Low-Gradient Severe AS Early AVR or Watchful Waiting

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Outcome of Asymptomatic Patients with Low-Gradient "Severe" Aortic Stenosis

In 619 asymptomatic patients (SEAS study), AV events* occurred in 48.5% pts with low-gradient "severe" AS (AVA < 1.0 cm² and mean gradient ≤ 40 mmHg) versus 44.6% with moderate AS (AVA: 1.0-1.5 cm²) during 46 months of follow-up (P= 0.37)
Outcome of low-gradient "severe" AS and normal ejection fraction similar to that of moderate AS

AV events*: CV death, AVR and CHF

Jander N, et al. Circulation 2011;123:887

Outcome in Low-Gradient "Severe" AS



Jander N, et al. Circulation 2011;123:887







Clavel MA et al., Eur Heart J, 2016

Low-Gradient AS with Depressed LVEF LVEF < 40% $\Delta P < 40$ EOA < 1.0 **Dobutamine Stress Echo** 1 SV > 20% 1 SV < 20% LV Flow Reserve **No LV Flow Reserve** (EOA Proj < 1.0-1.2)* (CT Ca > 1650) AP < 40" & EOA > 1.2" AP > 40" & EOA < 1.2" (EOAproi > 1.0-1.2) (EOA_{Proj} < 1.0-1.2) (CT Ca < 1650) (CT Ca > 1650) Yes No **True-Severe AS True-Severe AS Pseudo-Severe AS** SAVR (High Op. Risk) SAVR + CABG MEDICAL Rx TRIAL TAVR?

Pibarot P et al. J Am Coll Cardiol 2012:1845-53

Atrial Fibrillation

Impaired Longitudinal Systolic function

Impaired Diastolic Filling

Reduced Forward Stroke Volume Mitral Stenosis

Pronounced Concentric Remodeling

Reduced Transvalvular flow rate Tricuspid Regurgitation

Mitral

Regurgitation

Low-Flow, Low gradient AS with Preserved LVEF

Pibarot P, Dumesnil JG. Circulation 2013:1729

Paradoxical Low-flow, Low-gradient Severe AS with Preserved LVEF

Hachicha et al. Circulation. 2007

AVR Versus Medical Therapy in Symptomatic LGAS

Ozkan et al. Circulation 2013;128:622-631

Outcome of Low-flow Severe AS in PARTNER Trial

PARTNER-I B (inoperable): Medical vs. TAVR

Herrman HC et al, Circulation , 2013

Outcome of Low-flow Severe AS in PARTNER Trial

PARTNER-I A: TAVR ≈ SAVR

Herrman HC et al, Circulation , 2013

PARTNER Trial Included High-Gradient Severe AS

Inclusion Criteria
 Aortic valve area < 0.8 cm² with mean gradient
 > 40 mmHg or peak aortic jet velocity > 4 m/s

 Only 16% patients had normal EF and low flow, low gradient severe AS

Herrmann HC et al, Circulation, 2013

AVR for Symptomatic LG Severe AS

2012 ESC guidelines

- LF, LG AS with reduced EF and flow reserve (IIa)
- LF, LG AS and reduced EF without flow reserve (IIb)
- Low-flow, low-gradient AS with normal EF (IIa)

2014 ACC/AHA guidelines

- Dobutamine stress echo (IIa)
- LF, LG AS with reduced EF and flow reserve (IIa)
- Low-flow, low-gradient AS with normal EF (IIa)

Long Term Outcome of Low-Gradient AS, Moderate AS, and High-Gradient AS Under Medical Management

Tribouilloy C, et al. J Am Coll Cardiol. 2015;65: 55-66

Comparison of Survival Benefit of AVR Between LG/LF AS and HG AS

Low-gradient, Low flow AS

High-gradient AS

Tribouilloy C, et al. J Am Coll Cardiol 2015;65: 55-66

Impact of AVR on Survival in LF-LG aortic stenosis

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% Cl	Hazard Ratio IV, Random, 95% Cl
Belkin et al 2011	-0.7141	0.6902	0.0%	0.49 [0.13, 1.89]	
Clavel et al 2012	-1.124	0.2758	17.9%	0.32 [0.19, 0.56]	
Eleid et al 2013	-1.2448	0.3572	15.9%	0.29 [0.14, 0.58]	-0-
Grupper et al 2014	-0.6733	0.2707	0.0%	0.51 [0.30, 0.87]	
Herrmann et al 2013	-0.7955	0.4066	0.0%	0.45 [0.20, 1.00]	
Jander et al 2011	-0.1793	0.7269	8.5%	0.84 [0.20, 3.47]	
Maes et al 2014	-0.7508	0.4079	0.0%	0.47 [0.21, 1.05]	
Melis et al 2012	0.839	0.5269	12.0%	2.31 [0.82, 6.50]	
Mohty et al 2013	-1.4697	0.4787	13.0%	0.23 [0.09, 0.59]	
Ozkan et al 2013	-0.7133	0.2855	0.0%	0.49 [0.28, 0.86]	
Ozkan LF	-0.4539	0.1668	20.3%	0.64 [0.46, 0.88]	Ð
Pai et al 2008	-0.9113	0.884	0.0%	0.40 [0.07, 2.27]	
Tarantini et al 2011	-1.3243	0.3575	0.0%	0.27 [0.13, 0.54]	
Tarantini LF	-2.3645	0.8725	6.7%	0.09 [0.02, 0.52]	
Tribouilloy et al 2015	-0.2525	0.9529	5.9%	0.78 [0.12, 5.03]	
Yamashita et al 2015	-1.3218	816.4965	0.0%	0.27 [0.00, Not estimable]
Total (95% CI)			100.0%	0.46 [0.27, 0.79]	
Heterogeneity: Tau2 = 0 Test for overall effect: Z	9.33; Chi2 = 22.35, df = 7 (2 = 2.85 (P = 0.004)	P = 0.002); I2	= 69%		0.02 0.1 1 10 50 AVR Conservative

Dayan V, et al. J Am Coll Cardiol 2015;66:2594-2603

Outcome and Impact of AVR in the Different Subtypes of Flow/Gradient Aortic Stenosis

Mortality According to Subtypes of Aortic Stenosis

Mortality According to type of Treatment

Dayan V, et al. J Am Coll Cardiol 2015;66:2594-2603

Algorithm for Management of Symptomatic Low-Gradient Severe AS

Pibarot P et al. J Am Coll Cardiol 2016:2359-2363

Low gradient Severe AS with Preserved LVEF

- Paradoxical Low-flow, Low-gradient severe AS
 - Severe concentric LVH and smaller LV cavity size
 - High valvuloarterial impedance and low stroke volume
- Normal-flow, Low-gradient severe AS
 - Measurement error
 - Small body surface area
 - Inconsistency between cutoff values
 - of AVA and gradient

Relation of AV Area to the Mean Pressure Gradient

Aortic valve area (cm ²)	Mean gradient (mmHg)	
3.0	2.9	
2.0	6.6	
1.0	26	
0.9	32	
0.8	41	
0.7	53	
0.6	73	

Carabello BA. N Engl J Med 2002;346:677

AV Area vs. Mean Pressure Gradient

Minners J, et al. Eur Heart J 2008

Algorithm for Management of Symptomatic Low-Gradient Severe AS

Pibarot P et al. J Am Coll Cardiol 2016:2359-2363

Watchful Observation Versus Early Aortic Valve Replacement for Patients with Normal flow, Low-Gradient Severe Aortic Stenosis Duk-Hyun Kang, Jeong Yoon Jang, Sung-Ji Park, Dae Hee Kim, Jong-Min Song, Seung Woo Park, Jae-Kwan Song, Jae Won Lee, Seung-Jung Park

Asan and Samsung Medical Center

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Kang DH, et al. Heart 2015;1375-81

Study Flow

Normal flow LG AS (n = 284)

Early AVR Group (n = 98, 35%)

Watchful Observation Group (n = 186, 65%)

Early elective AVR within 6 months after initial echocardiography

Referred for late AVR

Symptoms worsened Aortic jet velocity > 4 m/s Mean gradient > 40 mmHg

Clinical and Echocardiographic follow-up until June 2014

Kang DH, et al. Heart 2015;1375-81

Overall Mortality Early AVR vs Watchful observation

Cardiovascular Mortality Early AVR vs Watchful observation

Overall Mortality Propensity-matched Cohort

Take Home Messages

- Flow-gradient pattern, AVA, EF, symptoms and operative risk should be considered in a decision for AVR in severe AS
- Clinical trials are required to evaluate benefit of AVR and optimal timing of AVR for LG severe AS
- Further studies are also needed to determine whether TAVR is superior to surgical AVR in low-flow LG severe AS