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Is there an outcome penalty linked to guideline-based class-I indications for valvular surgery? long-term analysis of patients with high gradient severe aortic stenosis

D. De Azevedo[1], M. Boute[1], V. Hanet[1], C. Tribouilloy[2], S. Marechaux[3], A. Altes[3], Y. Bohbot[2], D. Rusimaru[2], N. Thellier[3], A.C. Pouleur[1], A. Pasquet[1], B.L. Gerber[1], J.L. Vanoverschelde[1], D. Vancraeynest[1]

[1]Cliniques Universitaires St Luc (UCL), Bruxelles, Belgium
[2]University Hospital of Amiens, Cardiology, Amiens, France
[3]Lille Catholic Institute Hospitals Group, Cardiology, Lomme, France

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Background: Current ACC/AHA guidelines recommend aortic valve replacement (AVR) as class-I triggers in patients with high-gradient severe aortic stenosis (HGSAS) in presence of symptoms and/or left ventricular dysfunction (LVEF<50%). Whether waiting for these triggers could be associated with long-term outcome penalty after AVR remains poorly studied.

Objective: To examine the impact of guideline-based class-I triggers on long-term post-operative survival in patients with HGSAS.

Methods: We used an international registry including consecutive patients operated on for HGSAS between 2000 and 2017. 2030 Patients were included in the analysis and retrospectively classified according to the guideline-based indication: no Class-I trigger (no symptoms and LVEF>50%, n=853), Symptoms with LVEF>50% (n=965), or LVEF<50% (regardless of symptoms, n=212). Survival was compared in a multivariate Cox-model and after inverse probability weighting-[IPW] for relevant variables. Finally, we explored the most sensitive left ventricular ejection fraction threshold for predicting mortality risk.

Results: 10-years survival was better among patients without any class-I trigger than with symptoms or LVEF<50% (67±3 vs 56±3 vs 53±7% respectively, p<0.001). After adjustment for covariates, risk of death increased significantly when patients were operated on with symptoms (HR: 1.48, [95%CI: 1.17-1.86]) or with LVEF<50% (HR: 1.47, [95%CI: 1.05-2.06]) compared to patients with no class-I trigger. Furthermore, LVEF<55% emerged as a more sensitive threshold for the prediction of post-operative mortality in comparison with LVEF<50% (see table), allowing a better separation of survival curves and indicating that patients with LVEF 50-55% are already at risk with long term consequences even after AVR. Interestingly, among asymptomatic patients with LVEF >55%, performing AVR restituted a normal life expectancy (comparable to the Belgian population of same age, see figure). Finally, the outcome penalty after AVR when waiting for symptoms or LVEF<55% was confirmed in IPW analysis (HR: 1.43, [95%CI: 1.13-1.82] and HR: 1.63, [95%CI: 1.19-2.23], respectively).

Conclusions: Guideline-based Class-I triggers for AVR in patients with HGSAS is associated with profound outcome consequences on long-term postoperative mortality. Our data argue that patients with HGSAS should be operated on before the onset of these triggers. Finally, our data suggest that a threshold of LVEF<55% is a stronger predictor of outcome than LVEF<50%.

Table : Multivariate Cox Model for 10 years post operative survival

Survival Models	Variables	Hazard Ratio (95% CI)	P Value	Chi² test to remove	LHR
Basal Model	Age (per 5 y)	1,25 (1,15-1,36)	<0,001	27,4	108,7
	Male gender	1,25 (1,01-1,55)	0,035	4,4	
	Diabetes	1,43 (1,14-1,80)	0,002	9,1	
	CAD	1,28 (1,03-1,59)	0,023	5,2	
	GFR (per 5ml/')	0,94 (0,92-0,97)	<0,001	15,7	
Additional prognostic variables to basal model					
		Hazard Ratio (95% CI)	**P Value**	**Chi² test to enter**	**LHR**
Model 1	Symptoms	1,49 (1,19-1,85)	<0,001	13,1	127,3
	LVEF by 5%	0,95 (0,91-0,99)	0,031	4,5	
Model 2	No class I trigger	ref	-		120,2
	Symptoms + EF>50%	1,48 (1,17-1,86)	<0,001	12,4	
	EF<50%	1,47 (1,05-2,06)	0,026		
Model 3	No Symptoms + EF>55%	ref	-		129,8
	Symptoms + EF>55%	1,52 (1,18-1,94)	<0,001	22,0	
	EF<55%	1,93 (1,45-2,57)	<0,001		

Figure : 10 years adjusted survival – Cox Model 2 (Class I triggers) and 3 (modified LVEF threshold)