A Systematic Approach to Multivalvular Disease

James D. Thomas, MD, FACC, FASE
Director, Center for Heart Valve Disease
Bluhm Cardiovascular Institute
Professor of Medicine, Feinberg School of Medicine, Northwestern University
Chicago, Illinois

Conflicts of interest: GE, Abbott, Edwards, Caption Health (honoraria and spouse employment)
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
• **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**
• Peak/mean grad 51/29 mmHg
• AVA = 0.6 cm², DI = 0.17
• SVI = 28 mL/m²

Paradoxical LF/LG 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

Secondary:
• Malcoaptation (LV/LA/RV/RA/Ao dilation)

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

Clinical Effect

- **Grading severity:** Does the addition of a second lesion:
  1. Modify the actual severity of the primary lesion?
  2. Affect the quantification of the primary lesion?
  3. Adversely impact patient sx and outcomes?
**Table 17 Impact of multivalvular disease on assessment of valvular regurgitation with Doppler echocardiography and CMR**

<table>
<thead>
<tr>
<th>By this Valvular Lesion</th>
<th>AR</th>
<th>MR</th>
<th>PR</th>
<th>TR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AS</strong></td>
<td>Little impact, although hemodynamically significant AR will increase AS gradient. For CMR: phase-contrast plane better in LVOT.</td>
<td>For constant ROA, RVol increases in proportion to square root of excess pressure; jet area exaggerated beyond this, ROA may increase if LV dilates.</td>
<td>Little impact unless PH ensues.</td>
<td>Little impact unless PH ensues.</td>
</tr>
<tr>
<td><strong>AR</strong></td>
<td>NA</td>
<td>LV dilatation may increase ROA (especially in secondary MR). Mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVTs). For CMR: MV RVol = LVSV - aortic forward flow; MR Reg fraction = MR RVol/ (LVSV - AR RVol).</td>
<td>Little impact unless PH ensues.</td>
<td>Little impact unless PH ensues.</td>
</tr>
<tr>
<td><strong>MS</strong></td>
<td>Little direct impact, although the delayed LV filling might theoretically lengthen AR pressure half-time.</td>
<td>If MV is heavily calcified, may shadow and decrease jet area and appearance of jet.</td>
<td>Lesion most likely to increase PAP and thus worsen RVol and jet area.</td>
<td>Lesion most likely to increase PAP and thus worsen RVol and jet area.</td>
</tr>
<tr>
<td><strong>MR</strong></td>
<td>Little direct impact, but mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVTs). Rapid early filling may decrease AR pressure half-time.</td>
<td>Little impact, although PR will exacerbate PS gradient. For CMR: phase-contrast plane better in RVOT.</td>
<td>Little impact, although PR will exacerbate PS gradient.</td>
<td>Increased RVSP will worsen RVol and jet area. If RV dysfunction occurs, may increase ROA.</td>
</tr>
<tr>
<td><strong>PS</strong></td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Increased RV volume may increase ROA, which will worsen RVol and jet area. For CMR: TVRVol + RVSV - pulmonic forward flow. TR Reg fraction = TR RVol/ (RVSV - PR RVol).</td>
<td>NA</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Increased RV volume may increase ROA, which will worsen RVol and jet area. For CMR: TVRVol + RVSV - pulmonic forward flow. TR Reg fraction = TR RVol/ (RVSV - PR RVol).</td>
<td>Increased RV volume may increase ROA, which will worsen RVol and jet area. For CMR: TVRVol + RVSV - pulmonic forward flow. TR Reg fraction = TR RVol/ (RVSV - PR RVol).</td>
</tr>
<tr>
<td><strong>TS</strong></td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Little direct impact, although TR will exacerbate TS gradient.</td>
<td>Little direct impact, although TR will exacerbate TS gradient.</td>
</tr>
<tr>
<td><strong>TR</strong></td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Rapid RV filling from TR may further shorten PR pressure half-time, and color PR jet more brief.</td>
<td>NA</td>
</tr>
</tbody>
</table>

**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, RCS, RDMS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Elsey Foster, MD, FASE, Paul A. Grayburn, MD, FASE, Rebecca T. Hahn, MD, FASE, Yuschi Han, MD, MMSc, Judy Hung, MD, FASE, Roberto M. Lang, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMSc, Stanton Sherman, MD, FASE, Paaladinesh Thavendiranathan, MD, MSc, FASE, James D. Thomas, MD, FASE, and Neil J. Weissman, MD, FASE, Houston and Dallas, Texas; Durham, North Carolina; Chicago, Illinois; Rochester, Minnesota; San Francisco, California; New York, New York; Philadelphia, Pennsylvania; Boston, Massachusetts; Toronto, Ontario, Canada; and Washington, DC.
AS and MR

How does AS affect MR?

Mitral Regurgitation + Aortic Stenosis = 

Increased Transmitral Gradient

Increased Regurgitant Volume

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 =

http://www.cvphysiology.com/Heart%20Disease/HD004
Jet size is dependent on jet momentum ($M$): flow x velocity

- Momentum is conserved throughout the jet
- $Flow (Q) = Av$
- $M = Qv = Av^2$

**Simplified Bernoulli:** $\Delta p = 4v^2$

- $v \propto \sqrt{\Delta p}$

$\therefore Q \propto \sqrt{\Delta p}$ AND $M \propto \Delta p$, if ROA is constant

Jet size increases roughly linearly with $\Delta p$, $Rvol$ roughly half as fast

Quantification of Jet Flow by Momentum Analysis

An In Vitro Color Doppler Flow Study

Circulation 1990; 81: 247-259

James D. Thomas, MD, Chun-Ming Liu, MD, Frank A. Flachskampf, MD, John P. O’Shea, MB, BS, Ravin Davidoff, MB, BCh, and Arthur E. Weyman, MD

\[ J_{A} = K \int_{A_{0}}^{\infty} u^{2} \, dr \]

This integral is expressible in closed form through a series of substitutions. First, let \( \xi = u_{0}/7.8\sqrt{M} \) yielding

\[ J_{A} = K \int_{A_{0}}^{\infty} \xi \left( \frac{7.8\sqrt{M}}{u_{0}} \right) \frac{d\xi}{\ln(1/\xi)} \]

where \( K = (2\pi \times 7.8/M)(9.7u_{0}) = 12.5M/\xi^{2} \) and \( \xi = u_{0}/7.8\sqrt{M} \) that ranges from 0 to 1. Next, let \( r = \sqrt{\ln(1/\xi)} \) yielding

\[ J_{A} = 2K \int_{A_{0}}^{\infty} \xi^{2} e^{-\xi^{2}/2} \, dv \]

where \( r = \sqrt{\ln(1/\xi)} \), which ranges from 0 for unconstrained jets to \( + \) for infinitesimally small receiving chambers. This expression may be integrated by parts \((\int_{u}^{\infty} x \, dv = -u \, f + f \, dv)\) with \( u = u_{0} \) and \( dv = \frac{e^{-\xi^{2}/2}}{2} \, dv \).

\[ J_{A} = K \int_{A_{0}}^{\infty} \xi^{2} e^{-\xi^{2}/2} (\sqrt{\pi/2} \, \text{erf}(2\xi)) \]

Backsubstituting for \( \xi, K \), and \( r \) yields

\[ J_{A} = \pi^{3/2} M^{1/2} \left( \frac{\ln(7.8\sqrt{M}/u_{0})}{u_{0}} \right) \]

\[ + 3.93 M \left( \frac{\ln(7.8\sqrt{M}/u_{0})}{u_{0}} \right)^{1/2} \text{erf} \left( \sqrt{2} \frac{\ln(7.8\sqrt{M}/u_{0})}{u_{0}} \right) \]

This function is displayed graphically in Figure 7 and discussed in the text.
Momentum: Physical Determinant of Jet Size

**Free jet**

v = 500 cm/sec  
Q = 63 cm³/sec  
ROA = 0.13 cm²

**Flow**  
(Q)  
Rises due to entrainment of flow

**Momentum**  
(Q·v)  
Constant along jet

**Energy**  
(Q·v²)  
Falls due to turbulent dissipation

---

Northwestern Medicine®
AS and MR

How does AS affect MR?

Mitral Regurgitation + Aortic Stenosis =

Increased Transmirtal Gradient

Increased Regurgitant Volume

Δp: 85 ⇒ 175 mmHg (2.06x)
Rvol ↑’s by $\sqrt{2.06} = 1.43x$
Jet area ↑’s by 2.06x

http://www.cvphysiology.com/Heart%20Disease/HD004
Echo Evaluation

AS Evaluation

Don’t confuse AS and MR jets! Timing is critical!!

Treatment Strategy for Nonsurgical Candidates

**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!)

Case 1 Treatment: TAVR first with #34 Evolut

Very mild paravalvular AR

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

Trivial AR

Gradient normalized
2 Month Follow Up

Improved but still persistent Class 2 sx

MR EROA = 0.4 cm$^2$
Mitral Regurgitant Volume = 61 mL
Mitral Mean Grad = 3 mmHg (HR 72)

Continued severe organic MR
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 the next summer!

OK, that’s a lie, but he was Class 1, riding a stationary bike daily
Case 2

84 yo woman with MR + AR and heart failure

- Normal LV Ejection Fraction
- Severely Dilated LA and LV
Severely prolapsed vs. flail posterior leaflet with severe MR
AR

Difficult to quantify but short $P^{1/2}t$ suggests severe

$P^{1/2}t = 249 \text{ ms}$
Multivalvular Disease

Same questions!

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

Mitral Regurgitation

LV Volume Overload

Aortic Regurgitation

Very Poorly tolerated Post-operatively:

- High incidence of LV Dysfunction
- Reduced survival
- Often persistent symptoms

LV dilation \(\Rightarrow\) increased mitral ROA

Adapted from Katz, Physiology of the Heart (3rd ed), 2001
## Table 17 Impact of multivalvular disease on assessment of valvar regurgitation with Doppler echocardiography and CMR

<table>
<thead>
<tr>
<th>By this Valvar Lesion</th>
<th>AR</th>
<th>MR</th>
<th>PR</th>
<th>TR</th>
</tr>
</thead>
</table>
| **AS**               | Little impact, although hemodynamically significant AR will increase AS gradient. 
For CMR: phase-contrast plane better in LVOT | For constant RDA, RVol increases in proportion to square root of excess pressure; jet area exaggerated beyond this, RDA may increase if LV dilates. | Little impact unless PH ensues. | Little impact unless PH ensues. |
| **AR**               | NA | LV dilatation may increase RDA (especially in secondary MR). Mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVOT). For CMR: MV RVol = LSVV + aortic forward flow; MR Reg fraction = MR RVol/ (LSVV – AR RVol). | Little impact unless PH ensues. | Little impact unless PH ensues. |
| **MS**               | Little direct impact, although the delayed LV filling might theoretically lengthen AR pressure half-time. | If MS is heavily calcified, may shadow and decrease jet area and appearance of jet. | Lesion most likely to increase PAP and thus worsen RVol and jet area. | Lesion most likely to increase PAP and thus worsen RVol and jet area. |
| **MR**               | Little direct impact, but mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVOT). Rapid early filling may decrease AR pressure half-time. | NA | Likely to increase PAP and thus worsen RVol and jet area. | Likely to increase PAP and thus worsen RVol and jet area. |
| **PS**               | Little direct impact | Little direct impact | Little impact, although PR will exacerbate PS gradient. 
For CMR: phase-contrast plane better in RVOT. | Increased RVSP will worsen RVol and jet area. If RV dysfunction occurs, may increase RDA. |
| **PR**               | Little direct impact | Little direct impact | NA | Increased RV volume may increase RDA, which will worsen RVol and jet area. 
For CMR: TVRVol = RVSP - pulmonic forward flow, TR Reg fraction = TR RVol/ (RVSP - PR RVol). |
| **TS**               | Little direct impact | Little direct impact | Little direct impact | Little direct impact, although TR will exacerbate TS gradient. |
| **TR**               | Little direct impact | Little direct impact | Rapid RV filling from TR may further shorten PR pressure half-time, and color PR jet more brief. | NA |

AS, Aortic stenosis; MS, mitral stenosis; NA, not applicable; PAP, pulmonary artery pressure; PH, pulmonary hypertension; PS, pulmonic stenosis; Reg, regurgitant; RDA, regurgitant orifice area; RVSP, right ventricular systolic pressure; TS, tricuspid stenosis. CMR-related considerations are in bold.
**AR and MR**

**Volumetric Methods**

Reference Stroke Volume:

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

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

**SV}_{RVOT} can be used**

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
Excellent example of PISA overestimation due to proximal constraint
Solution: estimate constraint (~50%) or use higher aliasing velocity
Regardless, it’s

Severe MR
AR and MR

Mitral inflow very high E wave

Short AR Pressure Half-Time

Severe MR shortens AV PHT so overestimates severity of AR
TEE

Flail P2

Less flow constraint at higher $v_a$
TEE

AR is only mild to moderate
MitraClip Procedure Performed

Two clips placed on A2-P2

Mild MR w/ mean $\Delta p$ 6 mmHg @ HR 113
1 Month Follow Up

Symptoms improved; no need to intervene on the AR

Mild Aortic Regurgitation

Mild-mod MR (eccentric, anteriorly directed)
Case 3 88 yo man w/ severe MR and TR

s/p remote CABG, previously active, now progressive DOE and edema

Severe TR, severely dilated RV and RA
Echo

Severe MR – 2 jets (big A1-P1, smaller A3-P3), EROA 0.5 cm²
### 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, RCS, RDMS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Elsye Foster, MD, FASE, Paul A. Grayburn, MD, FASE, Rebecca T. Hahn, MD, FASE, Yuchi Han, MD, MMSc, Judy Hung, MD, FASE, Roberto M. Lang, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMSc, Stanton Sherman, MD, FASE, Paulalinesha Thavendiranathan, MD, MSc, FASE, James D. Thomas, MD, FASE, and Neil J. Weissman, MD, FASE, Houston and Dallas, Texas; Durham, North Carolina; Chicago, Illinois; Rochester, Minnesota; San Francisco, California; New York, New York; Philadelphia, Pennsylvania; Boston, Massachusetts; Toronto, Ontario, Canada; and Washington, DC

---

<table>
<thead>
<tr>
<th>By this Valvular Lesion</th>
<th>AR</th>
<th>MR</th>
<th>PR</th>
<th>TR</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>Little impact, although hemodynamically significant AR will increase AS gradient. For CMR: phase-contrast plane better in LVOT</td>
<td>For constant RAO, RVol increases in proportion to square root of excess pressure; jet area exaggerated beyond this, RAO may increase if LV dilates.</td>
<td>Little impact unless PH ensues.</td>
<td>Little impact unless PH ensues.</td>
</tr>
<tr>
<td>AR</td>
<td>NA</td>
<td>LV dilatation may increase RAO (especially in secondary MR). Mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVOT). For CMR: RVol/LVSV = aortic forward flow; MR Reg fraction = MR RVol/ (LVSV − AR RVol)</td>
<td>Little impact unless PH ensues.</td>
<td>Little impact unless PH ensues.</td>
</tr>
<tr>
<td>MS</td>
<td>Little direct impact, although the delayed LV filling might theoretically lengthen AR pressure half-time. If MV is heavily calcified, may shadow and decrease jet area and appearance of jet.</td>
<td>Lesion most likely to increase PAP and thus worsen RVol and jet area.</td>
<td>Lesion most likely to increase PAP and thus worsen RVol and jet area.</td>
<td>Likely to increase PAP and thus worsen RVol and jet area. If RV dysfunction occurs, may increase RAO.</td>
</tr>
<tr>
<td>MR</td>
<td>Little direct impact, but mixed regurgitant lesions render volumetric methods challenging, as one must find some location reflective of net forward flow (e.g., RVOT). Rapid early filling may decrease AR pressure half-time.</td>
<td>NA</td>
<td>Likely to increase PAP and thus worsen RVol and jet area.</td>
<td>Likely to increase PAP and thus worsen RVol and jet area. If RV dysfunction occurs, may increase RAO.</td>
</tr>
<tr>
<td>PS</td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Little impact, although PR will exacerbate PS gradient.</td>
<td>Decreased RVSP will increase RAO, which will worsen RVol and jet area. For CMR: TVRVol + RVSP - pulmonic forward flow, TR Reg fraction = TR RVol/ (RVSP - PR RVol).</td>
</tr>
<tr>
<td>PR</td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>NA</td>
<td>Increased RV volume may increase RAO, which will worsen RVol and jet area.</td>
</tr>
<tr>
<td>TR</td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Little direct impact</td>
<td>Little direct impact, although TR will exacerbate TS gradient.</td>
</tr>
</tbody>
</table>

AS: Aortic stenosis; MS: mitral stenosis; NA, not applicable; PAP: pulmonary artery pressure; PH, pulmonary hypertension; PS: pulmonic stenosis; Reg, regurgitant; RAO, regurgitant orifice area; RVSP, right ventricular systolic pressure; TS, tricuspid stenosis. CMR-related considerations are in bold.
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**

STS > 8% + 2 elements of frailty

Plan: Address the MR first, reassess TR for emerging therapy

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

Symptoms improved enough that he chose not to have TR treated
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
Enjoy Echo Hawaii, join us again next January