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Sound Saves Lives

A Systematic Approach to Multivalvular Disease

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Conflicts of interest: GE, Abbott, Edwards, Caption Health (honoraria and spouse employment)

Objectives

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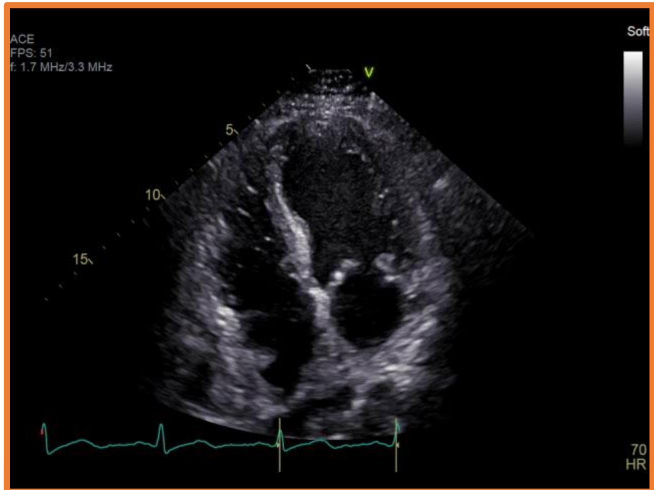
Considerations in management of multivalvular disease

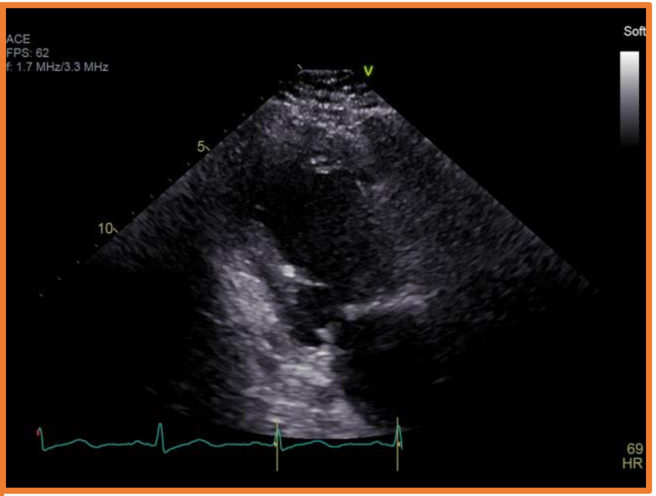
- Net clinical effect of multiple valvular lesions
- Challenges in grading severity of each lesion by echocardiography
- Treatment strategies

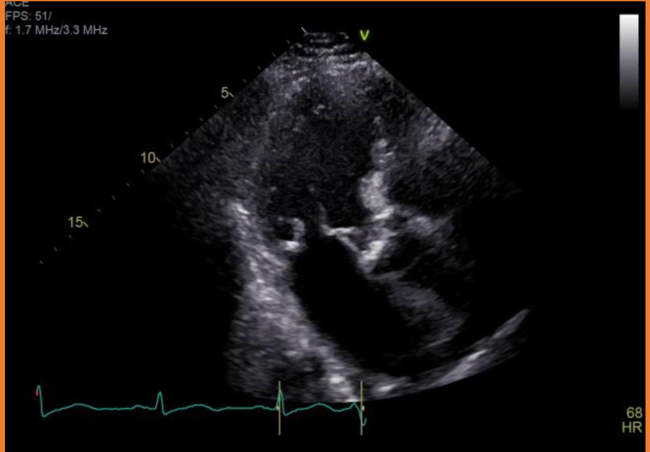
Case Discussions

Case 1: AS + MR

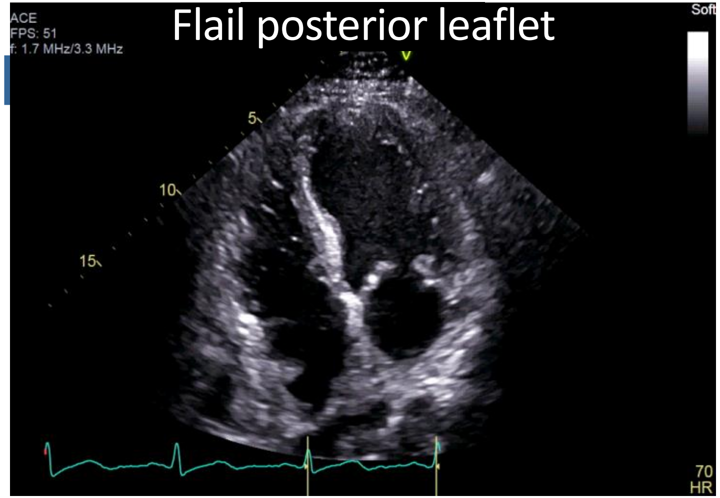
91M in CHF w/ CAD, CKD, AS, MR,& AF-RVR

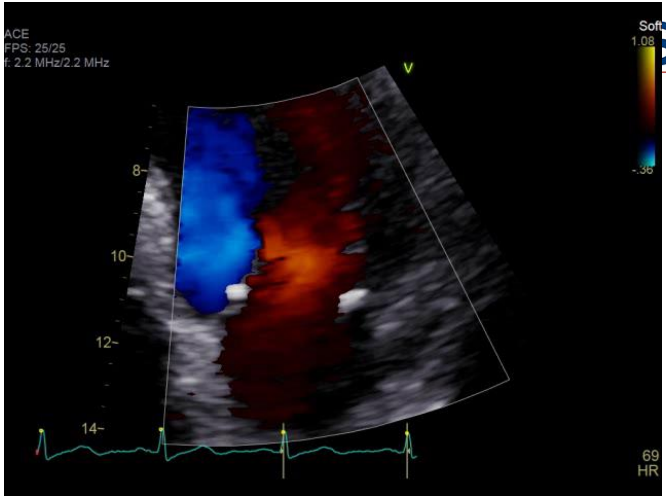


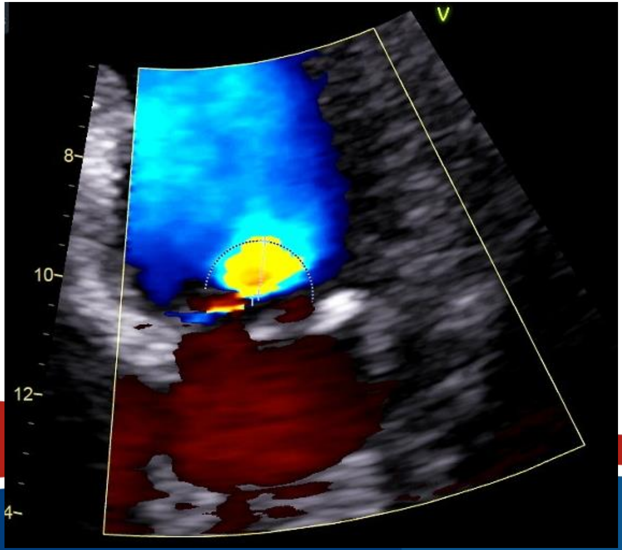




Normal LV EF, myxomatous MV, sclerotic AV







- ***PISA radius = 1.1 cm @ ~40 cm/s***
- ***EROA = 0.49 cm^2***
- ***Regurgitant Volume 78 mL***
- ***Systolic flow reversal noted in pulmonary veins***
- ***Severe MR***

AS

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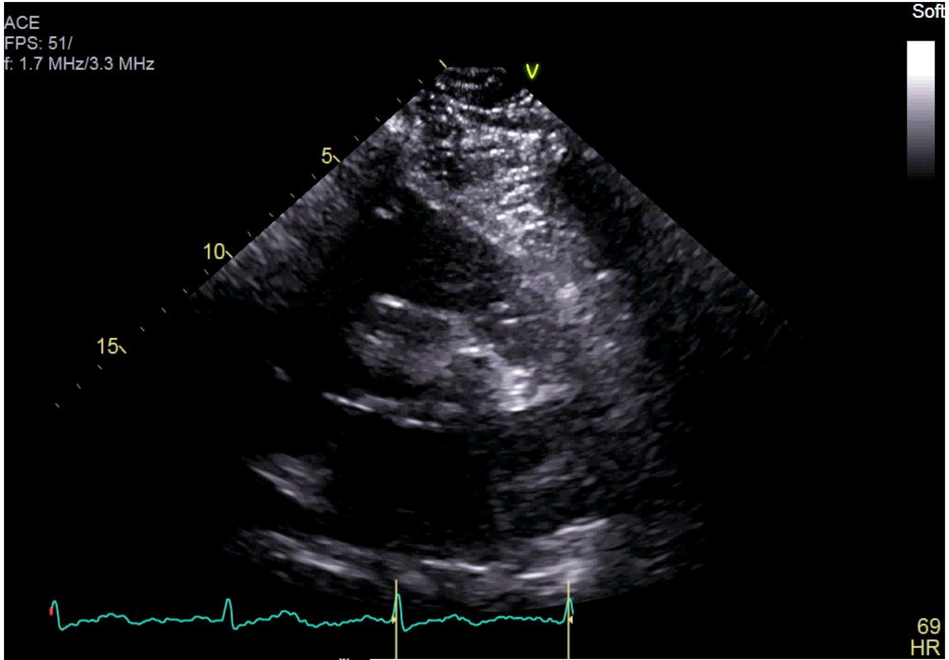
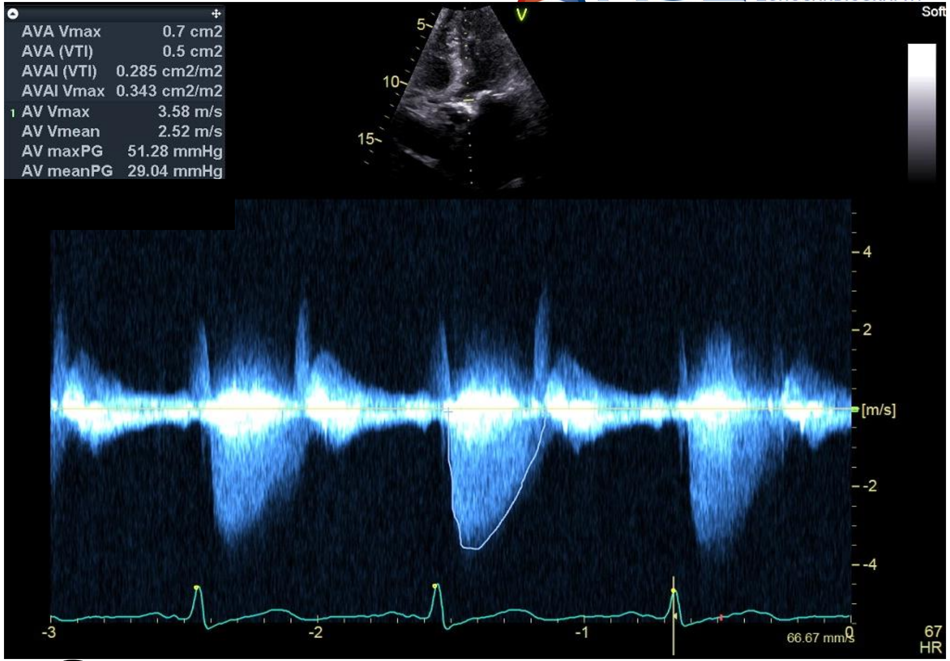
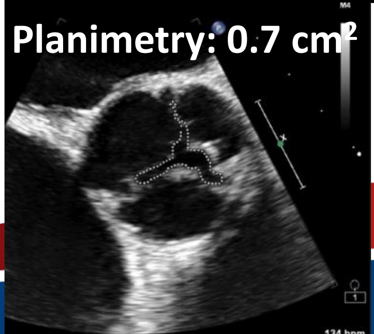






- Peak/mean grad 51/29 mmHg
- AVA = 0.6 cm^2, DI = 0.17
- SVI = 28 mL/m2

} **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

>90%

Other Causes:

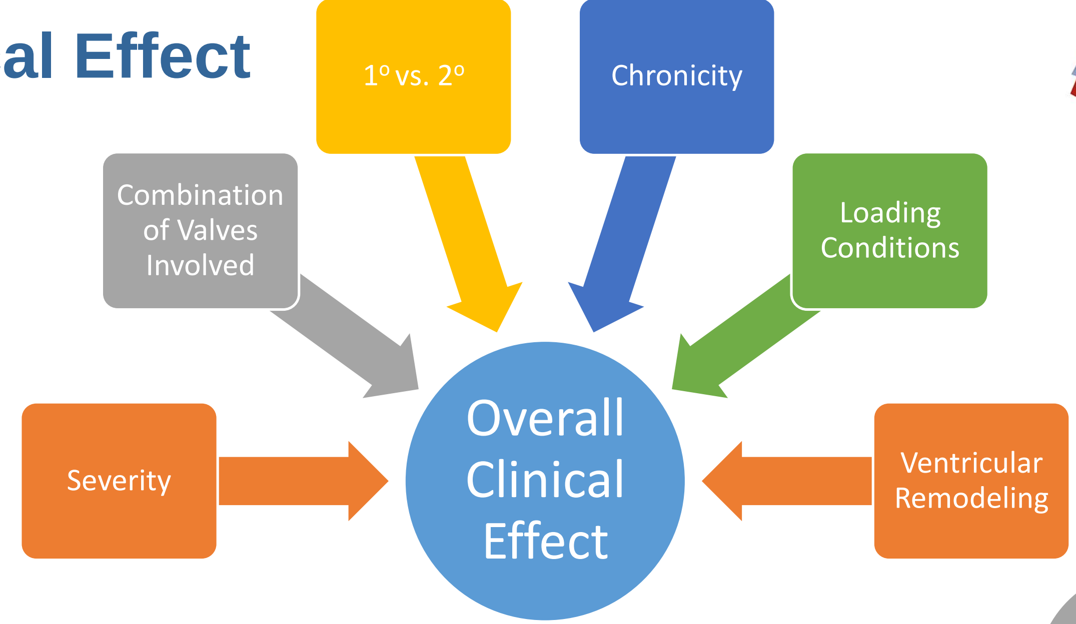
- Endocarditis
- Radiation
- Drugs (i.e. fen-phen)
- Connective tissue disease
- Genetic syndromes

Secondary:

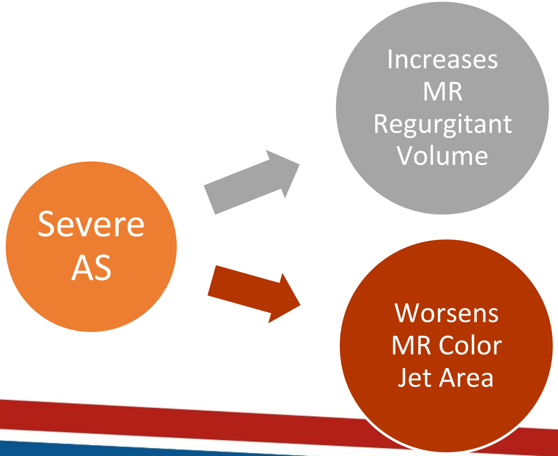
- Malcoaptation (LV/LA/RV/RA/Ao dilation)

Unger, Philippe, et al. "Pathophysiology and management of multivalvular disease." *Nature Reviews Cardiology* (2016).

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?



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, RDCS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Elyse 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 Shernan, 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*

Table 17 Impact of multivalvular disease on assessment of valvular regurgitation with Doppler echocardiography and CMR

	Impact on this Regurgitant Lesion			
By this Valvular Lesion	AR	MR	PR	TR
AS	Little impact, although hemodynamically significant AR will increase AS gradient. **For CMR: phase-contrast plane better in LVOT**	For constant ROA, RVol increases in proportion to square root of excess pressure; jet area exaggerated beyond this. ROA may increase if LV dilates.	Little impact unless PH ensues.	Little impact unless PH ensues.
AR	NA	LV dilation 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., RVOT). **For CMR: MV RVol = LVSV - aortic forward flow; MR Reg fraction = MR RVol/ (LVSV - 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 MV 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. If RV dysfunction occurs, may increase ROA.
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. If RV dysfunction occurs, may increase ROA.
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 ROA.
PR	Little direct impact	Little direct impact	NA	Increased RV volume may increase ROA, which will worsen RVol and jet area. **For CMR: TV RVol = RVSV - pulmonic forward flow. TR Reg fraction = TR RVol/ (RVSV - 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; *ROA*, regurgitant orifice area; *RVSP*, right ventricular systolic pressure; *TS*, tricuspid stenosis. CMR-related considerations are in bold.

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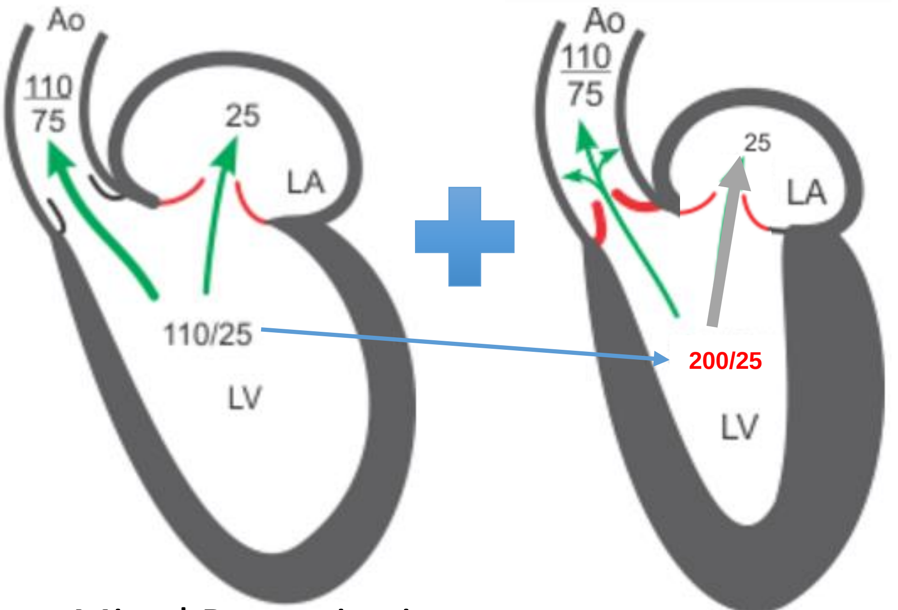
Zoghbi et al. JASE 2017; 40: 303-371

AS and MR

How does AS affect MR?



Mitral Regurgitation

Aortic Stenosis

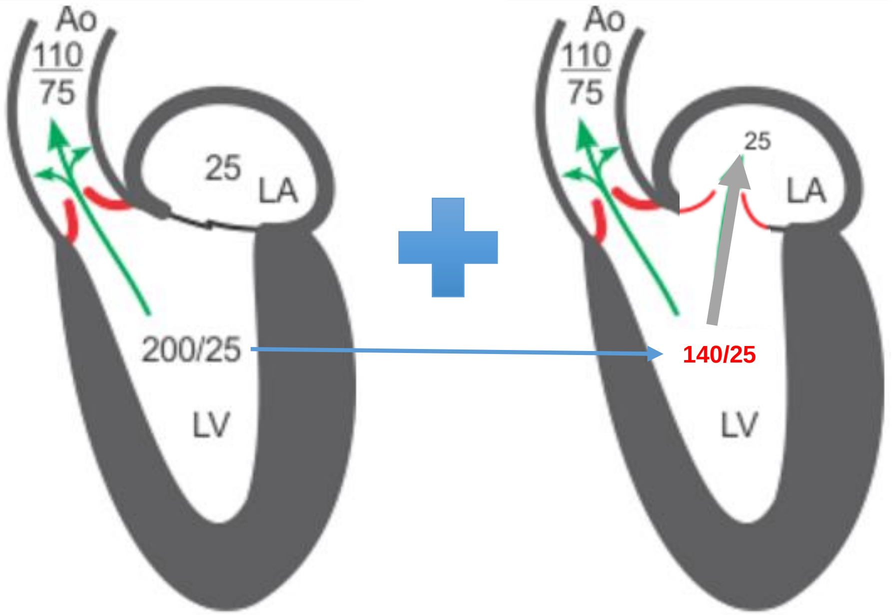
Increased Transmitral Gradient

Increased Regurgitant Volume

Thomas *et al.* Circulation 1990; 81: 247-259
http://www.cvphysiology.com/Heart%20Disease/HD004

AS and MR

How does MR affect AS?



Aortic Stenosis + Mitral Regurgitation =

Low Flow State

↓

Lower Transaortic Pressure Gradient

↓

Lower Cardiac Output

Thomas *et al.* Circulation 1990; 81: 247-259
http://www.cvphysiology.com/Heart%20Disease/HD004

Echo Evaluation

Color Jet Area

Jet size is dependent on jet momentum (M): flow x velocity

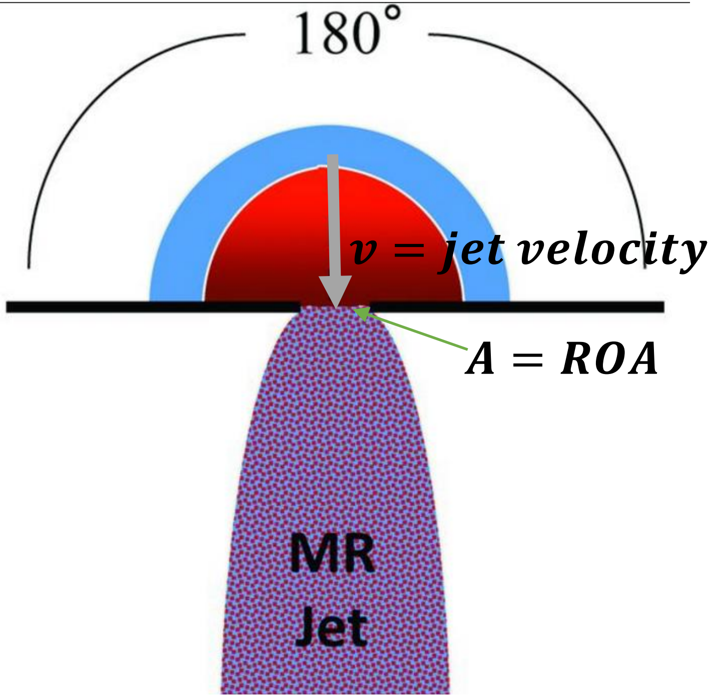
- Momentum is conserved throughout the jet
- $Flow\ (Q) = Av$
- $M = Qv = Av^2$

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

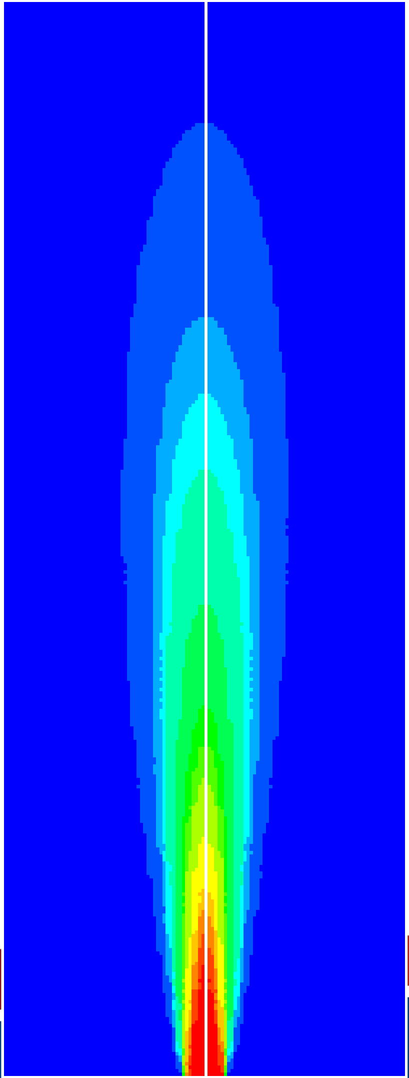
- $v \propto \sqrt{\Delta p}$

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

Jet size increases roughly linearly with Δp, Rvol roughly half as fast



Jet Size $\propto M$

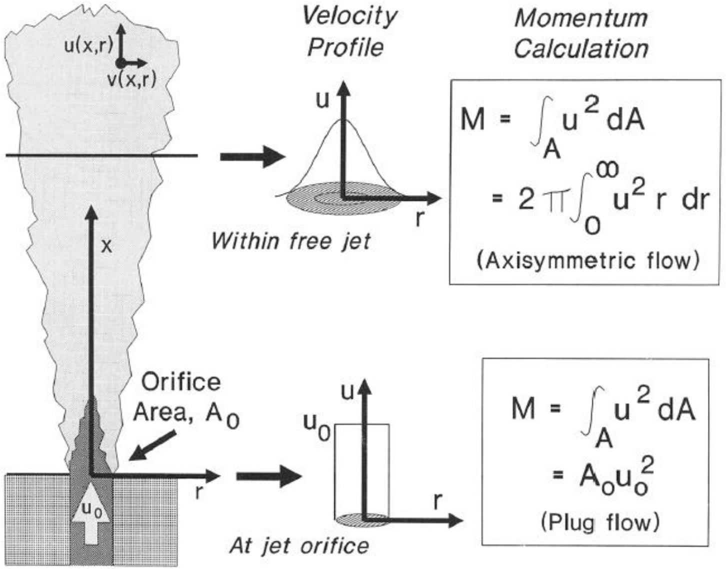


Quantification of Jet Flow by Momentum Analysis

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



$$JA(M,x_c,u_c)=2\int_0^{x_c}\frac{x}{9.7}\left(\ln\frac{7.8\sqrt{M}}{u_c x}\right)^{1/2}dx$$

This integral is expressible in closed form through a series of substitutions. First, let $\xi=u_c x/7.8\sqrt{M}$ yielding

$$JA=K\int_0^{\xi_c}\xi\sqrt{\ln(1/\xi)}\,d\xi$$

where $K=(2\times7.8^2M)/(9.7u_c^2)=12.5M/u_c^2$ and $\xi_c=u_c x_c/7.8\sqrt{M}$ that ranges from 0 to 1. Next, let $\nu=\sqrt{\ln(1/\xi)}$ yielding

$$JA=2K\int_{\nu_c}^{\infty}\nu^2e^{-2\nu^2}\,d\nu$$

where $\nu_c=\sqrt{\ln(1/\xi_c)}$, which ranges from 0 for unconstrained jets to ∞ for infinitesimally small receiving chambers. This expression may be integrated by parts ($\int u\,dv=uv-\int v\,du$) with $u=\nu$ and $dv=\nu e^{-2\nu^2}\,d\nu$:

$$JA=K[\tfrac{1}{2}\nu_c e^{-2\nu_c^2}+(\sqrt{\pi}/4\sqrt{2})\,\mathrm{erfc}(\sqrt{2}\nu_c)]^*$$

Backsubstituting for ν, ξ, and K yields

$$JA(M,x_c,u_c)=\frac{x_c^2}{9.7}\left(\ln\frac{7.8\sqrt{M}}{u_c x_c}\right)^{1/2}+\frac{3.93M}{u_c^2}\,\mathrm{erfc}\left[\sqrt{2}\left(\ln\frac{7.8\sqrt{M}}{u_c x_c}\right)^{1/2}\right]\quad (A3)$$

This function is displayed graphically in Figure 7 and discussed in the text.

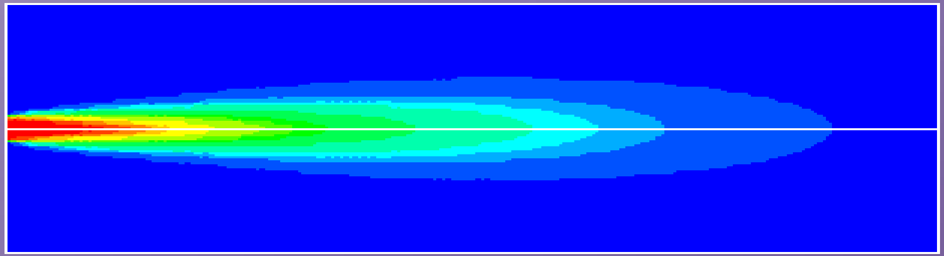
Momentum: Physical Determinant of Jet Size

Free jet

v = 500 cm/sec

Q = 63 cm^3/sec

ROA = 0.13 cm^2



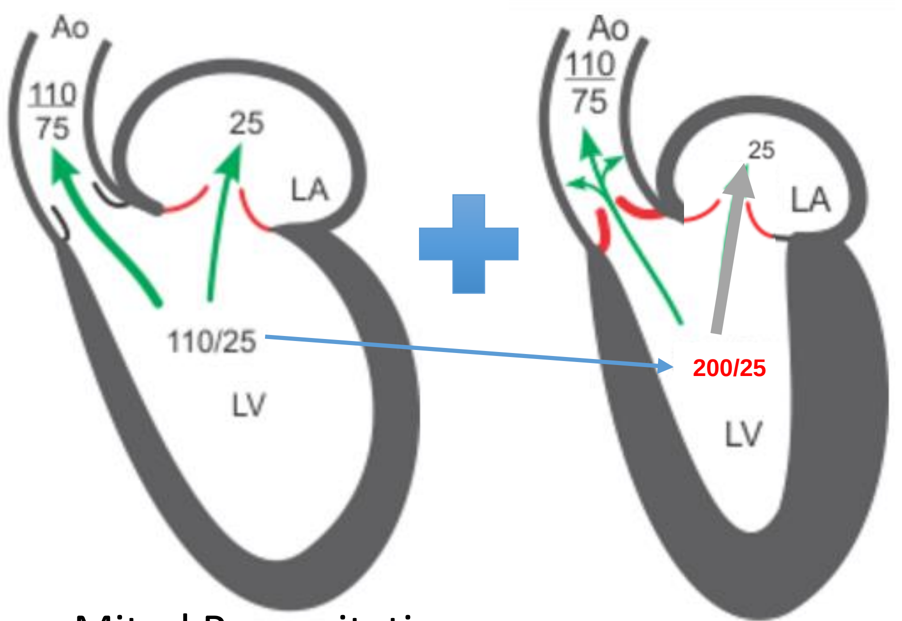
Flow
(Q)

Momentum
($Q \cdot v$)

Energy
($Q \cdot v^2$)

AS and MR

How does AS affect MR?



Mitral Regurgitation + Aortic Stenosis =

Increased Transmitral Gradient

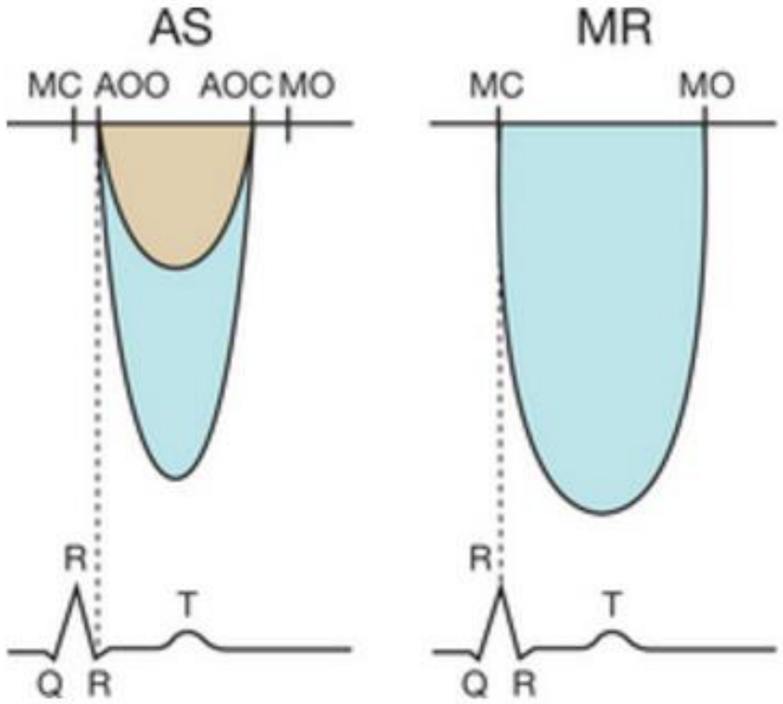
Increased Regurgitant Volume

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

Thomas *et al.* Circulation 1990; 81: 247-259
http://www.cvphysiology.com/Heart%20Disease/HD004

Echo Evaluation

AS Evaluation



Don’t confuse AS and MR jets!

Timing is critical!!

"Cardiac Valves." Thoracic Key. N.p., 04 June 2016. Web. 12 May 2017. <https://thoracickey.com/cardiac-valves/>.

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

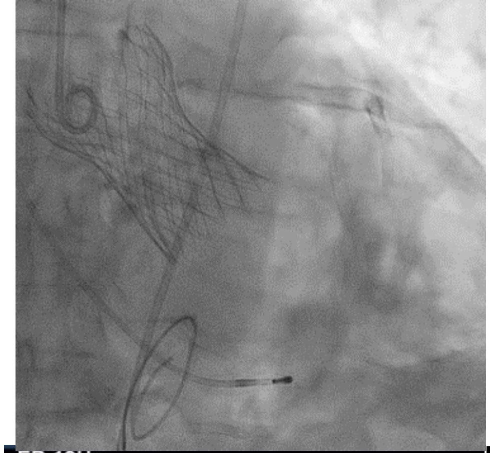
- Reassess and consider MitraClip if still severe, symptomatic MR

No increased risk or technical complexity of MitraClip in the presence of prior TAVR (assuming no distortion of the MV annulus)

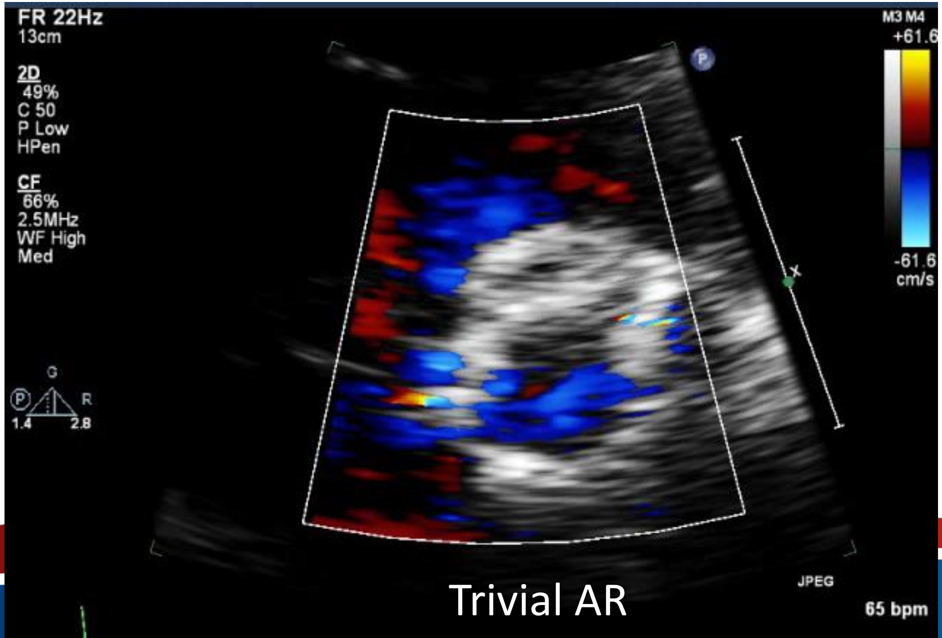
Simultaneous treatment has been described – consider in primary MR unlikely to recover significantly (may be tough to get paid for both!)

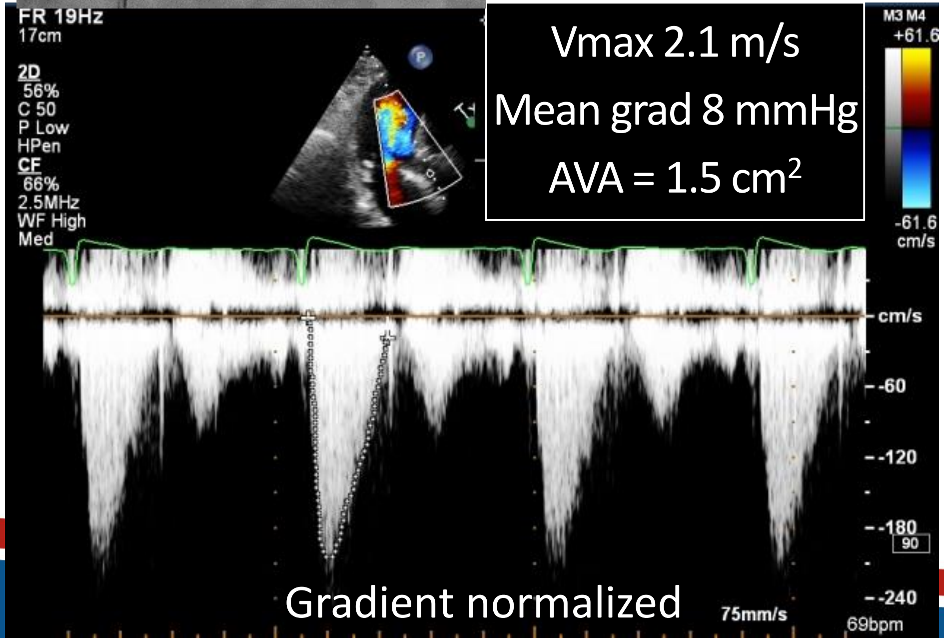
Kische, Stephan, et al. "Staged total percutaneous treatment of aortic valve pathology and mitral regurgitation: institutional experience." Catheterization and Cardiovascular Interventions 82.4 (2013): E552-E563.

Case 1 Treatment: TAVR first with #34 Evolut



Very mild paravalvular AR





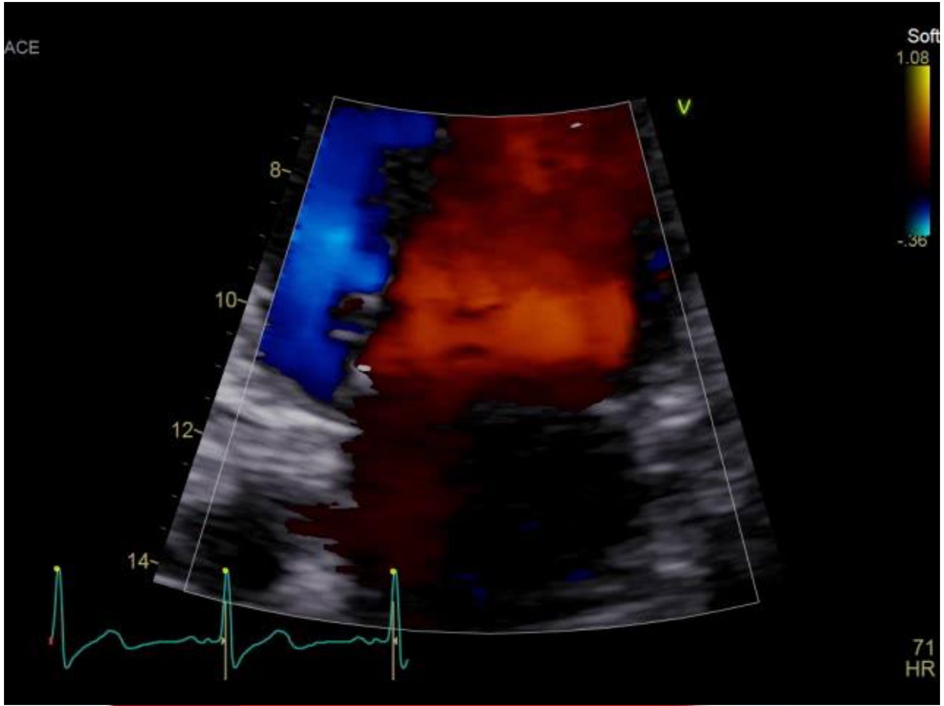
2 Month Follow Up

Improved but still persistent Class 2 sx

MR EROA = 0.4 cm^2

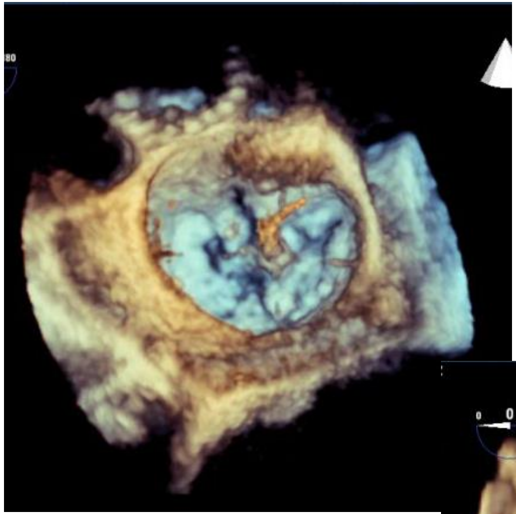
Mitral Regurgitant Volume = 61 mL

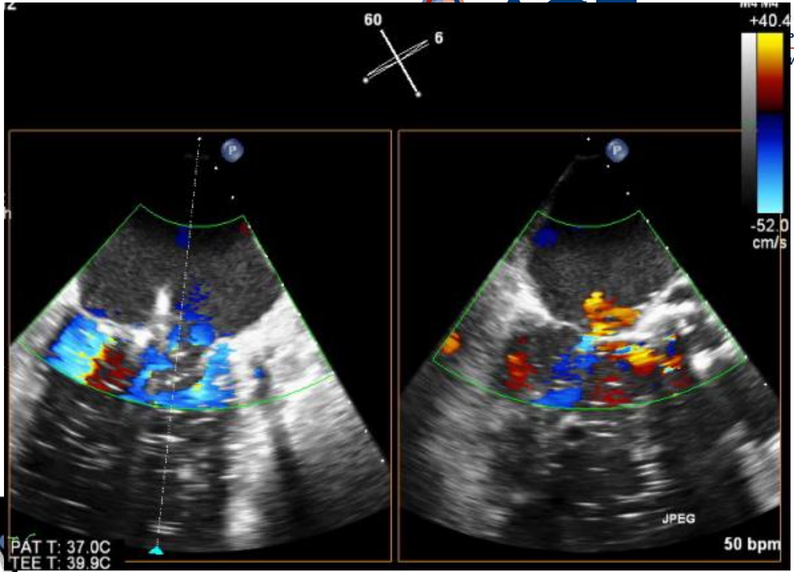
Mitral Mean Grad = 3 mmHg (HR 72)



Continued severe organic MR

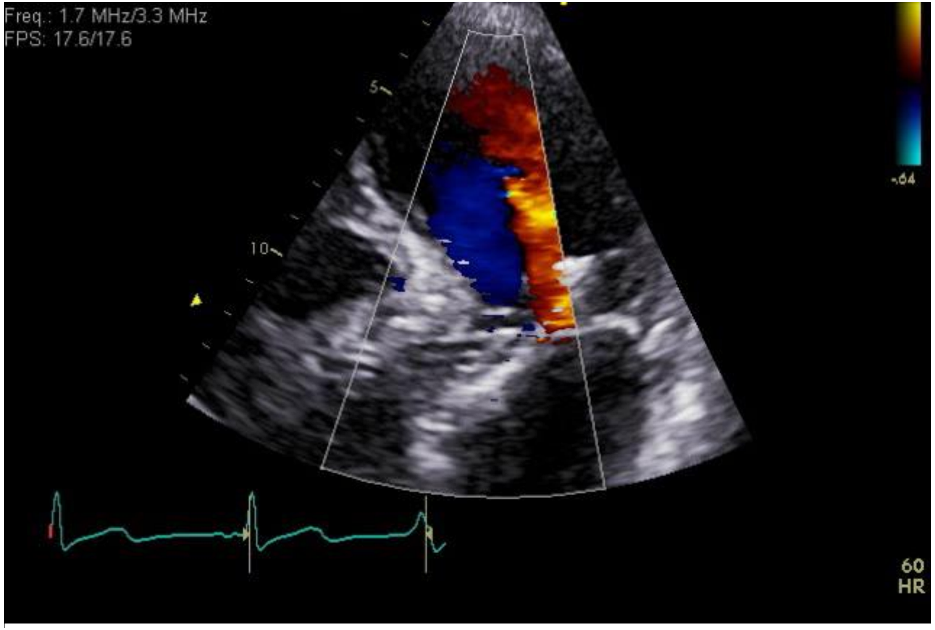
MitraClip: 2 clips on A2-P2

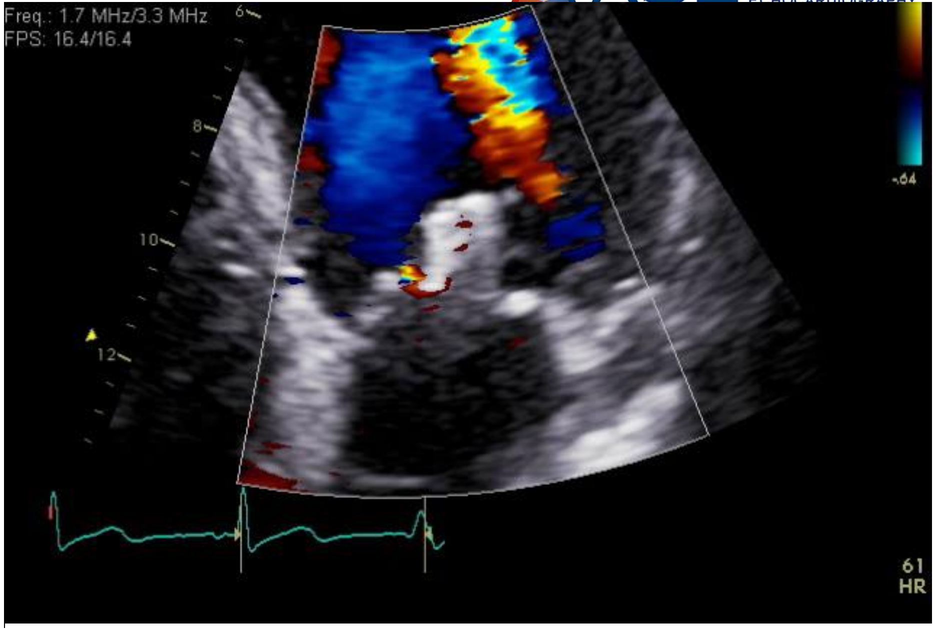




Final Result:
Trivial MR
Mean MV gradient = 4 mmHg
(HR 50)

1 Month Follow Up





Vmax = 2.1 m/s
Mean AV gradient = 9 mmHg
AVA = 1.23 cm^2

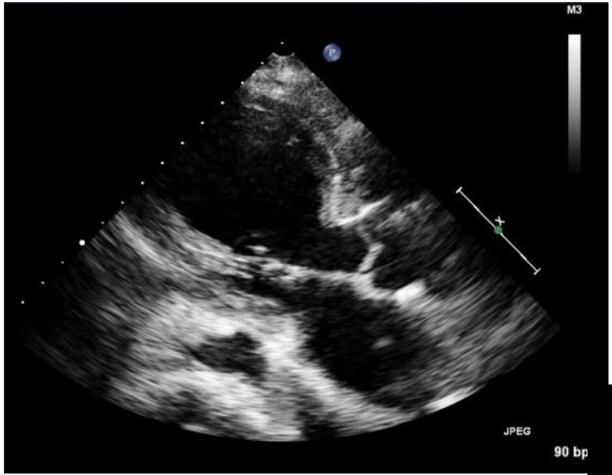
Trivial to mild MR
Mean MV gradient = 4 mmHg (HR 61)

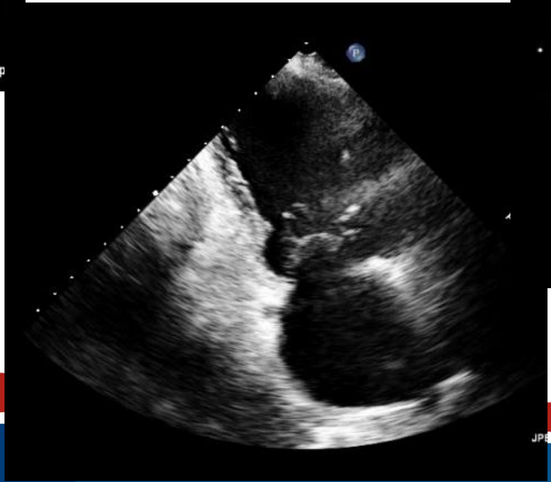
Climbed Kilimanjaro the next summer!

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

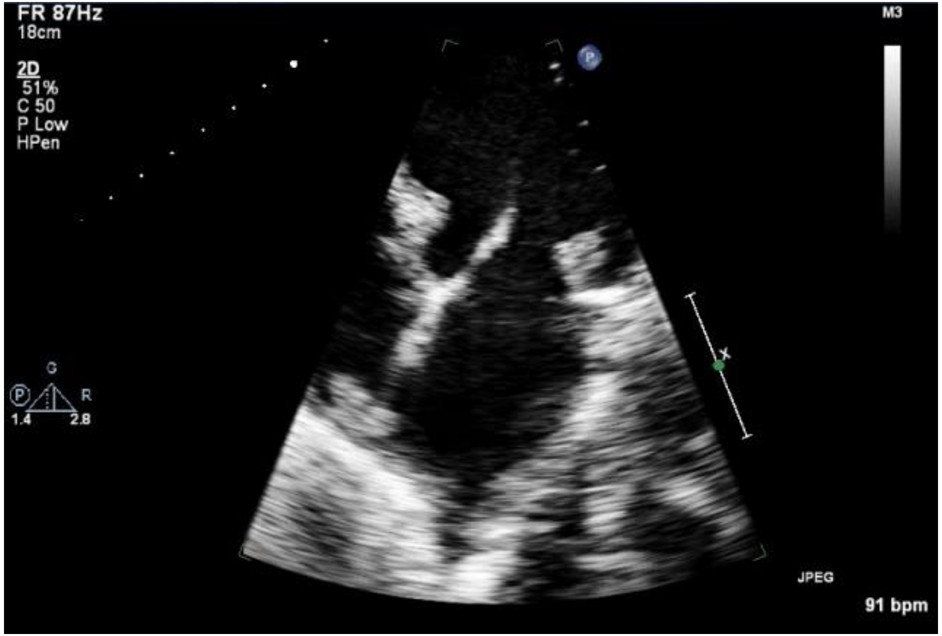


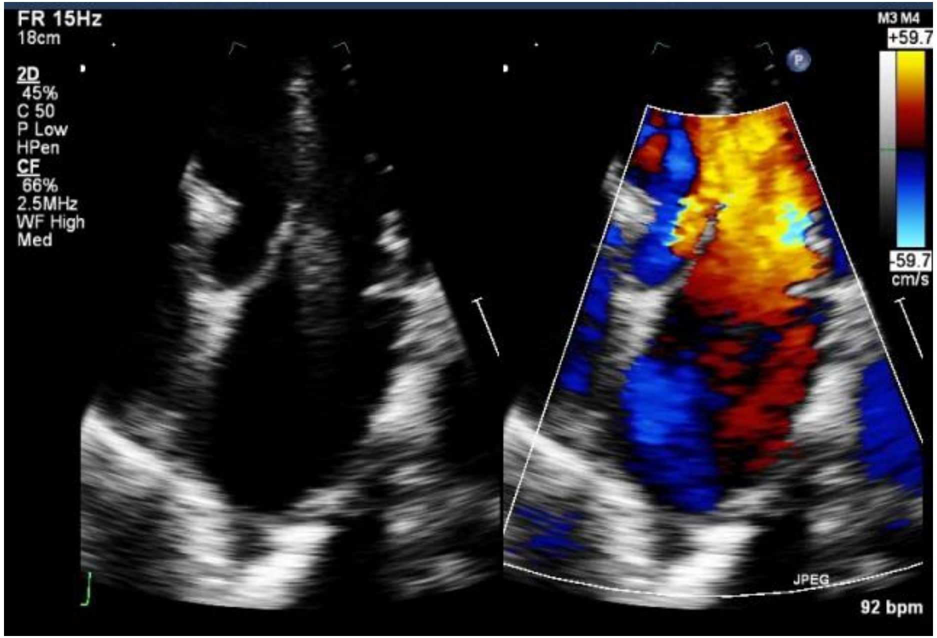


- Normal LV Ejection Fraction
- Severely Dilated LA and LV

MR

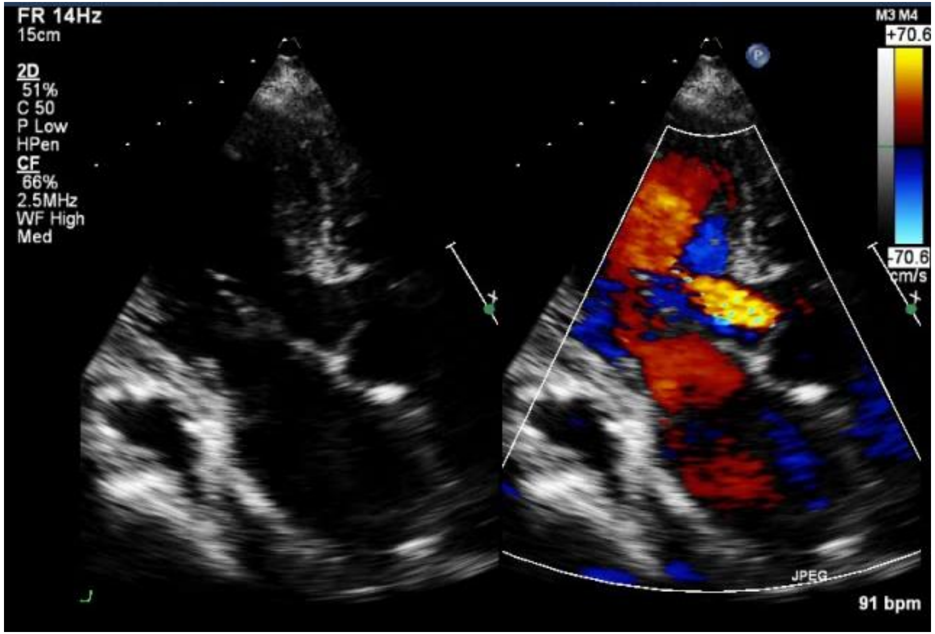
Severely prolapsed vs. flail posterior leaflet with severe MR

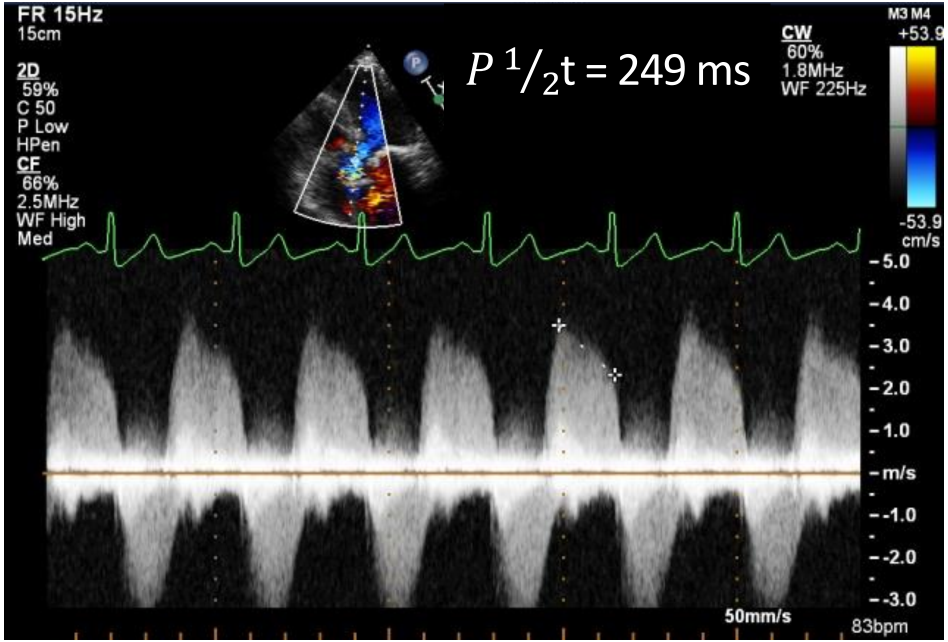




AR

Difficult to quantify but short P½t suggests severe





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?

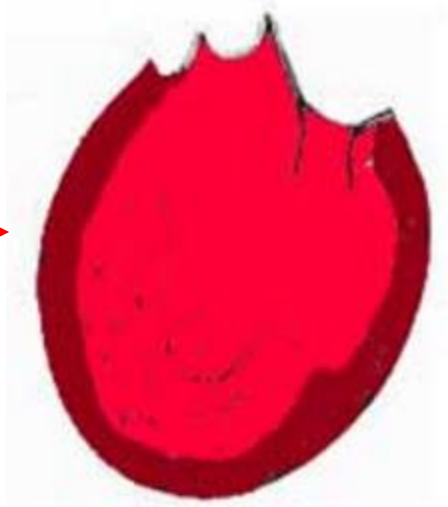
AR and MR

Clinical Impact – Severe Volume Overload

Mitral Regurgitation

Aortic Regurgitation

LV Volume Overload



Eccentric

Very Poorly tolerated

LV dilation ⇒ increased mitral ROA

Post-operatively:

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

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

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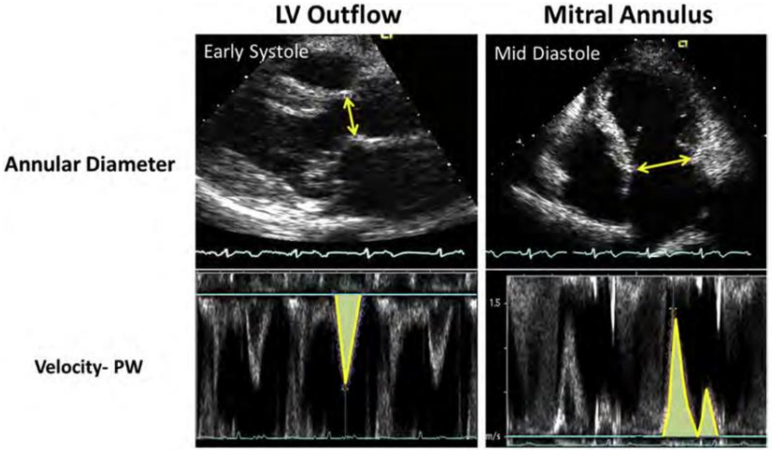
TR	Little direct impact	Little direct impact	Rapid RV filling from TR may further shorten PR pressure half-time, and color PR jet more brief.	NA

AS, Aortic stenosis; *MS*, mitral stenosis; *NA*, not applicable; *PAP*, pulmonary artery pressure; *PH*, pulmonary hypertension; *PS*, pulmonic stenosis; *Reg*, regurgitant; *ROA*, 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:



$SV_{LVOT} = CSA_{LVOT} * VTI_{LVOT}$
$= 0.785 * d^2_{LVOT} * VTI_{LVOT}$

$SV_{MV} = CSA_{MV} * VTI_{MV}$
$= 0.785 * d^2_{MV} * VTI_{MV}$

~~$Reg\ Vol_{MR} = SV_{MV} - SV_{LVOT}$~~

~~$Reg\ Vol_{AR} = SV_{LVOT} - SV_{MV}$~~

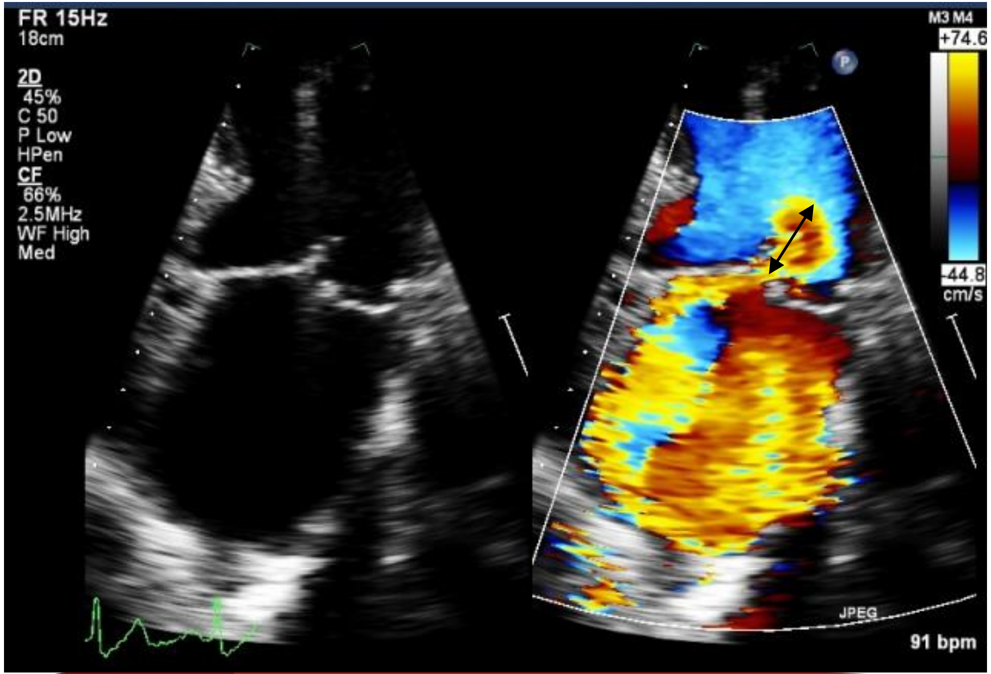
SV_{RVOT} **can be used**

Direct measurement of forward and reverse flow by CMR

Zoghbi, William A., et al. "Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation." *Journal of the American Society of Echocardiography* 30.4 (2017): 303-371.

Echo Evaluation

Grading MR



PISA Radius = 2 cm

ERO = 1.6 cm^2

Regurgitant Volume = 167 ml

Systolic flow reversal noted in pulmonary veins

Excellent example of PISA overestimation due to proximal constraint

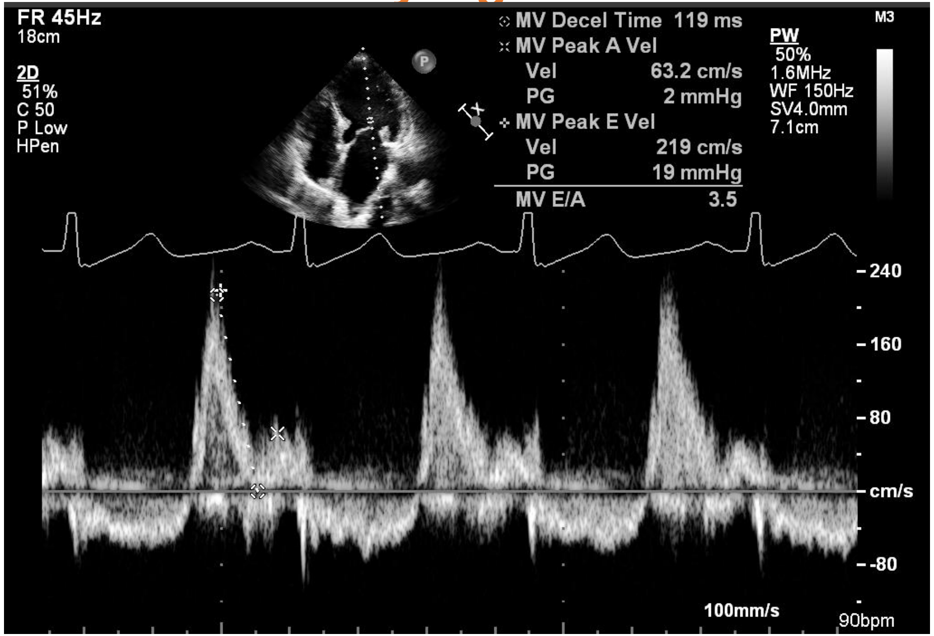
Solution: estimate constraint (~50%) or use higher aliasing velocity

Regardless, it’s

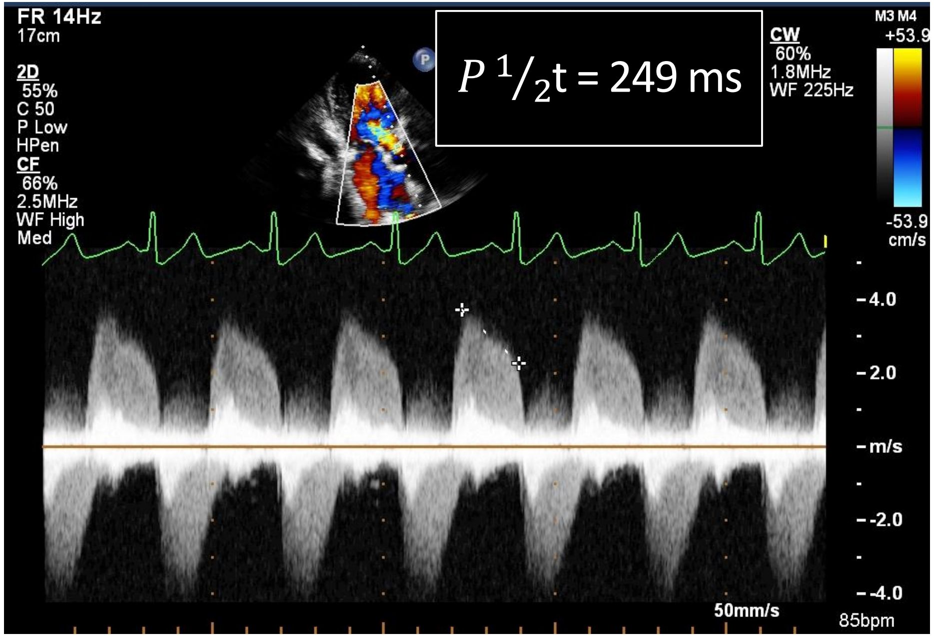
Severe MR

AR and MR

Mitral inflow very high E wave



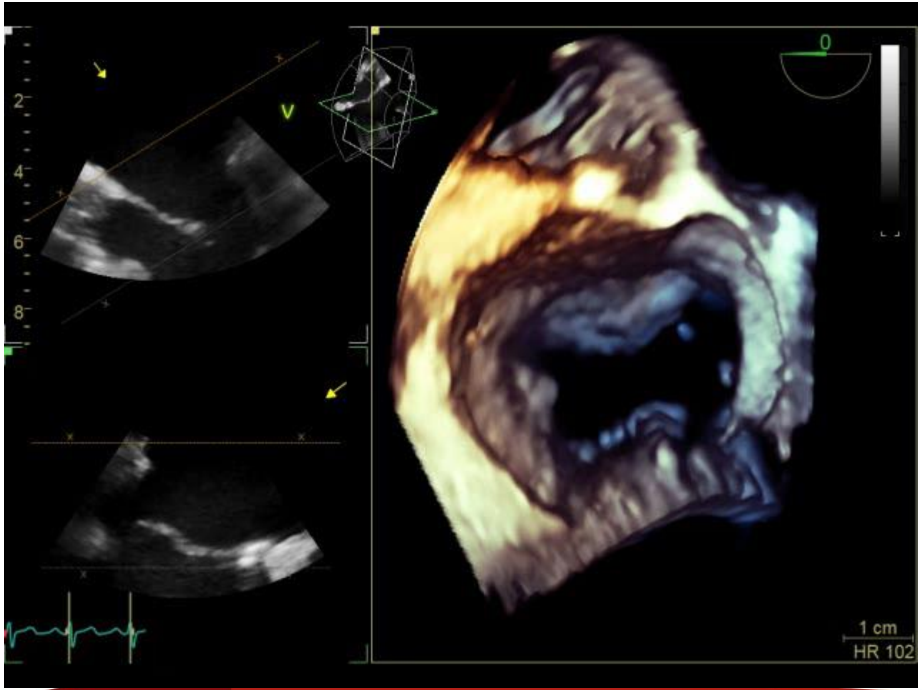
Short AR Pressure Half-Time



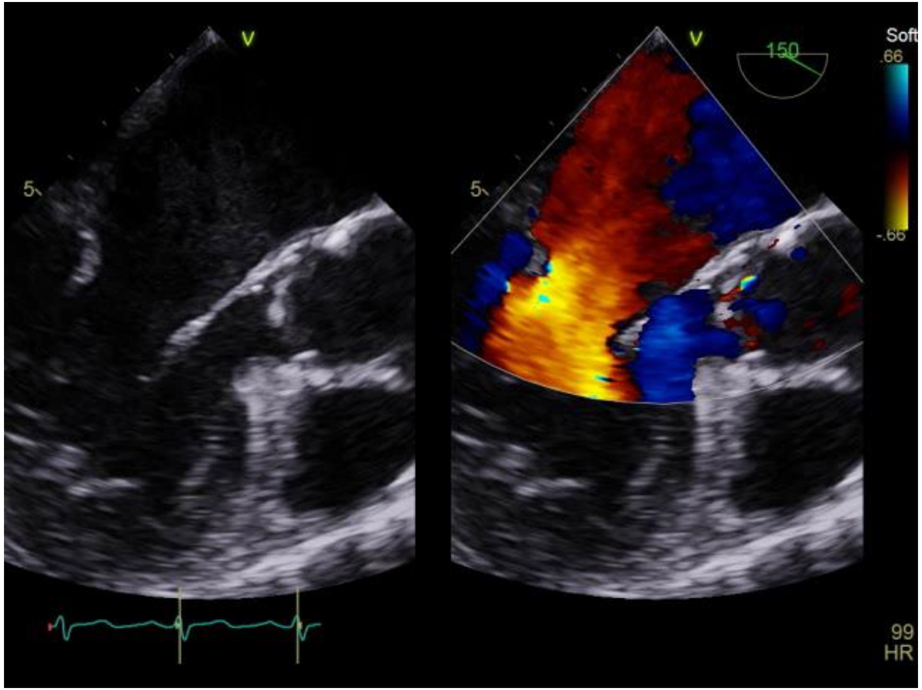
Severe MR shortens AV PHT so overestimates severity of AR

TEE

Flail P2

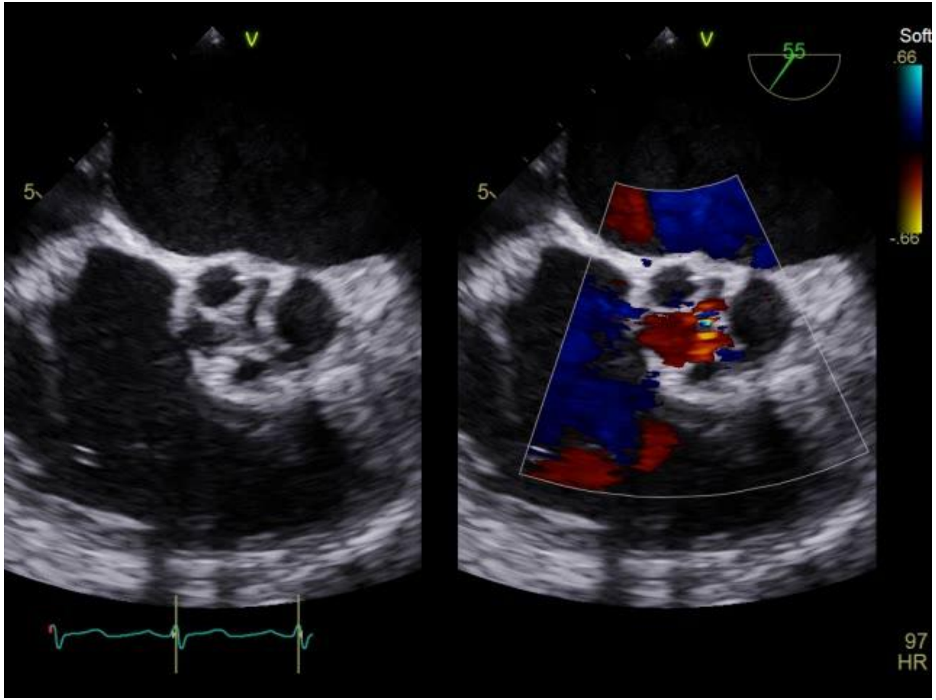


Less flow constraint at higher v_a



TEE

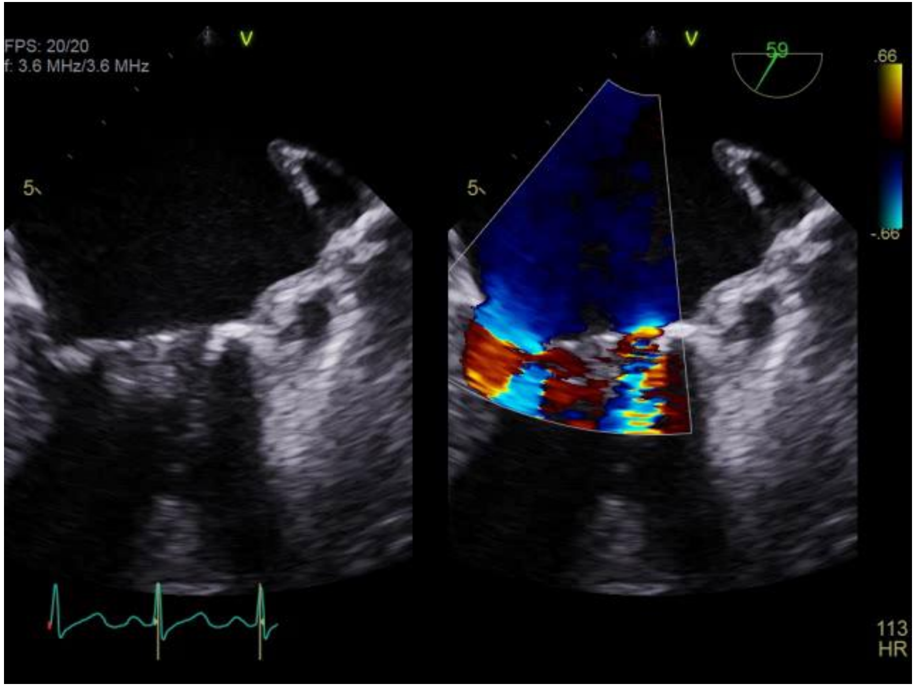
AR is only mild to moderate



MitraClip Procedure Performed

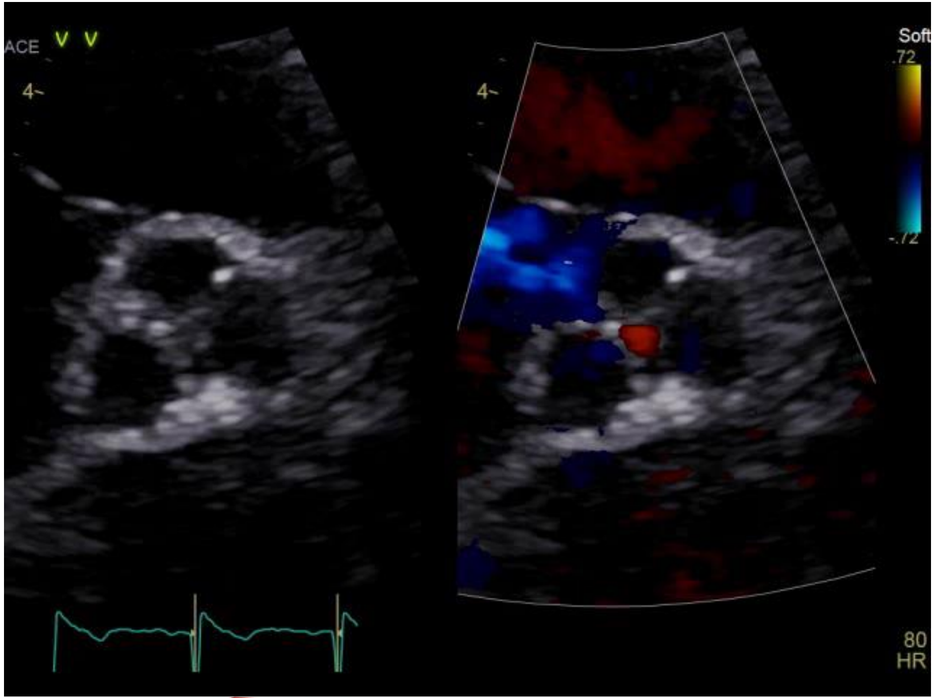
Two clips placed on A2-P2

Mild MR w/ mean ∆p 6 mmHg @ HR 113

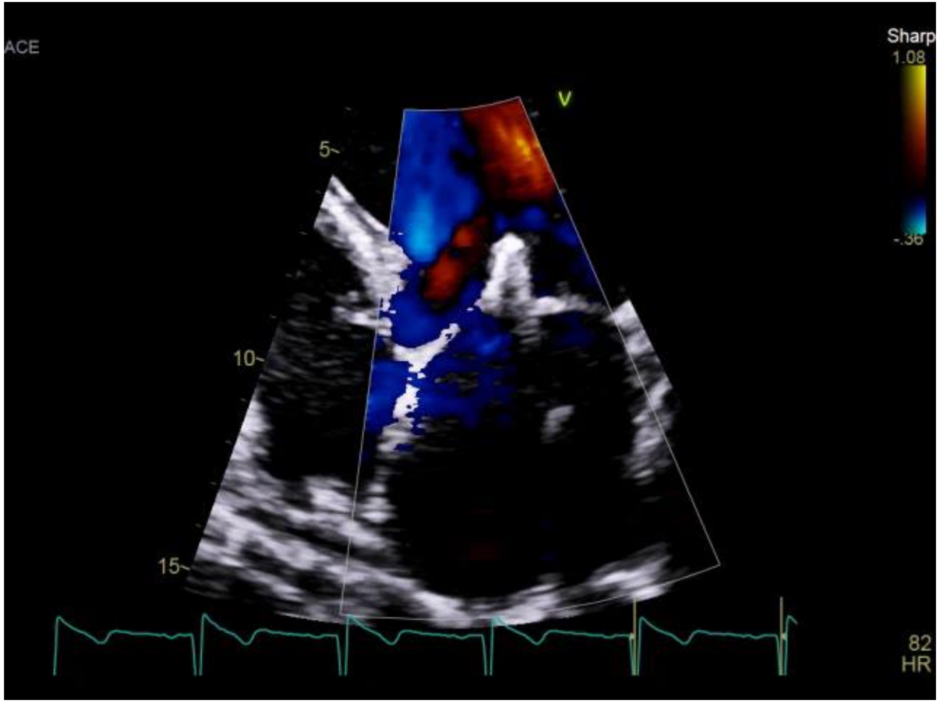


1 Month Follow Up

Symptoms improved; no need to intervene on the AR



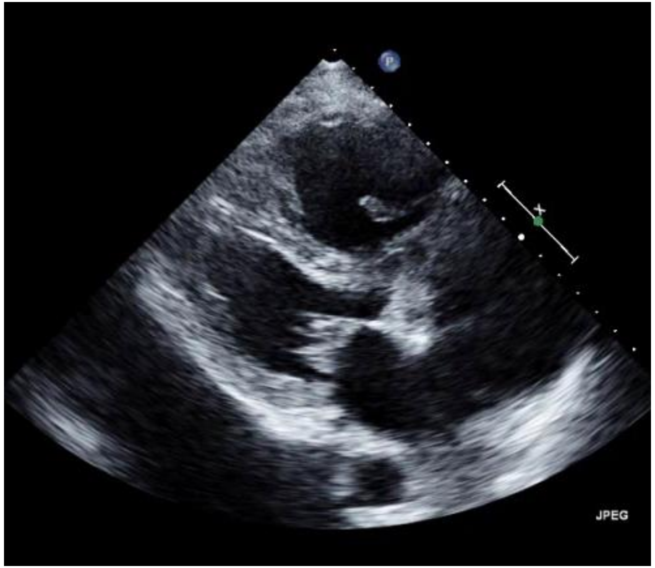
Mild Aortic Regurgitation

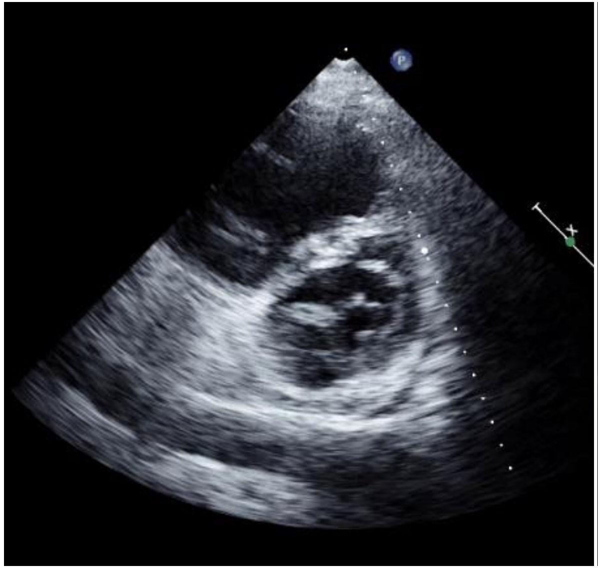


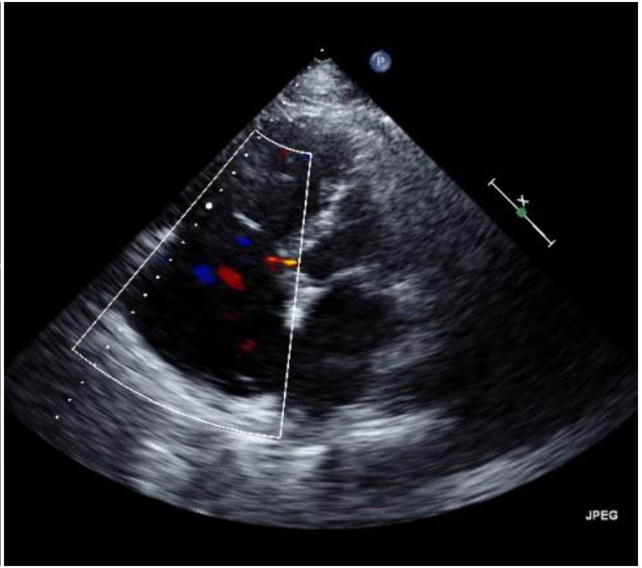
Mild-mod MR (eccentric, anteriorly directed)

Case 3 88 yo man w/ severe MR and TR

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



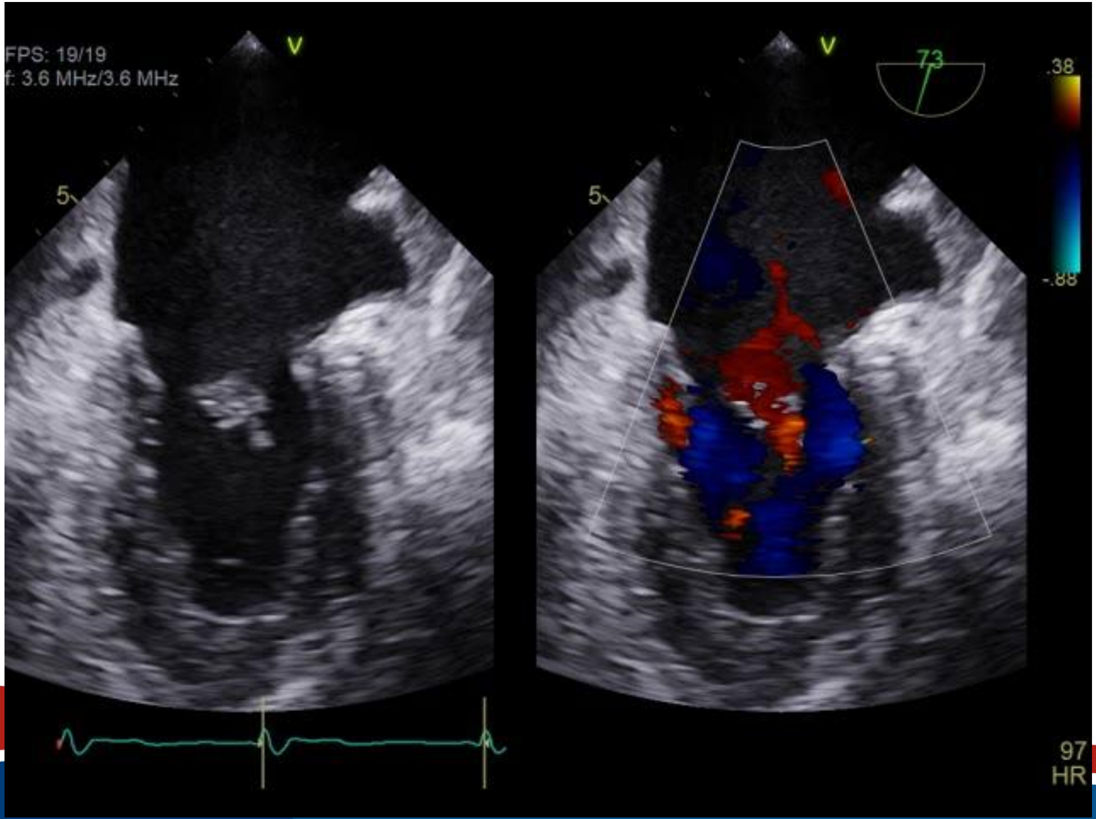




Severe TR, severely dilated RV and RA

Echo

Severe MR – 2 jets (big A1-P1, smaller A3-P3), EROA 0.5 cm^2



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, RDCS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Elyse 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 Shernan, 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*

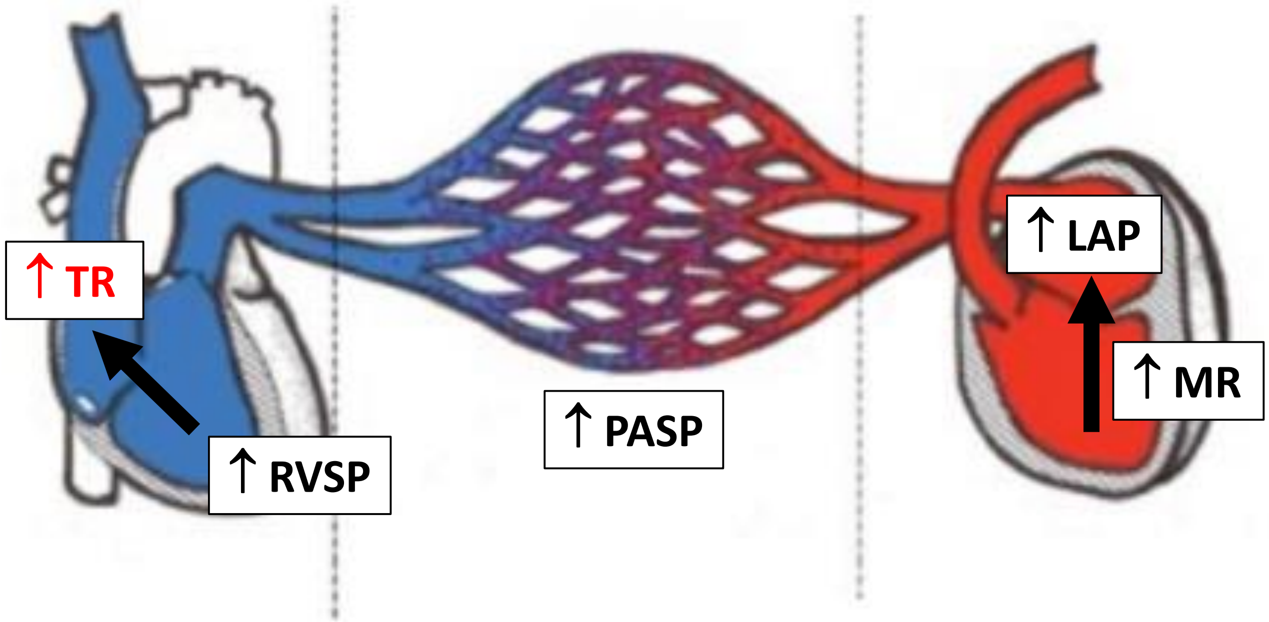
Table 17 Impact of multivalvular disease on assessment of valvular regurgitation with Doppler echocardiography and CMR

	Impact on this Regurgitant Lesion			
By this Valvular Lesion	AR	MR	PR	TR
AS	Little impact, although hemodynamically significant AR will increase AS gradient. **For CMR: phase-contrast plane better in LVOT**	For constant ROA, RVol increases in proportion to square root of excess pressure; jet area exaggerated beyond this. ROA may increase if LV dilates.	Little impact unless PH ensues.	Little impact unless PH ensues.
AR	NA	LV dilation 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., RVOT). **For CMR: MV RVol = LVSV - aortic forward flow; MR Reg fraction = MR RVol/(LVSV - 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 MV 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. If RV dysfunction occurs, may increase ROA.
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. If RV dysfunction occurs, may increase ROA.
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 ROA.
PR	Little direct impact	Little direct impact	NA	Increased RV volume may increase ROA, which will worsen RVol and jet area. **For CMR: TV RVol = RVSV - pulmonic forward flow. TR Reg fraction = TR RVol/(RVSV - 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; *ROA*, 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

http://www.rtmagazine.com/2010/08/pulmonary-hypertension-and-the-respiratory-therapists-role-in-diagnosis-and-treatment/

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