Relationship Between Insulin Resistance and Progression of Left Ventricular Hypertrophy in Patients with Aortic Stenosis: A Substudy of the ASTRONOMER Trial

Romain Capoulade1, Marie-Annick Clavel1, Jean G. Dumesnil1, Kwan L. Chan2, James W. Tam3, Koon K. Teo4, Nancy Côté1, Patrick Mathieu1, Jean-Pierre Després5, Philippe Pibarot1

1- Centre de recherche de l’Institut universitaire de cardiologie et de pneumologie de Québec, Québec, Canada 2- University of Ottawa Heart Institute, Ottawa, Ontario, Canada 3- St Boniface General Hospital, Winnipeg, Manitoba, Canada 4- McMaster University- Hamilton Health Sciences, Hamilton, Ontario, Canada

Abstract

Background: We had reported that metabolic syndrome (MetS) was associated with increased prevalence of concurrence hypertrophy in patients with aortic stenosis (AS). Insulin resistance could be a mediator of this association. The objective of this substudy from the ASTRONOMER trial was to investigate the relationship between insulin resistance and progression of left ventricular (LV) hypertrophy and global LV hemodynamic load in AS patients.

Methods: Newly diagnosed AS patients (n = 263) were enrolled in ASTRONOMER (2005-2009). LV mass index (LVMi) was calculated with the modified ASE formula and was indexed to a 2.7 power of height (LVMi = \( \frac{1}{2.7} \times (IVS + PWT + LVID)^2 - LVID \)). LV hypertrophy was defined as LVMi > 47 g.m\(^{-2.7}\) for women, > 49 g.m\(^{-2.7}\) for men. For an estimate of the LV global hydraulic load, we calculated the valvular arterial impedance (Zva) as: Zva = Systolic Blood Pressure + Mean gradient. Zva was indexed to the body surface area (Zva/BSA). LV remodeling was assessed using the Homeostatic Model Assessment (HOMA) index was used as an index of insulin resistance.

Results: There was a significant (p<0.0001) increase in LVMi among patients (n = 134) with no LV hypertrophy at baseline but not in those with pre-existing LV hypertrophy (p = 0.12). In the former subset of patients, annualized progression rate of LVMi was significantly higher in those with higher Zva (p<0.0001) after further adjustment for the latter variable. HOMA index was also an independent predictor (p = 0.03) of the progression of LVMi.

Conclusion: This study reports that insulin resistance is an independent predictor of faster progression of global LV hemodynamic load and LV hypertrophy in patients with AS. Given that the most prevalent form of insulin resistance is associated with visceral obesity, the findings of this study provide strong impetus for the elaboration of interventional studies targeting visceral obesity and other conditions predisposing to insulin resistance.

Background

- Severe LV hypertrophy (LHV) is independently associated with adverse events in patients with aortic stenosis (AS).
- We had recently reported that metabolic syndrome is associated with higher prevalence of concurrence hypertrophy in patients with AS. Given that this prevalent form of insulin resistance is associated with visceral obesity, the findings of this study provide strong impetus for the elaboration of interventional studies targeting visceral obesity and other conditions predisposing to insulin resistance.

Objective

To examine the association between insulin resistance and progression of LV hypertrophy and global LV hemodynamic load in patients with AS.

Methods

- ASTRONOMER study
- Multicentre, double-blind, placebo-controlled trial to assess cholesterol lowering on AS progression
- 23 Canadian sites
- 263 patients with mild to moderate AS
- Inclusion criteria: age comprise between 18 and 82 years, peak aortic jet velocity comprise between 2.5 and 4 m.s\(^{-1}\)
- Exclusion criteria: severe or symptomatic AS, severe AR, mitral valve disease, coronary artery disease, chronic heart failure, diabetes, needs for lipid lowering treatment

Mean follow-up time: 3.1±1.2 years

- Global LV hemodynamic load
  - Valvular arterial impedance\(^1\): Zva = Systolic Blood Pressure + Mean gradient
  - LV mass index
  - Homeostatic Model Assessment: HOMA index = \( \frac{(Fasting insulin + Fasting glucose) \times 2}{Fasting glucose + Fasting insulin} \)

- Left ventricular mass index
  - Modified ASE formula: LVMi = \( \frac{(IVS + PWT + LVID)^2 - LVID}{2.7} \)

- Index of insulin resistance
  - Homeostatic Model Assessment (HOMA)

Clinical Data

- Patients without LVH at Baseline
- LVH at Baseline
- LVH at Baseline

- Age, yr
- Male gender, %
- Body mass index
- Waist circumference, cm
- History of smoking, %
- Systolic Blood Pressure
- Triglycerides, mmol/L
- Apo B, g/L
- Fasting glucose, mmol/L
- Fasting insulin, \( \mu \text{g/L} \)

Laboratory Data

- Patients without LVH at Baseline
- LVH at Baseline

- L.D.R. cholesterol, mmol/L
- HDL cholesterol, mmol/L
- Triglycerides, mmol/L
- Fasting glucose, mmol/L
- Fasting insulin, \( \mu \text{g/L} \)
- HOMA index
- Creatinin, µmol/L

Doppler-Echocardiographic Data

- Patients without LVH at Baseline
- LVH at Baseline

- Mean transvalvular gradient, mmHg
- Mean transvalvular flow, m.s\(^{-1}\)
- Relative wall thickness ratio
- LV mass index, g.m\(^{-2.7}\)
- LV ejection fraction, %

Dynamics of LV Hypertrophy and global LV hemodynamic load in patients with AS

- Annualized systolic blood pressure - NS
- Mean gradient - NS
- Zva - p=0.001
- Zva index - p=0.001
- HOMA index - p<0.0001

Prevalence of LV Remodelling Pattern at Baseline and Last Follow-Up

- LVH at Baseline
- LVH at Baseline

- Patients without LVH at Baseline

Independent predictors of progression rate of LVH

- Age: \( p=0.0002 \)
- Hypertension: \( p=0.001 \)
- Male gender: \( p=0.02 \)

Annualized Progression Rate of LV Mass index In Patients without LVH at Baseline

- Patients without LVH at Baseline
- Patients without LVH at Baseline

- LVH at Baseline
- LVH at Baseline

- LVH at Baseline
- LVH at Baseline

- LVH at Baseline

Correlation between HOMA index and Progression rate of Global LV Hemodynamic Load

- HOMA index
- HOMA index

Acknowledgements

References

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