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ASE Guidelines: The clinical Use of Stress Echocardiography in Non-Ischemic Heart Disease







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Disclosures

- Speaker: Philips Healthcare, Boston Scientific, Medtronic, Edwards Lifescience
- Consultant: St. Jude Medical, Abbott Vascular

The Clinical Use of Stress Echocardiography in Non-Ischaemic Heart Disease: Recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography

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Lancellotti, P et al. J Am Soc Echocardiogr 2017;30:101-38

Types of Stress Tests

- Exercise stress testing preserve the integrity of the electromechanically response and provides valuable information regarding functional status
 - It is the test of choice for most applications
 - Echocardiography at the time of exercise also allows links to be drawn among symptoms, cardiovascular workload, wall motion abnormalities, and haemodynamic responses, such as pulmonary pressure and transvalvular flows and gradients.

Choice of Exercise

Treadmill stress

- Higher maximum heart rate (2-3x baseline)
- SBP $\uparrow \geq 50\%$ with \downarrow SVR
- ↑Contractility 3-4×
- Functional aerobic capacity well-defined
- Associated with increase in LVED volume initially, followed by smaller volumes with [↑]HR.

Bicycle stress

- Higher blood pressure in supine position
- Shorter duration of exercise/max workload and lower HR in setting of earlier leg fatigue.
- Allows continuous imaging and Doppler assessment, including peak stress

Types of Stress Tests

- Pharmacologic Stress does not replicate the complex hemodynamic and neurohormonal changes triggered by exercise.
 - Dobutamine stress is a useful modality for the evaluation of contractile and flow reserve, wall motion. Contraindicated in HCM
 - Vasodilator stress is particular useful for the assessment of both wall motion and coronary flow reserve. Can be used in HCM

Pharmacologic Stress

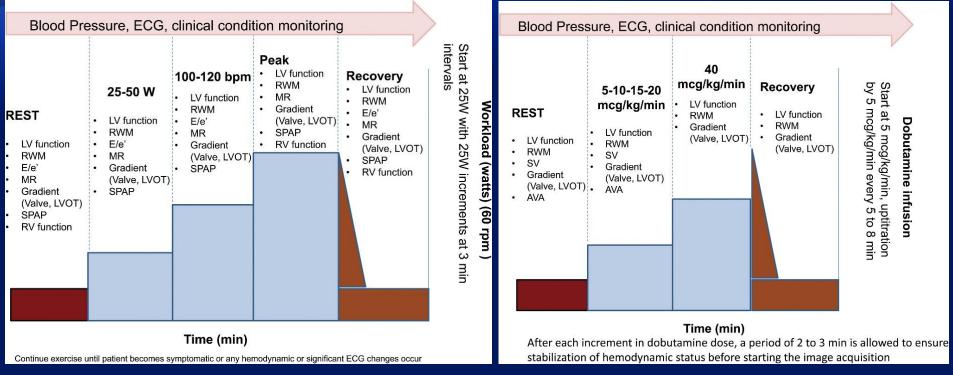
Dobutamine stress

- THR (2-3x) and contractility (>4x)
- Mild ↑BP (1.5-2x) initially with ↓BP (vasodilator) at higher doses
- Less recruitment of venous blood volume (LV volumes and wall stress less than exercise stress)
- Vasodilator stress (dipyridamole, adenosine or regadenoson)
 - Small \downarrow BP, \uparrow HR and minor \uparrow contractility
 - Generates a supply-demand mismatch and ↓subendocardial flow in areas of coronary stenosis

Stress Protocols

Exercise echocardiography protocol and parameters

Dobutamine echocardiography protocol and parameters



DSE:

- 5-8 minute stages starting at 5 μ g/kg/min, titrating in increments of 2.5-5 μ g/kg/min up to 20 μ g/kg/min
- 40 μ g/kg/min may be required for inotropic reserve in patients with HR or on β -blockers

Diagnostic end-points, causes of test cessation and definition of abnormal stress test

Diagnostic end-points	Causes of test cessation	Abnormal test (≥ 1 criteria)
 Max dose/Workload Target heart rate Obvious ECG positivity Obvious Echo positivity Severe chest pain 	 Intolerable symptoms Muscular exhaustion Hypertension (220/120 mmHg) Symptomatic hypotension (>40 mmHg decrease) Arrhythmias (SVT, AF, frequent or complex ventricular ectopy) 	 Symptoms: angina, dyspnea, dizziness, syncope or nearsyncope, fatigue at low workload Ischemia ≥ 2 mm ST segment depression in comparison to baseline level New or worsening RWMA Arrhythmias (NS and SVT) Specific targeted features*

 Asterisk indicates specific targeted features relates to cutoff values associated with poor outcome in defined population (i.e. >50 mmHg intraventricular obstruction).

Definitions

Interventricular
 Obstruction

LVOT gradient >50mmHg

Contractile Reserve

↑ LVEF by≥5%
↑ GLS by≥2%

- Flow Reserve
- Ischemia
- Recruitable viable myocardium

- ↑ forward stroke volume by ≥ 20%.
- New or worsening wall motion abnormality
- Improvement of RWM motion by ≥ 1 grade in dysfunctioning segments

Asymptomatic Patients with Severe Valve Disease

Disease State

- Severe MR
 Exercise
- Severe MS
 Exercise
- Severe AR
 Exercise
- Severe AS
 Exercise

Flow AS (low EF)

Aim of Test

- Assess symptoms and ex-tolerance, ±
 SPAP ↑ >60 mmHg, EF ↑<4%, ± GLS ↑<-2%
- Assess symptoms and ex-tolerance, ± ↑ Mean grad >15 mmHg, ± SPAP ↑ >60 mmHg
- Assess symptoms and ex-tolerance and contractile reserve
- Assess symptoms and ex-tolerance, ±LVEF ↓, ±SBP ↓ or <20 mmHg rise, ST depression, RWMA, contractile reserve, GLS, SPAP ↑>60 mmHg, ↑ mean gradient >18-20 mmHg
- Flow reserve, gradient, valve area

Definitions

- Dynamic primary MR
 Exercise
- Dynamic Secondary MR *Exercise*
- Fixed AS
 Exercise
- Fixed MS *Exercise DSE*
- Abnormal Prosthetic Mitral Valve ESE or DSE
- Abnormal Prosthetic Aortic Valve
 ESE or DSE
- RV Dysfunction

An increase by ≥ 1 grade in MR SPAP ≥ 60 mmHg, and a lack of contractile reserve (<5% increase in EF or <2% increment inGLS

- △EROA ≥10-13 mm²
- ► ► MPG↑ ≥18-20 mmHg
- MPG¹>15 mmHg
 MPG¹>18 mmHg
 - ____ ◆ MPG↑>10 mmHg
 - MPG¹>20mmHg
 - TAPSE <19 mm (Primary MR)

Exercise

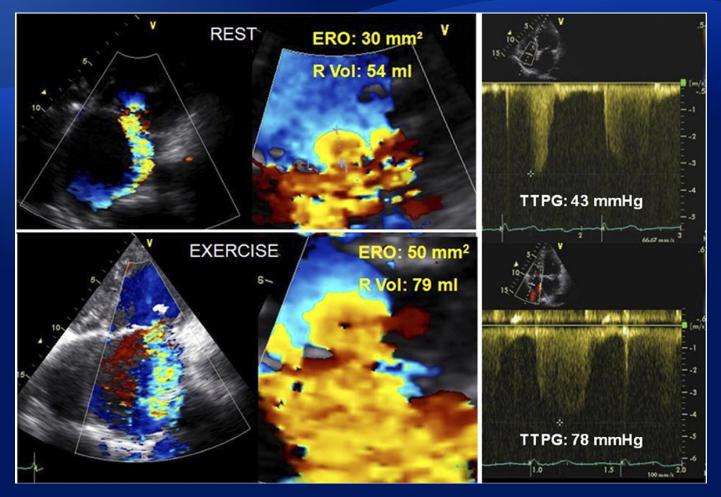
Exercise Stress Testing for MR

- Exercise capacity itself is a predictor of the development of symptoms or LV dysfunction in asymptomatic patients with MR
- In symptomatic patients with mild MR at rest, exercise echocardiography may be useful in elucidating the cause of symptoms
 - Increase in severity of MR
 - Increase in pulmonary arterial pressure
 - PASP >60 mm Hg during exercise has been suggested as a threshold value above which asymptomatic patients with severe MR might be referred for surgical valve repair
- Response of LV similar to pts with AR
 - Prognostic importance unknown
 - Strain imaging may be useful

Ischemic MR

- Mitral regurgitation should be quantitated at rest and during exercise
 - The regurgitant jet area is not reproducible and should preferably not be used
 - The PISA (proximal isovelocity surface area) method is reproducible and reliable if the flow-convergence region is appropriate.
 - The Doppler method is an alternative in patients with a suboptimal flow-convergence definition.
 - Regurgitant volumes calculated by the Doppler method are usually slightly larger than those obtained with the PISA method
 - The results of the two methods may therefore be averaged.
- The ERO area appears to be the most robust parameter for quantifying mitral regurgitation at rest and during exercise.
 - ERO ≥ 20 mm2 is prognostically significant
 - An increase in ERO ≥13 mm² during exercise is associated with both mortality and hospital admission for worsening heart failure

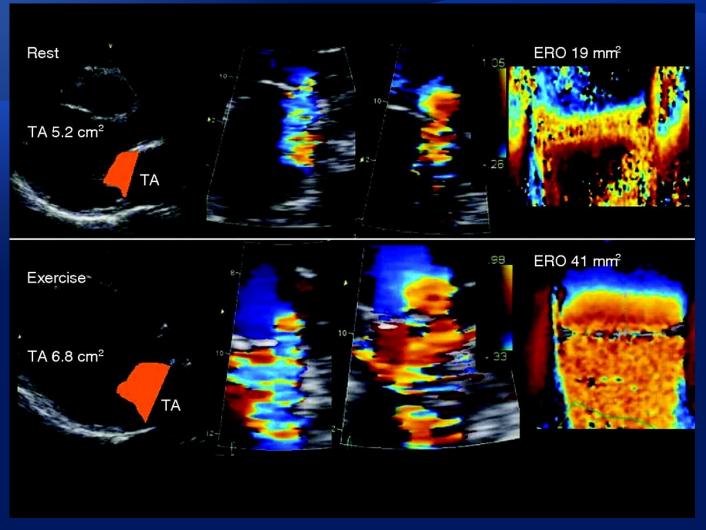
Exercise Echocardiography in Ischemic Mitral Regurgitation



Picano, E. et al. J Am Coll Cardiol 2009;54:2251-2260



End-systolic stop frame images and proximal flow-convergence region at rest and during exercise in a patient with chronic posterior myocardial infarction and functional mitral regurgitation.



Piérard L A , Lancellotti P Heart 2007;93:766-772



Exercise Stress Testing for AR (Case courtesy of Linda Gillam)

32 yr. old Male (asymptomatic but sedentary)

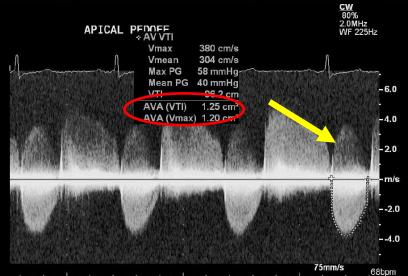
 History: Bicuspid Aortic valve with mixed valvular disease (moderate to severe AR, moderate AS)

Indication:

- Functional capacity
- -Ventricular response to exercise
- -Transvalvular gradients

Baseline





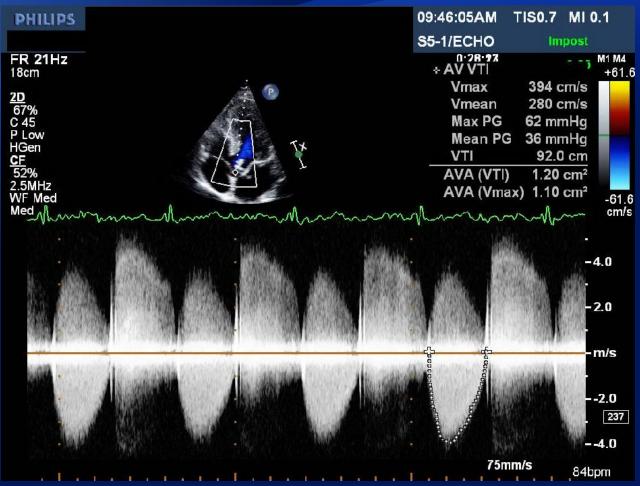
Aortic mean PG of 40mmHg, Peak PG of 58mmHg a AVA of 1.2cm2 PHT is 353millisec

Stress Echo Performed

- Exercised for 9 min. Bruce protocol /14% grade, speed 3.4 mph/10 METs; stopped because of dyspnea
 - -Exercise tolerance reduced for age -Symptomatic based on response at low level exercise

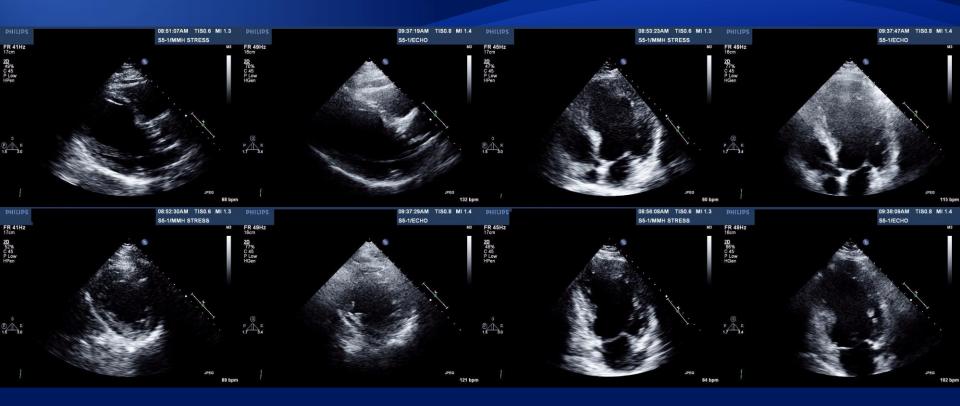
Achieved Peak HR: 155bpm & BP: 148/62mmHg

Peak - Aortic PG & AVA



Mean Ao PG 36mmHg/Peak Ao PG 62mmHg AVA 1.20cm2 PHT shortens

AR Stress: Contractile Reserve



 EF at Baseline (66%) vs. EF Peak exercise (55%)
 LVEDd/LVESd cavity size change (Base) = 6.9/4.2(cm) vs. (Peak) 7.0/4.7(cm)

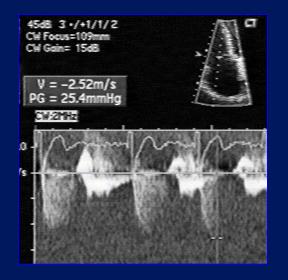
Case MS



50 year old woman with history of asthma and rheumatic fever who presents with exertional dyspnea (Class III NYHA).

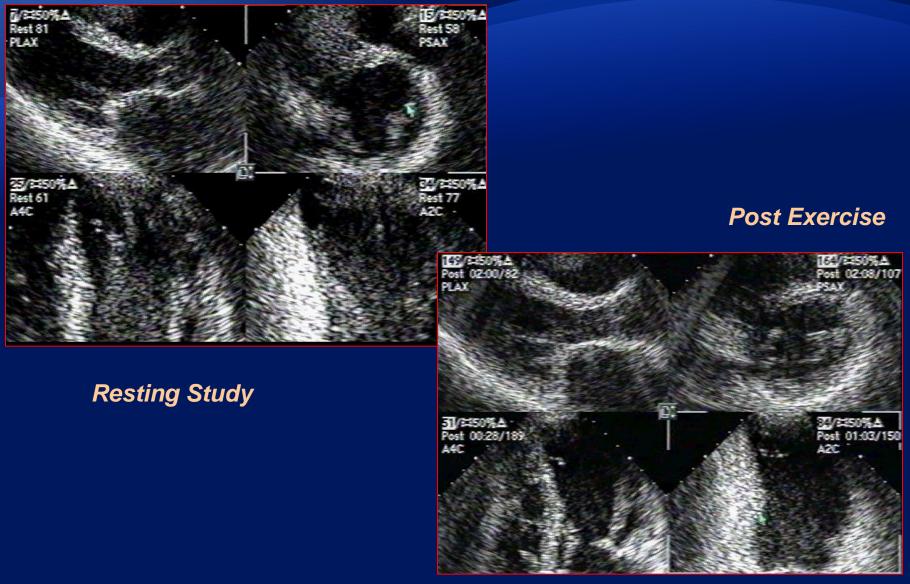


MOVA by PHT = 1.6 cm² Mean gradient = 10 mmHg

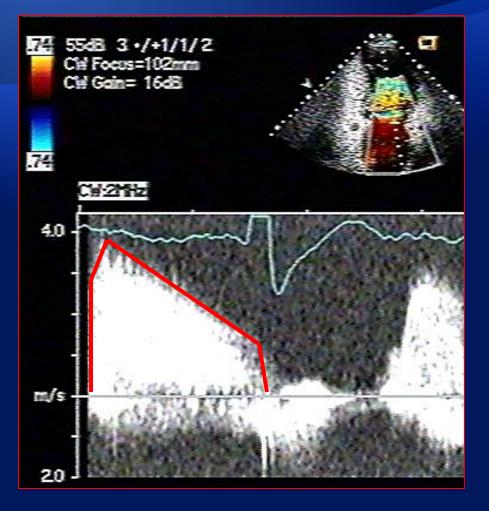


TR = 2.5 m/s

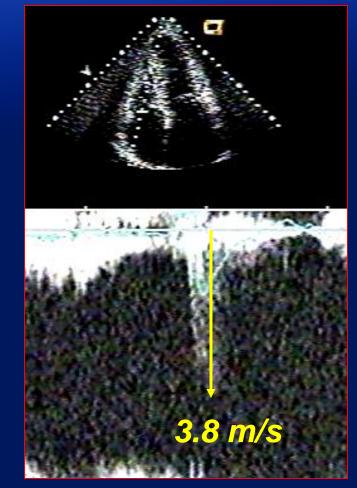
Case MS



Case MS



Mean gradient = 25 mmHg



TR = 3.8 m/s Gradient = 58 mHg (add assumed RAP)

Stress Echo in Mitral Stenosis

- Calculation of mitral valve area by Doppler methods is controversial
 - Reliability of PHT calculation questionable
- Mean transmitral gradients and peak tricuspid regurgitant velocities are reliable
- Patient's symptoms reliable

Exercise-induced pulmonary hypertension(>60-70 mmHg) warrants close follow-up

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

STATE-OF-THE-ART REVIEW

Natural History, Diagnostic Approaches, and Therapeutic Strategies for Patients With Asymptomatic Severe Aortic Stenosis

Philippe Généreux, MD,^{a,b,c} Gregg W. Stone, MD,^{a,b} Patrick T. O'Gara, MD,^d Guillaume Marquis-Gravel, MD,^c Björn Redfors, MD, PHD,^{b,e} Gennaro Giustino, MD,^f Philippe Pibarot, DVM, PHD,^g Jeroen J. Bax, MD, PHD,^h Robert O. Bonow, MD,ⁱ Martin B. Leon, MD^{a,b}

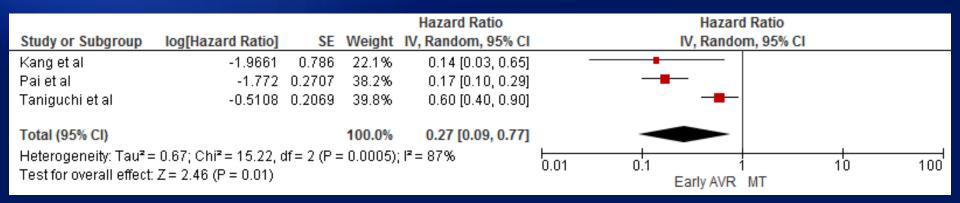
Généreux et al J Am Coll Cardiol. 2016 May 17;67(19):2263-88

Observational Studies of comparing AVR vs. Observation in Asymptomatic Severe AS Patients

Authors	AS definition	Ν	Age	Female	Follow-up (median)
Pellikka et al 1990	Severe AS Doppler PV ≥4m/s	143 30 AVR 113 Medical	72 (mean) 40 to 94	38%	AVR 21 m Medical 20 m
Otto et al 1997	Moderate-severe AS; Doppler PV ≥2m/s	123	63±16 22 to 84	30%	2.5 ±1.4 yrs
Pai et al 2006	Severe AS AVA <0.8cm²	338 99 AVR 239 Medical	71±15	49%	3.5 years
Kang et al 2010	Very severe AS AVA ≤0.75 cm² AND PV≥4.5 m/s or a MG ≥50 mmHg	197 102 AVR 95 Medical	63±12	50%	AVR 1265 d Medical 1769 d
Taniguchi et al 2015	Severe AS AVA: <1cm2 MG: >40mmhg PV: >4m/s	1808 291 AVR 1517 Medical	AVR 71.6±8.7 Medical 77.8±9.4	60%	1361 d

Généreux et al J Am Coll Cardiol. 2016 May 17;67(19):2263-88

All-Cause Mortality: AVR vs. Medical Therapy in Asymptomatic Severe AS



Adjusted: ~3.7 fold increase in all-cause Mortality

Généreux et al J Am Coll Cardiol. 2016 May 17;67(19):2263-88

Meta-Analysis of Prognostic Value of Stress Testing in Patients With Asymptomatic Severe Aortic Stenosis

Asim M. Rafique, MD^a, Simon Biner, MD^{a,b}, Indraneil Ray, MD^a, James S. Forrester, MD^a, Kirsten Tolstrup, MD^a, and Robert J. Siegel, MD^{a,*}

	Normal	Abnormal	Odds Ratio		Odds Ratio		
Study or Subgroup	Stress Test	Stress Test	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI		
Alborino 2002	2/12	14/18	7.1%	0.06 [0.01, 0.38]			
Amato 2001	3/22	35/44	11.4%	0.04 [0.01, 0.17]			
Das 2005	10/79	26/46	22.3%	0.11 [0.05, 0.27]			
Lancellotti 2005	4/43	14/26	13.3%	0.09 [0.02, 0.32]			
Marechaux 2007	10/26	20/24	12.6%	0.13 [0.03, 0.47]			
Peidro 2007	10/35	37/67	22.5%	0.32 [0.13, 0.78]			
Takeda 2001	13/36	10/13	10.9%	0.17 [0.04, 0.73]			
Total	52/253	156/238	100.0%	0.12 [0.07, 0.21]	•		
Heterogeneity: Tau ² = 0.13; Chi ² = 8.08, df = 6 (P = 0.23); I ² = 26%					0.01 0.1 1	10 100	
Test for overall effect: Z = 7.63 (P < 0.00001)			Reduced risk	Increased risk			

Abnormal stress test associated with ~8 fold increase in CV Events

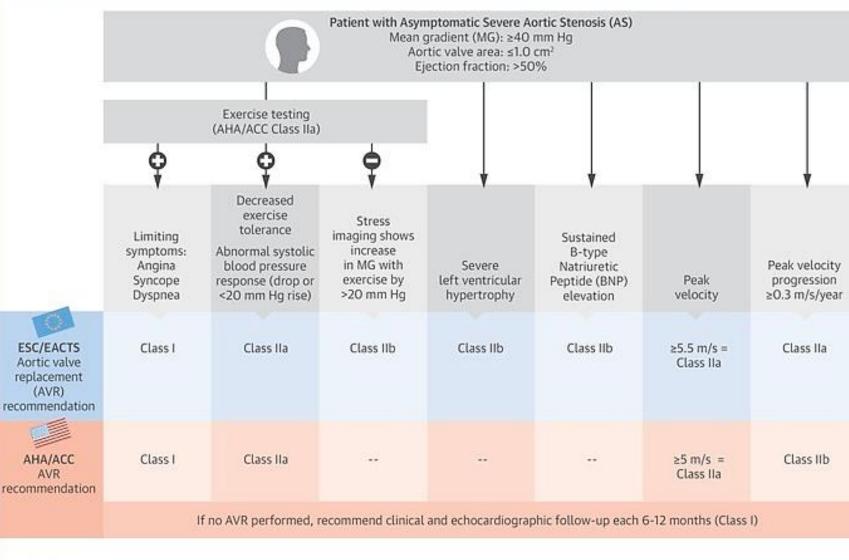
Rafique et al. Am J Cardiol 2009;104:972–977

AHA/ACC Guidelines

- Exercise testing can also identify a limited exercise capacity, abnormal BP response, or arrhythmia.
- An abnormal hemodynamic response
 - Hypotension or failure to increase BP (<20 mm Hg increase) with exercise
 - Symptoms
 - ST-segment abnormalities with
 - However, electrocardiographic ST-segment depression is seen in >80% of patients with AS with exercise and is nonspecific for diagnosis of CAD.
 - Ventricular tachycardia was reported in early exercise studies but has not been reported in contemporary series.

Nishimura R et al. 2014

CENTRAL ILLUSTRATION: Treatment Algorithm for Asymptomatic Severe Aortic Stenosis: Basis of Current American and European Guidelines



Généreux, P. et al. J Am Coll Cardiol. 2016;67(19):2263-88.

Evaluation of a Strategy of Transcatheter Aortic Valve Replacement Compared to a Strategy of MedicaL Observation in the Treatment of As Ymptomatic Severe Aortic Stenosis: EARLY-TAVR trial

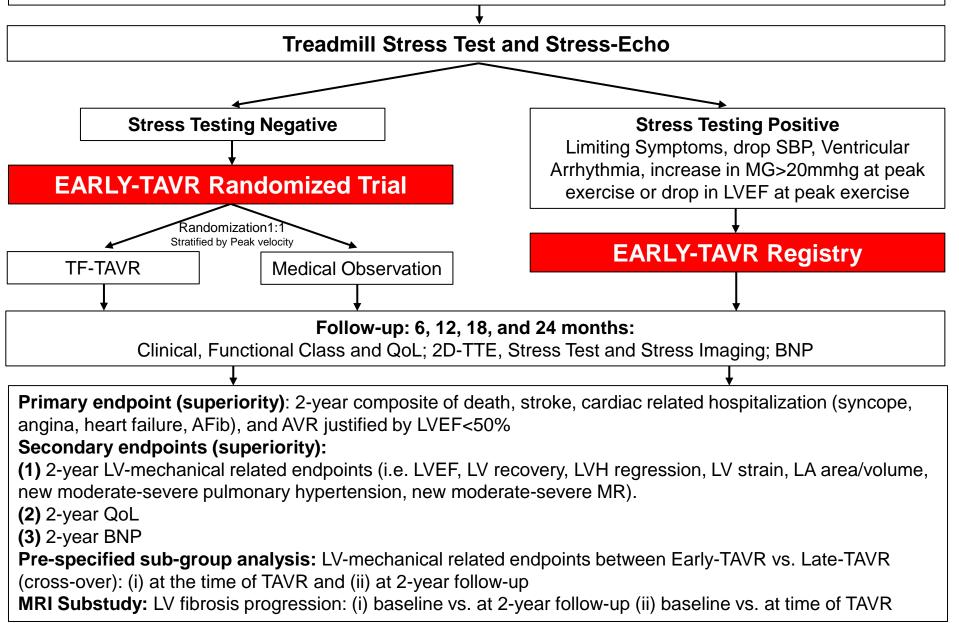
Philippe Généreux, MD, Gregg W. Stone, MD, Ori Ben-Yehuda, MD, Martin B. Leon, MD

October 10th, TCT 2015, San Francisco,





Asymptomatic Severe AS per questionnaire and 2D-TTE (PV ≥4m/s and AVA ≤1 cm²) Exclusion if patients clinically symptomatic, EF<50%, other concomitant surgical indications Exclusion if not anatomically suitable for TF-TAVR



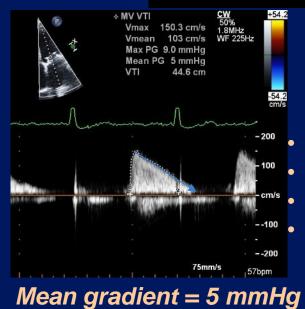
Symptomatic Patients with Non-severe Valve Disease

Disease State	Aim of Test		
 Non-severe regurgitation (MR and AR) Exercise 	 Assess increase in regurgitation, ± SPAP ↑ >60 mmHg, EF ↑<4% 		
 Non-severe MS Exercise or low-dose DSE 	 ↑ Mean grad >15 mmHg (ex) or >18 mmHg (DSE), ± SPAP ↑ >60 mmHg 		
 Non-severe AS or paradoxical low-flow AS Exercise 	 Assess peak/mean gradient, increase and change in valve are 		
 Equivocal PPM (AVR or MVR) Exercise or low-dose DSE 	 Assess gradient and valve area change 		
 Mitral Annuloplasty resting mean gradient >3 mmHg 	 Mean gradient ≥7 mmHg, peak exercise SPAP ≥ 50 mmHg 		

MVR







- 27 mm CE MVR 2 years ago Persistent DOE MVOA calculated to 1.7 cm2
- Deceleration time = 120 msec



TR Vmax = 2.1 *m*/s

Approach to High Gradient in an Mitral Prosthetic Valve

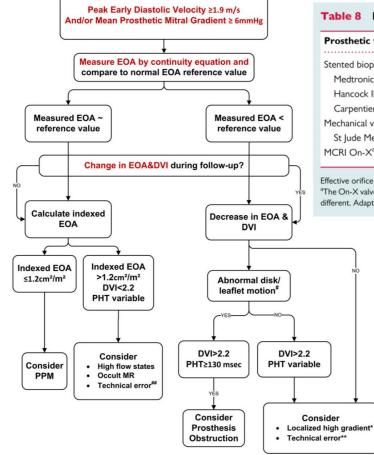


Table 8 Normal reference values of effective orifice areas for the prosthetic mitral valves

Prosthetic valve size (mm)	25	27	29	31	33
Stented bioprosthetic valves					
Medtronic Mosaic	1.5 ± 0.4	1.7 ± 0.5	1.9 ± 0.5	1.9 ± 0.5	-
Hancock II	1.5 ± 0.4	1.8 ± 0.5	1.9 ± 0.5	2.6 ± 0.5	2.6 ± 0.7
Carpentier-Edwards Perimount	1.6 ± 0.4	1.8 ± 0.4	2.1 ± 0.5	-	-
Mechanical valves					
St Jude Medical Standard	1.5 ± 0.3	1.7 ± 0.4	1.8 ± 0.4	2.0 ± 0.5	2.0 ± 0.5
MCRI On-X ^a	$\textbf{2.2} \pm \textbf{0.9}$	$\textbf{2.2} \pm \textbf{0.9}$	$\textbf{2.2} \pm \textbf{0.9}$	$\textbf{2.2} \pm \textbf{0.9}$	2.2 ± 0.9

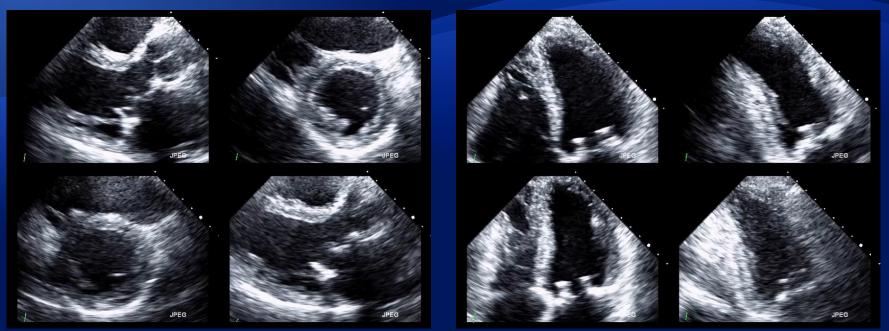
Effective orifice area is expressed as mean values available in the literature. Further studies are needed to validate these reference values.

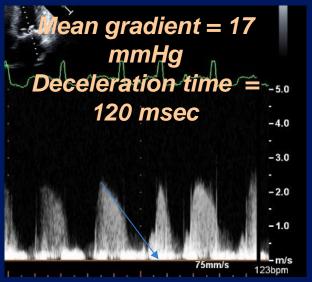
^aThe On-X valve has just 1 size for 27 to 29 and 31 to 33 mm prostheses. In addition, the strut and leaflets are identical for all sizes (25 to 33 mm); only the size of the sewing cuff is different. Adapted with permission from Ref. 7.

- 27 mm CE MVR 2 years ago
- Persistent DOE
- MVOA calculated to 1.7 cm2

Lancellotti P et al. Eur Heart J Cardiovasc Imaging. 2016 Jun;17(6):589-90.

MVR: Stress







Symptomatic patient-prosthesis mismatch

S.B.

Clinical History				
Age	83 years			
Gender	Female			
Medical history	Heart Failure Arterial Hypertension Hypercholesterolemia			
Rx	ASA 81 mg QD Metoprolol ER 50 mg QD Furosemide 40 mg QD Spironolactone 37.5 mg QD Atorvastatin 20 mg QD			

- Heart Failure NYHA class III, ACC/AHA stage C
- Creatinine o.81 mg/dL
- NT pro-BNP 9 952 pg/mL
- ECG: Sinus rhythm. LBBB

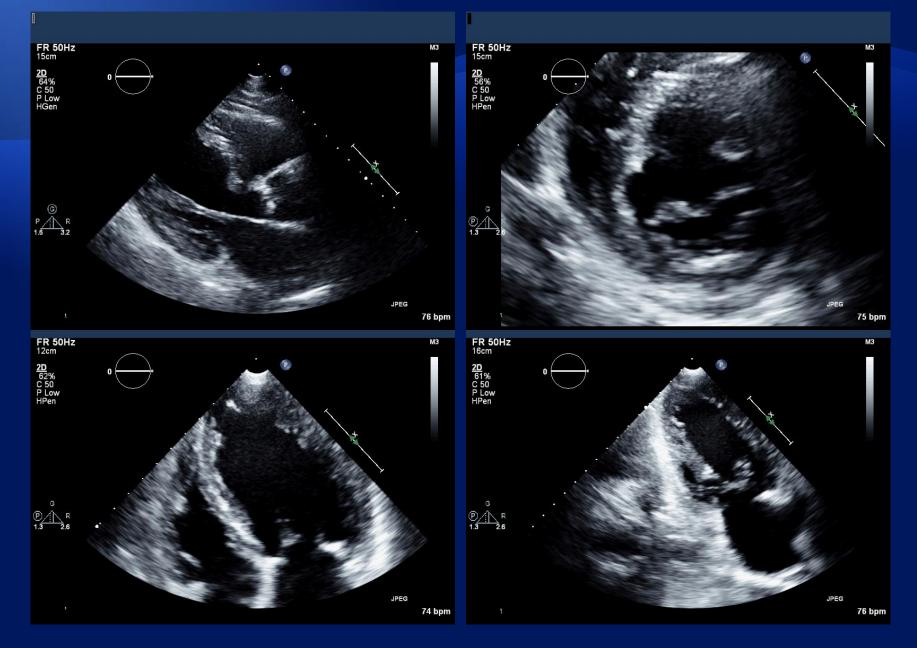
Physical Examination

Height: 5ft 3in Weight: 115 lbs BSA 1.53 m²

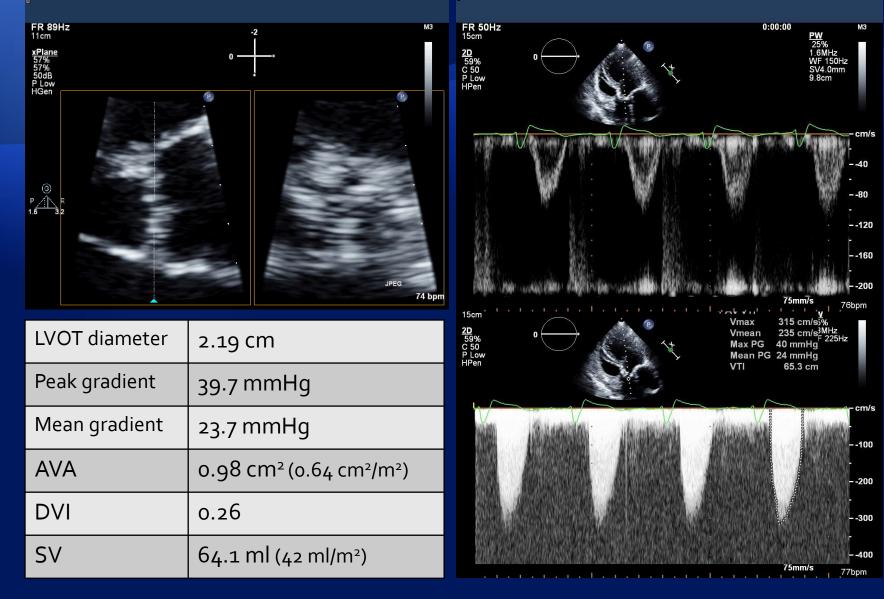
BP 124/70; HR 68 bpm

No jugular venous distention Soft S₂ III/VI SM RUSB Clear lungs No edema

S.B. Baseline Echo LVEF 35%



S.B. Baseline Echo



DSE

Baseline		Low dose (5 mcg/kg/min)		Peak dose (15 mcg/kg/min)	
Peak gradient	34.4 mmHg	Peak gradient	39.7 mmHg	Peak gradient	55.7 mmHg
Mean gradient	19.0 mmHg	Mean gradient	23.7 mmHg	Mean gradient	25.3 mmHg
AVA	0.98 cm ² (0.64cm ² /m ²)	AVA	1.17 cm ² (0.76cm ² /m ²)	AVA	1.28 cm ² (0.84cm ² /m ²)
DVI	0.26	DVI	0.31	DVI	0.34
SV	64.1 ml (42 ml/m²)	SV	70.2 ml (46 ml/m²)	SV	71.3 ml (47 ml/m²)
LVEF	35%	LVEF	40%	LVEF	50%

Negative stress echo for ischemia 11% increase in stroke volume with increase AVA with dobutamine

Follow-up ECHO with GDMT



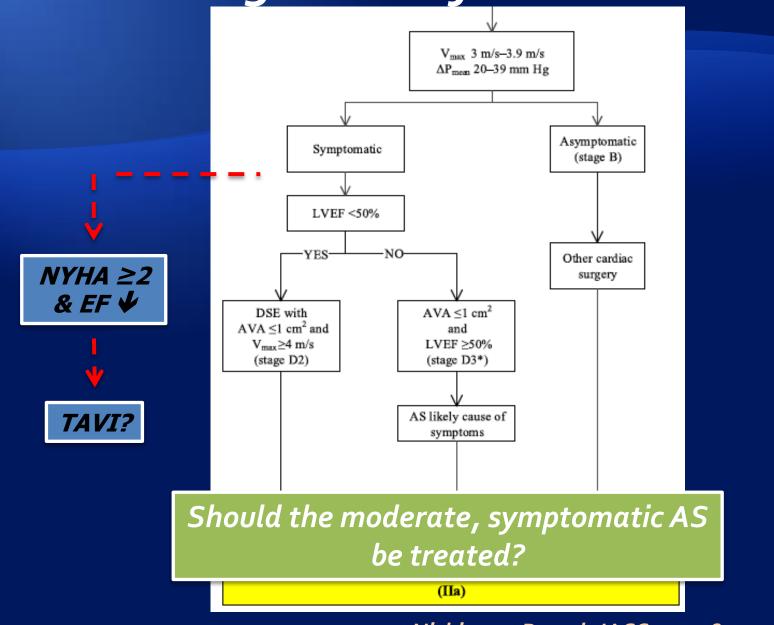






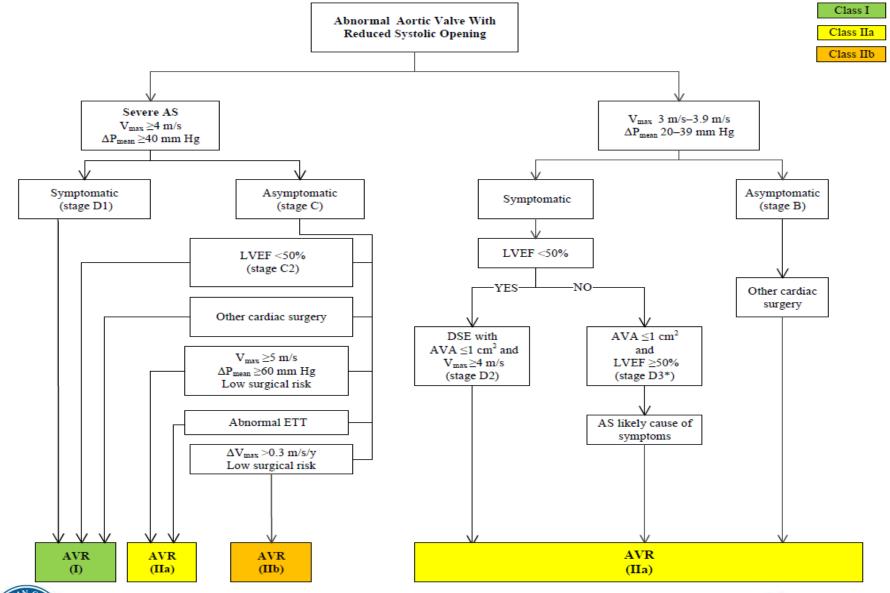
LVEF 46%,BP 113/59 HR 56 bpm NYHA Class II

Management of Moderate AS



Nishimura R et al. JACC 2014;63:e57-185.

Indications for Aortic Valve Replacement in Patients With Aortic Stenosis





Helping Cardiovascular Professionals Learn. Advance. Heal.









TAVR UNLOAD TRIAL

- NewYork-Presbyterian

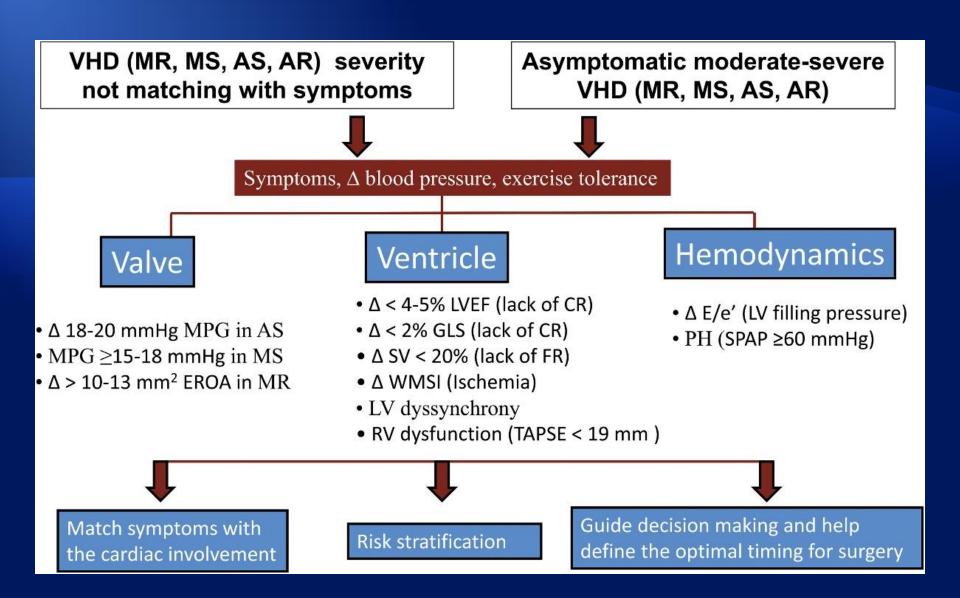


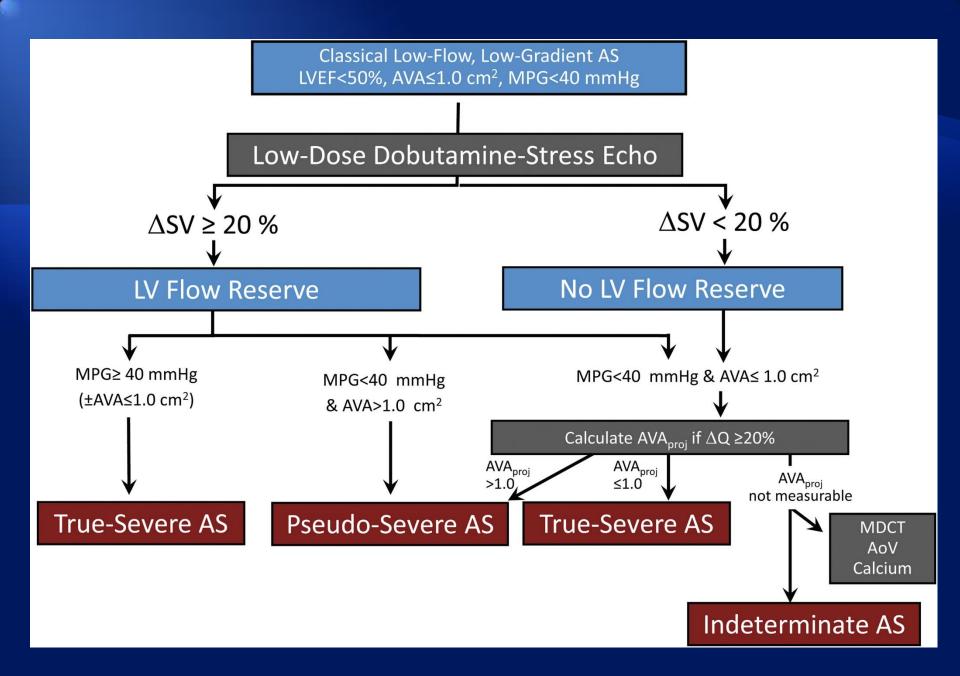


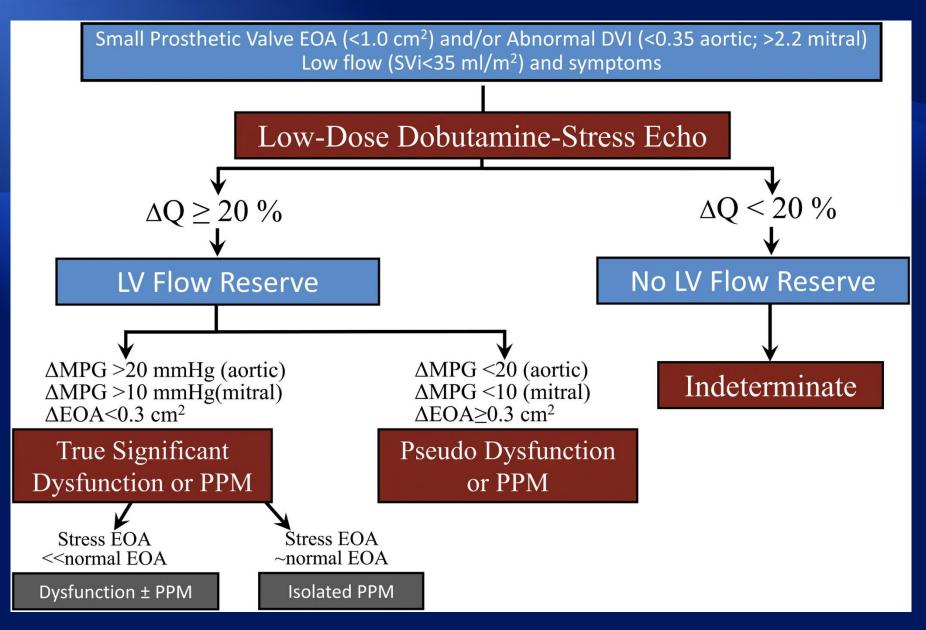


INSTITUT UNIVERSITAIRE DE CARDIOLOGIE ET DE PNEUMOLOGIE DE QUÉBEC









Evaluation of aortic/mitral prosthetic valves function in patients with low flow.

The Clinical Use of Stress Echocardiography in Non-Ischaemic Heart Disease: Recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography

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Thomas Ryan, MD, FASE, Jeane M. Tsutsui, MD, PhD, and Albert Varga, MD, PhD, FESC, *Liège, Belgium; Bari* and Pisa, Italy; Rochester, Minnesota; Leuven, Belgium; New York, New York; Rennes, France; Oslo, Norway; London, UK; Seoul, South Korea; Atlanta, Georgia; Toronto and Québec, Canada; Columbus, Ohio; São Paulo, Brazil; and Szeged, Hungary

Lancellotti, P et al. J Am Soc Echocardiogr 2017;30:101-38

Targeted Parameters

Disease State

Aim of Test

- Diastolic Stress Echo Exercise
- HCM
 Exercise

Dilated COM

Exercise

- E/e' increase ± ↑SPAP
- LVOTO $\pm \uparrow$ SPAP, E/e' increase $\pm \uparrow$ SPAP, Δ MR, RWMA

• Δ Contractility, E/e' increase ± \uparrow SPAP, RWMA, Lung comets, Δ MR

Congenital Heart Disease

Disease State

Aim of Test

- Atrial septal defect
 Exercise or DSE
- Tetralogy of Fallot
 Exercise
- Aortic Coarctation
 Exercise
- Univentricular hearts
 Exercise

- [↑]SPAP, RV Contractile Reserve
- LV/RV Contractile Reserve
- ↑Gradient, ↑LV contractility
- ↑contractility, AV valve regurgitation, ∆Gradients





THANKYOU!

