No diagnostic usefulness of Ivabradine in low-flow low-gradient aortic stenosis

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Background

In patients with low-flow low-gradient aortic stenosis (LF-LG AS) Dobutamine stress-echocardiography is the standard examination to differentiate truly severe and pseudo-severe AS. Up to 30 % do not increase stroke volume index (SVi) and the test is inconclusive. In theory, reduction in heart rate with Ivabradine may increase SVi and help differentiate.

The aim of this pilot study was to examine if Ivabradine was able to differentiate true severe AS from pseudo-severe AS better than Dobutamine.

Methods

Four patients with LF-LG AS scheduled for Dobutamine stress-echocardiography were evaluated at the cardiac intensive care unit Odense University Hospital. Patients underwent comprehensive echocardiography, right heart catheterization with continuous hemodynamic monitoring and continuous arterial blood pressure. First, a standard Dobutamine stress-echocardiography was performed and afterward, patients were examined every hour until 6 hours after Ivabradine administration.

Results

The group had a median age of 66 (57.5-70) years, 75 % male. At baseline was AVA 1.02 (0.72-1.41) cm^2 and mean gradient 20.75 (14.5-27.2) mmHg. Wilcoxon signed-rank test indicated that during Dobutamine stress echocardiography mean gradient raised, z=-1.83, *p*=0.068, as well as SVi, z=-1.604, *p*=0.11 and invasively measured heart rate, z=-1.46, *p*=0.14. There was no difference in Cardiac Output (CO), z=0, *p*=1.00. During Ivabradine signed-rank test indicated no difference in mean gradient, z=0.00, *p*=1.00. Median SVi raised z=-1.83, *p*=0.68 and CO decreased, z=1.83, *p*=0.068. Under Ivabradine the heart rate fell from 69 (64.5-71.5) bpm at baseline to 59.5 (55.5-64.5) z=1.83, *p*=0.068. However, none of the results were statistically significant due to small sample size.

Conclusion

This study was terminated because of lacking signal in the results and it would be unethical to examine further 21 patients. Ivabradine lowered the heart rate, but only raised SVi minimally, decreased CO and did not change mean gradient in patients with LF-LG AS and cannot replace dobutamine stress-echocardiography.

Table 1: Wilcoxon signed-rank test

Variable	***Median Baseline***	***Median Dobutamine 20 µg***	***Median Ivabradine***	***z***	***p***
Mean gradient	20.75 (14.5-27.2)	29.95 (20.2-32.8)		-1.83	0.068
Mean gradient	20.75 (14.5-27.2)		21.6 (14.85-27.05)	0.00	1.00
Stroke volume index	34.02 (32.64-42.23	37.10 (35.81-42.18)		-1.60	0.11
Stroke volume index	34.02 (32.64-42.23		37.18 (36.20-45.15)	-1.60	0.11
Heart rate	69 (64.5-71.5)	80.5 (70-99)		-1.46	0.14
Heart rate	69 (64.5-71.5)		59.5 (55.5-64.5)	1.83	0.068
Cardiac Output	4.8 (3.6-5.1)	4.1 (2.8-5.25)		0.00	1.00
Cardiac Output	4.8 (3.6-5.1)		4.6 (3.3-4.75)	1.83	0.068