

POSTER SESSION

1012 Clinical Factors Associated With Valvular Aortic Stenosis

Sunday, March 30, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 9:00 a.m.-10:00 a.m.

1012-21 Systemic Arterial Compliance in Patients With Aortic Stenosis: Relationship With Diastolic Dysfunction

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Background: Diastolic dysfunction (DD) in aortic stenosis (AS) does not always correlate to classical markers of hemodynamic severity and it has been hypothesized that other factors may be involved. In an acute animal model, we recently observed that a decrease in systemic arterial compliance (SAC) downstream to a severe AS was associated with a marked increase in peak LV systolic wall stress and a decrease in aortic diastolic pressure. Since both abnormalities may predispose to the development of DD, we hypothesized that SAC might have a significant impact on DD in patients with AS.

Methods: Relevant clinical and echocardiographic variables were measured in 226 consecutive patients (128 males, 98 females, mean age: 69±12 years) with at least moderate AS (Aortic Valve Area (AVA) <1.5 cm²). Total SAC was calculated as follows: Total SAC=SV/(SAP-DAP), where SAP and DAP are systolic and diastolic blood pressures measured at the time of stroke volume (SV) measurement.

Results: One hundred and eighty eight (188, 83%) patients had DD (abnormal relaxation: 114 pts, 50%; pseudo-normal: 68 pts, 30%; and restrictive: 6 pts, 3%). Patients with DD were older (71±11 vs. 61±14 years; p<0.001) and they had a smaller AVA (0.95±0.26 vs. 1.09±0.27 cm²; p=0.003), a lower radius-to-wall-thickness ratio (2.08±0.46 vs. 2.40±0.49; p<0.001), a lower total SAC (1.22±0.45 vs. 1.61±0.57 ml/mmHg; p<0.001), and higher incidence of systemic hypertension (72 vs 39%, p<0.001). However, in multivariate analysis, the only variables independently associated with DD were radius-to-wall-thickness ratio (p=0.009), AVA (p=0.03) and total SAC (p<0.0004).

Conclusion: In patients with moderate or severe AS, systemic arterial compliance is more closely associated to DD than the classical markers of stenosis severity. These results suggest that, beyond the stenosis severity and the degree of concentric LV hypertrophy, it is also important to consider the anatomic and hemodynamic factors involved downstream to the stenosis since they may have important implications regarding the LV function and thus the prognosis of these patients.

1012-22 Hypercholesterolemic Valvulopathy as an Aspect of Malignant Atherosclerosis

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Background: Aortic stenosis is frequently observed in young patients with homozygous familial hypercholesterolemia (FH). Some patients with heterozygous FH also affect not only coronary artery, but also the aortic valve resulting in aortic valve replacement (AVR). **Methods:** We reviewed 10 homozygous (25.7±16.5 years) and 39 heterozygous FH patients under age 60 years (47.4±7.4 years) on evolution and prevalence of the aortic valvular dysfunction by sequential catheterization and echocardiography for 2 decades. Surgically excised aortic cusps obtained from the patients with homozygous FH, heterozygous FH and non-FH calcific aortic stenosis were histopathologically examined. **Results:** Nine patients with homozygous FH had aortic regurgitation, 3 of them have aggravated transaortic pressure gradients more than 70mmHg and 2 patients received AVR at 20 and 31 years-old. The initial clinical sign was cusp thickening and the development of a regurgitant jet followed by increasing pressure gradient across the aortic valve despite of intensive cholesterol-lowering therapy. Ten of 39 heterozygous FH patients had aortic regurgitation with impaired distensibility of the ascending aorta. Pathological examination demonstrated that the earliest change in the cusp is thickening of the fibrosa with the infiltration of foam cells, macrophages stained by HAM-64 and T-lymphocytes stained with anti CD-45. The nature of the changes of FH valves were similar to the histopathological changes seen in the age-related calcific aortic stenosis that occurs in the non-FH population. **Conclusions:** Hypercholesterolemia affects the aortic valve which occurs in a short period of time in homozygous FH patients by extreme hypercholesterolemia, over an intermediate time period in heterozygous FH patients with several risk factors and over a number of years gradually in the elder non-FH population with additional risk factors and underlying mild hypercholesterolemia. Histopathological changes of the cusps are common in these patients with AVR. Aortic stenosis as hypercholesterolemic valvulopathy is a life-threatening complication as the primary clinical characteristic of malignant atherosclerosis.

1012-23 Do Statins Really Slow the Progression of Aortic Valve Stenosis? A Need for a Prospective Randomized Trial

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Background. It has been recently suggested in a retrospective study of 57 statin-treated patients with mild to moderate aortic stenosis (AS) that statins could slow the progression of AS.

Methods. From our echocardiographic database (1988-2001) we obtained 95 statin-treated patients with mild to moderate AS (initial peak aortic velocity 2-3.9 m/s) and with

at least two examinations >6 months one apart of the other (61 males, 34 females, mean age 67.6 ± 8.6 years, mean follow up 54 ± 36 months; initial aortic valve area 1.28 ± 0.26 cm²). As control group we randomly selected, from the remaining 759 patients with an initially similar degree of AS and with at least two examinations, 95 sex-age matched patients who did not receive treatment with a statin (61 males, 34 females, mean age 67.5 ± 8.7 years, mean follow up 51 ± 34 months; initial aortic valve area 1.28 ± 0.25 cm²).

Results. The rate of increase of peak aortic velocity was 0.15 ± 0.26 m/s/y in the statin group and 0.15 ± 0.20 m/s/y in the control group (p=ns). The rate of decrease of aortic valve area was -0.074 ± 0.095 cm²/y in the statin group and 0.069 ± 0.074 cm²/y in the control group (p=ns). The mean value of aortic valve area at the end of the study was 1.01 ± 0.31 cm² in the statin group and 1.04 ± 0.30 cm² in the controls (p=ns). A pattern of rapid progression of AS (increase of peak aortic velocity > 0.3 m/s/y) was observed in 20/95 (21%) of statin-treated patients and in 15/95 (16%) patients who did not receive statins (p=ns). A major clinical end point (death or aortic valve replacement) was found in 21/95 statin-treated patients (22%) and in 13/95 (14%) not treated patients (p=ns).

Conclusion. Despite the theoretical potential benefits of statins on aortic valve lesion, our study does not confirm the first results about their slowing effect on the progression of AS. A prospective randomized controlled trial is necessary before to extend the indications of the statins in patients with AS.

1012-24 C-Reactive Protein Is Increased in Aortic Stenosis but Not Aortic Regurgitation

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Introduction: Histological evidence of inflammation similar to that observed in atherosclerosis has been reported in aortic stenosis (AS), but not in aortic regurgitation (AR). **Aim:** To determine whether serum levels of C-reactive protein (CRP), a marker of inflammation, are elevated in AS and/or AR.

Methods: Transthoracic echocardiography was performed, and CRP was measured by high-sensitivity enzyme immunoassay in 20 patients with isolated non-rheumatic AS, mean age 67 ± 11 years, 19 patients with isolated non-rheumatic AR, mean age 45 ± 14 years, and in 31 controls, mean age 66 ± 4 years. Exclusion criteria for all subjects were history of cardiac failure, cerebrovascular disease, peripheral vascular disease, cancer, recent development of any active inflammatory or haematological disorder, left ventricular ejection fraction < 50%, and the presence of coronary stenosis >50% determined by coronary angiography (in all patients with AS and in 8 patients with AR). The other 11 AR patients had no symptoms of angina and no regional wall motion abnormalities on echocardiography. All controls were free of cardiovascular disease as determined by history, physical examination, exercise ECG and echocardiography.

Results: Mean ± SD echocardiographic measures for AS were: peak aortic velocity 4.6 ± 0.7 m/s, aortic valve area 0.77 ± 0.25 cm², and LV ejection fraction 62 ± 7%, and for AR, LV end-diastolic diameter 6.9 ± 0.8 cm and LV ejection fraction 58 ± 5%. CRP was increased in AS compared with controls, median (interquartile range) 2.98 (1.59-5.37) mg/l vs. 1.51 (0.75-2.09) mg/l, P=0.007, but not in AR compared with controls, 1.00 (0.35-2.00) mg/l, P=0.86 after adjusting for age. There were no significant correlations between CRP and echocardiographic measures of valve disease severity for AS or AR, P > 0.05 for all.

Conclusion: Serum levels of CRP are raised in patients with non-rheumatic aortic stenosis, but not in non-rheumatic aortic regurgitation. This data supports the hypothesis there is an active inflammatory component to non-rheumatic aortic stenosis.

1012-25 Cardiovascular Risk Factors in Patients With Aortic Stenosis Are Associated With the Prevalence of Coronary Artery Disease, but Not the Prevalence of Aortic Stenosis

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Background: Traditional cardiovascular risk factors have been associated with aortic stenosis and coronary artery disease (CAD). However, the profile of cardiovascular risk factors in patients with aortic stenosis has not been compared with the profile of controls matched for gender, age and CAD defined by left coronary angiography.

Methods: 523 patients referred for elective diagnostic left heart catheterization because of severe aortic stenosis formed the case population. 3925 patients referred for elective diagnostic left heart catheterization without valve disease formed the base control population. Out of these, 523 patients were pair matched to the case population for gender, age and prevalence of relevant CAD and formed the pair matched control population. In all patients the cardiovascular risk profile (male gender, hypertension, hypercholesterolemia, smoking, diabetes mellitus, family history for CAD) was assessed.

Results: None of the traditional cardiovascular risk factors was more prevalent in patients with aortic stenosis compared to the base control population or compared with the pair matched control population. However, male gender, hypercholesterolemia, smoking, diabetes mellitus, family history for CAD were significantly associated with the presence of additional CAD in patients with aortic stenosis.

Conclusions: Cardiovascular risk factors are frequently present in patients with aortic stenosis. They are significantly associated with the prevalence of CAD. However, compared to controls matched for age, gender and angiographic defined CAD no risk factor was associated with the prevalence of aortic stenosis itself.