Prognostic Value of Transaortic Flow Rate Compared to Ejection Fraction and Stroke Volume Index in Low-Gradient Severe Aortic Stenosis

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Disclosure of Relevant Financial Relationships

I, Mohamed Allam, DO NOT have any financial relationships to disclose.

Background

- Aortic stenosis (AS) is the most prevalent valvular heart disease in developed countries.
- Severe AS defined by a Vmax ≥4 m/s and/or an MG ≥40 mmHg. (Typically, AVA <1.0 cm^2)
- Discordance between MG and AVA is frequently observed in patients with reduced cardiac output, where diminished flow fails to generate a high-pressure gradient despite an AVA of less than 1 cm^2 ; ***"Low-flow low-gradient AS"***

Background

- *Symptomatic severe AS*
  - *Stage D1:* Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg. AVA typically ≤1.0
  - *Stage D2: AVA* ≤1.0 + *LVEF <50%*
  - *Stage D3: AVA* ≤1.0 + SVI <35 mL/m^2
- *EF and SVI are volume-based measures*
- Transaortic flow rate (TAFR): SV divided by LVET (mL/s), may provide a more physiologically relevant assessment of true flow

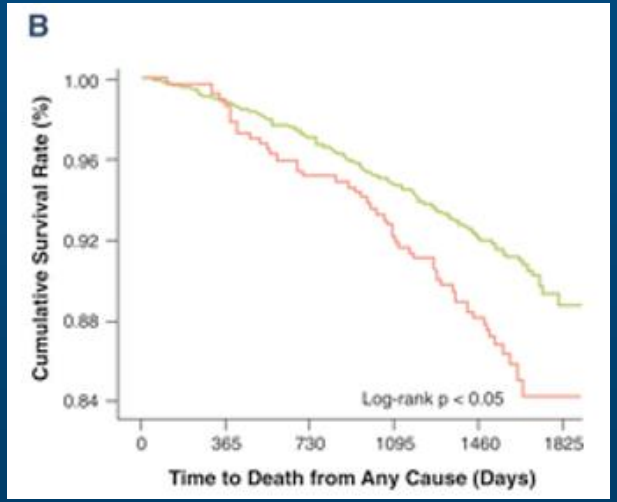
Background

TABLE 3 Prognostic Value of AVA ≤1.0 cm^2 by Flow Rate

	Hazard Ratio for Death* of AVA ≤1.0 cm^2	95% CI for HR	Sig.
Below median Q	1.25	0.92-1.68	NS (0.15)
Above median Q	1.66	1.19-2.33	0.003

Median Q 242 ml/s. *Cox proportional hazards model for time to death (all-cause mortality), adjusted for age, sex, and surgical or transcatheter aortic valve replacement (as time-dependent covariates).

AVA — aortic valve area; Q — transvalvular flow rate.



- *Mayooran Namasivayam et al. JACC 2020; 75:1758-1769.*
- Sahrai Saeed et al. J Am Coll Cardiol Img 2017; 10:912-920.

Methods

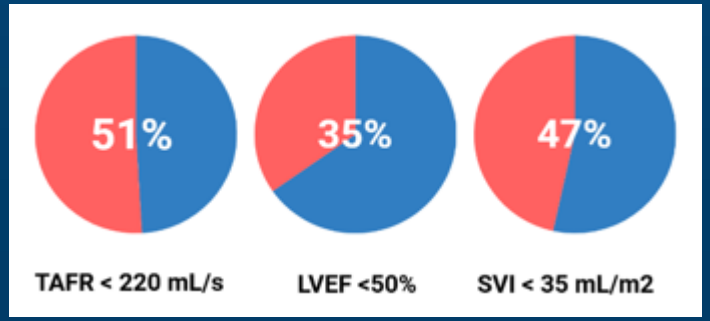
- Design:
  - Retrospective cohort study
  - Low-gradient severe AS: AVA ≤1cm^2 and Vmax <4 m/s or MG <40 who underwent TAVR
  - Baseline TTE done within 3 months
  - ViV, > mod. aortic insufficiency, supra or sub-valvular stenosis, no available baseline images excluded.
- Objective:
  - Evaluate the prognostic value of TAFR compared with LVEF and SVI

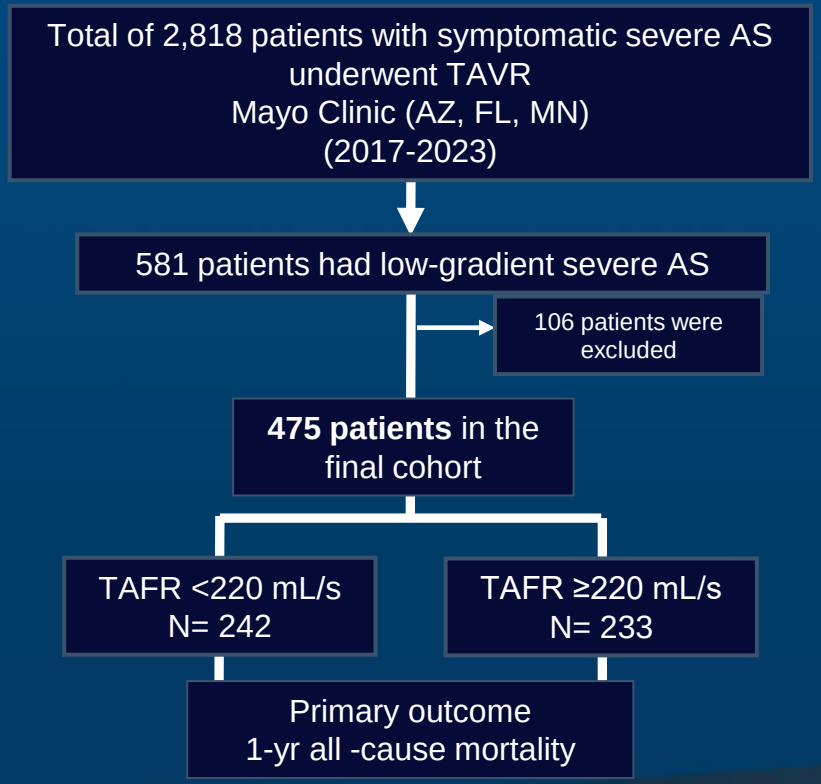
Statistical analysis

- Primary outcome was 1-year all-cause mortality.
- Optimal TAFR cutoff determined using Youden index from a ROC analysis (1-year mortality as the outcome).
- Variance inflation factor calculated for TAFR and SVI to test for multicollinearity.
- Survival assessed using Kaplan-Meier and Cox proportional hazards models (HR; 95% CI).
- Two-tailed p-value < 0.05

Results

- Prevalence of low-gradient severe AS was 21%.
- TAFR cutoff of 220 mL/s.





Results

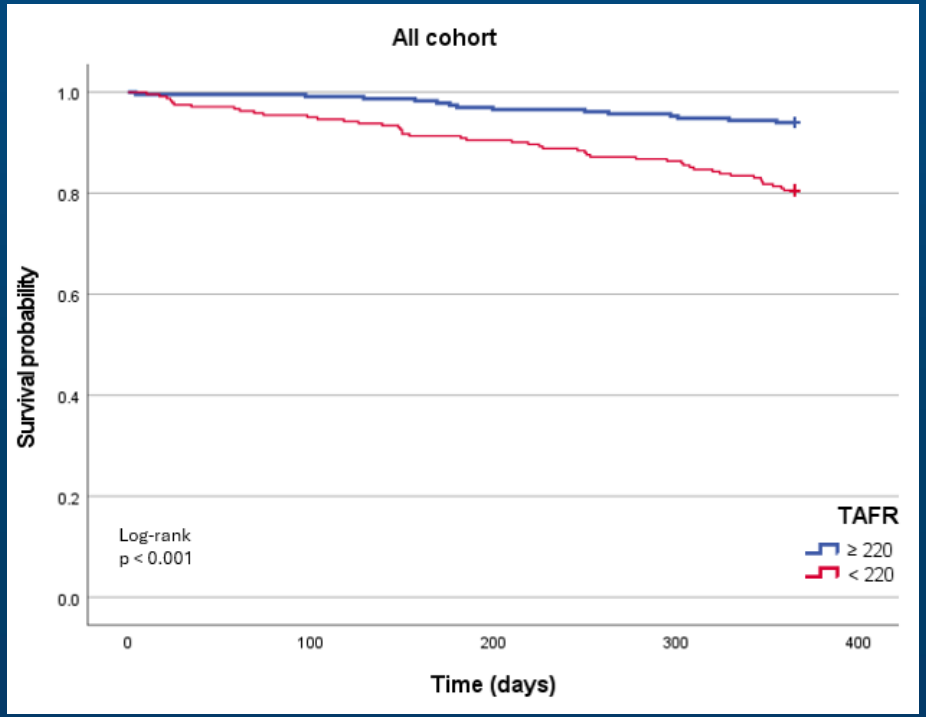
Baseline characteristics	TAFR ≥ 220 N = 233 (49 %)	TAFR < 220 N = 242 (51 %)	Overall N = 475	p-value
Age (years)	84 ± 8	86 ± 8	**85 ± 8**	0.023
Men	141 (61%)	103 (43%)	244 **(51%)**	<0.001
White race	227 (97%)	237 (98%)	464 (98%)	0.4
Diabetes Mellitus	99 (42%)	105 (43%)	204 (43%)	0.8
Hypertension	213 (91%)	213 (88%)	426 (90%)	0.2
Dyslipidemia	218 (94%)	208 (86%)	426 (90%)	0.006
Atrial Fibrillation	122 (52%)	**159 (66%)**	281 (59%)	0.003
Chronic Kidney Disease	110 (47%)	**162 (67%)**	272 (57%)	<0.001
Prior Revascularization	72 (31%)	73 (30%)	145 (31%)	0.9
Aortic calcium Score (men)	2,192 (1,748- 2,879)	2,349 (1,645- 2,786)	2,250 (1,715- 2,877)	**0.823**
Aortic calcium Score (women)	1,345 (1,002- 1,772)	1,216 (879- 1,745)	1,273 (920- 1,757)	**0.293**

Results

ECHO characteristics	TAFR ≥ 220 N = 233 (49 %)[1]	TAFR < 220 N = 242 (51 %)[1]	Overall N = 475[1]	p-value[2]
Peak velocity (m/s)	3.5 ± 0.3	**3.2 ± 0.4**	3.4 ± 0.4	<0.001
Mean gradient (mmHg)	32 ± 4	**26 ± 6**	29 ± 6	<0.001
Valve area (cm^2)	0.9 ± 0.1	**0.8 ± 0.1**	0.85 ± 0.1	<0.001
SBP at echo (mmHg)	134 ± 21	**125 ± 21**	129 ± 21	<0.001
Ejection Fraction < 50%	57 (24%)	108 (45%)	165 (35%)	<0.001
Stroke Volume Index < 35	56 (24%)	165 (68%)	221 (47%)	<0.001
LVMI (g/m^2)	105 ± 32	109 ± 35	107 ± 33	0.2
TAPSE (mm)	20 ± 5	17 ± 5	18 ± 5	<0.001
Aortic insufficiency (mild-moderate)	22 (9%)	21 (9%)	43 (9%)	>0.9
Mitral regurgitation > mild	58 (25%)	**102 (42%)**	160 (34%)	<0.001
Tricuspid regurgitation > mild	64 (27%)	**110 (45%)**	174 (37%)	<0.001

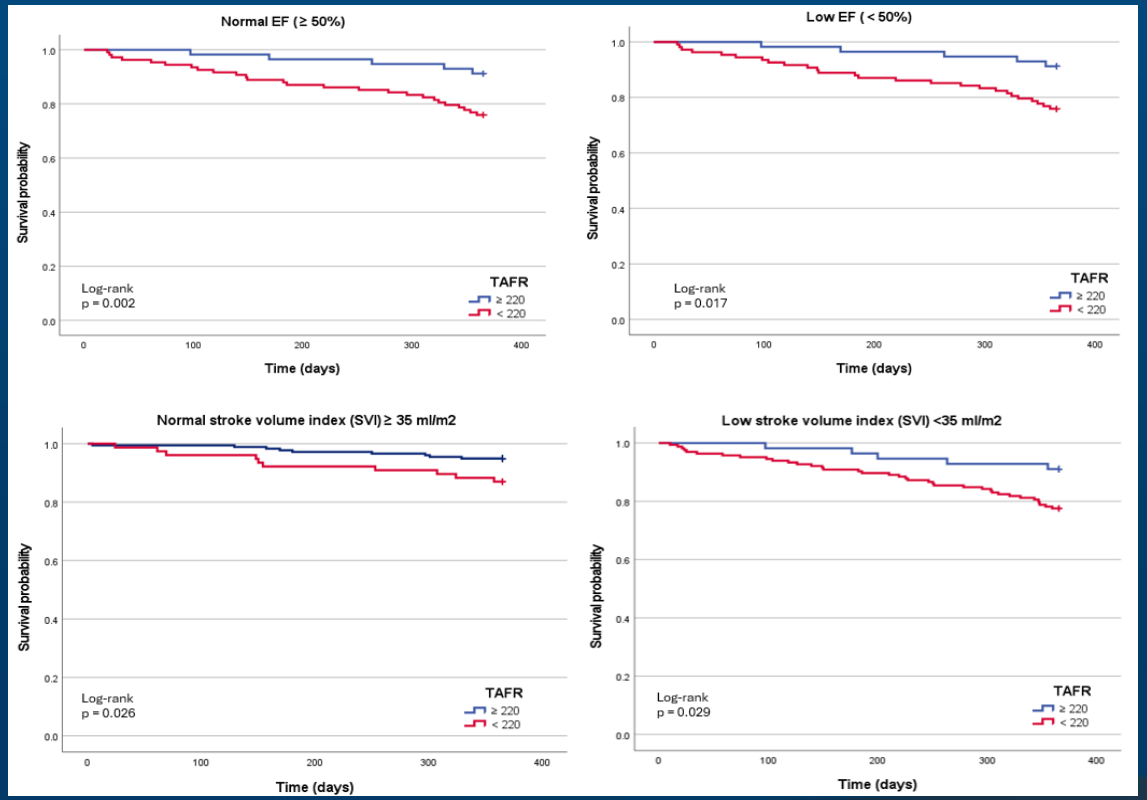
Results

- Overall mortality at 1 year by TAFR cut-off.
- Cumulative survival: 80.6% vs. 94.0%, log-rank p < 0.001



Results

- Overall mortality at 1 year for TAFR stratified by EF and SVI.
- The prognostic value of TAFR persisted when stratified by LVEF and SVI



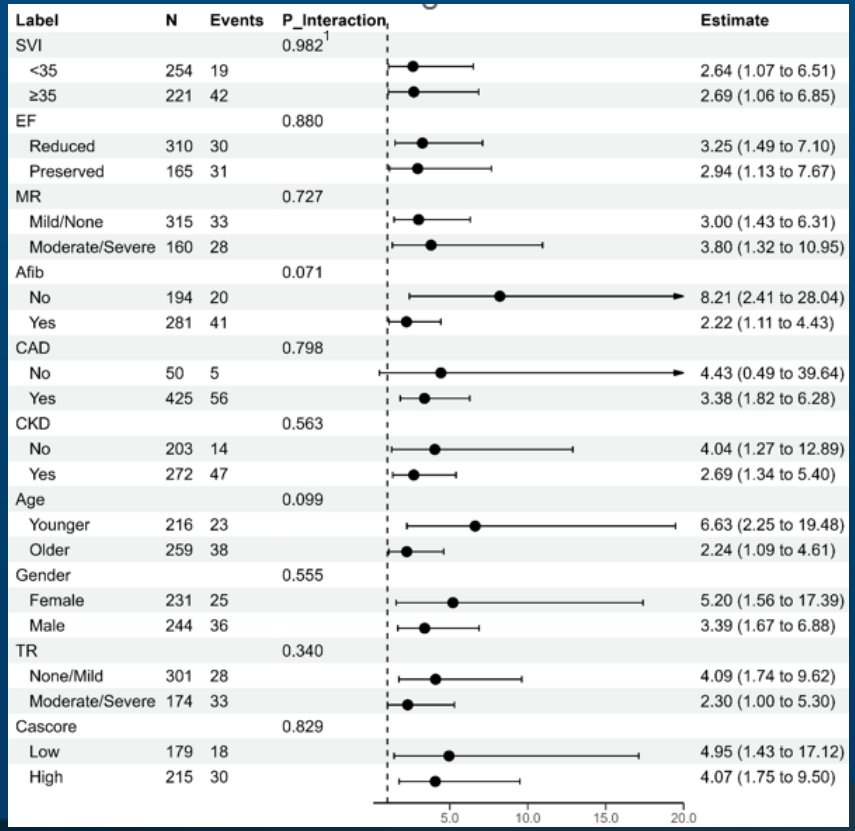
Results

Multivariable Cox regression analysis

OUTCOME	HR	CI 95%	*P*-Value
TAFR less than 220 mL/s	***2.75***	***1.21 - 6.26***	***0.016***
Reduced LVEF	**1.13**	**0.59 - 2.16**	**0.700**
SVI less than 35 mL/m²	**1.60**	**0.75 - 3.41**	**0.200**
Age	**1.00**	**0.96 - 1.04**	**>0.9**
Male sex	**1.37**	**0.73 - 2.56**	**0.300**
Coronary artery disease	**1.24**	**0.37 - 4.16**	**0.700**
Atrial fibrillation	**0.72**	**0.38 - 1.39**	**0.300**
Chronic kidney disease	**2.12**	**1.03 - 4.39**	**0.042**
MR more than mild	**1.84**	**0.99 - 3.41**	**0.052**
TR more than mild	**1.56**	**0.81 - 3.00**	**0.200**
High calcium score by sex	**1.57**	**0.86 - 2.88**	**0.140**

Results

- Subgroup analyses of the association between TAFR and 1-year all-cause mortality, stratified by clinical covariates, with p values for interaction.
- The interaction between TAFR and SVI was insignificant



Limitations

- Retrospective design
- All-cause mortality (not cardiovascular mortality or quality of life outcomes).
- Risk of overfitting cannot be excluded.
- Data on STS or other surgical risk scores not readily available

Conclusion

- TAFR was significantly associated with higher 1-year mortality even after stratifying by EF or SVI
- TAFR remained a significant predictor of mortality even among patients with normal SVI value
- Only TAFR was an independent predictor of mortality in multivariate analysis (HR 2.75; 95% CI 1.21-6.26; p=0.016)
- TAFR may offer more accurate measure of flow state for clinical staging.