

Metoprolol treatment reduces hemodynamic and metabolic overload in patients with asymptomatic aortic valve stenosis - a randomized double-blind placebo controlled trial

Hansson NH^a, Sørensen JB, Harms HJ^b, Kim WY^a, Nielsen R^a, Tolbod LP^b, Frøkiær JB, Bouchelouche K^b, Dodt KK^c, Sihm I^d, Poulsen SH^a, Wiggers H^a

^aDepartment of Cardiology, Aarhus University Hospital, Denmark, ^bDepartment of Nuclear Medicine & PET-Center, Aarhus University Hospital, Denmark, ^cDepartment of Cardiology, Horsens Regional Hospital, Denmark, ^dAarhus Hjerterklinik, Denmark

BACKGROUND

- No pharmacological treatment can modify the natural history of aortic valve stenosis (AS).
- Beta blockers are widely used in asymptomatic AS patients although no randomized data exist.

OBJECTIVES

To investigate the hemodynamic and metabolic effects of metoprolol in patients with asymptomatic AS.

METHODS

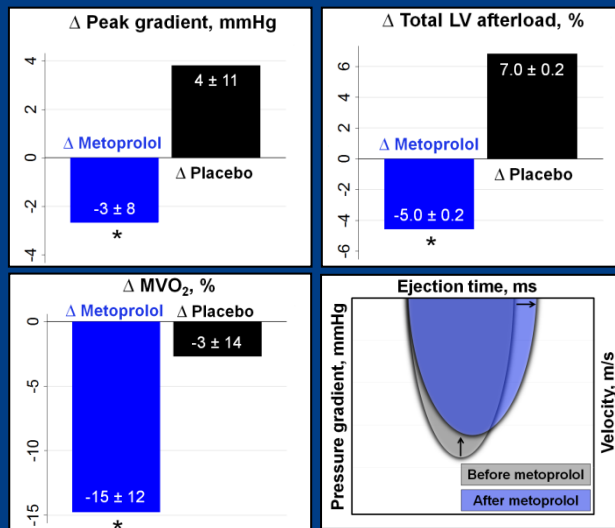
- Patients (n=40): moderate-severe asymptomatic AS (Table).
- Design: randomized, double-blind study.
- Treatment: placebo vs. metoprolol succinate.
- Duration and Target dose: 5 months and 200 mg x 1.
- Imaging: echocardiography, cardiac magnetic resonance (CMR), ¹¹C-acetate positron emission tomography.
- Key endpoints: valve gradients, total LV afterload¹, myocardial oxygen consumption (MVO₂), and myocardial external efficiency (MEE)².

¹Total LV afterload, mmHg/mL/m²

$$= \frac{\text{systolic blood pressure} + \text{net mean gradient}}{\text{Stroke volume index}}$$

²Myocardial external efficiency (MEE), %

$$= \frac{\text{Stroke work}}{\text{Total myocardial energy consumption}}$$



RESULTS

- 2 patients were protocol violations (CMR: severe aortic regurgitation, LVEF < 50%) → excluded.
- 2 pts with events in the metoprolol group (chest pain, edema) → intention to treat.
- Stable treatment dose of metoprolol succinate 100 ± 53 mg.

	ΔMetoprolol – ΔPlacebo	p
HR, min ⁻¹	-8 (-13, -3)	0.001
Ejection time, ms	26 (2, 50)	0.03
Systolic blood pressure, mmHg	-2 (-10, 6)	0.41
Peak gradient, mmHg	-7 (-13, 0)	0.05
Mean gradient, mmHg	-4 (-7, -1)	0.03
SV index, mL/m ²	3 (-2, 8)	0.16
Cardiac index, L/min	-0.2 (-0.5, 0)	0.10
Total LV afterload, mmHg/mL/m ²	-0.5 (-1, 0)	0.03
LVEF, %	-1 (-5, 2)	0.54
GLS, %	1.0 (-0.5, 2.4)	0.92
MEE, %	1.7 (-1.7, 5)	0.62

Patient characteristics	Placebo (n=19)	Metoprolol (n=19)
Age, years	71 ± 5	69 ± 5
Men, n (%)	14 (74)	10 (53)
AVA index, cm ²	0.5 ± 0.1	0.5 ± 0.1
Peak gradient, mmHg	56 ± 23	60 ± 29
LVEF, %	72 ± 5	73 ± 5

CONCLUSIONS

In patients with asymptomatic AS, metoprolol treatment:

- ↓ Aortic valve gradients
- ↓ Afterload
- ↓ Myocardial oxygen requirements

Metoprolol could improve outcome in asymptomatic AS.



Corresponding author:
Nils Henrik Hansson
Department of Cardiology
Aarhus University Hospital, Denmark
nilhan@rm.dk

Sources of Funding: Lundbeck Foundation, Arvid Nilssons Foundation, Health Research Fund of Central Denmark Region, Karen Elise Jensens Foundation, and Snedkermester Sophus Jacobsen and Hustru Astrid Jacobsens Foundation.

Declaration of interest: Henrik Wiggers has been the principal or a sub-investigator in studies involving the following pharmaceutical companies: MSD, Bayer, Daiichi-Sankyo, Novartis, Novo Nordisk, Sanofi-Aventis and Pfizer.