Evaluating Medical Therapy for Calcific Aortic Stenosis:

JACC State-of-the-Art Review

Brief title: Evaluating Medical Therapy for Calcific AS

Data Supplement

Supplementary Table 1. Retrospective Studies Evaluating Progression of Aortic Stenosis Severity over Time

First Author	Year	N	Mean follow-up when available (years)	Baseline population entry criteria and study design	Modality to assess progression	Baseline aortic valve measurements (and % with mild, moderate, and severe when available)	Annualized progression rate of AS severity (AVA, V_{peak}, ΔP, AVC score)
Roger et al. (1)	1990	112	2.1	Echocardiographic evidence of AS. V_{peak} ≥2m/s. At least three Doppler examinations during study period Retrospective	Echocardiography	V_{peak}: 2.9 ± 0.7 m/s ΔPmax: 35 ± 18 mmHg Mild (V_{peak}): 2.0 to 2.4 m/s: 33% 2.5 to 2.9 m/s: 21% Moderate (V_{peak}): 3.0 to 3.4 m/s: 21% Moderate to severe (V_{peak}): ≥3.5 m/s: 24%	Mild (V_{peak}): 2.0 to 2.4 m/s: 0.18 ± 0.22 m/s/y 2.5 to 2.9 m/s: 0.32 ± 0.38 m/s/y Moderate (V_{peak}): 3.0 to 3.4 m/s: 0.21 ± 0.33 m/s/y Moderate to severe (V_{peak}): ≥3.5 m/s: 0.24 ± 0.52 m/s/y
Brener et al. (2)	1995	394	2.8	Echocardiographic evidence of AS and at least two studies ≥1 year apart Retrospective	Echocardiography	N/A	AVA: -0.4 cm^2/y ΔPmean: 6.3 mmHg/y
Bahler et al. (3)	1999	91	1.8	Echocardiographic evidence of AS (initial AVA ≤2.0cm^2) and ≥2 studies separated by ≥6 months Retrospective	Echocardiography	AVA: 1.24 ± 0.34 cm^2 V_{peak}: 2.64 ± 0.62 m/s ΔPmean: 15.8 ± 9.27 mmHg	AVA: -0.04 cm^2/y V_{peak}: 0.19 ± 0.06 m/s/y Pmean: 2.8 ± 1.36 mmHg/y
Palta et al. (4)	2000	170	1.9	Echocardiographic evidence of AS with paired echocardiograms ≥3 months apart Retrospective	Echocardiography	AVA: 1.17 ± 0.38 cm^2 V_{peak}: 2.7 ± 0.07 m/s ΔPmean: 20 ± 10 mmHg	AVA: -0.10 ± 0.27 cm^2/y ΔPmean: 3.7 mmHg/y
Rosenhek et al. (5)	2004	176	4	Echocardiographic evidence of mild to moderate AS with peak velocity of 2.5-3.9 m/s and without symptoms Retrospective	Echocardiography	N/A	V_{peak}: 0.24 ± 0.30 m/s/y None/mild calcification: V_{peak}: 0.16 ± 0.19 m/s/y Moderate/severe calcification: V_{peak}: 0.35 ± 0.31 m/s/y
Ersboll et al. (6)	2015	1558	1.9 in moderate AS patients and 3.4 in mild AS patients*	Contemporary, unselected cohort of patients with AS with information available in clinical database and at least 1 follow-up echocardiogram ≥90 days from index study Retrospective	Echocardiography	ΔPmean: 19 (13-31) Mild (ΔPmean): 63% Moderate (ΔPmean): 23% Severe (ΔPmean): 14%	Mild: ΔPmean: 6.8% (95% CI 6.0-7.6) Moderate: ΔPmean: 7.1% (95% CI 4.8-9.3)
Capoulade et al. (7)	2015	220	3.5	Echocardiographic evidence of mild-to-moderate AS (Vpeak 2.5-4.0 m/s) without symptoms Retrospective analysis of prospective study	Echocardiography	AVA: 1.34 ± 0.42 cm^2 V_{peak}: 3.2 ± 0.4 m/s ΔPmean: 22 ± 7 mmHg	Lp(a) Tertiles 1 and 2 (≤58.5 mg/dL): V_{peak}: 0.17 ± 0.02 m/s/y Lp(a) Tertile 3 (>58.5 mg/dL):

							V_{peak}: 0.26 ± 0.03 m/s/y OxPL-apoB Tertiles 1 and 2: (≤5.5 nM): V_{peak}: 0.17 ± 0.02 m/s/y OxPL-apoB Tertile 3: (>5.5 mg/dL): V_{peak}: 0.26 ± 0.03 m/s/y
Nishimura et al. (8)	2016	140	3.9	Echocardiographic evidence of severe AS (AVA: 0.75-1.0 cm^2) and without symptoms Retrospective	Echocardiography	AVA: 0.90 ± 0.08 cm^2 V_{peak}: 3.68 ± 0.56 m/s ΔPmean: 33.1 ± 11.3 mmHg	AVA: -0.07 ± 0.10 cm^2/y V_{peak}: 0.27 ± 0.35 m/s/y
Tastet et al. (9)	2019	303 (CT N=220)	2.6* (echocardiography) and 2* (CT)	Echocardiographic evidence of at least mild AS (Vpeak ≥2.0 m/s and/or AVA <2.0cm^2) and with available repeat echocardiography or CT within >6 months. Prospective and retrospective data collection	Echocardiography and CT	Warfarin: V_{peak}: 2.5 ± 0.5 m/s AVC: 395 (63-991) AU DOAC: V_{peak}: 2.3 ± 0.5 m/s AVC: 322 (64-820) AU No Anticoagulation: V_{peak}: 2.7 ± 0.4 m/s AVC: 511 (254-1015) AU	Warfarin: V_{peak}: 0.14 (0.06-0.32) m/s/y AVC: 204 (48-317) AU/y DOAC: V_{peak}: 0.10 (-0.01-0.20) m/s/y AVC: 66 (11-86) AU/y No Anticoagulation: V_{peak}: 0.09 (0.04-0.19) m/s/y AVC: 94 (31-203) AU/y
Kebed et al. (10)	2020	916	1.4	Echocardiographic evidence of mild to severe AS with multiple TTEs during study period. Retrospective	Echocardiography	Mild (AVA): 32% Moderate (AVA): 51% Severe (AVA): 17%	Mild: AVA: -0.106 ± 0.005 cm^2/y Moderate: AVA: -0.068 ± 0.004 cm^2/y Severe: AVA: -0.032 ± 0.009 cm^2/y
Nayeri et al. (11)	2020	364	1.3*	Evidence of mild or moderate AS on echocardiography and ≥2 surveillance echocardiograms ≥6 months apart (without progression to severe by time of first repeat study) Retrospective	Echocardiography	V_{peak}: 2.7 (2.3-3.2) m/s ΔPmean: 15 (11-21) mmHg	V_{peak}: 0.11 (-0.09-0.32) m/s/y ΔPmean: 1.44 (-0.34-4.00) mmHg/y

Modified from 2021 ACC/AHA Guideline for Management of Valvular Heart Disease by Otto et al. *Median follow-up. Data are mean ± SD, median (IQR), or % (95% CI) as available. AS = aortic stenosis; AVA = aortic valve area; CT = computed tomography; ΔP = transaortic pressure gradient; IQR = interquartile range; RCT = randomized clinical trial; SD = standard deviation; V_{peak} = peak aortic valve velocity

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