Med. J. Cairo Univ., Vol. 62, No. 1, March: 23 - 29, 1994

Regression of Hypertrophy After Aortic Valve Replacement for Chronic Aortic Regurgitation

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Abstract

Factors influencing magnitude of regression of left ventricular hypertrophy after successful aortic valve replacement have been studied in 20 patients with chronic aortic regurgitation by cardiac catheterization, echocardiography and left ventricular muscle biopsy. Patients with preoperative value of left ventricular end diastolic pressure >20 mmHg and/or left ventricular end systolic dimension >5.6 cm are less likely to have normalization of their left ventricular mass index following aortic valve replacement. Preoperative left ventricular mass index does not predict changes following aortic valve replacement. Increased amounts of interstitial fibrosis appears to be related to incomplete regression of left ventricular hypertrophy after aortic valve replacement.

Introduction

LEFT ventricular hypertrophy (LVH) is an adaptive structural cardiac response to the load imposed by aortic regurge (AR). As such, it maintains a stable cardiac performance until further adaptation is no longer possible and then cardiac failure supervenes. Offsetting this beneficial effect is a distinct risk demonstrated by greater number of cardiovascular morbid and mortal events, more severe ischemic disease, cardiac dysrhythmia and sudden death [1].

Factors influencing the magnitude of regression of LVH after aortic valve replacement (AVR) have not been well studied [2,3,4]. In this work, echocardiography and histopathological studies were utilized in order to study factor(s) that may be responsible for lack of regression after AVR.

Patients and Methods

20 patients (pts) with isolated significant AR in whom surgery was indicated were included. Patients with additional valve disease or associated with medical disorders liable to affect left ventricular structure or function were excluded.

Study Patients:

This study is based on 20 patients (2 females) and 18 males, age range from 14 to

50 years, with severe aortic regurgitation who underwent a comprehensive echocardiographic examination between March 1988 to March 1991 at the National Heart Institute and Cairo University Hospitals. patients were subjected to full clinical evaluation, resting ECG, Chest X-ray, cardiac catheterization, left ventriculography and coronary arteriography to assess the severity of AR, measure left ventricular and diastolic pressure and exclude associated valvular or coronary disease. All patients were in sinus rhythm and all underwent aortic valve replacement within 30 days (range 1 to 36 days) after the echocardiographyic study. Repeat M-mode, two-dimensional and Doppler echocardiographic examinations were performed 6 months after successful aortic valve replacement in all patients. The severity of aortic regurgitation was judged by the root aortography and was graded according to the criteria of Grossman [5]. Seven patients were graded +4 and 13 patients were graded +3. All patients had left ventricular muscle biopsy at the time of surgery.

Histopathological Studies:

Biopsy material were fixed in 10% buffer formalin. Serial paraffin sections were prepared and properly stained by Hematoxylin and Eosin [6], Masson Trichrome stains and periodic Acid Schiff's (P.A.S.) reaction for histopathological examination. Assessment of collagen deposition was done by a semiquantitative technique by which the amount of interstitial fibrosis was measured as percentage in relation to adjacent muscle fibers. Muscle degeneration was assessed as absent (0), focal (+) and diffuse (++). Muscle hypertrophy was assessed as absent (0), slight (+) when myofiber diameter was increased to < 1.5 times normal and moderate (++) when diameter was increased > 1.5 times normal. Mucopolysaccharide (MPS) deposition was judged slight (+) or moderate (++) depending on the staining reaction to PAS. The inflammatory process was judged mild (+) when few scattered chronic inflammatory cells were found, moderate (++) when aggregation on one focus was found and significant (+++) when aggregation in more than one focus was found.

Echocardiography:

A Hewlett Packard 77020 A ultrasound phased array sector scanner was used for M-mode /two-dimensional /Doppler color flow imaging echocardiographic examination. Ultrasound transducer ranging from 2.25 to 5 MHz was used for examination. Examination was performed with the patient in the left lateral decubitus position.

The following variables were measured:

a- Left ventricular end diastolic and end systolic dimensions (LVEDD, LVESD).

b- Percent left ventricular fractional shortening (%FS).

c- Left ventricular and systolic wall stress (ESS) calculated as previously described by Sutton [7].

d- left ventricular mass index (LVMI); calculated by the method of Troy [8].

The upper limit of normal of LVMI for our laboratory was 110 gm/m^2 which represents two standard deviations above the mean value for measurements in a group of 280 normal healthy individuals (controls) that were age-matched and involving both males and females.

Data Analysis:

Data are presented as the mean ± 1 standard deviation. Statistical analysis as calculation of means, unpaired *t*-test for comparisons using the same variable be-

tween two different groups, Chi-square test for comparison between proportions and statistical difference of results, were performed by the standard methods. A p value less than 0.05 was considered statistically significant.

Results

Patients were divided into two groups based on the degree of regression of LVH 6 months after AVR; Group I (12 pts): had normalization of their left ventricular mass index (LVMI) (LVMI < 110 gm/m^2 and group II (8 pts): had incomplete regression (LVIM > 110 gm/m^2).

Group I patients was composed of 10 males and 2 females; their age ranged between 14 and 41 years with a mean of 25 ± 8 while group II were all males and their age ranged between 16 and 50 with a mean of 25 ± 11 years. There was no difference between both groups in relation to age or functional class (NYHA classification) neither before nor after surgery. Patients in both groups showed significant symptomatic improvement of at least one functional class.

Echocardiographic and hemodynamic Results (Table 1):

Table (1) shows comparisons of the mean values for echocardiographic and hemodynamic variables among groups I and II patients. Only preoperative left ventricular end systolic dimension and left ventricular end diastolic pressure showed significantly lower values in group I than group II (4.47 ± 0.92 versus 5.63 ± 0.65 cm, p = 0.03 and 10.16 ± 4.17 versus 20 ± 7.9 mmHg, p = 0.002, respectively). There was no significant difference between both groups in relation to preoperative values of LV end diastolic dimension, end systolic

Table (1): Hemodynamic and Echocardiographic Results in Group (I) and (II).

Parameter	Group I	Group II	p =
LVEDP-B	10.1 ± 4.1	20 ± 7.9	0.002
LVESD-B	4.70 ± 0.92	5.63 ± 0.65	0.03
LVESD-A	2.95 ± 0.50	3.87 ± 0.79	0.005
LVEDD-B	6.90 ± 0.90	7.57 ± 1.11	NS
LVEDD-A	4.43 ± 0.74	5.44 ± 0.80	0.01
ESS-B	96.7 ± 32.8	112.5 ± 19	NS
ESS-A	68± 16	94 ± 41	0.05
FS-B	31 ± 7	25 ± 6	NS
FS-A	33 ± 2.6	28 ± 6	0.05
LVMI-B	294 ± 73	340 ±85	NS
LVMI-A	83 ± 14	143 ± 22	0.0001
AVSG-A	23.8 ± 11.2	18.4 ± 12.5	NS

LVEDP : LV end diastolic pressure. LVESD : LV end systolic dimension in cm.
LVEDD: LV end diastolic dimension in cm. ESS : LV end systolic wall stress (10^3 dyne /cm^2).
FS : LV percent fractional shortening. LVMI : LV mass index in gm /m^2.
AVSG : Aortic valve prosthesis systolic gradient in mmHg B : Before aortic valve replacement.
A : 6 months after aortic valve replacement.

stress, percent fractional shortening or LV mass index. Six months postoperatively, group I patients had significantly lower values than group II patients in relation to LV end diastolic and end systolic dimensions, end systolic stress and LV mass index; while percent fractional shortening showed a higher value in group I than group II. It needs to be mentioned that there was no significant difference between both groups in the mean value for postoperative aortic valve prosthetic gradient.

Pathological Results (Tables 2 and 3):

Group I pts showed significantly lower percentage of interstitial fibrosis (using a semiquantitative technique) than group II patients. (3.3 ± 3.9 vs 10 ± 4.2 %, p 0.003, Figs. 1,2). Patietns in group I also showed significant lower value for muscle degeneration than group II when comparing absent or focal (0/+) with diffuse (++ or morc) pathology using chis quare test (p = 0.02). Furthermore, group I pts showed less deposition of A-MPS than group II pts when comparing absent or slight (0/+) with mild or moderate (++ or more) deposition (p = 0.04). However, there was no significant difference between both groups in relation to the presence of inflammatory cells or the degree of muscle hypertrophy.

Table (2): Pathologic Data in Group (I).

Case no.	Fibrosis	Degen.	Inflam.	Hypertr.	MPS
1	0	0	0	+	N
2	5	+	0	++	++
3	0	+	0	0	N
4	5	+	0	0	+
6	0	0	0	++	+
8	0	+	0	+	++
10	5	+	0	+	N
12	5	++	0	++	++
13	10	++	++	+	++
14	10	+	0	+	++
17	0	++	++	++	+
19	0	+	0	++	N
Mean ± SD	3.33±3.89				

Fibrosis : Percent fibrosis in relation to muscle fibers.
Degen : Degree of muscle fiber degeneration.
Inflam : Degree of inflammatory process.
Hypertr : Degree of muscle hypertrophy.
MPS : Degree of mucopolysaccharide deposition.
N : Normal amount.

Table (3): Pathologic Data in Group (II).

Case no.	Fibrosis	Degen.	Inflam.	Hypertr.	MPS
5	0	0	0	+++	++
7	10	++	++	+	N
9	15	++	++	++	++
11	15	+	0	++	++
15	10	++	0	++	++
16	10	++	0	+	++
18	10	++	0	++	++
20	10	++	0	++	++
Mean ±SD	10 ± 2.4				

Fibrosis : Percent fibrosis in relation to muscle fibers.
Degen : Degree of muscle fiber degeneration.
Inflam : Degree of inflammatory process.
Hypertr : Degree of muscle hypertrophy.
MPS : Degree of mucopolysaccharide deposition.
N : Normal amount.

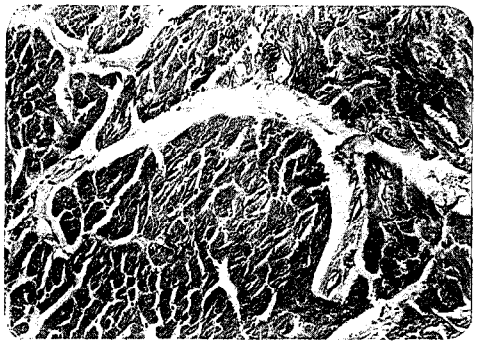

Fig. (1): Myocardial biopsy from case no. 1 showing no evidence of interstitial fibrosis.
(Hematoxylin and Eosin x 200)

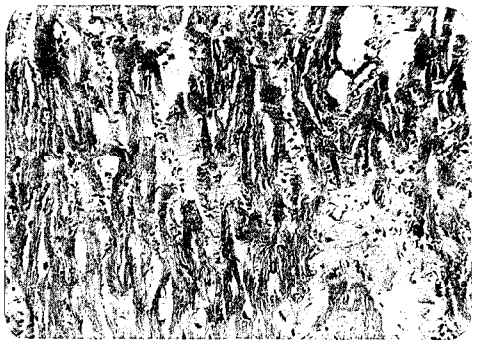

Fig. (2): Biopsy specimen from case no. 9 (in group II) showing patchy areas of interstitial fibrosis. Muscle fibers in between areas of fibrosis show some degenerative changes.
(Hematoxylin and Eosin x 100).

Discussion

Most studies of operative outcome after aortic valve replacement have focused on correlates and predictors of clinical states or ventricular performance, whereas few reports have systematically assessed the determinants and consequences of normalization of ventricular size and hypertrophy [2,3,4].

In this study, factors which influence

the rate and magnitude of regression of left ventricular hypertrophy (LVH) in patients with AR who have undergone successful AVR were examined. Results showed that two groups of patients could be identified; group I with normalization of LVMI at 6 months postoperatively and group II with incomplete regression of left ventricular mass.

The reversibility of myocardial hypertrophy after aortic valve replacement (AVR) for chronic aortic regurgitation (AR) has been well documented [2, 3, 9, 10, 11, 12, 13]. Normalization of LV mass was found in approximately two thirds (60%) of patients in the current study which agrees with many recent reports; Fioretti et al. [3] reported 65% after 3 years follow up; Roman et al. [14] reported 68% after 18 to 56 months and Kurnik et al. [15] reported 82% after 6 to 8 months postoperatively. Bonow et al. [13], reported a slightly lower proportion (54%) after 3-7 years postoperatively, a difference possibly attributed to more prevalent ventricular dysfunction before surgery, which was performed as early as 1976 in some patients. In contrast to the previous studies, preoperative LV and systolic dimension (LVESD) and the LV end diastolic pressure (LVEDP) in our study were highly reliable predictive factors for regression of LVH postoperatively, however, the preoperative symptoms and functional class were similar in both groups and had limited value in predicting the postoperative results. These findings were in agreement with Roman et al. [14] and Gaasch et al. [2] studies which was also true for all other echocardiographic parameters.

The present study confirmed the previous reports that echocardiographic and hemodynamic data, with the exception of preoperative LVESD and LVEDP, have limited value in defining the type or the degree of irreversible dysfunction, but we were able to document that increased pathological interstitial fibrosis and diffuse muscle degeneration were related to incomplete regression of LV hypertrophy and persistent dilatation.

In conclusion, patietns with preoperative value of LVEDP > 20 mmHg and/or LVESD > 5.5 CM are less likely to normalize their LVMI following AVR. Preoperative LVMI does not predict changes following AVR. Increased amounts of interstitial fibrosis appears to be related to incomplete regression of LVH after AVR.

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