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Research on the Effect of Aortic Valve Replacement with Mechanical Prosthesis on the Evolution of Ventricular Hypertrophy in Patients with Degenerative Aortic Stenosis

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Abstract*. Aortic valvulopathies, and especially aortic stenosis (AS), are the most common valvular disorders. Untreated, 50% of patients with severe AS will die within 2-3 years from the onset of symptomatology. The standard treatment consists in the surgical replacement of the aortic valve with mechanical or biological prosthesis. 40 patients were included in the study after replacement of the aortic valve with double disc mechanical prosthesis for severe degenerative AS. The disks of the prosthesis are made of pyrolytic carbon characterized by extreme hardness, which provides wear protection over the years. The ring is composed of a graphite substrate coated with pyrolytic carbon and attached to a suture collar made of polyethylene (polytetrafluoroethylene - PTFE) or polyester (Dacron® or Teflon®). This study evaluates mass regression and left ventricular mass index at three months and one year postoperatively. The regression of the left ventricular mass at 3 months after the surgery is 25.86%, and at one year after the surgery this regression was reduced - 15.11%. The regression of the mass of the left ventricle and especially the premature regression, correlated with the degree of hypertrophy of the left ventricle preoperatively, highlight the beneficial effect of the double disc mechanical prosthesis.*

Keywords: *carbon pyrolite, Dacron, mechanical prosthesis, degenerative aortic stenosis, left ventricular hypertrophy*

1.Introduction

Cardiovascular disease is a major health problem worldwide. According to the World Health Organization, in 2005, 17.5 million people died from cardiovascular disease, which represents 30% of the causes of mortality. A large percentage of these diseases are valvular heart disease, and the number of patients requiring heart valve replacement is estimated at approximately 290.000 in 2003 to over 850.000 by 2050 [1]. Aortic valvulopathies are the most frequent valvular disorders (44.3% of the total valvulopathies) [2], the most common being aortic stenosis (AS) almost 50%. If left untreated, 90% of patients with severe AS have a life expectancy of less than 10 years, and 50% of patients will die within 2-3 years of symptom onset [3, 4]. Degenerative AS is most commonly seen in elderly, hypertensive patients with cumulative cardiovascular risk factors [5, 6].

The golden standard treatment was the surgical replacement of the aortic valve, until 2007 when a new revolutionary procedure was introduced, the transcatheter implantation of the aortic valve used especially in inoperable patients, those with high surgical risk [7].

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Materials for mechanical prosthesis

The first mechanical ball prosthesis, made of a metal cage housing a silicone elastomer ball, was implanted in 1952 [8]. The technology of valve prostheses has evolved rapidly. If the concept of ball valve predominated between 1960-1970, mono-disc prosthesis, formed of a Teflon-coated metal ring containing a pyrolytic carbon disc responsible for the oscillatory movements of the prosthesis [9], are used in the clinic since 1969.

At the end of the next decade the first double-disc valves appear, the Saint Jude Medical valve formed from a ring with a graphite substrate coated with pyrolytic carbon and two hollow disk of the same composition quickly becomes the most used valve in the world [9, 10].

Throughout the 1990s it became the reference mechanical prosthesis due to the performances achieved: almost laminar central flow, low gradient, low risk of complications and excellent hemocompatibility [11].

The composition of the materials from which the prosthetic disks are formed has evolved over time, alloys such as chromium, cobalt, nickel, being gradually replaced by titanium and especially pyrolytic carbon, inert and thrombus-resistant material used alone to cover the disk or fittings, having the characteristics suitable for heart valves (Figure 1). The technological progress of these valves has led to the use of pyrolytic carbon which is required by its mechanical properties and biocompatibility [12].

Pyrolytic carbon components have been used in the manufacture of more than 25 different types of cardiac valve prostheses since the late 1960s, and have accumulated a clinical experience in the order of 16 million patient-years [13].

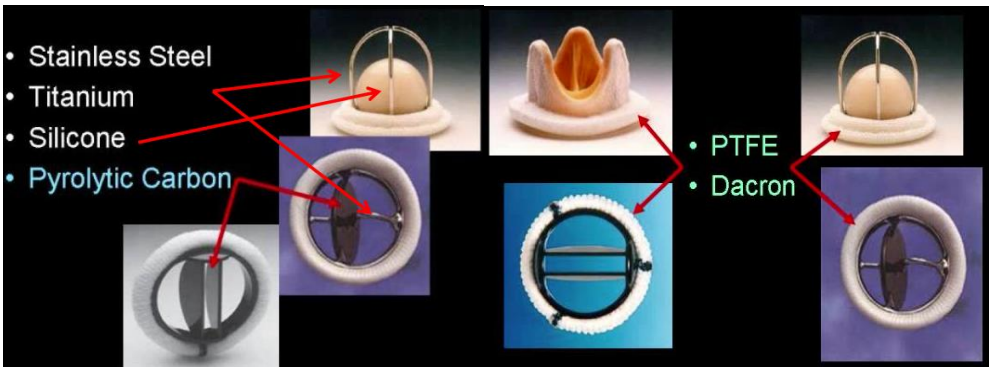

Figure 1. Valve prosthesis – structure

The mechanical prosthesis used are made of a rigid circular ring and disks. The disks of the valve were made of pyrolytic carbon, (which replaced the polymer disks used in the old valve models), characterized by extreme hardness, which provides protection over the years. Carbon fiber is created in the process of controlled pyrolysis of polyacrylonitrile (synthetic carbon fiber) and other organic polymers. It comprises large carbon structures similar to graphite and has mechanical durability. Pyrolytic Carbon is resistant to wear, strong, durable, is highly resistant to blood clotting and causes little damage to blood cells. It owes its unusual mechanical properties and its biocompatibility to a unique microstructure [13, 14].

The rigid circular ring is composed of a graphite substrate coated with pyrolytic carbon and attached to a radio-transparent suture collar made of polyethylene (polytetrafluoroethylene - PTFE) or polyester (Dacron® or Teflon®), which allows the prosthesis to be fixed to the aortic ring [13]. Dacron (terephthalate polyethylene fibers) is the trademark for a polyester fiber used to produce vascular, especially aortic, prosthesis, widely used in cardiovascular, but also in vascular surgery. Dacron is a condensation polymer obtained from ethylene glycol and terephthalic acid [15- 17].

Considerations regarding the causes of the use of aortic mechanical prosthesis

Doppler echocardiography is the method of choice for assessing the severity of aortic stenosis and the functionality of the prosthesis. Echocardiography is the paraclinical investigation that confirms the presence of aortic stenosis, evaluates the degree of valve calcification, function and degree of left ventricular hypertrophy. It also detects the presence of other associated valve disease or associated aortic pathology and provides prognostic information [3, 18, 19].

In patients with aortic stenosis, a major determinant of ventricular function is the overload of pressure that determines the compensatory occurrence of left ventricular hypertrophy (LVH) in the course of the disease. The development time of LVH is generally parallel to the evolution of stenosis severity in most patients [20].

There are studies that show that the degree of hypertrophy of the left ventricle is slightly correlated with the severity of obstruction of blood flow in aortic stenosis. In wide aortic stenosis the degree of hypertrophy is mainly conditioned by hypertension, whereas in patients with moderate/severe stenosis the determinants are the severity of the aortic obstruction and the age [21, 22, 23].

The purpose of this study is to highlight the effect of the mechanical prosthesis on the evolution of patients with aortic prosthesis for degenerative aortic stenosis, preoperatively, at 3 months and one year postoperatively. For this purpose, a comparative evaluation of the regression of left ventricular hypertrophy quantified by the size of the left ventricular telediastolic diameter (LVEDD), the thickness of the interventricular septum (IVST) and the posterior wall of the left ventricle (PWT), as well as the mass (LVM) and the left ventricular mass index (LVMI) was used.

2. Materials and methods

Materials

Included in the study were 40 patients (22 men and 18 women) with a mean age of 69 ± 11 years (age range 58-80) with aortic prostheses with mechanical prostheses for degenerative aortic stenosis and who were examined and monitored at the Timisoara Circumvallation Clinic.

Of the 40 patients, 8 patients (20%) underwent concomitant myocardial revascularization by aorto-coronary bypass.

Inclusion criteria

- patients with preoperative, at 3 months and one year postoperatively echocardiographic evaluation;
- patients with aortic valve replacement with mechanical prosthesis from composite biomaterials (carbon fiber coated metal);
- severe preoperative aortic stenosis defined by: maximum transvalvular flow velocity ($V_{max.}$) ≥ 4 m/s, transvalvular mean gradient (P_{med}) ≥ 40 mmHg and aortic valve area (AVA) ≤ 1 cm^2 [3, 21, 24];
- patients with normal left ventricular systolic function (LVEF ≥ 50%);
- patients with left ventricular concentric hypertrophy documented by echocardiography (IVST and PWT> 1cm in men and> 0.9cm in women; LVM > 224g in men and > 162g in women; LVMI > 115 g / m^2 in men and > 95 g / m^2 in women) [21, 24].
- double disc mechanical prosthesis (pyrolytic carbon), post-operative normofunctional.

Patients in whom aortic double mechanical cardiac prosthesis (Saint Jude Medical or Carbomedics) were used to replace the aortic valve were included in the study [12].

A standard method of noninvasive evaluation both pre- and postoperatively of the valvular patient is echocardiographic examination (both 2D and Doppler).

Tracking the evolution of left ventricular hypertrophy, the size of the heart cavities, the systolic and diastolic function of the left ventricle (LV), the severity of pulmonary hypertension (aortic valvulopathy from the onset and until the time of correction induces maladaptive or compensatory changes of the heart and circulatory system) [18, 19], was performed by echocardiography, which provided a complete assessment of cardiac hemodynamic status pre- and post-valve replacement.

After the clinical and biological balance, the patients were examined using the SonoScape SSI 8000 ultrasound.

The echocardiographic evaluation for the quantification of the echocardiographic parameters was performed preoperatively, respectively at 3 months and one year postoperatively. The post-operative echocardiographic examination allowed to establish the velocimetric profile and was used as a reference for the examinations carried out subsequently.

The measurement of the echocardiographic parameters of the LV was performed by the linear method, and as normal values were considered those recommended by the guides of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [21, 24]. Thus: IVST and PWT ≤ 1cm in men and ≤ 0.9cm in women; LVM ≤ 224g in men and ≤ 162g in women; LVMI ≤ 115 g / m^2 in men and ≤ 95 g / m^2 in women, were considered within normal limits, and above these values was defined left ventricular hypertrophy.

Statistical methods

The changes of mass and of the other parameters, over time, were evaluated by paired t test. All values are expressed as mean ± SD. A $p < 0.05$ was used to identify significant results.

3.Results and discussions

The patients were monitored on average one year after the surgery, without major incidents being reported during the follow-up period and no deaths were recorded.

The general characteristics of the patients included in the study are shown in table 1

Table 1. Preoperative general characteristics of patients

Variables	Aortic stenosis (n=40)
Age (years)	69±11
Gender (M/W) (%)	55/45
Body surface area (m^2)	1.83±0.17
NYHA class (n, %)	29
I	6 (15)
II	13 (32.5)
III	10 (25)
IV	0
Concomitant aorto-coronary bypass (n, %)	8 (20)
Hypertension (n, %)	19 (47.5)
ECG variable (n, %):	
- atrial fibrillation	9 (22.5)
- major block of left branch	7 (17.5)
- hypertrophy of LV	36 (90)
Echocardiographic variables:	
- LVEDD (mm)	53.5±2.4
- IVST (mm)	13.9±1.2
- PWT (mm)	13.7±1.1
- LVM (g)	264.09±74
- LVMI (g)	144.31±18
- EF (%)	58.3±7.1
- P_{med} preoperatively (mmHg)	50.6±10.2

Values: mean ± SD or n (%)

Within the group included in the study, all patients had hypertrophy of the left ventricle, detected either by electrocardiography or by echocardiography or by both methods.

Replacement of the aortic valve causes correction of hemodynamic disorders, especially afterloads, as well as the consecutive regression of the morphological and geometric adaptation of the left ventricle [25].

Quantifying the evolution of the echocardiographic parameters (telediastolic diameter, thickness of the interventricular septum, posterior wall of the left ventricle, mass and index of the mass of the left

ventricle) in the patients included in the study in which the surgery was performed, a different regression is observed.

Increased LVEDD as an adaptive mechanism for volume overload is more evident in patients with aortic insufficiency than in patients with aortic stenosis where the telediastolic diameter has generally fallen within normal limits. In these patients, concentric hypertrophy predominates, expressed by increased dimensions of the interventricular septum (IVST) and the posterior wall of the left ventricle (PWT).

Table 2 presents the medical effect of aortic prosthesis with mechanical prosthesis. The reduction of the telediastolic diameter in the protected patients was more evident in the first 3 months postoperatively, thus finding a reduction of 2 mm (3.73%), from 53.5 ± 2.4 mm to 51.5 ± 1.1mm, p <0.03, compared to the regression at one postoperative year where it was 0.9 mm (1.74%), from 51.5 ± 1.1mm to 50.6 ± 0.7mm, p <0.02.

Table 2. Dynamics of lvedd regression

	LVEDD (mm)
Preoperative	53.5±2.4
At 3 months	51.5±1.1
p<0.03	
At 3 months	51.5±1.1
At 1 year	50.6±0.7
p<0.02	

Values: mean ± SD

These results are consistent with the literature data indicating a 3-month postoperative reduction of LVEDD by 1.7 mm in patients with aortic stenosis and preoperative LV hypertrophy, compared with 0.8 mm in those without left ventricular hypertrophy [23 , 25].

The regression of left ventricular hypertrophy is evidenced not only by the reduction of LVEDD, but especially by decreasing the thickness of the interventricular septum and the posterior wall of the left ventricle.

Analyzing the dynamics of the regression of the thickness of the interventricular septum (IVST) and the posterior wall of the left ventricle (PWT) we notice a more pronounced reduction of them at 3 months after the surgical intervention, compared with the preoperative values.

The echocardiographic evaluation at 3 months postoperatively shows a regression of IVST of 12.23% (from 13.9 ± 1.2mm to 12.2 ± 0.9mm, p <0.001), 1.7mm, and at one year this regression compared to the first 3 months it is only 7.37% (12.2 ± 0.9mm to 11.3 ± 0.5mm, p <0.01), 0.9mm, as shown in figure 2.

An obvious improvement is also noticed in the PWT regression, which at 3 months postoperatively was 13.1% (from 13.7 ± 1.1mm to 11.9 ± 1mm p <0.001), respectively 1.8mm. At 1 year the regression of PWT thickness is lower compared to the first 3 months, thus showing a regression of 8.40% (from 11.9 ± 1mm to 10.9 ± 0.4mm p <0.01), respectively 1 mm, (Figure 2).

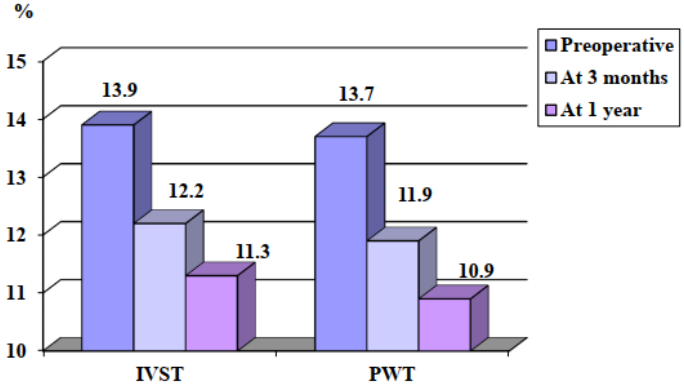

Figure 2. Dynamics of IVST and PWT regression

The results are in agreement with the study carried out by Karpuz and collaborators, which revealed, at 3 months postoperatively, a regression of 11% of IVST and 13% of PWT in patients with prosthesis for aortic stenosis and hypertrophy of the left ventricle [26].

In contrast, Kupari et al. [23] report a 3-month postoperative PWT regression of 1.3 mm in patients with aortic stenosis and left ventricular hypertrophy compared to those without hypertrophy where this regression was 0.1 mm.

Other reliable parameters for quantifying the regression of left ventricular hypertrophy are the left ventricular mass (LVM) and the left ventricular mass index (LVMI).

At 3 months after surgery, a regression of LVM is observed compared with preoperative values from 264.09 ± 74g to 195.79 ± 28g, ($p < 0.001$), (see table 3).

The data in table 3 show that the most obvious regression is in the first 3 months after the surgery, a less significant improvement of the LVM is observed one year after the surgery, from 195.79 ± 28g to 166.19 ± 5g ($p < 0.05$).

	LVM (g)	LVMI (g/m^2)
Preoperative	264.09±74	144.31±18
At 3 months	195.79±28	109.26±5
p	< 0.001	< 0.01
At 3 months	195.79±28	109.26±5
At 1 year	166.19±5	93.75±4
p	< 0.05	< 0.05

Table 3. Dynamics of LVM and LVMI regression

Our findings, from this experiment/study, are consistent with those in the literature that show a marked reduction of the LV mass with improvement of systolic function at 3 months postoperatively in patients with preoperative LV hypertrophy, whereas in those without preoperative hypertrophy, they are not significant postoperative changes in systolic structure and function of the left ventricle [23].

LVM regression at 3 months after surgery compared to preoperative values is 25.86%, and at one year after surgery this regression was 15.11%, which is shown in figure 3.

The results are in agreement with those in the literature that show a regression of LVM at 3 months postoperatively of approximately 25%, in patients with aortic stenosis and hypertrophy of the left ventricle [26].

As mentioned above, the quantification of the postoperative regression of LV hypertrophy can also be done through the LV mass index (LVMI).

In the case of LVMI at 3 months after surgery, the regression was from 144.31 ± 18 g/m^2 to 109.26 ± 5 g/m^2, ($p < 0.01$), and at one year from 109.26. ± 5 g/m^2 to 93.75 ± 4 g/m^2 to ($p < 0.05$), aspect shown in table 3.

At 3 months after surgery, the effective regression of LVMI was 24.28%, and at one year it was 14.19%, an aspect presented in figure 3.

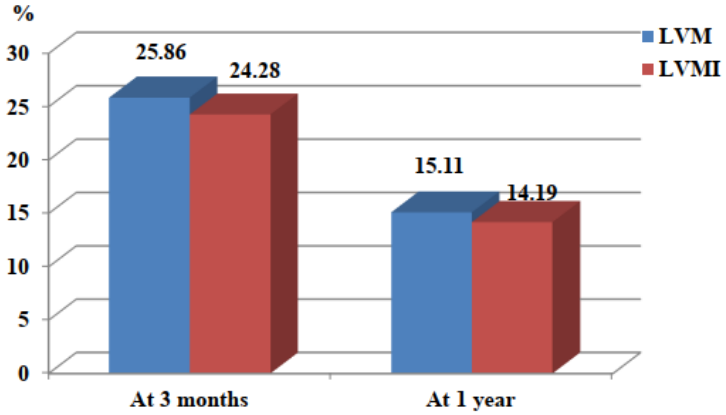

Figure 3. Effective regression of LVM and LVMI

These data are also in agreement with those in the literature that indicate a significant regression (p = 0.018) of the LVMI immediately postoperatively from 217.3 ± 64.6 g / m2 preoperatively to 153.2 ± 33.9 g / m2 postoperatively in patients with aortic stenosis [27, 28].

Also, Singh and co-workers [29] show a significant reduction of IMVS (p = 0.001) at 3 months after aortic prosthesis, regardless of the type of aortic valve (stenosis, insufficiency and aortic disease) for which the surgery was performed.

High blood pressure appears to have a significant negative effect on lowering LVMI, since hypertensive patients have higher preoperative LVMI, so its regression in the first 3 months postoperatively is much lower.

There seems to be a threshold of myocardial hypertrophy over which histological and functional normalization becomes impossible, even in the presence of echocardiographic evidence of regression. Before reaching this limit the echocardiographic decrease of the LVM reflects a real decrease of the hypertrophy; once this value is reached, LVM regression is only partially possible and is probably the main result of decreased hypertrophy in the less affected cells and fibrous remodeling of the left ventricle [30].

It is known that prosthesis of the aortic valve reduces pressure overload and consecutive parietal stress, leading to a reduction in the amount of hypertrophy in postoperative evolution. LVH regression in postoperative evolution is dependent on multiple factors, including prosthesis size and residual pressure gradient [20, 30, 31].

Also it is considered that although post-aortic prosthesis produces a significant regression of LVM and LVMI, survival and quality of life depend mainly on the degree of preoperative hypertrophy [32].

Finally, it may be speculative, but it is possible that early surgery (before reaching the irreversible critical threshold of ventricular hypertrophy and taking into account systemic condition and cardiac function) may improve postoperative survival in patients undergoing aortic prosthesis surgery [32].

4.Conclusions

Valve prosthesis with mechanical valves, such as those investigated in this paper, result in a significant early reduction of left ventricular hypertrophy, commonly encountered under tight aortic stenosis, over a period of several weeks or months, due to the significant reduction of transvalular gradients of left ventricular wall stress.

From the presented data results the regression of the left ventricular mass, and especially the premature regression, thus demonstrating the beneficial effect of the mechanical prosthesis on the postoperative evolution of patients with tight aortic stenosis.

A significant decrease in both the mass and the index of the left ventricular mass is observed in the first 3 months postoperatively, and at one year the regression of the hypertrophy is lower compared to the early postoperative one.

Left ventricular mass regression and especially premature regression are strictly correlated with the grade of the preoperatory left ventricular hypertrophy.

There by, the use of mechanical (biocompatible) prosthesis is beneficial, substantially improving the parameters and quality of life of patients.

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