

# Stented Bioprosthetic Valve Hemodynamics: Is the Supra-Annular Implant Better than the Intra-Annular?

Luigi P. Badano, Daisy Pavoni, Sergio Musumeci, Romeo Frassani, Pasquale Gianfagna, Mara Baldassi, Vincenzo Tursi, Enzo Mazzaro, Edlira Zakja, Paolo M. Fioretti, Ugolino Livi

Department of Cardiopulmonary Sciences, A.O. S. Maria della Misericordia, Udine, Italy

**Background and aim of the study:** The use of stented bioprostheses for aortic valve replacement (AVR) in elderly patients with a small aortic annulus may result in unsatisfactory hemodynamic performance of the prosthesis. To overcome this limitation, new bioprostheses have been designed for complete supra-annular implantation, but the actual hemodynamic advantage of the supra-annular implant over the intra-annular has not been fully investigated. Accordingly, the hemodynamic performance of the same stented bioprosthesis (except for sewing ring design) implanted in the supra-annular and conventional intra-annular seating was compared.

**Methods:** Twenty-two patients received an intra-annular implant, and 38 a supra-annular implant. Age ( $74 \pm 5$  versus  $76 \pm 5$  years,  $p = 0.54$ ), gender (55% versus 50% males,  $p = 0.79$ ) and body surface area ( $1.74 \pm 0.2$  versus  $1.81 \pm 0.2$  m<sup>2</sup>,  $p = 0.13$ ) were similar in both subgroups, who underwent echocardiography at  $8 \pm 2$  and  $6 \pm 2$  months after surgery, respectively ( $p = 0.09$ ).

**Results:** The two patient subgroups had similar preoperative left ventricular outflow tract diameters ( $2.06 \pm 0.2$  and  $2.1 \pm 0.2$  cm;  $p = 0.62$ ), average size of

implanted prosthesis (21.0 and 21.3 mm;  $p = 0.44$ ) and mean transprosthetic flow rate ( $246 \pm 70$  and  $218 \pm 58$  ml/s;  $p = 0.12$ ). Mean ( $8 \pm 3$  and  $19 \pm 8$  mmHg,  $p < 0.0001$ ), and peak ( $17 \pm 6$  and  $40 \pm 13$  mmHg;  $p < 0.0001$ ) transprosthetic gradients were lower, and mean effective orifice area (EOA) ( $1.78 \pm 0.4$  and  $1.45 \pm 0.5$  cm<sup>2</sup>,  $p = 0.006$ ) was higher in patients with supra-annular implants than in those with intra-annular. The incidence of patient-prosthesis mismatch (EOA index  $< 0.85$  cm<sup>2</sup>/m<sup>2</sup>) decreased from 50% to 34% ( $p < 0.0001$ ), with no case of severe mismatch using the supra-annular implant. During follow up, a left ventricular mass reduction occurred in patients with supra-annular implants (from  $225 \pm 110$  to  $173 \pm 59$  g/m<sup>2</sup>;  $p < 0.03$ ), but not in patients with intra-annular implants ( $173 \pm 62$  and  $186 \pm 64$  g/m<sup>2</sup>;  $p = 0.87$ ).

**Conclusion:** The study results showed that, compared to intra-annular implantation, supra-annular implantation of bioprosthetic stented valves in the aortic position was associated with a significantly better hemodynamic performance of the prosthesis and significant regression of left ventricular hypertrophy.

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Aortic stenosis is the most frequently identified valvular heart disease in Europe, with about 40% of patients undergoing aortic valve replacement (AVR) when aged over 70 years (1). Moreover, as the general population continues to age, the incidence of calcific aortic valve disease will rise further. Changes in the epidemiology of heart valve disease and in patient

demographics are associated with an increasing use of bioprosthetic valves (2-4). Tissue valves are the preferred prostheses in the elderly due to the patients' relatively shorter life expectancy (5,6), good durability of these valves in the elderly (6), and the increased potential for complications from long-term anticoagulation with age (7). Accordingly, there is a renewed interest in the hemodynamic performance of biological valves, because intermediate and long-term survival may be affected by the influence of valve prosthesis-patient mismatch on left ventricular mass regression, especially in patients with small aortic roots (8).

Several surgical options are available which aim to avoid valve prosthesis-patient mismatch. The first possibility is to implant stentless prostheses, but these are technically demanding and extensive calcification of

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Address for correspondence:

Luigi P. Badano, Cardiology Unit, Department of Cardiopulmonary Sciences, A.O. S. Maria della Misericordia, P. le S. Maria della Misericordia 15, 33100 Udine, Italy  
e-mail: badano.luigi@aoud.sanita.fvg.it

the aortic root may preclude their use. The second approach is to implant high-flow hemidisc prostheses, but these carry the risk of bleeding complications related to the chronic anticoagulation required with these devices. Hence, they are recommended only in elderly patients otherwise anticoagulated (2). The third method is to perform surgical enlargement of the aortic root, though there are many unsolved issues regarding the safety of this procedure (9,10). Finally, stented bioprostheses constructed for a complete supra-annular placement have recently become available (11).

The supra-annular implantation of stented bioprostheses is gaining popularity because it is easy to perform. Moreover, by allowing a precise alignment of the valve orifice to the patient's tissue annular orifice, blood flow should be maximized. In addition, it is thought that supra-annular implantation allows the use of valves one or two sizes larger than when using intra-annular implants, thereby improving the hemodynamic results and reducing the incidence of patient-prosthesis mismatch (12). However, actual improvements in valve hemodynamics achieved with supra-annular implantation of stented bioprostheses have not been fully addressed. Accordingly, the present study was designed to compare the hemodynamics of the same stented tissue valve available for implantation in either the supra-annular or intra-annular position in elderly patients with a small aortic annulus diameter.

## Clinical material and methods

### Patient population

A total of 60 patients (31 females, 29 males; mean age  $75 \pm 5$  years) was included in the study, which was designed in prospective fashion to assess the hemodynamic performance of the Soprano™ valve. For the purposes of the study, all patients who received the Pericarbon More™ valve during the 12-month period before introduction of the Soprano valve at the authors' institution were recalled for clinical assessment and echocardiographic evaluation. For data analyses, 60 one-month survivors were included. Patient selection was not randomized; the Soprano valve has been available at the authors' institution since May 2003, and thus the majority of patients implanted with the Pericarbon More valve were operated on earlier (between April 2002 and August 2003) than those receiving the Soprano valve (between May 2003 and December 2004). All patients underwent AVR with either the Pericarbon More (n = 22) or Soprano (n = 38) bioprosthesis.

Exclusion criteria included emergency surgery, aortic annulus measured at preoperative echocardiography >23 mm, multiple valve replacement, endo-

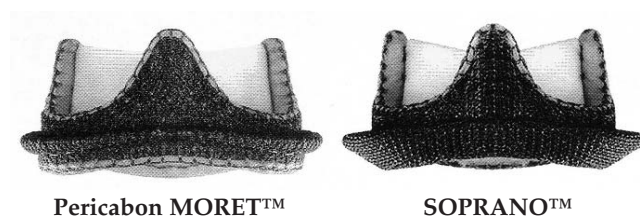


Figure 1: Lateral views of the Pericarbon More and Soprano pericardial tissue valves. The Soprano valve is an evolution of the Pericarbon More, which was designed for supra-annular implantation.

carditis, and coexistent illness known to have a high mortality or concomitant procedures other than coronary artery bypass grafting, mitral annuloplasty or ascending aorta replacement.

The study was approved by the hospital ethics committee on April 2003, and written informed consent to intervention was obtained from all patients.

### Valves

The Pericarbon More valve (Sorin Biomedica Cardio, Saluggia, Italy) is a stented valve, composed of two sheets of pressure-free glutaraldehyde-fixed pericardium mounted on a semi-flexible polymeric stent covered by with polyester fabric (Fig. 1). A tricuspid-shaped pericardium sheet is sutured to a second flat sheet using a Carbofilm™-coated thread. The sewing ring is Carbofilm-coated to enhance biocompatibility and hemocompatibility and to reduce the formation of pannus overgrowth. This valve has been used since 1985, with excellent clinical and hemodynamic outcome (13,14). The new Soprano valve (Sorin Biomedica Cardio) corresponds to the Pericarbon More in terms of tissue preparation and prosthetic material, but differs in stent design as it is intended for a totally supra-annular seating (Fig. 1). As a result, the base of the Soprano sewing ring is flat, while that of the Pericarbon More features a small protrusion, which extends into the annulus, and the stent which constitutes the Soprano is three sizes larger than the corresponding Pericarbon More (e.g., the stent of the 18-mm Soprano and 21-mm Pericarbon More are the same) (Fig. 2). Therefore, for similar-sized valves (e.g., 18-mm Soprano and 19-mm Pericarbon More) the profile of the Soprano is 1 mm higher than that of the Pericarbon More valve. In addition, the Soprano sewing ring filler is 'silicone', which helps penetration of the needle. The Pericarbon More sewing ring filler is composed of either Dacron or polytetrafluoroethylene (PTFE) felt.

### Surgical procedures

After median sternotomy, all patients underwent AVR with the Pericarbon More or Soprano prosthesis

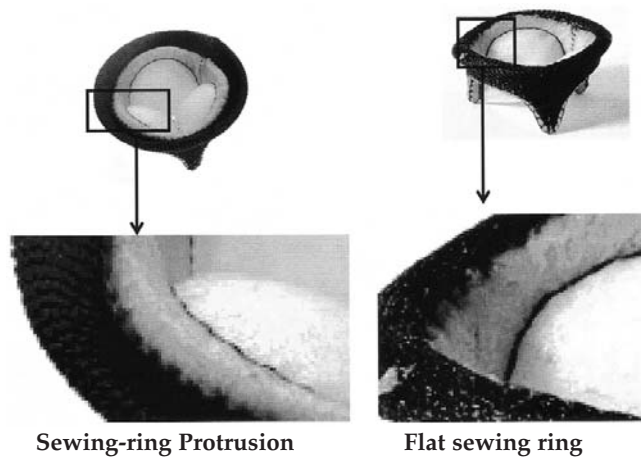


Figure 2: Magnifications of portion of the base of the sewing ring of the Pericarbon More (left) and Soprano (right) pericardial tissue valves, showing the main difference between the two valves. The base of the Pericarbon More sewing ring features a small white protrusion, which passes into the annulus, while that of the Soprano sewing ring is flat for complete supra-annular seating.

under mild-to moderate hypothermic cardiopulmonary bypass. Myocardial protection was achieved both by topical cooling and by intermittent infusion of cold crystalloid solution (St. Thomas' Hospital) directly into the coronary ostia, or in a retrograde manner via the coronary sinus. With regard to sizing of the prosthesis, the surgeon determined the largest size hosted by the annulus using specific sizers provided by the manufacturer, without applying any force and without dilating the annulus. The size of the annulus was also measured with a standard set of Hegar dilators to assess the actual patient annulus diameter. Both types of prosthesis were implanted using the same technique of multiple, interrupted, non-everting pledgetted vertical mattress sutures reinforced by subannular PTFE felts. All procedures were performed by the same surgical team.

### Echocardiography

All surviving patients underwent postoperative echocardiography between one and 12 months after intervention. This time frame was chosen to avoid the immediate postoperative hyperdynamic state of the left ventricle, to allow patients to compensate any postoperative relative anemia, and to reduce the possibility of early prosthesis degeneration. Complete M-mode, two-dimensional, spectral Doppler and color-flow studies were performed, using commercially available ultrasound instruments (SONOS 5500; Philips, Andover, USA).

Two-dimensional cine-loops, M-mode and Doppler

tracings were digitally recorded, with all hemodynamic measurements being made off-line by the same observer (L.P.B.), who was blinded to the prosthesis size, using a dedicated software for quantitative analysis (Compacs, MediMatic S.r.l., Genova, Italy). At least three cardiac cycles were averaged for those patients in sinus rhythm, and at least five cycles for those in atrial fibrillation. From two-dimensional directed M-mode tracings, the left ventricular minor axis internal dimension, posterior wall and septal thickness were measured at end-diastole, and left ventricular mass was calculated using the corrected formula of the American Society of Echocardiography (15). Left ventricular mass was indexed by body surface area (BSA) to obtain the left ventricular mass index (LVMI). Left ventricular volumes were calculated according to the biplane disk summation algorithm tracing the end-diastolic and end-systolic endocardial borders of the left ventricle in the apical two- and four-chamber views. The left ventricular ejection fraction (LVEF) was calculated using the method of disks. The left ventricular outflow tract (LVOT) diameter was measured in the parasternal long-axis view at early systole, with the use of the inner-edge-to-inner-edge method, and was used to derive the cross-sectional area of the LVOT (as  $\pi \text{LVOT diameter}^2/4$ ). In each patient, spectral Doppler tracings of velocities in the LVOT and through the valve prosthesis were recorded at 100 mm/s, and the area under the velocity curves, or time-velocity integrals were derived by digitizing the external contour of the darkest portion of the curves. Cardiac cycles with the highest peak velocity were selected for the measurements. The following measurements were obtained: peak and mean jet velocities; velocity-time integrals; and systolic ejection time. From these measurements, the left ventricular stroke volume was calculated from the product of the LVOT velocity-time integral and cross-sectional area, the cardiac output from the product of stroke volume and heart rate, and the mean transvalvular flow rate by dividing the stroke volume for systolic ejection time. The modified Bernoulli equation was used to calculate the instantaneous pressure gradients across the prosthesis. The velocities in the LVOT were considered in the peak and mean gradient calculation by including them in the equation. The effective orifice area (EOA) of the prostheses was calculated using the standard continuity equation (16), and then indexed for the patient's BSA (17).

### Statistical analysis

Statistical analyses were performed with the SPSS statistical software package (SPSS 10.1, Inc. Chicago, USA). Values were expressed as mean  $\pm$  SD and compared with non-parametric tests (Mann-Whitney).

Categorical variables were compared with contingency tables and the chi-square test (corrected with Yates' formula when necessary) or Fisher's Exact test. A p-value <0.05 was considered to be statistically significant.

## Results

Preoperatively, 47% of the patients were in NYHA class III or IV. The cause of aortic valve disease was stenosis in 67% of cases, mixed stenosis and regurgitation in 23%, and regurgitation in 10%. There were no significant differences in age, gender, and BSA between patients who had the valve implanted in the intra-annular or supra-annular position (Table I). Despite not reaching statistical significance, those patients who underwent AVR with the intra-annular prosthesis tended to have more mixed valve dysfunction (versus pure aortic stenosis), a lower LVMI, and more advanced symptoms before surgery (predominantly NYHA class III versus II) than patients implanted with the supra-annular prosthesis (see Table I). The diameter of the aortic annulus, and LVMI and function, assessed at preoperative echocardiography were similar in the two patient groups (Table I), as was the

annulus size measured with the Hegar dilator at the time of surgery ( $2.1 \pm 0.2$  cm).

At the time of AVR, 18 patients (30%) underwent concomitant coronary artery bypass, one patient (3%) had concomitant mitral annuloplasty, and one (3%) had ascending aorta replacement. Numbers of implanted valves with regard to the intra- or supra-annular position are listed in Table II. The average valve size implanted intra-annularly was similar to that of valves implanted supra-annularly (Table II). The time between AVR and echocardiography was similar in both groups (Table II). At the time of follow up, the NYHA class was significantly improved compared to the preoperative status, with only three patients (5%) showing class III functional impairment.

The hemodynamic performance of the valves in the intra- and supra-annular positions is detailed in Table III. The mean transprosthetic flow rate was similar in both groups, whereas peak and mean transprosthetic gradients were significantly lower (-58% and -58%, respectively) in patients undergoing supra-annular valve implantation (Table III). The EOA (+23%) and EOA index (EOAI) (+20%) were significantly larger, and prosthetic valve resistance was significantly lower (-54%) in patients with a supra-annular valve (Fig. 3;

Table I: Demographics and preoperative clinical characteristics of the study patients.

Parameter	Intra-annular (n = 22)	Supra-annular (n = 38)	p-value
Gender			0.79
Females	12 (55)	19 (50)	
Males	10 (45)	19 (50)	
Age (years)*	74 ± 5	76 ± 5	0.54
Body surface area (m <sup>2</sup> )*	1.74 ± 0.22	1.81 ± 0.15	0.128
Body mass index (kg/m <sup>2</sup> )*	25.9 ± 4.4	26.2 ± 4.4	0.84
Dominant valvular dysfunction			0.099
Stenosis	12 (56)	28 (74)	
Regurgitation	1 (5)	5 (13)	
Mixed	9 (39)	5 (13)	
Cardiac rhythm			0.364
Sinus	18 (80)	34 (89)	
Atrial fibrillation	4 (20)	3 (8)	
Pacemaker	-	1 (3)	
Aortic annulus (cm)*	2.01 ± 0.18	2.1 ± 0.18	0.625
LVMI (g/m <sup>2</sup> )*	173 ± 62	225 ± 110	0.11
LVEF (%)*	56 ± 13	58 ± 15	0.75
NYHA class			0.337
I	2 (9)	6 (16)	
II	6 (27)	19 (50)	
III	12 (54)	11 (28)	
IV	2 (9)	2 (6)	

\*Values are mean ± SD.

Values in parentheses are percentages.

LVEF: Left ventricular ejection fraction; LVMI: Left ventricular mass index.

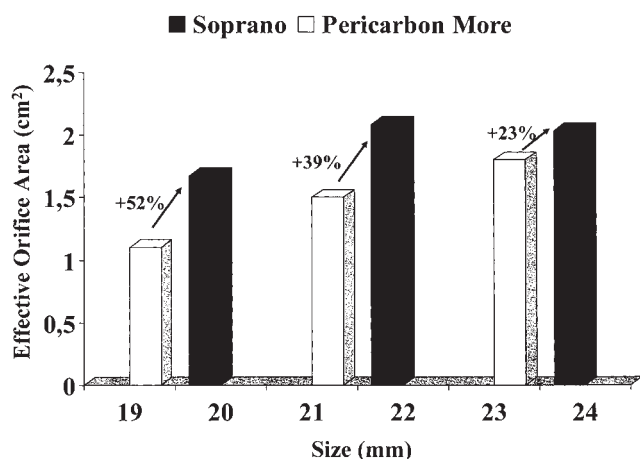


Figure 3: Comparison of effective orifice areas between the Pericarbon More and Soprano pericardial tissue valves.

Table III). The incidence of valve prosthesis-patient mismatch (EOAI  $\leq 0.85$  cm<sup>2</sup>/m<sup>2</sup>) was 50% (n = 11) in patients with intra-annular valves, and 34% (n = 13) in those with supra-annular valves (p <0.0001). Severe valve prosthesis-patient mismatch (EOAI  $\leq 0.6$  cm<sup>2</sup>/m<sup>2</sup>) was seen in four patients (18%) with intra-annular bioprostheses, but in no patients with supra-annular valves.

In comparison with the preoperative data, the post-operative LVEF showed a trend towards improvement in both patient groups (from  $56 \pm 13\%$  to  $64 \pm 12\%$ , and from  $58 \pm 15\%$  to  $63 \pm 13\%$  after intra- or supra-annular implantation, respectively; p <0.08). The LVMI showed a significant regression in patients with a supra-annular valve (from  $225 \pm 110$  g/m<sup>2</sup> to  $173 \pm 59$  g/m<sup>2</sup>; p = 0.032), but was unchanged in patients with intra-annular valves ( $173 \pm 62$  and  $186 \pm 64$  g/m<sup>2</sup>; p = 0.87).

Hemodynamic parameters of bioprostheses implanted in the intra-annular and supra-annular positions according to valve size are summarized in Table IV.

Table II: Intervention, and early clinical and left ventricular function data.

Parameter	Intra-annular (n = 22)	Supra-annular (n = 38)	p-value
Pump time (min)*	140 ± 47	125 ± 39	0.267
Cross-clamp time (min)*	109 ± 39	96 ± 31	0.237
Prosthesis size (mm)			
19	5 (23)	-	
20	-	14 (37)	
21	12 (54)	-	
22	-	24 (63)	
23	5 (23)	-	
Average	21.0	21.3	0.437
Concomitant CABG	7 (32)	11 (29)	0.55
Mean no. of grafts*	1.7 ± 0.8	2 ± 1	0.777
Mitral annuloplasty	-	1 (3)	
Ascending aorta replacement	-	1 (3)	
Time since implantation (months)*	8 ± 2	6 ± 2	0.534
Cardiac rhythm			0.625
Sinus	19 (86)	32 (84)	
Atrial fibrillation	3 (14)	5 (13)	
Pacemaker	-	1 (3)	
Heart rate (beats/min)*	70 ± 10	76 ± 11	0.07
LVEF (%)*	64 ± 12	63 ± 13	0.711
LVMI (g/m <sup>2</sup> )*	186 ± 64	173 ± 59	0.478
NYHA class			0.904
I	15 (68)	28 (74)	
II	6 (26)	8 (21)	
III	1 (6)	2 (5)	
IV	-	-	

\*Values are mean ± SD.

Values in parentheses are percentages.

CABG: Coronary artery bypass graft; LVEF: Left ventricular ejection fraction; LVMI: Left ventricular mass index.

\*, p <0.05 versus preoperative data.

Table III: Postoperative echocardiographic Doppler data.\*

Parameter	Intra-annular (n = 22)	Supra-annular (n = 38)	p-value
Mean flow rate (ml/s)	246 ± 70	218 ± 58	0.116
Peak transprosthetic gradient (mmHg)	40 ± 13	17 ± 6	<0.0001
Mean transprosthetic gradient (mmHg)	19 ± 8	8 ± 3	<0.0001
EOA(cm <sup>2</sup> )	1.45 ± 0.46	1.78 ± 0.41	0.006
EOAI (cm <sup>2</sup> /m <sup>2</sup> )	0.84 ± 0.25	1.02 ± 0.21	0.021
Valve resistance (dynes/s·cm <sup>-5</sup> )	1165 ± 812	535 ± 207	<0.0001

\*Values are mean ± SD.

EOA: Effective orifice area; EOAI: Effective orifice area index.

## Discussion

In the present study population of elderly patients with prevalent stenosis of the native aortic valve and small aortic annulus, supra-annular implantation of bioprosthetic stented valves was associated with a significantly better hemodynamic performance of the prosthesis and postoperative reduction of the left ventricular mass compared to the intra-annular implant. When compared to the same prosthesis in the intra-annular position, implantation in the supra-annular position led to a 23% increase in EOA, a 58% reduction in both peak and mean transprosthetic gradients, and a 54% reduction in the valve's resistance to flow.

The present results may have important clinical implications in assisting surgeons to select the optimal surgical strategy for individual elderly patients requiring AVR. In elderly patients with aortic stenosis, the use of a bioprosthetic valve would be desirable with regard to freedom from lifetime anticoagulant therapy and the greater durability enjoyed by the older age group (2). However, notwithstanding recent impressive technological progress in the design and construction of prosthetic valves, their hemodynamic

performance does not yet match that of the native aortic valve. In particular, the hemodynamic performance of small stented bioprosthetic valves may be suboptimal. The bulk of the prosthesis itself, as well as the stent, sewing ring, and other material to which the graft is attached, contribute towards reducing the final prosthetic functional area available to flow. Although appropriate annular-enlarging techniques are available, there is a reluctance to use them in older patients in whom extensive calcification may limit their applicability from the standpoint of increased morbidity and mortality (9,10). Stentless valves may be a logical alternative, but many surgeons are inexperienced in their use, and the extensive annular calcification frequently present in older patients compromises the implantation of these valves. An additional surgical option that is gaining popularity is to use stented valves that are suitable for complete supra-annular implantation (11).

The concept behind the design of stented bioprostheses for complete supra-annular implantation is to maintain the advantage of easy and safe implantation of stented valves, with the stent material placed on top of the annulus such that it does not impair the blood-

Table IV: Hemodynamic parameters of bioprostheses implanted in the intra-annular and supra-annular position according to valve size.\*

Parameter	Intra-annular valve size			Supra-annular valve size	
	19 mm (n = 5)	21 mm (n = 12)	23 mm (n = 5)	20 mm (n = 14)	22 mm (n = 24)
EOA (cm <sup>2</sup> )	1.15 ± 0.29	1.47 ± 0.41	1.83 ± 0.51	1.62 ± 0.23	1.90 ± 0.49
EOAI (cm <sup>2</sup> /m <sup>2</sup> )	0.72 ± 0.18	0.84 ± 0.25	0.87 ± 0.12	0.92 ± 0.14	1.04 ± 0.26
Mean flow rate (ml)	225 ± 65	237 ± 68	283 ± 78	203 ± 32	231 ± 69
Peak gradient (mmHg)	45 ± 14	40 ± 14	31 ± 10	18 ± 6	16 ± 7
Mean gradient (mmHg)	23 ± 9	18 ± 8	16 ± 5	9 ± 3	8 ± 4
Valve resistance (dynes/s·cm <sup>-5</sup> )	1510 ± 888	1183 ± 919	851 ± 434	618 ± 16	482 ± 219

\*Values are mean ± SD.

EOA: Effective orifice area; EOAI: Effective orifice area index.

stream. In addition, bioprostheses designed for supra-annular implantation, by allowing precise alignment of the valve orifice to the patient's tissue annular orifice, should result in maximal blood flow. However, the actual improvement in stented bioprosthesis hemodynamics gained using the supra-annular implant has not been fully addressed.

The main strength of the present study was that the hemodynamic performance of the same stented biological valve was evaluated after implantation either intra- or supra-annularly in patients of similar body size and aortic annulus diameter. This comparison was possible due to the fact that the supra-annular valve used was an evolution of its intra-annular counterpart, the only difference being in the sewing ring design. The base of the sewing ring designed for supra-annular implant is flat, whereas that designed for intra-annular implant features a small protrusion which enters the annulus and reduces the theoretical area available for flow. The present results confirm poor hemodynamic performance of the Pericarbon More valve implanted intra-annularly (18). In-vivo hemodynamic data for the Pericarbon More valve in the aortic position have not been reported, and consequently the present unfavorable hemodynamic data for this valve cannot be compared. However, the present patients who underwent intra-annular implantation were clinically stable with no morphological abnormality of the valve at echocardiography. Moreover, these patients were studied at a mean period after AVR of eight months, a time frame during which degeneration of the valve is highly unlikely to occur and to affect hemodynamic results. In addition, high residual transvalvular gradients and increased incidence of valve-related morbidity and mortality, compared to the St. Jude Medical valve, have been reported in elderly patients with aortic stenosis implanted with 19-mm and 21-mm Pericarbon More (i.e., intra-annular) valves (18). The same valve, when implanted in the supra-annular position, showed a much better hemodynamic performance. Good hemodynamic performance of the Soprano valve has been reported by Botzenhardt et al. (11), though the gradients measured in the present study were lower than those reported by this group. The difference may be explained by the fact that Botzenhardt and colleagues used a simplified form of the Bernoulli equation ( $4 \times V_{\max \text{ valve}}^2$ ) rather than the modified version [ $4 \times (V_{\max \text{ valve}}^2 - V_{\max \text{ LVOT}}^2)$ ] to calculate peak and mean transprosthetic gradients, and did not take into account the velocity of flow in the LVOT. The simplified Bernoulli equation can be used only for flow that is through a restrictive orifice (i.e., the inertial component is negligible) and when  $V_{\max \text{ valve}}$  is much higher than  $V_{\max \text{ LVOT}}$ .

Since new, normally functioning prosthetic valves

show non-restrictive orifices and low  $V_{\max \text{ valve}}$  values, use of the simplified Bernoulli equation to assess transprosthetic gradients of these valves may also cause a significant overestimation of calculated gradients in patients with  $V_{\max \text{ LVOT}} < 1$  m/s (19). Another important finding in the present study was the dramatic reduction in the incidence of patient-prosthesis mismatch associated with supra-annular implantation of a stented bioprosthesis. Usually, senescent calcification of the aortic valve is not associated with dilatation of the aortic valve annulus or proximal ascending aorta. Indeed, the aortic valve annulus is frequently small, especially in women who have a small BSA and who often receive 19-mm or 21-mm valves. The small aortic annulus presents the potential for iatrogenic 'valve prosthesis-patient mismatch'.

According to Rahimtoola, when the EOAI is  $< 0.9$   $\text{cm}^2/\text{m}^2$ , mismatch occurs between the valve prosthesis and patient body size, and the transprosthetic gradients increase (20). The incidence of valve prosthesis-patient mismatch in patients implanted with stented bioprostheses in the aortic position has been reported to be as high as 46 to 52% (21). Moderate to severe or severe valve prosthesis-patient mismatch has been reported to occur in 11% and 8% of these patients, respectively (21). Among the present study patients, a conservative EOAI cut-off value of 0.85  $\text{cm}^2/\text{m}^2$  was used to define the occurrence of valve prosthesis-patient mismatch (22). Despite this reduction in cut-off value, the incidence of valve prosthesis-patient mismatch in patients receiving an intra-annular valve was 50%, with 18% of these patients showing severe mismatch (EOAI  $< 0.6$   $\text{cm}^2/\text{m}^2$ ). Among patients receiving a supra-annular valve the incidence of valve prosthesis-patient mismatch was reduced to 34% and, more importantly, no case of severe mismatch occurred. A lack of regression of left ventricular hypertrophy (LVH) after AVR, as well as an increase in morbidity and mortality during follow up, has been reported in patients with valve prosthesis-patient mismatch (21,22). Accordingly, in the present patients the better hemodynamic performance of valves implanted supra-annularly was associated with a regression of LVH that was statistically significant at five months after surgery. Conversely, the left ventricular mass did not change or was slightly increased in those patients whose valves were implanted intra-annularly and studied eight months after surgery.

### Study limitations

The main limitations of the present study were the non-randomized nature and predominantly sequential use of the two prostheses. However, as all surgery was performed by the same team and echocardiography by

the same echocardiographer, these limitations were unlikely to have any significant effect on results. The comparable nature of the two patient groups was confirmed by identical valve sizes being implanted in both positions; this may be explained by the fact that the size of the Pericarbon More represented the external diameter of the stent, while the side of the Soprano represented the internal orifice diameter of the prosthesis. The non-randomized nature of the study did not permit the use of two patient cohorts that were perfectly matched regarding preoperative characteristics. Notably, the LVMI was lower in patients with intra-annular valves than in those with supra-annular valves. Differences in preoperative LVMI may be explained by the lower prevalence of pure aortic stenosis (56% versus 74%) in patients receiving the intra-annular valve. However, a lack of preoperative regression of LVH in patients with intra-annular prostheses is unlikely to be accounted for lower preoperative values, for several reasons. First, despite being lower than in patients who received a supra-annular valve, the LVMI of patients with intra-annular valves was well above the cut-off value for a diagnosis of LVH ( $173 \pm 62$  versus  $<125$  g/m<sup>2</sup>) (15). Second, there was no trend to LVMI decrease from preoperative to postoperative values ( $173 \pm 62$  versus  $186 \pm 64$  g/m<sup>2</sup>). Third, the high incidence (50%) of patient-prosthesis mismatch in patients with intra-annular prostheses (18% showed severe mismatch) may explain the lack of regression of LVH (21).

*In conclusion*, the results of the present study clearly demonstrated the great hemodynamic advantage of supra-annular over intra-annular implantation of a stented bioprosthesis. In comparison to intra-annular implantation, the same valve, when implanted supra-annularly, led to a mean increase in EOA of 23%, while transprosthetic gradients were halved, with regression of LVH occurring soon after AVR. Larger trials and a longer follow up period are required to evaluate the impact of the improved hemodynamics of stented bioprosthetic valves in the supra-annular position on patient mortality and morbidity.

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