

# 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





2





#### Incidence and Etiology of Multivalvular Disease

>90%

- 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

Other Causes:

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



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

Secondary:

Malcoaptation

3



By this Valvular Lesion	Impact on this Regurgitant 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; jot area exaggerated beyond this. ROA may increase if LV dilates.	Little impact unless PH ensues.	Little impact unless PH ensues.		
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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., RVCT). Rapid early filling may docrease 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 wil 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		

le 17. Impact of multivaluater disease on as

AS, Aortic stenosis; MS, mitral stenosis; NA, not applicable; PAP, pulmonary aftery 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.

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, Eyse Foater, MD, FASE, Faul A. Grayburn, MD, FASE, Rebeca T. Hahm, MD, FASE, Fuch Han, MD, MMSKs, \* Jost Hung, MD, FASE, Boberto M. Lang, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMSc, \* Statmon Sherman, MD, FASE, Paladinesh Tavendrianthan, MD, NKS, FASE, \* Janes D. Thomas, MD, FASE, Neil J. Weissman, MD, FASE, Houtan and Dallar, Teasty Durham, North Camlina; Chicago, Illinoic, Rechetter, Minnesota; San Francisco, California; New Tork, New Tork Philadelphia, Pennylvania; Bastan, Massachusetty Tarento, Ontarrio, Canada; and Washingten, DC



#### **Treatment for Multiple Valve Lesions**

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

	Class I	Class IIa	Class IIb
Severe AS	Х		
Moderate AS		Х	
Severe AR	Х		
Moderate AR		Х	
Severe 1° MR	Х		
Moderate 1º MR		Х	
Severe 2° MR		Х	
Moderate 2º MR			Х
Severe TR	Х		
TR and Annular Dilatation or Right Sided Failure		Х	
Moderate TR and Pulm HTN			Х

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

## 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



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

#### AS and MR

Clinical Impact for Each is Compounded by the Other



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



Increased Transmitral Gradient Increased Regurgitant Volume

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



# AS and MR

Effect on Ejection Fraction after Correction





#### 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) = Av

$$- M = Qv = Av^2$$

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

• 
$$v \propto \sqrt{\Delta p}$$
  
•  $\therefore Q \propto \sqrt{\Delta p}$  AND  $M \propto \Delta p$ 





#### **Echo Evaluation**

Grading MR

#### Effective Regurgitant Orifice Area (PISA):

Flow Convergence Method





Vena Contracta:



#### Northwestern Medicine

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.



#### Case 1: What is the optimal treatment strategy?

OR? Percutaneous? Fix AS? Fix MR? Fix Both?

- 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



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.

#### What Happens to MR after TAVR?

**Predictors** 

TABLE 2	Independent Predictors of Persistent MR After TAV	ł
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	OR	95% CI	p Value
Mitral leaflets calcification by MDCT (2 or 3)	3.942	1.208-12.864	0.023
Mitral annulus calcification by MDCT (2 or 3)	11.233	4.032-31.297	<0.001
Organic MR	2.594	0.858-7.845	0.091
NOAF	9.258	2.103-40.769	0.003
Persistent LBBB	2.503	0.921-6.800	0.072
SPPA	2.535	0.882-7.291	0.84
Mitral annulus diameter >35.5 mm	9.000	3.205-25.285	<0.001

Significant p values are in **bold**.

 $\mathsf{TAVR} = \mathsf{transcatheter}$  aortic valve replacement; other abbreviations as in Table 1.



#### Northwestern Medicine®

Cortés, Carlos, et al. "Mitral regurgitation after transcatheter aortic valve replacement: prognosis, imaging predictors, and potential management." JACC: Cardiovascular Interventions 9.15 (2016): 1603-1614.

## 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.

#### 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)



#### Northwestern Medicine<sup>®</sup>

Vollenbroich, René, et al. "The impact of functional vs degenerative mitral regurgitation on clinical outcomes among patients undergoing transcatheter aortic valve implantation." American Heart Journal 184 (2017): 71-80.





12

#### Post TAVR AV





# 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



Climbed Kilimanjaro last summer! Medicine 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





AR





#### Multivalvular Disease

- What is the net clinical effect of multiple valvular lesions?
- How do we grade severity of each lesion?
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	By this Valvular Lesion	AR	MR	PR	TR
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Native valvular Regurgitation	MS	Little direct impact,	If MV is heavily calcified,	Lesion most likely to	Lesion most likely to
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Northwestern	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

ment of valvular regurgitation with Doppler echocardio

aphy and CMR

Table 17 Impact of multivalvular disease on asse

AS, Aortic stenosis; MS, mitral stenosis; NA, not applicable; PAP, pulmonary artery pressure; PH, pulmonary hyper Reg, regurgitant: ROA, regurgitant orifice area; RVSP, right ventricular systolic pressure; TS, tricuspid stenosis. CMB-related providerations are in Indet ion: PS, pulmonic st



- Post-operatively:
  - High incidence of LV Dysfunction

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- 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?





http://www.mardil.com/overview/

#### AR and MR Volumetric Methods

#### Reference Stroke Volume:





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



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- PISA Radius = 2 cm
- ERO = 1.6 cm<sup>2</sup>
- Regurgitant Volume = 167 ml
- Systolic flow reversal noted in pulmonary veins

#### **Severe MR**

# AR and MR





May overestimate severity of AR



#### TEE Flail P2





#### TEE





Mild to moderate AR

#### Multivalvular Disease

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



#### 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%

#### Northwestern Medicine

Roy, David A., et al. "Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation." Journal of the American College of Cardiology 61.15 (2013): 1577-1584.

#### 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

# RIP 11/30/16



"Transcatheter options for the treatment of noncalcified aortic regurgitation." JACC: Cardiovascular Interventions 8.14 (2015).

# 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

Northwestern 1. htt Medicine 2. Sar

http://www.bostonscientific.com/en-US/products/transcatheter-heart-valve/lotus-edge-valve-system.html Saraf, Smriti, et al. "Use of the Lotus Transcatheter Valve to Treat Severe Native Aortic Regurgitation." The Annals of Thoracic Surgery 103.4 (2017): e305-e307.

#### Percutaneous Options for Aortic Regurgitation



С



N/V



В

- 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

<sup>&</sup>quot;Transcatheter options for the treatment of noncalcified aortic regurgitation." JACC: Cardiovascular Interventions 8.14 (2015).

#### 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



"Transcatheter options for the treatment of noncalcified aortic regurgitation." JACC: Cardiovascular Interventions 8.14 (2015).

#### 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.
- <u>Past Medical History</u>
  - 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 cm<sup>2</sup>





	Table IV Impact of	поличанова словазе от азвезатели от чанова тедогдлахот что соррнет еспосатоюдгарлу ало онит			
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Northwestern	TR	Little direct impact	Little direct impact	Rapid RV filling from TR may further shorten PR pressure half-time, and color DR international	NA

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#### MR and TR

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





#### MR and TR How does MR affect TR?



#### Northwestern Medicine®

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

#### 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)

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Rodés-Cabau, Josep, et al. "Transcatheter therapies for treating tricuspid regurgitation." Journal of the American College of Cardiology 67.15 (2016): 1829-1845.

#### 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

Medic North

Rodés-Cabau, Josep, et al. "Transcatheter therapies for treating tricuspid regurgitation." Journal of the American College of Cardiology 67.15 (2016): 1829-1845.

#### FORMA – Coaptation Device



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



Rodés-Cabau, Josep, et al. "Transcatheter therapies for treating tricuspid regurgitation." Journal of the American College of Cardiology 67.15 (2016): 1829-1845.

# 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 cm<sup>2</sup> to 11.3 +/- 2.7 cm<sup>2</sup>; p=0.02
- EROA reduction:
  - $0.51 + 0.18 \text{ cm}^2$  to  $0.32 + 0.18 \text{ cm}^2$ ; p = 0.02
- LVSV increase:
  - 63.6 +/- 19.9 ml to 71.5 +/- 25.7 ml; p=0.02

#### Northwestern Medicine

Hahn, Rebecca T., et al. "Early Feasibility Study of a Transcatheter Tricuspid Valve Annuloplasty: SCOUT Trial 30-Day Results." Journal of the American College of Cardiology 69.14 (2017): 1795-1806.

#### TriCinch



PREVENT study

Medicine

Rodés-Cabau, Josep, et al. "Transcatheter therapies for treating tricuspid regurgitation." Journal of the American College of Cardiology 67.15 (2016): 1829-1845.



Cardioband

Rogers, Toby, et al. "Transatrial intrapericardial tricuspid annuloplasty." JACC: Cardiovascular Interventions 8.3 (2015): 483-491. http://www.valtechcardio.com/our-products/cardioband-tricuspid/

# Percutaneous TV Replacement

Gate<sup>™</sup> Tricuspid Valved Stent





Outflow view of Replacement Valve

- 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



# ASE GUIDELINES AND STANDARDS Recommendations for Noninvasive Evaluation of A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular William A. Zoghbi, MD, FASE (Chair), David Adams, RCS, RDCS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Ehyse Foster, MD, FASE, Paul A. Grayhurn, MD, FASE, Rebecca T. Hahm, MD, FASE, Liopan J. Shah, MD, MMSK, \* Stanton Shernan, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMSK, \* Stanton Shernan, MD, FASE, Paladineh: Thu-wenfuranthan, MD, MSK, FASE', Tanse D. Thornas, MD, FASE, Neil J. Weissman, MD, FASE, Houtsen and Dallas, Texus Durbans, Nerth Carbina; Chicaga, Illinwic Roboterr, Minneona; San Francisco, California: New York, Nor Yor Fey Foliaddebia, Pannofpania; Boston, Masaedusett; Toronic, Ontaris, Canada; and Washington, DC

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Native Valvular Regurgitation

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