The Effect of Preoperative Left Ventricular Filling Patterns on Prognosis in Patients with Aortic Valve Replacement

AORTİK KAPAK REPLASMANI YAPILAN HASTALARDA PREOPERATIF DÖNEMDEKİ SOL VENTRİKÜL DOLUMUNUN PROGNOZA OLAN ETKİSİ

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Abstract

Objective: Although many studies have been performed to evaluate the effects of a variety of heart valves on left ventricular function, the alterations in diastolic function seen in patients with preoperatively restrictive filling patterns after aortic valve replacement (AVR) with various mechanical, stented or stentless prostheses have not been sufficiently examined. This study aimed to assess and compare the changes in diastolic function in such patients following AVR.

Material and Methods: In accordance with preoperative echocardiographic findings in patients of similar age groups and body size, 24 patients were selected as having restrictive filling patterns (i.e. deceleration time (DT)<150 msec, iso-volumetric relaxation time (IVRT)<100 msec). The patients underwent AVR with either St. Jude Medical (SJM) (n = 8) or CarboMedics (CM) mechanical valves (n = 6), or Medtronic Freestyle® (MF) (n = 6) or CryoLife-O’Brien (CO) (n = 4) stentless bioprostheses. Another 24 patients were selected as a non-restrictive, physiologic group. The effect of valve replacement on diastolic parameters was evaluated preoperatively and postoperatively at discharge and after 4 and 8 weeks by comparing the parameters before and after valve replacement.

Results: Improvement in DT, IVRT and ejection fraction occurred in all patients with restrictive filling patterns irrespective of valve type. Although the difference between the various types was not statistically significant, left ventricular mass regression was higher in patients with mechanical valves.

Conclusion: Preoperatively determined restrictive patterns appear to convey more benefit than that derived by patients with preoperative non-restrictive filling patterns. A greater improvement is to be expected in more advanced disease states in patients following AVR.

Key Words: Left ventricular, hypertrophy, aortic valve, heart valve prosthesis

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Although mechanical heart valves offer more durability and better hemodynamic profiles when compared with stentless bioprostheses, the requirement of lifetime anticoagulation is a decided drawback. Indeed, related
complications such as thromboembolism, hemoly-
sis and bleeding still constitute the major morbid-
ities. However, structural valve deterioration re-
 mains the major risk factor that has served to di-
minish the use of bioprosthetic valves. To date, 
there exists no unique guideline for decision-
making in prosthesis selection for elective valvular 
surgery.

The SJM (St. Jude Medical, Inc., St. Paul, 
MN) and CM (CarboMedics, Inc., Austin, TX) 
mechanical heart valves are both bileaflet me-
chanical prosthetic valves constructed of pyrolytic 
carbon with excellent in vitro and in vivo hemody-
namics and with proven reliability and freedom 
from adverse events.\textsuperscript{1,4} Bioprosthetic valves 
are made of biological materials treated with glutaral-
dehyde in order to prevent degeneration, which can 
in time lead to calcification.

The aim of the present study was to compare 
the prognostic efficacy of preoperative echocar-
diographic parameters as determinants of restric-
tive or non-restrictive filling patterns of diastolic 
function in patients following AVR with various 
types of mechanical and stentless bioprosthetic

\section*{Material and Methods}

In accordance with preoperative echocardi-
ographic findings, 24 patients were determined as 
having restrictive filling patterns (DT\textless;150 msec, 
IVRT\textless;100 msec) and another 24 patients with 
non-restrictive patterns (DT\textgreater;150 msec, IVRT\textgreater;100 
msec).\textsuperscript{5} The two groups were assigned to an equal 
distribution of various types of valves, i.e. the pa-
tients in each group underwent AVR with either 
SJM or CM mechanical valves, or MF (Medtronics, 
Inc., Minneapolis, MN) or CO (Cryolife, Inc., 
Kennesaw, GA) stentless bioprostheses. Patients 
were candidates for AVR due to aortic stenosis and 
regurgitation without previous history or evidence of 
arrhythmia, mitral valve disease, or coronary 
artery disease. Informed consent was obtained 
from all patients. The choice of valve type was 
individually determined by either patient option or 
some prevailing condition (i.e. age, contraindica-
tion for anticoagulation usage, etc.). The choice of 
stentless bioprosthesis valve was made intra-
operatively according to aortic valve pathology and 
aortic root morphology. In patients with mainly 
fibrotic aortic valve pathology, O’Brien valves 
were preferred. For those with larger aortic roots 
who may have been candidates for root inclusion, 
MF valves were preferred, as this type of valve 
more readily accommodates to this procedure.

The patients were divided into two groups ac-
cording to Doppler mitral flow velocity profiles: 
group A, consisting of 24 patients (10 females, 14 
males; mean age 59.6 ± 8.4; SJM: n = 8; CM: n = 6; 
MF: n = 6; CO: n = 4) with restrictive physiology, 
and group B, consisting of another 24 patients (9 
females, 15 males; mean age 61.2 ± 5.2; SJM: n = 
8; CM: n = 6; MF: n = 6; CO: n = 4) with non-
restrictive physiology.

All patients were evaluated preoperatively and 
postoperatively, at discharge and at 4 and 8 weeks 
by comparing echocardiographic parameters before 
and after valve replacement. Parameters measured 
in pre- and postoperative trans-thoracic echocardi-
ography were ejection fraction (EF), fractional 
shortening (FS), trans-aortic peak gradient, aortic 
regurgitation, left ventricular end-diastolic diame-
ter (LVEDD), left ventricular mass (LVM), inter-
ventricular septum thickness (IVS), and left ven-
tricular posterior wall thickness (PW).

LVM was calculated according to Penn’s 
modified 3D formula:

\begin{align*}
\text{LVM} &= 1.04\left[\left(LVID + IVS + PW\right)^3\right] - 13.6 \text{ g/m}^3
\end{align*}

Left ventricular mass index (LVM\textsubscript{I}) was 
calculated by dividing the values obtained from the 
formula by patient body surface area.

\section*{Operative Technique}

Standard operative technique was employed 
for all operations. Following cannulation of the 
ascending aorta and right atrium with a two-stage 
cannula, hypothermic cardiopulmonary bypass was 
established and myocardial preservation was ob-
tained by administering 500 mL of cold (+4°C) 
Plegisol (Abbott Laboratories, Abbott Park, IL) 
antegrade to the aortic root, followed by the infu-
sion of 500 mL of the same solution retrograde via 
the coronary sinus. Cardioplegic arrest was main-
tained by 400 mL of the same solution with retrograde application every 20 minutes. The native valve was excised through oblique aortomy, the annulus was decalcified and sized, and the prosthesis was implanted. SJM and CM mechanical valves were implanted in the aortic annulus with interrupted 2/0 non-absorbable sutures. The techniques used for MF stentless porcine valves were aortic root inclusion or total root replacement with interrupted pledged sutures. The coronary ostia were implanted on the prosthesis with 6/0 polypropylene sutures. O’Brien valves were implanted on the aortic root with a continuous suture technique, using three double 2/0 polypropylene sutures.

**Echocardiography**

All patients were followed by echocardiography. Examinations were performed before the operation and at 6 months. Acceleration times (AT), DT, IVRT, and LVMI were evaluated. Echocardiograms were performed by a single cardiologist using a Toshiba SSH-140A Ultrasound system in accordance with the specifications of the American Society of Echocardiography. After measuring the left atrial diameter using two-dimensional echocardiography in the parasternal plane, systolic and diastolic diameters as well as wall thicknesses were studied with M-mode echocardiography. The Teicholz method for left ventricular EF and the modified Simpson method for dyskinetic interventricular septi were used. Left ventricular diastolic filling patterns were determined by mitral flow pulse-wave Doppler examination with a 2.5-MHz transducer. In the apical 4-chamber view, the Doppler sample volume was infused into the middle of the left ventricular inflow tract, 1 cm below the mitral annulus plane between the mitral leaflet tips, where flow velocity is maximum in early diastole.

Statistical analysis

The variables of the groups were compared using the chi-square test, and comparisons of the continuous variables between groups were performed with Student’s t and Spearman’s correlation coefficient tests. When multiple pairwise comparisons were needed, Bonferroni corrections were made. The variables are presented as mean ± SD in the tables and a p value less than 0.05 was considered significant.

**Results**

The demographics of the patients including mean age, gender distribution, weight, and body mass index were similar in both groups (Table 1). All patients underwent AVR without statistically significant differences in prosthetic valve size.

All patients in the study manifested sinus rhythm and a normal heart rate of 82.0 ± 2.0/min.

Aortic stenosis was the most common pathology among patients. Only two patients in each group had severe aortic insufficiency and 4 had aortic stenosis as well as insufficiency (Table 1). In these patients, LVMI was higher when compared to the other patients. As the number of such pa-

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**Table 1. Patient characteristics.**

<table>
<thead>
<tr>
<th></th>
<th>Group A (restrictive)</th>
<th>Group B (non-restrictive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>59.6 ± 8.4</td>
<td>61.2 ± 5.2</td>
</tr>
<tr>
<td>Gender (females/males)</td>
<td>10 female/14 male</td>
<td>9 female/15 male</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.72 ± 0.12</td>
<td>1.71 ± 0.18</td>
</tr>
<tr>
<td>New York Heart Association class III-IV (%)</td>
<td>82</td>
<td>78</td>
</tr>
<tr>
<td>Preoperative aortic valve lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Insufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mixed</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
patients was equal in both groups, statistical comparison between the two groups was moot.

There were two operative mortalities in each group. In group A, two patients died in the early postoperative period due to low cardiac output. The first patient had undergone combined coronary bypass surgery and AVR with a MF aortic bioprosthesis. The second one died due to low cardiac output following SJM mechanical valve implantation. In group B, the first patient had undergone coronary bypass 7 years earlier and died due to blood loss after combined surgery for coronary bypass and O’Brien aortic valve implantation. The other fatality in this group was due to low cardiac output following MF aortic valve implantation.

Intra-operatively logged data indicated that the cross-clamp time and cardiopulmonary bypass duration were higher in patients receiving AVR with MF prosthesis.

All surviving patients were requested to present for echocardiographic evaluation of left ventricular performance at 4 and 8 weeks postoperatively. Significant regression was observed in both groups (Table 2). E/A ratios, left ventricular end-diastolic diameters and ejection fractions were significantly decreased in patients with restrictive physiology when preoperative and postoperative values were compared (2.2 ± 0.4 versus 1.2 ± 0.6, 56.4 ± 6.4 versus 42.6 ± 4.8, and 46.7 ± 4.2 versus 56.4 ± 6.6, respectively).

**Discussion**

Aortic valve pathologies lead to left ventricular hypertrophy, which is characterized by myocardial fibrosis and structural changes in the extracellular matrix.9 The aim of this study was to examine the prognostic impact of preoperatively-determined left ventricular diastolic filling patterns on diastolic function in patients following AVR with mechanical and stentless bioprosthetic valves.

In hypertrophic hearts, as in aortic stenosis, diastole abnormalities are common sequelae of a delayed onset of normal relaxation, and may precede systolic dysfunction. Impaired relaxation is associated with a lengthening of the atrial filling phase, so that the E/A ratio evinced in the mitral Doppler pattern declines. In the normal pattern, there is a large E wave and a small A wave. However, three abnormal patterns of mitral filling represent impaired left ventricular diastolic performance. “Delayed relaxation” is characterized by larger A waves (E<A), and the left ventricular DM is normal or prolonged. In the “pseudonormalized” pattern, the E wave is larger than the A wave (E>A), but with a shortened DT. In the restricted filling pattern, E is much larger than A (E>>A) with a very short DT.7,9

The Standard® St. Jude disk valve has been in clinical use for over 20 years. The valve in its current form is the consequence of some unfortunate developments during the late 1970s: High degeneration rates of xenograft valves and the frequent mechanical failure of the single-disc valve types.10 The valve has become very popular, and the standard valve together with its modifications remains the dominant mechanical valve currently, exhibiting a low rate of valve-related deaths, acceptably low thrombogenicity, and an absence of mechanical failure, all of which were verified through long-term studies of a large series of patients.10 The designers of the original St. Jude mechanical valve implemented further refinements of this prosthesis in creating the Advanced The Standard (ATS)® (ATS Medical, Inc., Minneapolis, MN).10

The other prosthetic valve included in this study was the CM bileaflet mechanical valve, which is introduced for clinical use in 1986.4 The CM device is a bileaflet pyrolytic carbon heart valve, and differs from the SJM prosthesis on several aspects, including the Biolute® carbon-covered blood-contacting surface on the sewing ring, the valve pivot design with its absence of pivot guards, the presence of a titanium stiffening ring, and particularly, the rotate-ability of the valve after implantation.4 The most comprehensive clinical experience with this prosthesis was described by Copeland et al in an international multi-center study featuring an average follow-up of 30.2 months.4
Table 2. Preoperative and postoperative echocardiographic data.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (restrictive)</th>
<th>Group B (non-restrictive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>46.7 ± 4.2</td>
<td>48.8 ± 2.8</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>54.6 ± 2.8</td>
<td>50.8 ± 4.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>56.4 ± 6.6</td>
<td>53.8 ± 6.8</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.05*</td>
<td>NS*</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>32.6 ± 7.8</td>
<td>33.6 ± 8.8</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>34.8 ± 4.2</td>
<td>35.8 ± 2.6</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>35.8 ± 6.4</td>
<td>36.0 ± 6.2</td>
</tr>
<tr>
<td>p</td>
<td>NS*</td>
<td>NS*</td>
</tr>
<tr>
<td>Transaortic peak gradient (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>72.4 ± 8.0</td>
<td>70.8 ± 2.4</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>38.8 ± 6.2</td>
<td>36.8 ± 6.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>16.4 ± 2.2</td>
<td>15.6 ± 6.8</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.01*</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Aortic regurgitation (preoperative)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Left ventricular end diastolic diameter (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>56.4 ± 6.4</td>
<td>52.8 ± 8.8</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>48.8 ± 4.2</td>
<td>48.8 ± 6.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>42.6 ± 4.8</td>
<td>46.2 ± 5.6</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.05*</td>
<td>NS*</td>
</tr>
<tr>
<td>Left ventricular mass index (g/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>210.2 ± 18.6</td>
<td>192.8 ± 18.4</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>180.8 ± 4.2</td>
<td>168.8 ± 4.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>162.8 ± 20.4</td>
<td>140 ± 14.6</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.01*</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Interventricular septum thickness (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>12.4 ± 3.2</td>
<td>11.7 ± 4.7</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>11.8 ± 4.2</td>
<td>10.8 ± 4.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>11.4 ± 5.2</td>
<td>10.2 ± 2.1</td>
</tr>
<tr>
<td>p</td>
<td>NS*</td>
<td>NS*</td>
</tr>
<tr>
<td>Left ventricular posterior wall thickness (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>12.4 ± 4.2</td>
<td>10.9 ± 6.2</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>11.8 ± 4.2</td>
<td>10.8 ± 5.2</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>11.4 ± 4.8</td>
<td>10.2 ± 3.2</td>
</tr>
<tr>
<td>p</td>
<td>NS*</td>
<td>NS*</td>
</tr>
<tr>
<td>E/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>2.2 ± 0.4</td>
<td>1 ± 0.2</td>
</tr>
<tr>
<td>Post (4 weeks)</td>
<td>1.8 ± 0.2</td>
<td>0.9 ± 0.8</td>
</tr>
<tr>
<td>Post (8 weeks)</td>
<td>1.2 ± 0.6</td>
<td>0.9 ± 0.8</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.05*</td>
<td>NS*</td>
</tr>
</tbody>
</table>

*: Pre vs post at 4 weeks.

The CO stentless porcine aortic bioprosthesis is of a composite design, constructed with non-coronary leaflets obtained from three porcine valves. Leaflets are carefully excised from valves fixed in glutaraldehyde under very low or near zero pressure. The matched set of leaflets are sutured together along the free edges of the aortic wall at the leaflet commissures. Having no Dacron reinforcement in the structure of the xenograft remains the significant difference between this and the other stentless valves. The O’Brien valve has exhibited a satisfactory early hemodynamic profile. Promising 5-year follow-up results have been cited in recent studies.11,12

The MF bioprosthesis is another stentless valve that was used in our patients. This is a porcine aortic root cross-linked in buffered glutaraldehyde solution with 40 mmHg pressure applied to the root and a zero pressure differential across the valve leaflets.
The valve is pre-treated with alpha-amino oleic acid to reduce the potential for leaflet calcification. The device is suitable for root replacement, mini-root inclusion cylinder AVR, partial scolloppect sub-coronary valve implantation or completely scalloped sub-coronary implantation.\textsuperscript{13,14}

This study examined outcomes with respect to hemodynamic function in 48 consecutive patients who underwent AVR with a variety of valves. Kon and Westaby demonstrated that the hemodynamic performance of stentless porcine aortic valves was to a degree dependent upon the implant technique employed. In patients receiving the valve as a sub-coronary implant, there was a decrease in gradient and increase in effective orifice area as a function of time. Therefore, it is important to compare similar groups with respect to surgical technique, which should ideally be identical in both groups.

According to deceleration and iso-volumetric relaxation times, patients were categorized as demonstrating restrictive versus non-restrictive physiology based on preoperative Doppler-echo assessment. Patients in the restrictive group were considered to have more severe aortic stenosis as evidenced by higher preoperative aortic valve gradients and a tendency towards greater left ventricular mass index. In both groups, a significant reduction in aortic valve gradient and left ventricular mass index was identified. Many studies demonstrated similar results, such as a lessening of LVM following AVR due to regression of myocardial cellular hypertrophy and interstitial fibrosis.\textsuperscript{15,16}

Before AVR, single mitral flow wave with a DM of less than 150 ms reflected the restrictive filling pattern of hearts. Four weeks after valve replacement the DM reached to over 500 ms, which suggests an improved left ventricle filling profile. These findings indicate that the restrictive filling pattern of the left ventricle in aortic stenosis may be reversed within 4 weeks of left ventricular offloading with the AVR. This interesting finding is similar to the results of the study by Westaby and associates, which shows the improvement in left ventricular filling profile in 4 weeks under ventricular assist device support.\textsuperscript{17} In another study, we showed that 40 days of unloading of left ventricle with left ventricular assist device (LVAD) led to recovery in the myopathic hearts.\textsuperscript{18} In fact, although LVAD implantation is unlike AVR, the two procedures have parallel effects such as unloading the left ventricle.

Restrictive pattern generally indicates elevated left atrial pressures (i.e. filling pressures) which suggest a more advanced clinical stage of dysfunction. This is consistent with higher preop gradients, dilated ventricles and greater wall thickness and muscle mass. A greater improvement is expected in more advanced disease states. The non-restrictive groups with less severe dysfunction have smaller margins for improvement. This finding is clinically significant, since surgery might have better outcomes in patients with more advanced disease states, who are candidates for AVR.

In several previous reports, an increase in EF as well as a decrease in ventricular wall thickness was observed in patients who had undergone AVR for aortic stenosis. Unfortunately, classification with regard to preoperative diastolic parameters was not noted in these studies. Pei-Ying and associates, however, divided their patients into restrictive and non-restrictive subgroups.\textsuperscript{6}

The association of preoperative restrictive patterns on echocardiography and mechanical heart valves seems to confer more benefit when compared with those patients with preoperative non-restrictive filling patterns who received bioprosthetic valves. In the present study, we were able to show significant improvements in DT and IVRT values in patients with preoperatively restrictive pattern, as did Pei-Ying. However, unlike our study, they found no improvement in patients with non-restrictive physiology.

In our patients, LVMI decreased independently of valve replacement type at 8 weeks after AVR. The hemodynamic performance of the stentless valves was similar to that of the mechanical valves, as demonstrated by low trans-valvular gradients and decreased LVMI percentages.

Until recently, many studies were performed to compare the effects and prognostic consequences between two valve types, prosthetic and mechanical.\textsuperscript{15,19} The comparison was performed in various parameters such as age, valve position, type and
size, myocardial status, functional status, anticoagulation requirements, complications, etc.\textsuperscript{9,10} The common consequences of these studies suggest that bioprosthetic valves do not offer a survival advantage over mechanical valves. The rates of survival and freedom from all valve-related complications were similar for patients who received mechanical heart valves and those who received bioprosthetic heart valves. However, structural failure was observed only with the bioprosthetic valves, whereas bleeding complications and anticoagulant-related mortality and morbidity were more frequent among patients who received mechanical valves.

In accordance with these studies, we showed that patients undergoing AVR had an improvement in functional status, as well as systolic and diastolic left ventricular function, and a reduction in LVM, irrespective of prosthesis size.\textsuperscript{9,10} In addition, we suggest that these parameters may be sensitive to the type of the valve as well as the physiologic status of the left ventricle. Mechanical valves are somewhat less obstructive than stented bioprosthetic valves of the same size. They are also associated with a concomitantly more pronounced reduction of LVM especially when implanted in an aortic position of a left ventricle, which shows restrictive filling pattern.

In conclusion, preoperatively determined restrictive patterns appear to convey more benefit than that derived by patients with preoperative non-restrictive filling patterns. A greater improvement is expected in more advanced disease states in patients following AVR.

REFERENCES


