

## Coronary perfusion: Impact of flow dynamics and geometric design of 2 different aortic prostheses of similar size

Vito Mannacio, MD, Luigi Di Tommaso, MD, Vincenzo De Amicis, MD, Paolo Stassano, MD, and Carlo Vosa, MD

**Background:** Aortic valve replacement leads to improvement of coronary flow but not to complete normalization. Coronary hypoperfusion contributes to higher left ventricular mass persistence, arrhythmias, congestive heart failure and sudden death. This prospective study compares 2 similarly sized aortic prostheses (mechanical and porcine) regarding coronary flow and hemodynamic performances in patients who underwent surgery for pure aortic stenosis.

**Methods:** Sixty patients having undergone aortic valve replacement for pure aortic stenosis with Medtronic Mosaic Ultra bioprosthesis 21 mm ( $n = 30$ ) or St Jude Regent mechanical valve 19 mm ( $n = 30$ ) were evaluated preoperatively and 12 months postoperatively comparing the coronary flow and the hemodynamic behavior. Echocardiography and cardiac positron emission tomography were performed at rest and during exercise or adenosine maximal stimulation, respectively.

**Results:** The St Jude Regent mechanical valve, compared with the Medtronic Mosaic Ultra bioprosthesis, had reduced coronary flow reserve ( $2.1 \pm 0.3$  vs  $2.3 \pm 0.2$ ;  $P = .003$ ), less favorable systolic/diastolic time ratio ( $0.87 \pm 0.02$  vs  $0.78 \pm 0.03$ ;  $P < .001$ ), and higher mean transprosthetic gradient ( $46 \pm 11$  vs  $38 \pm 9$ ;  $P = .003$ ) during exercise. Multivariate analysis of impaired coronary reserve related indexed effective orifice area less than  $0.65 \text{ cm}^2/\text{m}^2$  (risk ratio [RR], 1.9; 95% confidence intervals [CI], 1.5-2.8;  $P < .001$ ), mechanical valve (RR, 2.5; 95% CI, 1.7-3.3;  $P < .001$ ), and systolic/diastolic time ratio greater than 0.75 (RR, 2.6; 95% CI, 1.8-3.8;  $P < .001$ ), as well as high transprosthetic gradient (RR, 1.7; 95% CI, 1.3-2.4;  $P < .001$ ) during exercise with coronary reserve less than 2.2.

**Conclusions:** Improvement of coronary flow and reserve was more evident for bioprosthesis than for mechanical valves. The bioprosthesis demonstrated superior hemodynamics during exercise, which may have some impact on exercise capability during normal daily life. (J Thorac Cardiovasc Surg 2012;143:1030-5)

Myocardial blood flow (MBF) and coronary flow reserve (CFR) are reduced in patients with severe aortic stenosis. Aortic valve replacement (AVR) leads to improvement of coronary flow but not to complete normalization.<sup>1-4</sup> Chronic coronary hypoperfusion might contribute to cardiac events such as congestive heart failure and sudden cardiac death and might be related to persistence of high left ventricular mass.<sup>1,5-8</sup> Recent experimental studies hypothesized that, besides other variables, impaired coronary flow after AVR should be ascribed to a disturbed flow pattern in the proximal part of the aorta distal to the valve and suggested that valve size and design as well as residual transprosthetic gradient may influence coronary perfusion.<sup>9,10</sup> In addition, considering

coronary perfusion also influenced by diastolic time, which is usually impaired after AVR, few data are available on the relationships between diastolic duration and coronary perfusion regarding the different behavior of mechanical and biological valve substitutes.

This study was designed to evaluate the impact of aortic valve design on MBF by means of several pathophysiologic and hemodynamic parameters measured at rest and during exercise. Two homogeneous groups of patients who received a similarly sized aortic prosthesis, divided according to mechanical or biological prostheses implanted, were compared. Cardiac cycle abnormalities and hemodynamic parameters were measured by Doppler echocardiography at rest and during exercise. MBF and CFR were evaluated by cardiac positron emission tomography (PET) at rest and during pharmacologically induced hyperemia.

### MATERIAL AND METHODS

#### Description of the Implanted Prostheses

To obtain 2 homogeneous groups and avoid any misleading interference owing to comparison of prostheses different in size, design, and structure, we aimed to perform an "actual size" analysis between 2 valve substitutes and held more realistic to evaluate patients with an aortic annulus of 20 mm (the most common size of aortic annulus in prosthetic

From the Department of Cardiac Surgery, University of Naples Federico II, Naples, Italy.

Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication March 1, 2011; revisions received May 12, 2011; accepted for publication June 7, 2011; available ahead of print July 13, 2011.

Address for reprints: Vito Mannacio, MD, Via S. Domenico 62, 80127 Naples, Italy (E-mail: vitomannacio2@libero.it).

0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2011.06.011

### Abbreviations and Acronyms

AVR	= aortic valve replacement
CFR	= coronary flow reserve
CI	= confidence intervals
LVDT	= left ventricular diastolic time
LVET	= left ventricular ejection time
MBF	= myocardial blood flow
MMU	= Medtronic Mosaic Ultra
PET	= positron emission tomography
RR	= risk ratio
SJR	= St Jude Medical Regent

implants for pure aortic stenosis). For the purpose of this study, we selected the St Jude Medical Regent (SJR) (St Jude Medical Inc, St Paul, Minn) 19-mm valve as the mechanical valve and the Medtronic Mosaic Ultra (MMU) (Medtronic Inc, Minneapolis, Minn) 21-mm valve as the bioprosthesis.

Differently sized mechanical (SJR 19 mm) and biologic (MMU 21 mm) prostheses were chosen because of the sizer provided by the manufacturers; the 21-mm MMU is clearly smaller (19.5 mm) than the 21-mm SJR (21 mm) when measured with slide callipers.<sup>11</sup> Conversely, the actual external sewing ring diameter, which is the maximum diameter of a prosthesis, was similar in SJR 19-mm and MMU 21-mm valves (19 mm vs 19.5 mm, respectively), as well as the internal orifice diameter, which is the factor that mainly affects the effective orifice area (17.8 mm vs 17.5, respectively).

### Patient Population

Between January 2007 and August 2009, a total of 189 patients undergoing AVR for pure aortic stenosis with an aortic annulus of 19 to 21 mm, determined after adequate (transthoracic and/or transesophageal) echocardiographic examination, were evaluated for inclusion in the study. All patients had aortic maximum gradient greater than 50 mm Hg and/or aortic valve area less than 1.0 cm<sup>2</sup> and angiographically normal coronary arteries before surgery. Mean age was 62.2 ± 7.2 years (range, 55-69 years). To obtain a study population as homogeneous as possible and to avoid any confounding interference on results, we used the following exclusion criteria: age less than 55 years or over 70 years, active endocarditis, emergency surgery, previous cardiac surgery, bicuspid aortic valve, associated aortic diseases, simultaneous mitral or tricuspid replacement or repair, poor cardiac function as indicated by ejection fraction less than 40%, chronic atrial fibrillation, severe comorbidities (dialysis, hepatic failure, autoimmune disease), impediments to exercise test (neurologic or osteoarticular), and contraindications to receive adenosine (heart block or reactive respiratory disease). Thirty patients received a 21-mm MMU bioprosthesis (MMU group) and 30 a 19-mm SJR mechanical bileaflet valve (SJR group). The choice was based on history of thromboembolism or bleeding disorders, liver disease, and preference of the patient or cardiologist.

All patients from both groups underwent echocardiographic (transthoracic or transesophageal) evaluations and PET scans at rest within a 2-week preoperative period. Postoperative echocardiographic assessment at rest and during exercise as well as PET scans at rest and during maximal adenosine stimulation were performed 12 months after surgery. Follow-up was started at 12 months because prosthetic gradients usually change during the first postoperative year with significant impact either on the exercise capability or on the hemodynamic results.<sup>11</sup>

The Institutional Research Ethics Committee of the University of Naples approved this study and all patients provided written informed consent.

### Surgical Technique

The surgical approach consisted in median sternotomy, hollow-fiber oxygenators, and a centrifugal blood pump. The ascending aorta and right atrium were cannulated. Pump flow was kept at about 2.5 L · min<sup>-1</sup> · m<sup>-2</sup> and the arterial pressure at about 70 mm Hg. The myocardium was protected by intermittent cold crystalloid cardioplegia. Aortic annulus diameter was measured by Hegar dilators. Thereafter, prosthetic valve size was determined by using the original sizer by each manufacturer. All prostheses were implanted with 2-0 polyester nonpledget-supported, interrupted, non-everting mattress sutures. Mean aortic crossclamping time was 65.4 ± 20.3 minutes. The MMU valves were implanted according to the manufacturer recommendations regarding the asymmetric design. The SJR valves were implanted respecting the optimum hemodynamic orientation achieved with one orifice facing the right coronary cusps.<sup>8</sup> Patients with the SJM valve received postoperative lifelong warfarin anticoagulation. Patients with the MMU bioprosthesis received warfarin for 8 to 12 weeks only.

### Echocardiographic Measurements and Calculations

The echocardiographic examinations were performed according to the recommendations of the American Society of Echography.<sup>12</sup> Left ventricular function was evaluated by the ejection fraction calculated by the Simpson rule. The left ventricular mass was normalized to body surface area. Left ventricular hypertrophy was defined as indexed left ventricular mass more than 130 g/m<sup>2</sup> in men and more than 100 g/m<sup>2</sup> in women.<sup>13</sup> The peak and mean prosthetic gradients were calculated from continuous-wave Doppler measurements using the modified Bernoulli equation. Stroke volume was indexed for body surface area. The continuity equation was used to calculate the effective orifice area.

Valve regurgitation was assessed by color flow Doppler mapping and continuous-wave Doppler (transthoracic or transesophageal) as the total backflow volume occurring after the aortic prostheses was fully closed. The evaluation of the SJR was possible only by the optimal orientation of the viewing plane as a consequence of the more complex arrangement of regurgitant jets.

Left ventricular ejection time (LVET) was measured on the continuous-wave Doppler trace from opening to closing of the aortic valve. Left ventricular diastolic time (LVDT) was determined as R-R interval-LVET. LVET/LVDT ratio was assessed as well. All measurements are given as the average of 3 consecutive cardiac cycles at rest or 10 cycles during exercise.

### Exercise Protocol

Stress test was performed in all patients 5 days after therapy withdrawal. The exercise test was performed with the patients exercising in the supine position and was conducted according to a standard protocol starting from a workload of 25 W and increased by 25 W at 2-minute intervals. The reference workload for healthy individuals was 2.5 W/kg in women and 3.0 W/kg in men between 21 and 30 years, minus 10% for each decade. Tests were limited by symptoms, blood pressure greater than 180/100 mm Hg, arrhythmias, and exhaustion or achievement of 100% of age and/or sex reference workload. The evaluation of LVET and LVDT was obtained at a heart rate of 100 beats/min while peak prosthetic gradient, mean prosthetic gradient, and effective orifice area were assessed at peak exercise.

### Quantification of MBF

Cardiac PET was performed on a Siemens ECAT EXACT 3-dimensional positron scanner (Siemens AG, Munich, Germany). PET perfusion tracer was <sup>13</sup>NH<sub>3</sub> given intravenously as a bolus. Rest and stress arterial radiopharmaceutical administration consisted of 370 to 740 MBq (10-20 mCi) of <sup>13</sup>NH<sub>3</sub>. All substances that interfere with adenosine metabolism, such as caffeine and other methylxanthine derivatives, were withheld 12 hours before the study. Regions of interest were septal, anterior, lateral, and posterior walls of the left ventricle in the apical, mid, and basal

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