EXCESSIVE LEFT VENTRICULAR HYPERTROPHY IN MODERATE DEGENERATIVE AORTIC STENOSIS WITH CONCOMITANT MILD RENAL IMPAIRMENT: AN INEFFECTIVE COMPENSATORY MECHANISM TRIGGERED BY PRIMARY MYOCARDIAL DYSFUNCTION?

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INTRODUCTION & BACKGROUND

- Moderate aortic stenosis (AS) frequently poses a clinical challenge. Notably, depressed LV performance, like symptomatic status, may be due to non-valvular causes, e.g. CAD, primary myocardial dysfunction, hypertension or non-cardiac diseases.
- LV hypertrophy (LVH), traditionally perceived as an adaptive mechanism to preserve LV systolic function, frequently develops already in moderate AS.
- Inappropriately high LV mass, i.e. disproportionate to LV afterload, predicts adverse outcome in AS and hypertension.
- In concentric LVH, indices based on LV midwall mechanics reflect LV function more accurately than EF which overestimates LV performance.

AIM

To assess whether renal function is related to LV systolic performance and the appropriateness of LVH in real-world patients with moderate AS.

METHODS

We reviewed hospital records of 150 subjects with moderate degenerative AS, out of whom 70 with pure AS in sinus rhythm, with EF>40%, stable in-hospital creatinine and without clinical instability or coexistent diseases except for diabetes, entered the final analysis.
- Variables were compared between GFR categories by: ANOVA or Kruskal-Wallis ANOVA (continuous data) or Chi-square test (categorical data).
- Trend effects along decreasing GFR categories were assessed by Spearman’s rank correlation (rho) for the both types of data.
- To detect independent determinants of excess of LV mass and LV midwall fractional shortening, multiple linear regression was performed, with a ridge regression option was introduced to avoid co-linearity of predictors.

INVESTIGATED PARAMETERS – CALCULATED FROM MEDICAL RECORDS AND ECHOCARDIOGRAPHY

LV mass index (g/m²)

by the classical Devereux formula

Relative wall thickness (RWT) - an index of LV concentricity

RWT = (Post. wall thicknesss 平均 + IV septum thicknesss 平均) / LVID

Valvulo-arterial impedance (Zva)

Zva = (SBP + mean aortic gradient) / stroke volume index (mm Hg / [ml/m²])

Excess of LV mass (ELVM) [%]

A percent deviation from the LV mass predicted from the individual hemodynamic load, height and gender by a validated formula

Circumferential end-systolic LV wall stress (cESS) [hPa] and LV midwall fractional shortening (mwFS) [%]

Vectors of LV midwall stress and shortening are oriented in the same direction, because circumferential fibers predominate at the midwall equator, in contrast to the subendocardial layer.

> Eliminates EF overestimation at eccentric LV geometry.

Midwall fractional shortening (mwFS)

(0.7) = (LVID + Hz/2) – (LVIS + Hz/2) / (LVID + Hz/2) x 100%

A positive correlation of midwall fractional shortening and GFR

An inverse correlation of excess of LV mass and LV midwall fractional shortening

A positive correlation of midwall fractional shortening and GFR

A positive correlation of excess of LV mass and LV midwall fractional shortening

An inverse correlation of excess of LV mass and LV midwall fractional shortening

70 patients with moderate aortic stenosis (AVA: 1.0–1.5 cm²)

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
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<tbody>
<tr>
<td>(GFR&lt;85)</td>
<td>(GFR&gt;85-60)</td>
<td>(GFR&gt;15-59)</td>
</tr>
<tr>
<td>n=18</td>
<td>n=30</td>
<td>n=22</td>
</tr>
<tr>
<td>Age, years</td>
<td>68±7</td>
<td>77±8</td>
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<tr>
<td>AVA, cm²</td>
<td>1.2±0.1</td>
<td>1.2±0.1</td>
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<tr>
<td>LV mass, g</td>
<td>178±49</td>
<td>203±45</td>
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<tr>
<td>ELVM, %</td>
<td>-2(-6–13)</td>
<td>21(1–57)</td>
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<tr>
<td>EF, %</td>
<td>61±8</td>
<td>59±7</td>
</tr>
<tr>
<td>mwFS, %</td>
<td>17±3</td>
<td>14±4</td>
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<tr>
<td>RWT</td>
<td>0.42±0.09</td>
<td>0.49±0.1</td>
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<tr>
<td>cESS, hPa</td>
<td>181±65</td>
<td>147±62</td>
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<tr>
<td>Zva, mmHg/[ml/m²]</td>
<td>4.2±1.4</td>
<td>5.4±2.6</td>
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<tr>
<td>LVID, cm</td>
<td>5.1±0.7</td>
<td>4.9±0.6</td>
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RESULTS

- Except for age, clinical characteristics were similar across the 3 groups.
- The 3 groups did not differ in AVA, EF, indices of afterload (Zva and cESS), LV mass, prevalence of CAD or diabetes.
- ELVM increased gradually across decreasing GFR (p<0.01 for trend).
- Compared to group A, group B subjects had lower mwFS (p<0.05) and higher estimates of LV concentricity, i.e. RWT and LV mass/volume ratio (p<0.05), all of which were yet similar in groups B and C.

CONCLUSIONS

Progressive GFR deterioration seems associated with excessive LVH and LV dysfunction at the midwall level in moderate AS, irrespective of global LV afterload and EF.

Excessive LVH can be triggered by slightly reduced LV contractility already in mild renal impairment as a compensatory, yet ineffective, mechanism aimed at restoring LV performance by lowering LV wall stress via Laplace law.

DISCUSSION

Our results supplement earlier reports of increasingly higher prevalence of excessive LV hypertrophy and depressed mwFS along progression of renal dysfunction in hypertensive subjects but without coexisting AS. Therefore, our study is first to show early renal impairment as a contributor to excessive LV hypertrophy in AS.

The gradual development of excessive LV hypertrophy could be initiated by load-independent primary myocardial dysfunction coexisting with AS, and enhanced by coexistent renal dysfunction, as shown in hypertension.

As the degree of LV hypertrophy predicted poor outcome on medical therapy and after valve replacement in AS, prevention of excessive LVH can improve prognosis on a long-term basis.

ACEI or ARB, a standard of nephroprotection and LVH inhibition, are avoided in severe AS due to fear of hypotension. However, their use was safe and slowed LVH progression in mild or moderate AS in the SEAS trial.

CLINICAL IMPLICATIONS

Prevention of early renal function decline in less-than-severe AS may slow the development of excessive LV hypertrophy and improve long-term prognosis.