Prognostic value of left ventricular ejection fraction and symptom severity in patients with moderate aortic stenosis

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Background: Moderate aortic stenosis (MAS) is associated with an increased risk of adverse events. Risk assessment in these patients, however, has not been thoroughly investigated.

Purpose: To investigate the independent determinants of survival in patients with MAS, stratified by left ventricular ejection fraction (LVEF) and severity of symptoms at the time of first diagnosis.

Methods: Patients with an echocardiographic diagnosis of tricuspid MAS (aortic valve area >1.0 and ≤1.5cm^2) were identified. Patients were stratified by LVEF (LVEF ≥60%, LVEF 50–59%, or LVEF <50%) and NYHA functional class (NYHA I, NYHA II, or NYHA III-IV) at time of MAS diagnosis. The relationship between LVEF, NYHA Class, and the composite of death or aortic valve replacement (AVR) was explored using univariable and multivariable proportional hazards regression.

Results: Of 2003 patients with MAS (mean age 73±10 years, 51% men, AVA 1.22±0.15 cm^2), 1063 (53%), had LVEF≥60%, 550 (27%) LVEF 50–59% and 390 (20%) LVEF<50%. Among 1763 patients with available NYHA class data, 1036 (59%) patients were in NYHA I, 435 (25%) in NYHA II and 292 (16%) in NYHA III-IV. During a median follow-up of 34 (13–60) months, 1323 (67.1%) patients underwent AVR (31.1%) or died (36.0%) without AVR. Patients with LVEF<50% and within the 50–59% range had significantly higher event rates compared with patients with an LVEF≥60% (log rank p<0.001; figure 1A). Likewise, patients with NYHA II and NYHA III-IV had significantly worse outcomes compared with patients in NYHA I (log rank p<0.001, figure 1B). On multivariable analysis, LVEF 50–59% (HR: 1.17; 95% CI: 1.02 – 1.35; p=0.028), LVEF <50% (HR: 1.36; 95% CI: 1.15 – 1.61; p<0.001), NYHA II (HR: 1.84; 95% CI: 1.59 – 2.13; p<0.001) and NYHA III-IV (HR: 2.38; 95% CI: 2.03 – 2.79; p<0.001) were independently associated with worse outcome (figure 2).

Conclusions: Baseline LVEF and symptom severity are associated with worse outcomes in patients with MAS. Although current guidelines recommend conservative management for MAS, randomized trials appear warranted to determine whether AVR at an earlier stage would be beneficial in these patients.

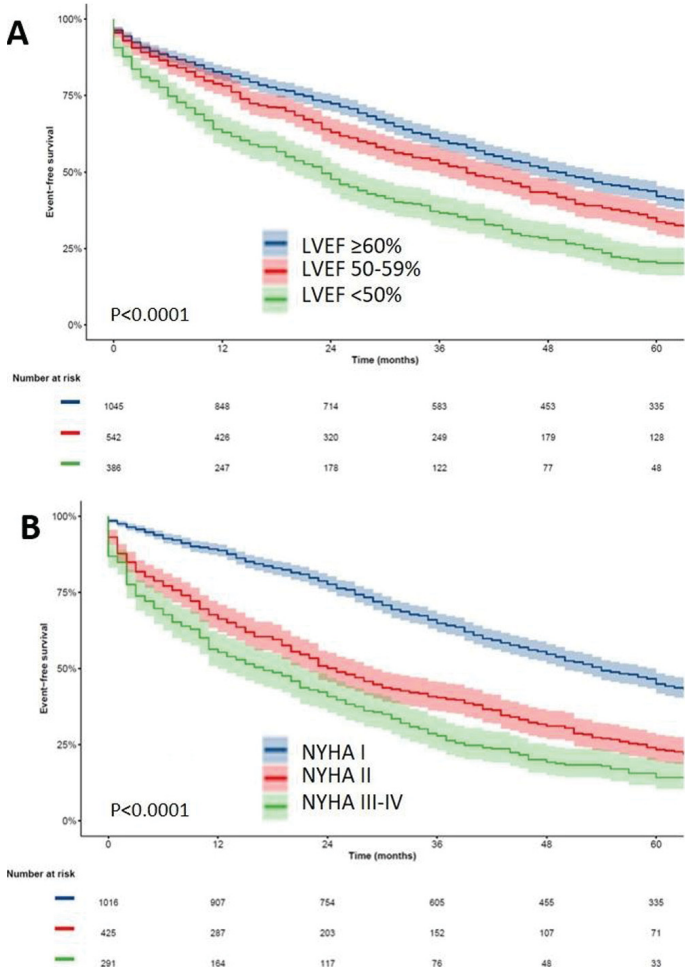

Figure 1. Kaplan-Meier outcome curves

	AVR or all-cause mortality			AVR or all-cause mortality	
	HR (95% CI)	P value		HR (95% CI)	P value
Univariable analysis			**Univariable analysis**		
LVEF ≥60%	*Reference group*		NYHA I	*Reference group*	
LVEF 50-59%	1.210 (1.065 – 1.375)	0.003	NYHA II	1.939 (1.696 – 2.217)	<0.001
LVEF <50%	1.831 (1.596 – 2.101)	<0.001	NYHA III-IV	2.657 (2.292 – 3.080)	<0.001
Multivariable analysis*			**Multivariable analysis****		
LVEF ≥60%	*Reference group*		NYHA I	*Reference group*	
LVEF 50-59%	1.172 (1.018 – 1.349)	0.028	NYHA II	1.840 (1.592 – 2.126)	<0.001
LVEF <50%	1.362 (1.154 – 1.608)	<0.001	NYHA III-IV	2.378 (2.026 – 2.792)	<0.001

*Adjusted for age, sex, diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, previous MI, atrial fibrillation, estimated glomerular filtration rate, NYHA class II to IV, stroke volume index and aortic valve area.

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Figure 2. Cox regression analysis