Ischemic Cardiomyopathy with/without Functional MR

Sitaramesh Emani, MD
Director of Heart Failure Clinical Trials
April 20, 2018
Disclosures

- Abbott Labs – consultant, grant support, steering committee
- Medtronic – consultant
- CHF Solutions – consultant
- Respicardia – consultant
- Abiomed – travel support
- Relypsa – speakers bureau

I will discuss investigational therapies
Cardiomyopathy Definition

- Historical definition
  - First used by W Brigden in 1972 to describe myocardial disease in the absence of CAD

- AHA Definition:
  - Heterogeneous group of diseases of the myocardium
  - Exhibit inappropriate ventricular hypertrophy or dilatation
  - From a variety of causes

Therefore, *Ischemic Cardiomyopathy* is …

- A bit of an oxymoron

- Used in modern medical vernacular to describe cardiac dysfunction resulting from ischemic injury
Ischemic Cardiomyopathy

ACS

Chronic Ischemia

Ischemic Injury

Fibrosis / changes in cellular pathways

Remodeling

LV Enlargement

Systolic Dysfunction

Gheorghiade M, Bonow RO, Circ 1998
HF Maladaptation (Simplified)

\[ CO = SV \times HR \]

- **Remodeling** (β stimulation)
- \( \uparrow \) Afterload
- \( \downarrow SV \) \( \rightarrow \) \( \downarrow CO \)
- \( \uparrow \) Afterload
- **Remodeling** (AT\(_2\) pathways)

**Sympathetic Tone**

- \( \uparrow \) HR
  - \( \uparrow O_2 \) Demand
  - \( \uparrow \) Symptoms

- \( \downarrow \) Renal Perfusion
  - \( \uparrow \) RAAS
  - \( \downarrow \) Na\(^+\) + H\(_2\)O Retention

**Apoptosis**
Treating HF (Simplified)

- CO
- SV
- HR
- Renal Perfusion
- Sodium + Water Retention
- RAAS
- O₂ Demand

- β-Blockers: ↑Sympathetic Tone
- Diuretics
- ACEi/ARBs
- Aldo-antagonism
- ARNIs
- Nitrates*
- Hydralazine*
- Ivabradine

↓SV → ↓CO → ↑Afterload

↓Renal Perfusion → ↑O₂ Demand → ↑RAAS
Beta Blocker Dose Matters: (And a little is better than none)

In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality

- **Class I recommendation**
- **LOE B-R**

Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest

- **Class IIa**
- **LOE B-R**

Yancy CW, et al., *Circ* 2016
Consequences of Ischemic Remodeling

Displacement of papillary muscles
+/-
Dilatation of annular structure
leads to loss of leaflet coaptation

Various Forms of Mitral Regurgitation

- Normal mitral valve
- Degenerative MR caused by mitral valve prolapse
- Degenerative MR caused by flail leaflet
- Functional MR
Does FMR Matter?

- MR after an MI is associated with worse outcomes
- Does chronic, severe FMR contribute to ongoing remodeling?

- Hemodynamic consequences
  - Contributes to worsening HF symptoms
  - Can contribute to worsening PHTN

Watanabe N, et al, Prog Cardiovasc Dis 2017
Treating FMR

Treat the underlying problems!

- Revascularization
- Aggressive GDMT for HF
- Appropriate device based therapies (e.g. CRT)
- Aggressive therapy may lead to improved MR in 33% of patients

Liu E, Emani S, unpublished data
Direct Valve Therapies

- Surgical options
  - Repair
  - Replacement
- Minimally invasive “repair”
  - MitraClip*
  - Percutaneous ring annuloplasty*
- Transcatheter MV Replacement*

*under investigation
MitraClip

- Approved for organic MR
- Currently in trials for FMR (COAPT)

Feldman T, Young A, JACC 2014
tMVR Options

- Currently in trials
- Several versions
New FMR Technologies

- Awaiting trial results for efficacy & safety
- Will still be adjunctive to good medical therapy
Thank You

Sitaramesh.emani@osumc.edu