Objectives

• Considerations in management of multivalvular disease
  - Net clinical effect of multiple valvular lesions
  - Challenges in grading severity of each lesion by echocardiography
  - Treatment strategies

• Case Discussions
Case 1: AS + MR
91M in CHF w/ CAD, CKD, AS, MR, & AF-RVR

- Normal LV EF, myxomatous MV, sclerotic AV

- Flail posterior leaflet

- PISA radius = 1.1 cm @ ~40 cm/s
- EROA = 0.49 cm²
- Regurgitant Volume 78 mL
- Systolic flow reversal noted in pulmonary veins
- Severe MR
AS

- Vmax 3.6 m/s
- Mean grad 29 mmHg
- AVA = 0.6 cm$^2$
- DI = 0.17
- SVI = 28 mL/m$^2$

Paradoxical low-flow/low-gradient AS

Incidence and Etiology of Multivalvular Disease

- EuroHeart Survey: 14.6% of patients undergoing valve surgery
- STS Database: 10.9% of 623,039 patients undergoing valve surgery
  - 57.8%: Aortic + Mitral Valve surgery
  - 31.0%: Mitral + Tricuspid Valve surgery
  - 3.3%: Aortic + Tricuspid Valve surgery
  - 7.9%: Triple valve surgery

Primary:
- Rheumatic Heart Disease
- Degenerative Valve Disease >90%

Secondary:
- Malcoaptation

Other Causes:
- Endocarditis
- Radiation
- Drugs (i.e. fen-phen)
- Connective tissue disease
- Genetic syndromes

• **Grading severity**: Does the addition of a second lesion:
  1. Modify the actual severity of the primary lesion?
  2. Affect the quantification and grading of the primary lesion?
Treatment for Multiple Valve Lesions

If you’re already going to the OR, what is the indication to treat:

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe AS</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate AS</td>
<td></td>
<td>X</td>
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<tr>
<td>Severe AR</td>
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<td></td>
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<tr>
<td>Moderate AR</td>
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<tr>
<td>Severe 1° MR</td>
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<tr>
<td>Moderate 1° MR</td>
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<td>X</td>
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<tr>
<td>Severe 2° MR</td>
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<td></td>
<td>X</td>
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<tr>
<td>Moderate 2° MR</td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Severe TR</td>
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<td>X</td>
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<tr>
<td>TR and Annular Dilatation or Right Sided Failure</td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Moderate TR and Pulm HTN</td>
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<td>X</td>
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</tbody>
</table>


Treatment

Surgical Risk

- EuroHeart Survey:
  - 6.5% in hospital mortality for multi-valve surgery compared with 0.9%-3.9% for single valve surgery

- STS Database:
  - 10.7% in hospital mortality for multi-valve surgery compared with 5.7% for single valve surgery
    - 10.7% for combined AV and MV surgery
    - 4.9% for isolated AV surgery
    - 6.9% for isolated MV surgery

- Good long-term survival and clinical improvement at experienced centers
  - Preferred treatment strategy

What if surgery is not an option?

- Percutaneous Options?
- Staged Approach vs. Simultaneous Treatment
AS and MR
Clinical Impact for Each is Compounded by the Other

Increased Transmitral Gradient
Increased Regurgitant Volume

Mitral Regurgitation
Aortic Stenosis


http://www.cvphysiology.com/Heart%20Disease/HD004
AS and MR
How does MR affect AS?

Low Flow State
Lower Transaortic Pressure Gradient
Lower Cardiac Output

Aortic Stenosis
Mitral Regurgitation

AS and MR
Effect on Ejection Fraction after Correction

<table>
<thead>
<tr>
<th></th>
<th>MR</th>
<th>AS</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect on EF</td>
<td>↓</td>
<td>↑</td>
<td></td>
</tr>
</tbody>
</table>

http://www.cvphysiology.com/Heart%20Disease/H004
Multivalvular Disease

- What is the net clinical effect of multiple valvular lesions?
- How do we grade severity of each lesion?
- What is the optimal treatment strategy?

**Echo Evaluation**

**Color Jet Area**

- Jet size is highly dependent on jet momentum \( (M) \)
  - Momentum is conserved throughout the jet
  - \( Flow \ (Q) = A v \)
  - \( M = Qv = Av^2 \)
- Simplified Bernoulli: \( \Delta p = 4v^2 \)
  - \( v \propto \sqrt{\Delta p} \)
- \( \therefore Q \propto \sqrt{\Delta p} \) AND \( M \propto \Delta p \)

Echo Evaluation

Grading MR

Effective Regurgitant Orifice Area (PISA):

Flow Convergence Method

\[ \text{Reg Flow} = 2 \pi r \times V_a \]

\[ \text{EROA} = \frac{\text{Reg Flow}}{\text{PKV}_{\text{reg}}} \]

\[ \text{R Vol} = \text{EROA} \times \text{VTI}_{\text{reg}} \]

Vena Contracta:


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Echo Evaluation

AS Evaluation

Don’t confuse AS and MR jets!

Case 1: What is the optimal treatment strategy?

- **Surgical Risk Prohibitive**
  - 2 elements of frailty
  - STS Scores:
    - SAVR: 7.6%
    - Mitral Valve Repair: 10.0%
    - Mitral Valve Replacement: 14.1%
    - No way to score double valve but certainly greater than 20%

- **Plan for Percutaneous Approach**
  - Simultaneous or staged?
  - Which order?

Percutaneous Double Valve Treatment
Feasibility of Staged Treatment

- 22 patients between Jan 2010 and Feb 2012 with severe AS and MR treated initially with TAVR
- 3 month follow up – 5 patients – the MR reduced to moderate with improvement in functional class (all functional without ischemic cardiomyopathy)
- 17 patients (77.3%) had persistent severe MR after 3 months
  - 12 patient had persistent symptoms and were treated with MitraClip
- Significant improvement in LVEF, MR grade, and functional status at 6 month follow up

What Happens to MR after TAVR?

Predictors

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Independent Predictors of Persistent MR After TAVR</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td>Mitral leaflets calcification by MDCT (2 or 3)</td>
<td>3.942</td>
</tr>
<tr>
<td>Mitral annulus calcification by MDCT (2 or 3)</td>
<td>11.233</td>
</tr>
<tr>
<td>Organic MR</td>
<td>2.594</td>
</tr>
<tr>
<td>NOAF</td>
<td>9.258</td>
</tr>
<tr>
<td>Persistent LBBB</td>
<td>2.503</td>
</tr>
<tr>
<td>SPPA</td>
<td>2.535</td>
</tr>
<tr>
<td>Mitral annulus diameter &gt;35.5 mm</td>
<td>9.000</td>
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</table>

Significant p values are in bold.

TAVR = transcatheter aortic valve replacement; other abbreviations as in Table 1.

Staged vs. Simultaneous

- Always fix AS first
  - May result in cardiac decompensation after MV repair in the presence of elevated afterload due to AS
- MR reduction in 60% of patients with moderate functional MR after isolated SAVR
- MR reduction in 30% of patients after TAVR
- LV Dysfunction, Afib, MV annular calcification, left atrial enlargement associated with MR progression
- Therefore, TAVR + maximal medical therapy
  - Reassess and consider MitraClip if still severe, symptomatic MR
- No increased risk or technical complexity of MitraClip in the presence of prior TAVR (assuming no distortion of the MV annulus)
- Simultaneous treatment has been described – consider in primary MR unlikely to recover significantly (may be tough to get paid for both!)

Functional vs. Degenerative MR after TAVR

- 603 patients undergoing TAVR in single center for severe, symptomatic AS
- 149 (25%) with moderate or severe MR
  - 53 (36%) with functional MR (FMR)
  - 96 (64%) with degenerative MR (DMR)


Case 1 Treatment: TAVR first with #34 Evolut
Post TAVR AV

Vmax 2.1 m/s
Mean grad 8 mmHg
AVA = 1.5 cm²

2 Month Follow Up
Improved but still persistent Class 2 sx

MR EROA = 0.4 cm²
Mitral Regurgitant Volume = 61 mL
Mitral Mean Grad = 3 mmHg (HR 72)

Continued severe organic MR
Flail P2 with severe MR

Small central leak laterally

MitraClip: 2 clips on A2-P2

Final Result:
Trivial MR
Mean MV gradient = 4 mmHg (HR 50)
1 Month Follow Up

Vmax = 2.1 m/s
Mean AV gradient = 9 mmHg
AVA = 1.23 cm²

Trivial to mild MR
Mean MV gradient = 4 mmHg (HR 61)

Climbed Kilimanjaro last summer!

OK, that’s a lie, but he’s Class 1 FC, riding a stationary bike daily

Case 2

• 84 year old female presents as an external transfer for MitraClip evaluation during an admission for a heart failure exacerbation, chest pain and tachycardia.

• Past Medical History
  - PE s/p IVC filter
  - HTN
  - HL
  - Breast Ca s/p Right mastectomy
  - GERD
Case 2

- Normal LV Systolic Function
- Severely Dilated LA and LV

MR
Severely prolapsed vs. flail posterior leaflet
Multivalvular Disease

- What is the net clinical effect of multiple valvular lesions?
- How do we grade severity of each lesion?
- What is the optimal treatment strategy?
AR and MR

Clinical Impact – Severe Volume Overload

- Very Poorly tolerated
- Post-operatively:
  - High incidence of LV Dysfunction
  - Reduced survival
  - Often persistent symptoms

Adapted from Katz, *Physiology of the Heart* (3rd ed), 2001
Multivalvular Disease

- What is the net clinical effect of multiple valvular lesions?
- How do we grade severity of each lesion?
- What is the optimal treatment strategy?

AR and MR

How does AR affect MR?

- Increased ROA

http://www.mardil.com/overview/
AR and MR
Volumetric Methods

Reference Stroke Volume:

\[
\text{Reg Vol}_{MR} = SV_{MV} - SV_{LVOT}
\]

\[
\text{Reg Vol}_{AR} = SV_{LVOT} - SV_{MV}
\]

\[
SV_{RVOT}?
\]

- Direct measurement of forward and reverse flow by CMR


Echo Evaluation
Grading MR

- PISA Radius = 2 cm
- ERO = 1.6 cm²
- Regurgitant Volume = 167 ml
- Systolic flow reversal noted in pulmonary veins

Severe MR
AR and MR
AR Pressure Half-Time

May overestimate severity of AR

TEE
Flail P2
TEE

Multivalvular Disease

• What is the net clinical effect of multiple valvular lesions?
• How do we grade severity of each lesion?
• What is the optimal treatment strategy?
Case 2
Treatment

- **Surgical Risk Prohibitive**
  - 2 elements of frailty
  - STS Scores:
    - Mitral Valve Repair: 6.1%
    - Mitral Valve Replacement: 10.5%

- Treat MR with MitraClip
MitraClip
Positioning First Clip – Mid A2-P2

MitraClip
Second Clip at lateral aspect of A2-P2
Final Result

- Mild residual MR (central and lateral jets)
- Mean MV gradient = 6 mmHg (HR 113)

1 Month Follow Up

- Mild Aortic Regurgitation
- Mild-mod MR (eccentric, anteriorly directed)
- Mean MV gradient = 9 mmHg (HR 82)
Percutaneous Options for Aortic Regurgitation

CoreValve Evolut R (Medtronic)

- Self-expandable
- Repositionable (after partial deployment)
- More than mild residual AR in 20.9% (n=43)
  - 8 required second valve
- 30 day stroke incidence 4.7%
- 12 month all cause mortality 21.4%


Percutaneous Options for Aortic Regurgitation

Direct Flow (Direct Flow Medical Inc.)

- Inflatable
- Repositionable after full deployment
- 11 high risk patients with pure, severe AR
- AR reduced to mild or less in all 11
- 1 patient required surgery for unstable valve
- 30 days:
  - 9% mortality
  - 0 strokes

Percutaneous Options for Aortic Regurgitation
Lotus (Boston Scientific)

- Mechanically expanded
- Fully repositionable and retrievable
- Valve skirt allows anchoring to annulus and LVOT
- Limited experience
- Case series (3 patients)
  - No more than trace residual AR
  - Significant symptomatic improvement at follow up


Percutaneous Options for Aortic Regurgitation

- **A**: Accurate (Symetic SA)
- **B**: J-Valve (JieCheng Medical Technology)
- **C**: Engager (Medtronic)
- **D**: JenaValve (JenaValve Technology)

- Self-seating geometry
  - Facilitates optimal positioning within the annulus
- Not repositionable
- Limited data is favorable for all of these

Percutaneous Options for Aortic Regurgitation
Healio Transcatheter Dock with SAPIEN XT (Edwards Lifesciences)

• Nitinol frame placed in aortic root behind native leaflets
• Balloon-expandable valve deployed within
• Very limited data


Case 3

• 88 year old male presents was referred to NMH for consideration for percutaneous options for severe MR and TR. He was very active until about 6 months prior to presentation. Now with severe fatigue, LE edema, and dyspnea on exertion.

• Past Medical History
  - CAD s/p LIMA-LAD bypass
  - Atrial Fibrillation
  - Prostate Ca
Echo
Severe TR, severely dilated RV and RA

Echo
Severe MR – 2 Jets (A1-P1, A3-P3), EROA 0.5 cm²
MR and TR

- Secondary TR is highly prevalent in patients with left-sided valvular disease

Table 51: Impact of multivariable disease on assessment of valvular regurgitation with Doppler echocardiography and CMR

<table>
<thead>
<tr>
<th>By the Valve Location</th>
<th>AR</th>
<th>MR</th>
<th>PR</th>
<th>TR</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td>Little direct impact, although highly prevalent and significant AR will vary</td>
<td>Little impact unless PR evident</td>
<td>Little impact unless PR evident</td>
<td>Little impact unless PR evident</td>
</tr>
<tr>
<td>MR</td>
<td>Little impact unless PR evident For CMR please contrast plane better in LVOT</td>
<td>For gradient TR, there is an increase in proportion to square root of aortic valve orifice area (AO) and engagement beyond the AO; PW may increase LV dilatation</td>
<td>Little impact unless PR evident</td>
<td>Little impact unless PR evident</td>
</tr>
<tr>
<td>PR</td>
<td>Little impact unless PR evident</td>
<td>Little impact unless PR evident</td>
<td>Little impact unless PR evident</td>
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</tr>
</tbody>
</table>

Techniques for CMR/MR-TR little
- LVOT: aorta proximal to LVOT Reg (b) - MR (c) (AO - AO free)

MR and TR

- Secondary TR is highly prevalent in patients with left-sided valvular disease

RV Enlargement and Dysfunction

Pulmonary Hypertension

RV Free Wall Annular Dilatation

Tricuspid Regurgitation

Right Atrial Enlargement

ASE GUIDELINES AND STANDARDS

Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation

A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance

William A. Zoghbi, MD, FASE (Chair), David Adams, RCSE, RDMS, FASE, Robert O. Bonow, MD, Martha Enriquez-Sarano, MD, Elroy Frenster, MD, FASE, Paul A. Gershwin, MD, FASE, Rebecca T. Hahn, MD, FASE, Toshi Hiro, MD, MMS,1,2 Saady Hwang, MD, FASE, Roberto M. Lang, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMS,1,2 Stanton Shuman, MD, FASE, Paulinenko T. Theodosiou-Stavrou, MD, MSc, FASE, James D. Thomas, MD, FASE, and Neil J. Weisman, MD, FASE, Houston and Dallas, Texas, Denver, North Carolina, Chicago, Illinois, Rochester, Minnesota; San Francisco, California; New York, New York; Philadelphia, Pennsylvania; Boston, Massachusetts; Toronto, Ontario, Canada, and Washington, DC.
MR and TR

How does MR affect TR?

1. Increased Regurgitant Volume for given ROA
2. Increased Color Jet Area (out of proportion to increased Regurgitant Volume)
3. Increased ROA due to TV annular dilation

Case 3

Treatment

- Surgical Risk Prohibitive
  - 2 elements of frailty
  - STS Scores:
    - Mitral Valve Repair: 5%
    - Mitral Valve Replacement: 8%

- MR - MitraClip
- TR - MitraClip at the same time vs. return at a later date for percutaneous TV repair

MitraClip

Final Result:
2 Clips (A1-P1, A3-P3)
Mild residual MR
MV mean gradient = 2 mmHg (HR 87)

CAVI – Caval Valve Implantation

- Tric Valve
  - Designed for SVC and IVC
  - Self Expandable
- SAPIEN
  - Requires preparation of landing zone with a self-expanding stent
  - TRICAVAL and HOVER


FORMA – Coaptation Device

- Rail which anchors to the RV apex
- Spacer that increases coaptation surface to reduce malcoaptation
- Feasibility trial ongoing

SCOUT – Mitralign
30 Day Results

- 15 patients between Nov 2015 and June 2016
- Technical success rate 80%
  - 3 patients with single-pledget annular detachment
- TA area reduction:
  - 12.3 +/- 3.1 cm² to 11.3 +/- 2.7 cm²; p=0.02
- EROA reduction:
  - 0.51 +/- 0.18 cm² to 0.32 +/- 0.18 cm²; p = 0.02
- LVSV increase:
  - 63.6 +/- 19.9 ml to 71.5 +/- 25.7 ml; p=0.02


TriCinch

- Corkscrew anchor
- Self-expanding nitinol stent deployed in the IVC
- Dacron band connecting both
- PREVENT study

Percutaneous TV Replacement
Gate™ Tricuspid Valved Stent

- Nov 2016: World’s first transcatheter tricuspid valved stent (transatrial)
- April 2017: Transjugular and placed into a failed annuloplasty ring
- Up to 48-50cm in diameter without protrusion into atria or ventricle

https://www.navigatecsi.com/about/
Take Home Points

- Multivalvular Disease is common
- Complex inter-relationship resulting in overall clinical picture
- Grading severity can be a challenge
  - Actual severity and echo appearance affected
- Many new transcatheter options are in development