primary endpoint at 12 months change in EROA
- EROA -0.058±0.095 vs -0.018±0.105 cm² p=0.032
- Regurg Vol: -7.3 [-12.6 to -1.9] p=0.009

Kang DH et al Circulation 2018
- ATTEND registry – 4842 patients with ADHF
- Association of FMR and all-cause mortality and HF readmission, stratified by HFpEF/HFrEF

![Figure 3](image_url)

Kajimoto K et al Eur J Heart Fail 2016

**Remodeling after MitraClip**

![Graphs showing changes in LVEF, LVEDV, LA Vol, and LVESV with MitraClip](image_url)

One year remodeling (FMR and HFrEF)

- 41 patients
- Rx w/ MitraClip
- Median age: 77
- LVEF 33±3%
- CI 2.0±0.2
- LVESD 50±2
- Mean PA 37±3.1

LVEF ≤ 30%


Do transcatheter therapies impact neurohormones?

- 21 patients with mR undergoing MitrClip
- Noradrenaline level – no change
- Sympathetic nerve activity – MSNA burst frequency from 130±78/min to 74±21/min

What about bivalvular FR?

- 1021 consecutive HFrEF patients
  - Median 62y, 80% male
  - 41% NYHA III and 17% NYHA IV
  - 34% CRT
- 32% had moderate/severe BVFR
  - 45% FMR, 35% FTR (in general)
- Severe BVFR associated with excess mortality, adverse symptoms, adverse remodeling and NH activation
- Severe BVFR associated with excess mortality, independent of clinical and echo parameters, GDMT, and NH activation
- BVFR conveys deleterious impact of global regurgitation load on failing heart

Thank you!

Peter.Eckman@allina.com
The Intersection of Heart Failure and Structural Heart Disease

Paul Sorajja, MD
Roger L. and Lynn C. Headrick Family Chair
Valve Science Center
Minneapolis Heart Institute Foundation
Abbott Northwestern Hospital

Disclosures

• **Consulting or Advisory Board:** Abbott Structural, Admedus, Boston Scientific, Edwards Lifesciences, Medtronic, Gore
• **Research:** Abbott Structural, Boston Scientific, Edwards Lifesciences, Medtronic
• **Speaking:** Abbott Structural, Boston Scientific, Edwards Lifesciences, Medtronic
• **National P.I.:** Tendyne in MAC, Alt-FLOW, TRILUMINATE II Pivotal
Key Points
Heart Failure and Structural Heart Disease

• Heart failure and SHD beget each other

• SHD therapy improves symptoms and saves lives even in late HF stages

• MHI and MHIF is leading the way for innovative trials in these patients, and we need your help!
A Different Paradigm

Structural Heart Disease → Heart Failure

Aortic Stenosis Pathophysiology
A One-way Highway

Pressure hypertrophy

AVR, curative?
Aortic Stenosis and Heart Failure
Any Myocardial Disease is Adverse

11,292 TAVR patients in TVT

Baron SJ et al. J Am Coll Cardiol 2016;67:2349-68

Aortic Stenosis and Heart Failure
LVEF <50% and Moderate AS

Poor Survival
4 year death = 36%

TAVR Unload Study
800 patients
Moderate AS
LVEF <50%
TAVR vs. GDMT

Van Gils et al., J Am Coll Cardiol 2017;69:2383-92
Dweck et al., J Am Coll Cardiol 2011
Aortic Stenosis and Heart Failure
More Than Just EF

Cavalcante JL, JACC Cardio Intv 2016;9:399-405

Mitral Regurgitation
Classical Dogma of Pathophysiology

“EF drops and patients can do worse.”
Modern Experiences with TMVR

Severe LV dysfunction, no MR

EF = 30%
EF = 20%

Transcatheter MVR

First 100 Tendyne Patients

No procedural deaths
30-day O/E = 0.76
87% NYHA I/II at 1-yr
KCCQ = +22 pts

Now in SUMMIT, U.S. pivotal trial

Sorajja P, et al. J Am Coll Cardiol [In press]
Severe Mitral Annular Calcification
Tendyne Early Feasibility Study

Nat’l Principal Investigators: Paul Sorajja, MD, Vinod Thourani, MD

Enrolling Now!

Sorajja P et al. JACC Intv 2017

79 year-old man on GDMT
Severe secondary MR, EF = 30%
Left atrial pressure

Cardiovascular Outcomes Assessment of MitraClip Percutaneous Therapy (COAPT)
MitraClip vs. GDMT for Secondary MR

One of the lowest NNTs to save a life, ever

The COAPT Trial
MR and HF beget each other

Baseline 12 months

GDMT
MitraClip

LVEDV (ml)

194 ± 76
196 ± 69
211 ± 94

192 ± 77

P<0.001

35 year-old Woman, NYHA III

8 cm

6.5 cm
Percutaneous Ventricular Therapy

AccuCinch

“Thank you for saving my life..”
Percutaneous Ventricular Therapy
ACCUCINCH Trials at MHIF

AccuCinch EFS
• LV dysfunction with moderate or severe MR

CorCinch – HFrEF
• NYHA III with LVEDD >55 mm, EF 20 to 40%

CorCinch - PMVI
• Secondary MR with prior failed surgery or MC

82 year-old Woman with TR
10-year survival, 14%
A Natural History Construct for TR

Survival and Sx

Moderate

Impairment already

Severe

Years of indolence

Massive

Torrential

Very steep both ways

RV failure, a late phenomenon

Years

Baseline TR Severity

3 (Severe) 4 (Massive) 5 (Torrential)

TRILUMINATE EFS

KCCQ at 30 days (n=60)

50% with still severe TR

BUT

KCCQ still 15 points better

Baseline 30 Day

34 of 39
TRILUMINATE II
U.S. Pivotal Study for TR

National Principal Investigators
Paul Sorajja, MD and David Adams, MD

Tri-Clip vs. Medical Therapy
Launch Q2 2019

Unexplained Dyspnea Evaluation

PCWP = 39
Atrial Shunting for Heart Failure

Corvia

V Wave

8 mm diameter

5 mm valve

Both ↓ exercise PCWP
Alt-FLOW Early Feasibility Study
Multicenter Study of ROOT Device
National Principal Investigator: Paul Sorajja, MD

- Ambulatory HFpFEF or HFrEF
- PCWP >15 at rest or >25 at exer.
- Stable GDMT >4 weeks
- No significant valve disease
Key Points
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• SHD therapy improves symptoms and saves lives even in late HF stages

• MHI and MHIF is leading the way for innovative trials in these patients, and we need your help!

Thank you!

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Tel: 507-513-1357
MitraClip Trials for Secondary MR

<table>
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<tr>
<th>Age (yr)</th>
<th>72</th>
<th>=</th>
<th>70</th>
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<tbody>
<tr>
<td>EF (%)</td>
<td>31</td>
<td>=</td>
<td>33</td>
</tr>
<tr>
<td>LVEDVI (ml/m2)</td>
<td>101</td>
<td>&lt;</td>
<td>135</td>
</tr>
<tr>
<td>ERO (cm²)</td>
<td>41</td>
<td>&gt;</td>
<td>31</td>
</tr>
<tr>
<td>Implanted (%)</td>
<td>95</td>
<td>&gt;</td>
<td>73</td>
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Aortic Stenosis and Heart Failure
Paradoxical LFLGSAS

“Normal” EF
LVH, small LV
Low SV
HTN

Better with AVR, but remain at risk