Original Research

The Role of Sex and Biochemical Markers of Inflammation in Left Ventricular Remodelling, Before and After Surgery, in Elderly Patients with Aortic Valve Stenosis

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Key words:
Elderly patients, aortic stenosis, left ventricular remodelling inflammatory markers.

Introduction: The aim of this study was to determine whether sex and biochemical markers of inflammation have a role in left ventricular (LV) remodelling after aortic valve replacement in elderly patients with aortic valve stenosis.

Methods: We studied 52 elderly patients with aortic valve stenosis (32 men, mean age 65 ± 11 years and 20 women, mean age 68 ± 9 years). Body surface area did not differ between men and women (1.81 ± 0.15 versus 1.84 ± 0.20, respectively). All patients underwent a complete echocardiographic examination for the determination of ejection fraction (EF), LV mass and mass index, peak and mean systolic pressure gradient, aortic valve area, early (E) and late (A) transmitral flow wave velocities and their ratio (E/A), tissue Doppler indexes of the mitral annulus (Sa, Ea, Aa), and the E/Ea ratio. In addition, levels of high sensitivity C-reactive protein (hsCRP), tumour necrosis factor-alpha (TNF-α) and monocyte chemoattractant protein-1 (MCP-1) were measured from venous blood samples taken before, and 10 days, 3 months and 6 months after aortic valve replacement.

Results: LV mass decreased from 297 ± 99.7 g before aortic valve replacement to 210 ± 67 g 3 months after surgery and to 210 ± 74 g 6 months after surgery ($p<0.001$). LV EF did not change significantly ($p=0.836$). Peak and mean systolic pressure gradients decreased, whereas aortic valve area increased after valve replacement ($p<0.001$). These changes were similar in men and women. In women Sa was greater ($p=0.017$) and the E/Ea ratio lower ($p=0.025$) than in men. The long-term changes in peak and mean pressure gradients, aortic valve area and LV mass after aortic valve replacement were well correlated with the long-term changes in hsCRP, TNF-α and MCP-1 in both men and women.

Conclusions: LV remodelling is similar in elderly men and women with aortic valve disease who have similar body surface area. Although inflammatory markers are not correlated with echocardiographic parameters before aortic valve replacement, a strong correlation exists after operation. This correlation is similar in men and women.

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Left ventricular (LV) remodelling in aortic valve stenosis is an adaptive mechanism for reducing myocardial tension and maintaining cardiac output.[1,2] This ability of the LV to adapt to an increase in afterload is determined by many endogenous and exogenous factors, which results in a reaction by the LV that is highly variable from patient to patient.[3-5] Many studies have reported that the adaptive remodelling of the LV in patients with aortic valve stenosis is different in men

and women.[5-8] However, there are conflicting results in the literature regarding the role of sex in this process.[9-10]

In addition, Hein et al, in a study of myocardial biopsies from patients with aortic valve stenosis and LV hypertrophy, found a mild inflammatory reaction by monocytes and T-lymphocytes, and expression of inflammatory agents in the myocardium.[11] According to the view of these and other researchers, the expression of inflammatory agents in the hypertrophic or pathological myocardium, via autocrine/paracrine or endocrinal action, plays a significant role in the process of LV remodelling.[11-16]

A recent study of ours, as well as observations by other investigators, suggest that inflammatory markers, such as high sensitivity C-reactive protein (hsCRP), tumour necrosis factor-alpha (TNF-α) and monocyte chemoattractant protein-1 (MCP-1), have elevated levels in the peripheral blood of patients with aortic valve stenosis. In addition, the changes in these markers follow almost the same curve in men and women.[17]

These observations raise the following two questions that were addressed by the present study: 1) does sex influence LV remodelling in elderly patients with aortic valve stenosis? 2) do inflammatory markers in peripheral blood (hsCRP, TNF-α, MCP-1) play a role in LV remodelling before and after surgical replacement of the aortic valve?

Methods

We studied 52 patients who satisfied clinical and haemodynamic criteria for severe aortic valve stenosis and underwent surgical valve replacement. Thirty-two patients were men (age 65 ± 11 years) and 20 were women (age 68 ± 9 years). Patients with any of the following were excluded from the study: coronary artery disease and regional LV wall motion disturbances; atrial fibrillation; chronic renal failure or chronic, active inflammatory disease; aortic regurgitation >1+; or other valvular disease.

All patients underwent a detailed echocardiographic examination before and after surgery and blood samples were taken for the quantitative determination of the biochemical markers hsCRP, TNF-α and MCP-1. Venous blood samples were immediately centrifuged and the serum was stored at -70°C. The echo examination and analysis of blood samples were repeated 10 days, 3 months and 6 months after the operation. Measurements of biochemical markers of inflammation were made after completion of the study protocol.

Echocardiographic examination

A Philips echocardiograph (Sonos 5500, Andover MA, USA) was used, equipped with a 2.5 and 3 MHz transducer. Two-dimensional echocardiography was performed in the standard manner, using the left parasternal view along long and short axes, and the apical 4- and 2-chamber views. M-mode recording was guided by the two-dimensional long-axis echo, in accordance with the guidelines of the American Heart Association.[18] The recording of transmitral diastolic flow was made using pulsed Doppler from the apical 4-chamber view, with the Doppler flow sample (4 × 4 mm) at the coaptation point of the mitral valve leaflets.

In all patients, continuous Doppler was used to record the peak flow velocity through the aortic valve. Peak systolic flow velocity was defined as the highest value recorded at one of the standard sites (apical, right parasternal, suprasternal) used for recording trans-aortic flow velocity. The systolic flow velocity and the diameter of the LV outflow tract were also measured, for determination of the area of the aortic valve.

All recordings were stored on videotape for later analysis and measurement of echo parameters. A separate videotape was used for each patient and the same tape was used for recording the follow-up examinations.

Echocardiographic measurements

M-mode

The following parameters were measured: end-diastolic diameter (EDD), end-diastolic thickness of the interventricular septum (IVST), thickness of the LV posterior wall (PWT). Measurements were made in accordance with the guidelines of the American Heart Association. These parameters were used in the calculation of LV mass, according to Devereux' formula,[19]

$$\text{LV mass (g)} = 0.81(1.04.\ [\text{IVST}+\text{EDD}+\text{PWT}]^3-\text{EDD}^3)+0.6$$

and of LV mass index,

$$\text{LV mass index} = \text{LV mass} / \text{body surface area.}$$

LV ejection fraction (EF) was estimated by inspection from the apical 2- or 4-chamber view by two experienced echocardiographers.

Echo Doppler

Transmitral flow was measured from the height of E and A waves, and their ratio E/A was calculated. From the peak aortic systolic flow velocity the peak systolic

pressure gradient of the aortic valve was calculated, using the Bernoulli $4V^2$ equation, as was the mean systolic pressure gradient, by planimetry of the peak systolic flow velocity through the aortic valve. The aortic valve area (AVA) was calculated from the following equation:[20]

$$AVA\ (cm^2) = \pi(D/2)^2.\ LVOT\ VTI\ /\ AV\ VTI$$

where D is the valve diameter, VTI is velocity time integral, LVOT is LV outflow tract, and AV is aortic valve.

Pulsed tissue Doppler

The following parameters were measured at the mitral annulus over 10 consecutive cardiac cycles: the height of the systolic wave (Sa), the Ea wave and the Aa wave. The ratio E/Ea was also calculated.[21]

Determination of biochemical inflammatory markers

The quantitative determination of hsCRP was made by nephelometry using a Date Behring reagent. TNF-α and MCP-1 levels were measured by the ELISA method using a Biomedica reagent.

Statistical analysis

Continuous variables are given as mean ± standard deviation of the mean, whereas discrete variables are given as percentages. Consecutive measurements were compared using 1-way analysis of variance (ANOVA), while comparison between two time intervals was made using Tukey's test for honestly significant differences. Linear correlations between inflammatory markers were sought using Pearson's correlation test. A p-value <0.05 was the criterion of significance throughout. All statistical tests were performed using the statistical program SPSS 11.0 (SPSS, Inc., Chicago IL, USA).

Results

Table 1 shows that age, height, weight, body surface area and body mass index did not differ significantly between men and women. Tables 2, 3 and 4 show the M-mode, two-dimensional, echo Doppler and mitral annulus tissue Doppler parameters measured before surgery, and 10 days, 3 and 6 months after aortic valve replacement, in the entire patient population, and in men and women separately.

IVS and PW thickness decreased to a significant degree ($p=0.001$, $p<0.001$, respectively) during the follow-up period, but EDD showed no significant change. LV mass and LV mass index also showed a significant reduction ($p<0.001$). LVEF did not change significantly. In only 6 patients was LVEF ≤40%. The values of the above echo parameters and of EDD were similar in men and women and showed a similar time course over the study period (Figure 1). However, the change in LV mass and LV mass index was statistically significant only in men ($p=0.001$).

The E wave deceleration time was significantly reduced 10 days after valve replacement ($p=0.015$), but this change subsequently almost disappeared and the value at the end of the study was not significantly different from that at the start (Figure 2).

Peak and mean transvalvular pressure gradients decreased significantly ($p<0.001$), while AVA showed a significant increase ($p<0.001$) (Figures 3 & 4).

None of the other echocardiographic parameters changed significantly during the study period, either for the whole patient population, or for men and women considered separately. The time course of all these variables was similar in men and women.

Tissue Doppler

The height of the systolic Sa wave changed significantly during the study period ($p=0.005$, Table 2), whereas

Table 1. Patient characteristics comparing men and women.

	All patients (n=52)	Men (n=32)	Women (n=20)	p
Age (years)	67.1 ± 10.4	66.0 ± 11.0	68.9 ± 9.3	0.335
Height (m)	1.66 ± 0.08	1.66 ± 0.09	1.67 ± 0.08	0.711
Weight (kg)	74.3 ± 12.2	73.5 ± 9.6	75.5 ± 15.7	0.575
BMI (kg/m^2)	26.9 ± 3.9	26.9 ± 3.6	27.0 ± 4.4	0.870
BSA (m^2)	1.82 ± 0.17	1.81 ± 0.15	1.84 ± 0.20	0.616

BMI – body mass index; BSA – body surface area.

Table 2. Echocardiographic parameters in all patients before and after aortic valve replacement (p-values are from ANOVA).

	Before	10 days after	3 months after	6 months after	p-value
EDD	4.70 ± 0.69	4.65 ± 0.74	4.62 ± 0.57	4.43 ± 0.65	0.318
IVST	1.36 ± 0.24	1.34 ± 0.26	1.22 ± 0.24	1.17 ± 0.27	0.001
PWT	1.28 ± 0.23	1.26 ± 0.22	1.15 ± 0.19	1.07 ± 0.18	<0.001
LVOT	1.82 ± 0.23	1.77 ± 0.22	1.69 ± 0.17	1.74 ± 0.20	0.086
Dec-E	248.2 ± 74.9	214.7 ± 51.0	245.9 ± 52.6	253.6 ± 52.1	0.015
E	77.4 ± 25.5	84.4 ± 32.6	83.0 ± 31.3	84.2 ± 27.4	0.620
A	100.8 ± 33.0	92.6 ± 30.4	90.1 ± 31.7	84.2 ± 27.4	0.448
E/A	0.86 ± 0.44	0.98 ± 0.52	1.03 ± 0.54	1.07 ± 1.28	0.585
Sa	9.23 ± 2.79	11.22 ± 2.71	11.05 ± 3.15	10.29 ± 2.77	0.005
Ea	9.01 ± 4.00	10.17 ± 3.48	10.00 ± 3.09	10.06 ± 3.05	0.371
Aa	13.58 ± 4.82	13.58 ± 4.84	12.55 ± 4.55	13.56 ± 4.95	0.813
E/Ea	11.01 ± 9.03	9.61 ± 6.24	10.17 ± 9.31	9.53 ± 7.57	0.987
Grad-P	90.93 ± 20.44	23.89 ± 9.36	21.14 ± 9.13	22.92 ± 9.84	<0.001
Grad-M	55.11 ± 14.00	13.37 ± 5.51	11.08 ± 4.03	13.15 ± 5.96	<0.001
EF	56.18 ± 7.85	55.23 ± 11.41	56.96 ± 6.53	56.71 ± 6.52	0.836
AVA	0.60 ± 0.27	1.42 ± 0.46	1.46 ± 0.51	1.81 ± 1.10	<0.001
AVAI	0.33 ± 0.15	0.79 ± 0.29	0.81 ± 0.30	0.99 ± 0.57	<0.001
LVmass	297.8 ± 99.7	279.1 ± 93.5	243.1 ± 67.8	210.4 ± 74.0	<0.001
LVImass	164.0 ± 52.9	151.2 ± 48.0	133.6 ± 43.3	115.1 ± 37.7	<0.001
LVS	0.104 ± 0.070	0.126 ± 0.069	0.093 ± 0.044	0.087 ± 0.041	0.026

AVA – aortic valve area; AVAI – aortic valve area index; Dec-E – deceleration time of the E wave; E, A – early and late transmitral flow wave velocities; EDD – end-diastolic diameter; EF – ejection fraction; Grad-M, Grad-P – mean and peak systolic pressure gradient; IVST – interventricular septum thickness; LVImass – left ventricular mass index; LVmass – left ventricular mass; LVOT – left ventricular outflow tract; LVS – left ventricular stiffness; PWT – posterior wall thickness; Sa, Ea, Aa – systolic, early and late waves at the mitral annulus measured by pulsed tissue Doppler.

Ea, Aa and the E/Ea ratio did not. Considering the sexes separately, the change in Sa was only statistically significant in men (p=0.001). However, the difference between the initial value of Sa and the value 6 months after aortic valve replacement was not significant (Figure 5). The values of Sa and the E/Ea ratio at baseline differed significantly between men and women (p=0.017, p=0.025, respectively).

Biochemical markers of inflammation

The values of biochemical inflammatory markers are presented in Table 5. TNF-α and MCP-1 decreased progressively over the study period, whereas hsCRP increased dramatically 10 days after valve replacement and subsequently decreased again at 3 and 6 months, with final values close to those at baseline.

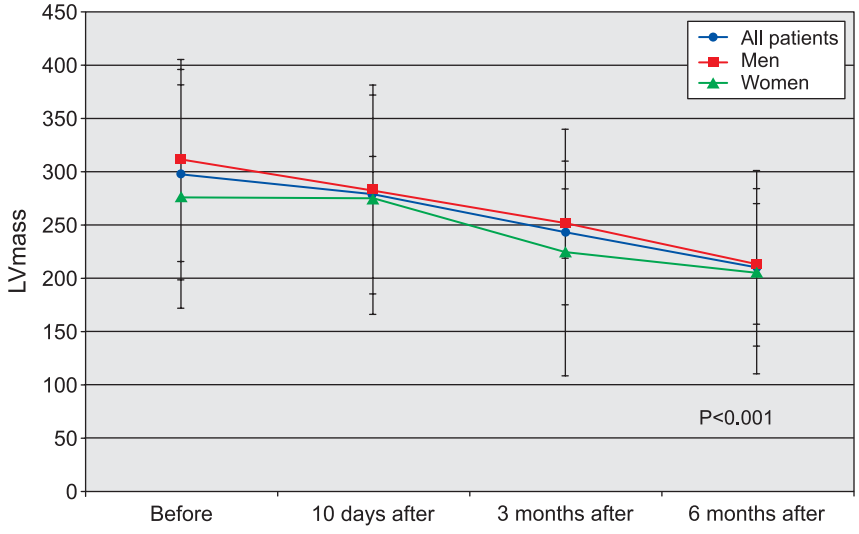

Figure 1. Time course of changes in left ventricular mass (LVmass) after aortic valve replacement, for the whole patient population and for men and women separately.

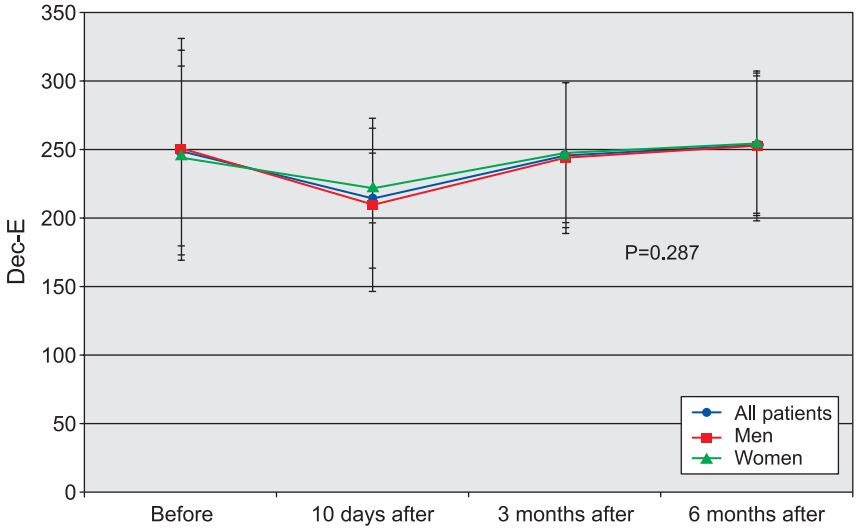

Figure 2. Time course of changes in E wave deceleration time (Dec-E) after aortic valve replacement, for the whole patient population and for men and women separately.

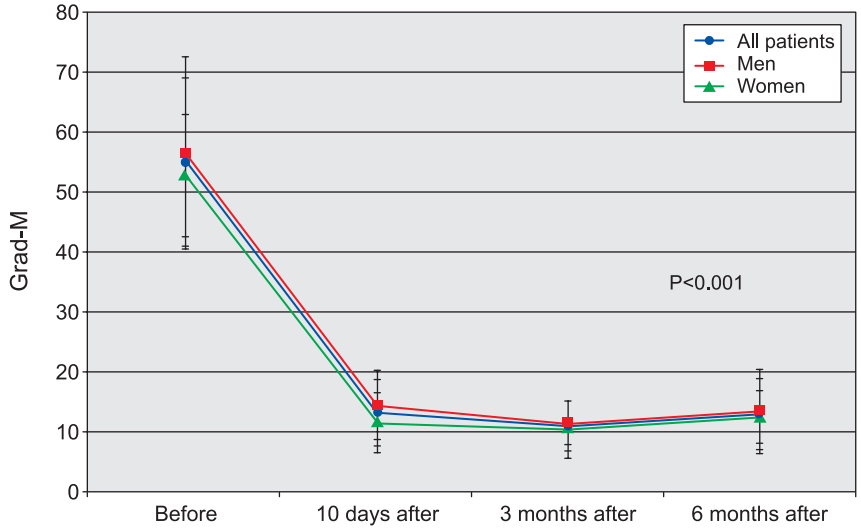

Figure 3. Time course of changes in mean systolic pressure gradient (Grad-M) after aortic valve replacement, for the whole patient population and for men and women separately.

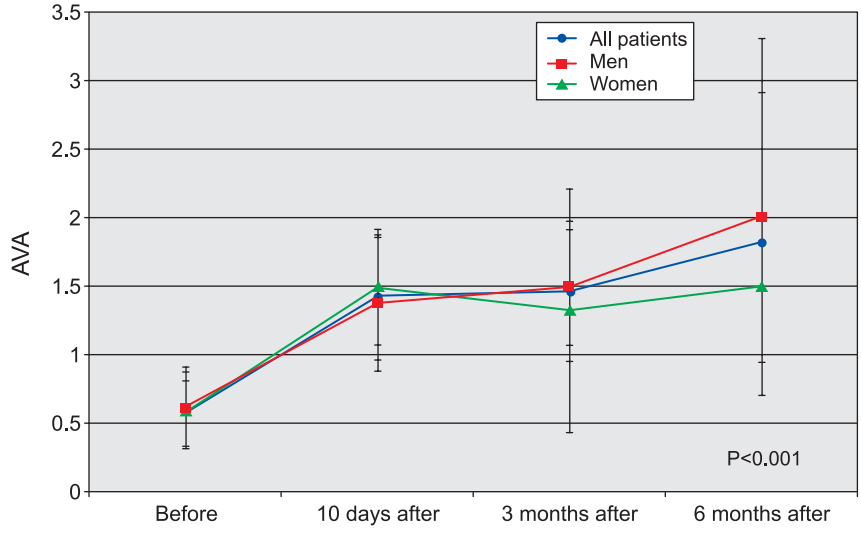

Figure 4. Time course of changes in aortic valve area (AVA) after aortic valve replacement, for the whole patient population and for men and women separately.

Table 3. Echocardiographic parameters in men before and after aortic valve replacement (p-values are from ANOVA).

	Before	10 days after	3 months after	6 months after	p-value
EDD	4.78 ± 0.70	4.70 ± 0.76	4.68 ± 0.43	4.54 ± 0.64	0.660
IVS	1.37 ± 0.19	1.29 ± 0.19	1.24 ± 0.23	1.18 ± 0.15	0.008
PW	1.31 ± 0.19	1.29 ± 0.17	1.15 ± 0.17	1.04 ± 0.13	<0.001
LVOT	1.82 ± 0.23	1.76 ± 0.23	1.69 ± 0.17	1.73 ± 0.20	0.251
Dec-E	250.1 ± 80.9	209.7 ± 63.0	244.5 ± 55.2	253.4 ± 54.7	0.082
E	84.8 ± 24.4	96.3 ± 36.8	88.1 ± 35.2	89.7 ± 31.0	0.597
A	101.8 ± 38.6	96.2 ± 33.8	87.7 ± 35.1	97.7 ± 34.4	0.678
E/A	0.97 ± 0.51	1.10 ± 0.64	1.11 ± 0.46	1.28 ± 1.64	0.706
Sa	8.51 ± 2.48	10.83 ± 2.53	11.31 ± 3.08	11.16 ± 2.65	0.001
Ea	9.03 ± 4.51	10.00 ± 3.67	9.41 ± 2.89	10.87 ± 3.33	0.393
Aa	12.93 ± 4.65	12.95 ± 5.22	12.90 ± 4.30	14.29 ± 5.80	0.780
E/Ea	12.40 ± 10.11	11.19 ± 7.03	11.51 ± 11.34	9.81 ± 9.57	0.928
Grad-P	94.03 ± 22.64	25.08 ± 10.48	23.39 ± 7.97	24.31 ± 10.25	<0.001
Grad-M	56.58 ± 15.99	14.54 ± 5.67	11.58 ± 3.50	13.53 ± 6.96	<0.001
EF	55.81 ± 8.77	55.77 ± 7.96	56.92 ± 7.78	56.91 ± 6.42	0.934
AVA	0.61 ± 0.30	1.37 ± 0.49	1.49 ± 0.42	2.00 ± 1.30	<0.001
AVAI	0.34 ± 0.17	0.76 ± 0.31	0.82 ± 0.22	1.10 ± 0.65	<0.001
LVmass	311.2 ± 95.5	282.3 ± 32.3	213.7 ± 56.7	213.7 ± 56.7	0.001
LVImass	172.8 ± 53.8	153.8 ± 44.4	139.6 ± 16.7	119.5 ± 31.3	0.001
LVS	0.102 ± 0.056	0.142 ± 0.085	0.092 ± 0.035	0.089 ± 0.045	0.013

Abbreviations as in Table 2.

Table 4. Echocardiographic parameters in women before and after aortic valve replacement (p-values are from ANOVA).

	Before	10 days after	3 months after	6 months after	p-value
EDD	4.57 ± 0.68	4.57 ± 0.70	4.55 ± 0.73	4.27 ± 0.66	0.582
IVS	1.37 ± 0.31	1.41 ± 0.33	1.18 ± 0.27	1.15 ± 0.38	0.094
PW	1.24 ± 0.28	1.22 ± 0.29	1.15 ± 0.22	1.12 ± 0.23	0.554
LVOT	1.82 ± 0.24	1.77 ± 0.20	1.68 ± 0.18	1.76 ± 0.21	0.517
Dec-E	245.1 ± 66.0	221.9 ± 25.5	247.6 ± 51.5	254.0 ± 50.0	0.291
E	65.6 ± 23.2	68.4 ± 16.2	76.4 ± 25.6	76.4 ± 20.0	0.370
A	99.1 ± 22.1	87.9 ± 25.6	93.2 ± 28.0	97.3 ± 19.9	0.508
E/A	0.68 ± 0.22	0.83 ± 0.25	0.93 ± 0.63	0.76 ± 0.10	0.201
Sa	10.45 ± 2.94	11.72 ± 2.94	10.72 ± 3.34	9.04 ± 2.54	0.095
Ea	8.98 ± 3.06	10.38 ± 3.30	10.77 ± 3.32	8.92 ± 2.24	0.246
Aa	14.71 ± 5.03	14.40 ± 4.31	12.09 ± 5.02	12.50 ± 3.27	0.308
E/Ea	8.62 ± 6.35	7.49 ± 4.31	8.46 ± 5.94	9.14 ± 3.34	0.682
Grad-P	86.13 ± 15.80	22.18 ± 7.39	18.22 ± 10.11	20.84 ± 9.16	<0.001
Grad-M	52.83 ± 10.15	11.67 ± 4.94	10.44 ± 4.75	12.61 ± 4.35	<0.001
EF	56.75 ± 6.34	54.44 ± 15.33	57.00 ± 4.83	56.43 ± 6.91	0.873
AVA	0.57 ± 0.24	1.49 ± 0.42	1.32 ± 0.89	1.49 ± 0.55	<0.001
AVAI	0.31 ± 0.13	0.83 ± 0.27	0.76 ± 0.57	0.81 ± 0.36	<0.001
LVmass	276.5 ± 105.1	274.2 ± 107.9	224.6 ± 115.8	205.8 ± 94.8	0.191
LVImass	149.9 ± 49.5	147.1 ± 54.4	120.8 ± 76.1	109.0 ± 45.4	0.119
LVS	0.108 ± 0.089	0.103 ± 0.023	0.093 ± 0.054	0.085 ± 0.035	0.665

Abbreviations as in Table 2.

The hsCRP levels at baseline and 6 months after operation were higher in women than in men ($p<0.001$). Values of the other markers did not differ significantly according to sex (Tables 6 & 7).

Correlation between echo parameters and inflammatory markers

A comparative analysis of the echocardiographic parameters and levels of inflammatory markers in pe-

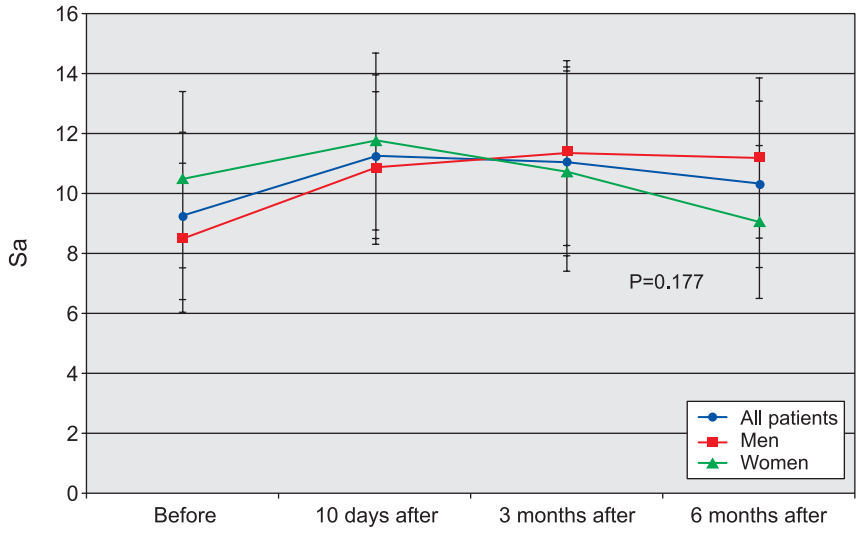

Figure 5. Time course of changes in the systolic Sa wave after aortic valve replacement, for the whole patient population and for men and women separately.

Table 5. Values of tumour necrosis factor alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and high sensitivity C-reactive protein (hsCRP) in all patients, before and after aortic valve replacement.

	Before	10 days after	3 months after	6 months after	p-value
TNF-α (pg/ml)	231.5 ± 144.4	135.4 ± 43.3	137.0 ± 28.2	46.8 ± 9.7	<0.001
MCP1 (pg/ml)	151.7 ± 48.2	125.5 ± 15.0	53.3 ± 12.2	29.9 ± 6.8	<0.001
hsCRP (mg/dl)	6.36 ± 6.56	50.33 ± 32.72	7.39 ± 6.72	5.70 ± 5.67	<0.001

Table 6. Values of tumour necrosis factor alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and high sensitivity C-reactive protein (hsCRP) in men, before and after aortic valve replacement.

	Before	10 days after	3 months after	6 months after	p-value
TNF-α (pg/ml)	212.4 ± 119.5	121.6 ± 47.7	134.7 ± 25.3	48.7 ± 8.8	<0.001
MCP1 (pg/ml)	157.0 ± 64.8	128.6 ± 18.8	49.0 ± 12.4	29.1 ± 6.4	<0.001
hsCRP (mg/dl)	5.34 ± 5.71	49.11 ± 32.15	5.85 ± 5.04	3.41 ± 0.83	<0.001

Table 7. Values of tumour necrosis factor alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and high sensitivity C-reactive protein (hsCRP) in women, before and after aortic valve replacement.

	Before	10 days after	3 months after	6 months after	p-value
TNF-α (pg/ml)	255.7 ± 171.3	150.0 ± 33.5	138.6 ± 30.9	44.9 ± 10.5	<0.001
MCP1 (pg/ml)	145.6 ± 13.4	122.7 ± 10.3	56.6 ± 11.5	30.6 ± 7.3	<0.001
hsCRP (mg/dl)	7.64 ± 7.46	51.63 ± 34.33	8.49 ± 7.69	7.84 ± 7.32	<0.001

ripheral blood at baseline found no statistically significant correlations. In contrast, a similar analysis of the data obtained after aortic valve replacement found very good correlations between the variation over time of several indexes of LV remodelling and biochemical markers (Table 8). The time course of changes in inflammatory markers and echo parameters after valve replacement was similar in men and women regarding the correlation of hsCRP with mean gradient and AVA, the correlation of TNF-α with peak and mean

Table 8. Correlations between the changes in markers of inflammation and echocardiographic parameters in all patients, after aortic valve replacement.

	hsCRP	TNF-α	MCP-1
EDD (cm)	0.688	0.646	0.013*
Dec-E (cm/s)	0.018*	0.974	0.557
Grad-P (mmHg)	0.001*	<0.001*	<0.001*
Grad-M (mmHg)	0.001*	<0.001*	<0.001*
AVA (cm^2)	0.234	0.002*	<0.001*
LVmass (kg)	0.638	0.074	<0.001*

Table 9. Correlations between the changes in markers of inflammation and echocardiographic parameters in men, after aortic valve replacement.

	hsCRP	TNF-α	MCP-1
EDD (cm)	0.802	0.111	0.036*
Dec-E (cm/s)	0.119	0.715	0.551
Grad-P (mmHG)	0.004*	0.001*	<0.001*
Grad-M (mmHg)	0.005*	0.001*	0.001*
AVA (cm^2)	0.002*	0.368	0.088*
LVmass (kg)	0.761	0.006*	0.005*

Table 10. Correlations between the changes in markers of inflammation and echocardiographic parameters in women, after aortic valve replacement.

	hsCRP	TNF-α	MCP-1
EDD (cm)	0.663	0.561	0.190
Dec-E (cm/s)	0.043*	0.658	0.874
Grad-P (mmHg)	0.061*	<0.001*	<0.001*
Grad-M (mmHg)	0.044*	<0.001*	<0.001*
AVA (cm^2)	0.004*	0.063*	0.013*
Lvmass (kg)	0.224	0.795	0.006*

*Statistically significant correlation. Abbreviations as in previous tables.

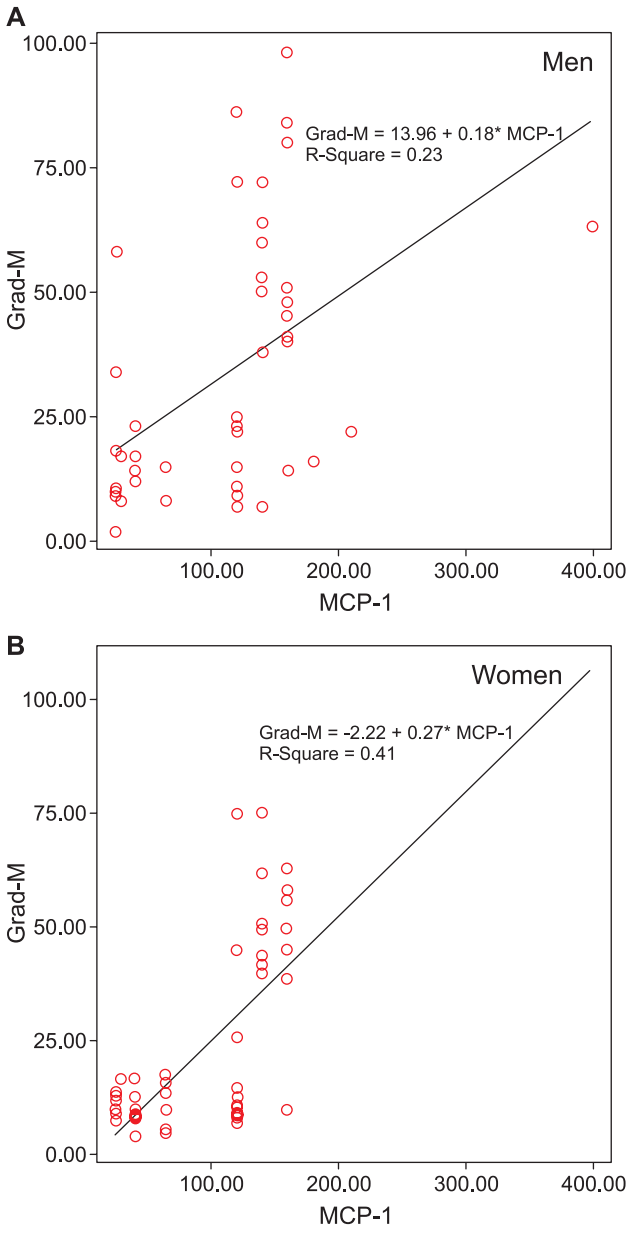

Figure 6. Correlation between mean systolic pressure gradient (Grad-M) and monocyte chemoattractant protein-1 (MCP-1) after aortic valve replacement, in men (A) and in women (B).

gradient, and the correlation of MCP-1 and peak and mean gradient and LV mass. Differences between men and women are shown in Tables 9 and 10. The correlations between MCP-1 and the mean gradient in men and women are shown in Figure 6.

Discussion

The most important findings of this study are that the degree of LV remodelling and the rate of reversal of remodelling and improvement in cardiac function after the surgical treatment of elderly patients with aortic valve stenosis are similar in men and women who have the same body surface area. Before surgery, there is no correlation between biochemical markers of inflammation and echocardiographic parameters. In contrast, after operation there is a good correlation between the long-term changes in inflammatory markers and the corresponding changes in the most important echo parameters. These findings apply similarly to men and women.

LV remodelling after aortic valve replacement

The adaptive remodelling of the LV to an increase in afterload, as occurs in aortic valve stenosis, varies from

patient to patient.[9] The most important factors that play a part in LV remodelling are age, body surface area, the size of the haemodynamic load, and LV performance.[9] Also, some experimental and clinical studies have shown that LV remodelling in women with severe aortic stenosis is different from that in men who have the same increase in afterload.[9,22,23] In women who have aortic stenosis the LV usually reacts with concentric hypertrophy and hyperdynamic systolic function.[5,7,24] In contrast to these observations, Milavetz et al[10] did not find statistically significant differences in LV geometry or function between men and women. In the present study, where the patients' body surface area did not differ significantly between men and women, although LV mass and LV mass index were higher in men than women, the difference did not reach statistical significance. Thus, our findings agree with those of Milavetz[10] and Douglas.[23] However, they differ from those of Kostkiewicz et al, who found a higher LV mass index in women than in men, although again the difference was not significant. At this point it should be noted that the patients in our study were older than those in the other studies above.

Our findings confirm those of older studies that showed a significant reduction in transvalvular systolic pressure gradient and LV mass, and an increase in AVA after aortic valve replacement.[26-28] The long-term change in these echo parameters after surgery was similar in men and women (Figures 1, 3, 4). Our findings also confirm the observation of older studies that LV systolic function improves (increase in Sa wave) early (within 10 days) after surgery.[27-30] In contrast, over the same period the E wave deceleration time decreases (though non-significantly), suggesting impairment of LV diastolic function.[31,32] However, the values of Sa and E wave deceleration time 6 months after operation in our study did not differ from the baseline values before surgery (Figures 2 & 5). The absence of such a significant difference is probably due to the small number of patients studied, and to the fact that 6 of the 52 patients had an LVEF ≤40%. The most interesting finding of our study was that, not only were the changes in Sa and E wave deceleration time from baseline to 6 months after treatment not statistically significant, but also that there was no statistically significant difference between men and women in the curves showing the time course of these two variables over the study period (Figures 2 & 5). Thus, in contrast to other studies[9,23] our findings clearly show that sex plays no special role in LV remodelling in elderly patients with aortic valve stenosis and similar body surface area. Even though this finding may have been due to random statistical variability, its interpretation could be considered as suggesting that the biological rules that determine the reaction of the hormonal system and the adaptability of the LV to severe aortic valve stenosis are the same in men and women, when the hormonal system of elderly women is not fully functional.

Relation between inflammatory markers and echo parameters

The determination of biochemical markers of inflammation in the peripheral blood is not considered to have clinical value early after surgery as a way of documenting a reduction in chronic inflammation. In a previous study, we showed that this indeed applies in the case of hsCRP, where we found significantly elevated levels 10 days after operation, compared with baseline values. In contrast, values of TNF-α and MCP-1 decreased 10 days after surgery and continued to decrease at 3 and 6 months after aortic valve replacement (Tables 5, 6, 7).

In the literature there are conflicting views regarding the relation between inflammatory markers and echocardiographic parameters that express LV morphology and function in patients with aortic stenosis.[34,35] According to the findings of our study, before valve replacement surgery there is no significant relation between hsCRP, TNF-α and MCP-1, and the echo parameters that express LV remodelling in aortic stenosis. However, after operation there was a good correlation between the time course of values of inflammatory markers and the echo parameters at 10 days, 3 and 6 months of follow up (Tables 8, 9, 10). It is difficult to interpret these findings, and they may have been the result of chance statistical variability. However, the products of inflammation seem to have an inhibitory effect on the myocardium, resulting in a modification of LV remodelling and the lack of a good correlation between inflammatory markers and echo parameters. The significant decrease in afterload after valve replacement restores cardiac function, while at the same time the markers of inflammation gradually return to normal. Thus, a correlation between the changes in the levels of those markers and the more important echo parameters is perhaps to be expected during this period. An interesting finding of our study is that about the same relation was observed in both men and women (Figure 6).

Conclusions

LV remodelling is similar in elderly men and women with aortic valve stenosis. Although biochemical markers of inflammation show no correlation with echocardiographic parameters before aortic valve replacement, they show a strong correlation after operation. This correlation is similar in men and women.

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