Comparison of the Performance of a Sutureless Bioprosthesis With Two Pericardial Stented Valves on Small Annuli: An In Vitro Study

Giordano Tasca, MD, Riccardo Vismara, PhD, Andrea Mangini, MD, Claudia Romagnoni, MD, Monica Contino, MD, Alberto Redaelli, PhD, Gianfranco Beniamino Fiore, PhD, and Carlo Antona, MD

Cardiovascular Department, Cardiac Surgery Unit, Ospedale "A. Manzoni" di Lecco, Lecco; Department of Electronics, Information, and Bioengineering, Politecnico di Milano, Milan; FoRCardioLab, Fondazione per la Ricerca in Cardiochirurgia ONLUS, Milan; and Cardiovascular Surgery Department, "L. Sacco" Hospital, Università degli Studi di Milano, Milan, Italy

Background. **Aortic valve replacement has evolved recently with the development of the sutureless bioprosthesis. One such valve is the Perceval bioprosthesis, which is built by mounting leaflets of bovine pericardium to a thin stent; this approach has the potential to provide an excellent fluid dynamic performance. We undertook an in vitro study to compare the hydrodynamic performance of the sutureless bioprosthesis with two standard pericardial stented bioprostheses (Crown and Magna).**

Methods. **Tests were conducted using a mock loop, testing on two sizes of the three prostheses. The prosthesis sizes were chosen to house the valves in porcine aortic roots with a native annulus diameter of 19 mm (n = 6) or 21 mm (n = 6). The stroke volume ranged from 25 mL to 105 mL at a simulated heart rate of 70 beats per minute.**

Results. **Mean pressure drop and energy loss rose with increasing stroke volume in all of the valves tested ($p < 0.001$), with the sutureless valve showing the lowest values for both variables ($p < 0.001$). Effective orifice area values were stable across the stroke volume intervals and were larger in the sutureless valves ($p < 0.001$).**

Conclusions. **All of the valves tested provided good fluid dynamic performances. The sutureless bioprosthesis provided the best performance with the least hindrance to flow behavior. From the hydrodynamic perspective, the sutureless prosthesis may present an advance in the evolution of bioprostheses, ensuring low gradients and potential for low incidence of patient-prosthesis mismatch even in small annuli.**

The sutureless prosthesis offers a promising evolution in the development of biologic artificial heart valves [1, 2]. These bioprostheses can be implanted without the need for a surgical suture, offering advantages in terms of procedure simplification, including shortening the cross-clamp time. The sutureless Perceval valve (PV [Sorin Group, Saluggia, Italy]) was developed by mounting a pericardial stentless valve inside a very thin stent. This design may improve the transvalvular gradient and thus reduce the incidence of patient-prosthesis mismatch. Indeed, some degree of residual gradient persists after standard aortic valve replacement, compared with that in the native valve [3]. That is especially the case when small size prostheses are implanted, with a possible negative effect on patient survival and quality of life [4–7].

Valve implantation is a complex process. The main factor that affects fluid dynamics—prosthesis size—depends on the manufacturer's sizing strategy [8], the surgeon's attitude and experience, and the aortic root characteristics [9]. Each type and size of valve has geometric dimensions that are related both to the stent (material and design) and the leaflet characteristics. Other factors may influence pressure drop, such as the inflow characteristics. These are related to the left ventricular outflow tract (LVOT) shape and the annulus-prosthesis interaction [3], which are influenced by the suture technique [10]. Clearly, a prosthesis that has an efficient design and excellent intrinsic fluid dynamic performance tends to blunt the effects of an implanted suboptimal-size valve.

The aim of this study was to compare the fluid dynamic performances of the PV aortic valve and two state-of-the art stented valves, Magna (MG [Edwards Lifesciences, Irvine, CA]) and Crown PRT (CR [Sorin Group]).

Material and Methods

FoRCardioLab Pulsatile Mock Loop

The mock loop used in this study, FoRCardioLab (Foundation for Research in Cardiac Surgery, Milan, Italy), has

Address correspondence to Dr Tasca, Cardiac Surgery Unit, Ospedale "A. Manzoni" di Lecco, Via Dell'Eremo 9/11, Lecco 23900, Italy; email: giordano.tasca67@gmail.com.

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been already described in detail [11–13]. In brief, the loop consists of a computer-controlled volumetric pump that can replicate left ventricular flow wave forms, a sample test section in which is housed a swine aortic root unit (ARU), and an adjustable hydraulic afterload mimicking the hydraulic impedance of the systemic circulation.

For this study, the mock loop was instrumented with a transit-time flow meter (HT100R; Transonic System, Ithaca, NY). The 1-inch probe was placed downstream of the ARU sample, with three pressure transducers (PC140 series; Honeywell, Morristown, NJ), one immediately upstream, one immediately downstream of the ARU, and the third placed at the inlet section of the hydraulic afterload. A high-speed digital camera (Phantom Miro2; Vision Research, Morristown, NJ) was placed downstream of the sample to acquire an aortic view of the working prostheses. Data were acquired at 200 Hz by an A/D board (USB 6210; National Instrument, Austin, TX).

Sample Preparation and Prostheses Sizing

Twelve fresh whole swine hearts were selected, 6 samples with a native aortic annulus measuring 21 mm and 6 with an annulus measuring 19 mm. The native aortic annuli were measured with a metric go/no go gauge. To replicate the operating theater setting, prosthesis sizing was performed using the probes provided by the manufacturer of each prosthesis on the 12 whole porcine hearts, to select a prosthesis that fit the ARU according to the standard operating procedure. The probes that fit the MG valve had the label size of 19 for annuli measuring 1.9 cm, and 21 for those measuring 2.1 cm. Corresponding labels for the CR valve were 21 and 23, respectively. For the PV, the label sizes were selected according to the manufactures guidelines that corresponded to the "small" (for 19 mm) and "medium" (for 21 mm) aortic annulus diameters.

The ARU samples were harvested by two experienced surgeons and prepared as described previously [3, 11–13].

Experimental Design

Tests were conducted by setting the pump at stroke volumes of 25 mL, 40 mL, 60 mL, 70 mL, 90 mL, and 105 mL. The systolic ejection time was set at one third of the entire cardiac cycle, and the heart rate at 70 beats per minute, with a mean simulated arterial pressure ranging from 80 mm Hg to 104 mm Hg. After housing each ARU sample in the test section holder and testing it for basal points, the three bioprostheses were implanted in a randomized sequence and data were acquired. For each experimental point, data were evaluated over five consecutive simulated heart cycles.

The CR and MG valves were implanted by means of a continuous suture technique using 2-0 polypropylene (Premilene 2/0; B. Braun Surgical SA, Barcellona, Spain). After each implantation, and before testing in the mock loop, the prostheses were visually inspected by the digital video in working conditions, qualitatively assessing their integrity and correct functioning. The flow rate, the pressures upstream from and downstream of the aortic root, and the pressure in the afterload were acquired. The following measurements were obtained through post-processing the raw data:

MEAN SYSTOLIC PRESSURE DROP. Mean systolic pressure drop (Δp_m, mm Hg) across the ARU was evaluated as the difference between the pressures measured upstream from and downstream of the prosthesis, averaged over the systolic interval.

EFFECTIVE ORIFICE AREA. Effective orifice area (EOA [cm^2]) was calculated from the following formula:

$$EOA(cm^2) = \frac{Q_{rms}}{k\sqrt{\Delta p_m}}$$

where Q_{rms} (L/min) is the root mean square systolic flow rate, Δp_m (mm Hg) the mean systolic pressure drop across the sample, and k a conversion factor (k = 3.1 to yield the EOA cm^2).

SYSTOLIC ENERGY LOSS. Systolic energy loss (mJ): the amount of the energy provided by the pump in the systole that is lost when the fluid passes through the prosthesis. It was calculated as the time integral of the product of the pressure drop across the valve and the flow rate. Time integral was evaluated over the systolic period.

Statistical Analysis

Continuous variables are expressed as mean ± SD and were compared using analysis of variance for repeated measures, with the Bonferroni correction used in post-hoc analysis. Values are reported with 95% confidence interval. All *p* values less than 0.05 were considered significant. The data were analyzed by means of SPSS 17 (SPSS Inc, Chicago, IL).

Results

None of the valves displayed significant structural problems in any of the test sessions, and none had to be discarded. Energy loss (Table 1) and mean pressure drop (Fig 1) increased with stroke volume in all of the valves tested. The PV valve showed lower values compared with the two standard prostheses (Table 1, Fig 1). The differences were greater when the data from the subgroup implanted in the 19-mm aortic annulus size were analyzed (Table 1, Fig 1). The EOA values were stable across the stroke volume interval, and were in accordance with the pressure drop. The PV showed the greatest value for EOA (Table 1, Fig 2). The two standard bioprostheses showed similar fluid dynamics, with the CR valve exhibiting a slightly lower pressure drop and larger EOA, but without statistical significance (Fig 2).

Comment

The results from this in vitro study show that the tested sutureless valve provides better hydrodynamic performance than the two standard stented bioprostheses. The mean pressure drops, as well as the energy loss, were statistically significantly reduced for the PV at each stroke volume in the two subgroups with different annulus sizes.

Table 1. Hydrodynamic Results According to Annulus Size

Variable	Stroke Volume 25 mL	40 mL	60 mL	70 mL	90 mL	105 mL	Effect	p Value
Annulus 19 mm								
Δp_m, mm Hg								
Native valve	0.2 ± 0.2	0.4 ± 0.5	1.1 ± 0.8	1.7 ± 0.8	3.1 ± 1.2	4.4 ± 1.7		
CR	2.0 ± 0.95	4.7 ± 1.5	8.8 ± 2.3	13.8 ± 2.5	19.5 ± 2.3	26.1 ± 2.7	Valve	<0.001
MG	3.3 ± 0.82	7.6 ± 1.5	12.2 ± 2.5	18.4 ± 3.3	25.2 ± 4.6	32.7 ± 5.0	Time (SV)	<0.001
PV	0.86 ± 0.8	2.3 ± 0.8	4.0 ± 0.7	6.4 ± 0.96	9.1 ± 0.5	12.4 ± 0.94	Interaction	<0.001
Energy loss, mJ								
Native valve	1 ± 2	1 ± 5	7 ± 9	22 ± 14	44 ± 21	77 ± 34		
CR	8 ± 4	31 ± 11	83 ± 26	173 ± 37	295 ± 46	481 ± 51	Valve	<0.001
MG	15 ± 2	54 ± 9	123 ± 27	237 ± 44	396 ± 79	601 ± 98	Time (SV)	<0.001
PV	5 ± 4	18 ± 6	43 ± 8	87 ± 13	152 ± 13	237 ± 14	Interaction	<0.001
EOA, cm^2								
Native valve	2.1 ± 0.4	2.4 ± 0.3	2.3 ± 0.1	2.3 ± 0.1	2.3 ± 0.1	2.4 ± 0.2		
CR	1.52 ± 0.4	1.50 ± 0.27	1.49 ± 0.19	1.51 ± 0.15	1.53 ± 0.14	1.59 ± 0.12	Valve	<0.001
MG	1.26 ± 0.20	1.25 ± 0.15	1.30 ± 0.13	1.33 ± 0.12	1.38 ± 0.12	1.40 ± 0.13	Time (SV)	<0.001
PV	2.05 ± 0.43	2.38 ± 0.34	2.34 ± 0.14	2.32 ± 0.11	2.35 ± 0.10	2.36 ± 0.17	Interaction	<0.001
Annulus 21 mm								
Δp_m, mm Hg								
Native valve	0.4 ± 0.2	0.2 ± 0.3	0.6 ± 0.5	1.1 ± 0.7	2.4 ± 1.4	2.4 ± 0.2		
CR	1.0 ± 0.64	2.2 ± 1.1	4.6 ± 1.3	7.6 ± 2.2	11.0 ± 3.1	14.6 ± 4.1	Valve	<0.001
MG	1.3 ± 0.75	3.2 ± 1.1	5.7 ± 1.7	8.6 ± 2.3	12.6 ± 3.0	16.4 ± 4.0	Time (SV)	<0.001
PV	0.41 ± 0.38	1.01 ± 0.70	2.03 ± 1.02	3.36 ± 1.16	5.1 ± 1.64	6.87 ± 2.01	Interaction	<0.001
Energy loss, mJ								
Native valve	2 ± 1	2 ± 1	2 ± 1	13 ± 10	44 ± 30	71 ± 40		
CR	4 ± 3	14 ± 7	43 ± 14	92 ± 32	168 ± 62	261 ± 91	Valve	<0.001
MG	6 ± 2	23 ± 8	57 ± 20	103 ± 36	195 ± 53	298 ± 82	Time (SV)	<0.001
PV	2 ± 3	8 ± 6	22 ± 11	48 ± 19	83 ± 29	130 ± 43	Interaction	<0.001
EOA, cm^2								
Native valve	3.3 ± 0.1	5.4 ± 1.7	5.8 ± 3.4	5.4 ± 1.7	4.5 ± 1.1	4.2 ± 0.6		
CR	2.36 ± 0.74	2.28 ± 0.54	2.04 ± 0.17	2.05 ± 0.18	2.05 ± 0.18	2.07 ± 0.16	Valve	<0.001
MG	2.23 ± 0.67	1.96 ± 0.28	1.94 ± 0.20	1.96 ± 0.17	1.96 ± 0.18	2.00 ± 0.17	Time (SV)	<0.001
PV	3.50 ± 1.27	3.31 ± 0.65	3.65 ± 0.81	3.43 ± 0.63	3.30 ± 0.47	3.29 ± 0.43	Interaction	<0.001

CR = Crown valve; Δp_m = mean pressure drop; EOA = effective orifice area; MG = Magna valve; PV = Perceval valve; SV = stroke volume.

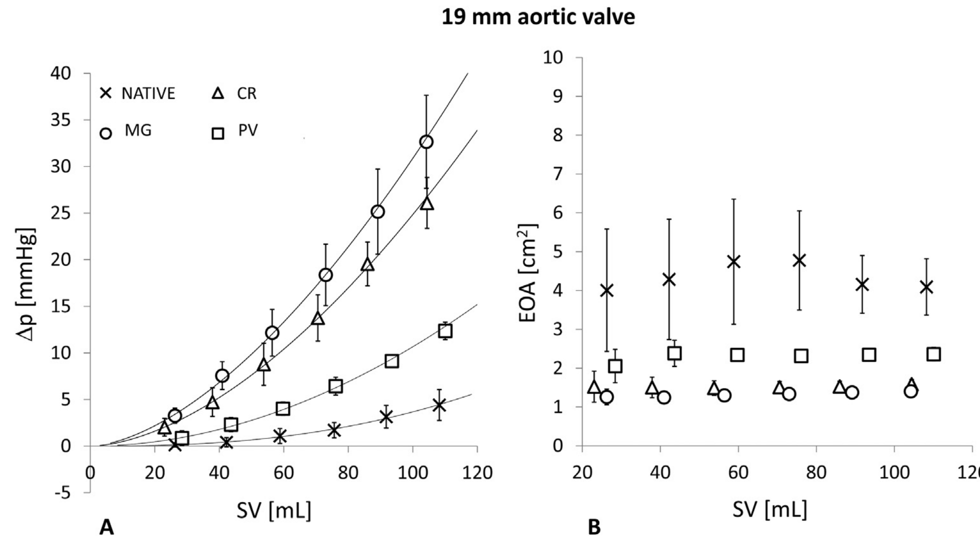
Consistent findings were obtained for the EOAs. Pressure drop is caused by the interaction between flow and the geometric area of the prosthesis orifice, of which only a portion is used by the flow as EOA. This geometric area, in turn, is related to the internal diameter of the prosthesis and to the leaflet aperture according to the nature and position of the leaflets as well as the design of the stent [14]. The size of the valve geometric area is specific for each label size and type of prosthesis and is the main determi-nant of the pressure drop for a given flow. The implantation process affects the size of the geometric area implanted because the valve selection depends on the manufacturer's sizing strategy, the surgical procedure adopted by the surgeon, and the aortic root characteristics. The manufac-turer's sizing strategy, specific for each valve brand, implies that prostheses with different label sizes, but made by different manufacturers, may fit the same aortic root [8]. Moreover, the anatomy of the aortic root plays an important role, because patients with the same aortic annulus size may be implanted with different size bioprostheses owing to their specific anatomy [9]. Finally, the size selection also depends on the surgeon's aptitude and experience—variables that are very difficult to measure [10, 15].

Another factor that may affect valve pressure drop is the native annulus-prosthesis interaction [3], which is related to the LVOT anatomic characteristics and the suture technique [10, 15]. In this regard, the suture technique may influence the transprosthesis pressure drop, especially when it gathers tissue underneath the prosthesis, causing an abrupt discontinuity between LVOT and valve, and is typical of the mattress suture with pledgets [10].

In Vitro Results

Even for implanted valves in the smallest annulus diameter, the PV resulted in mean pressure drops ranging from 2 mm Hg to 4 mm Hg at physiologic stroke

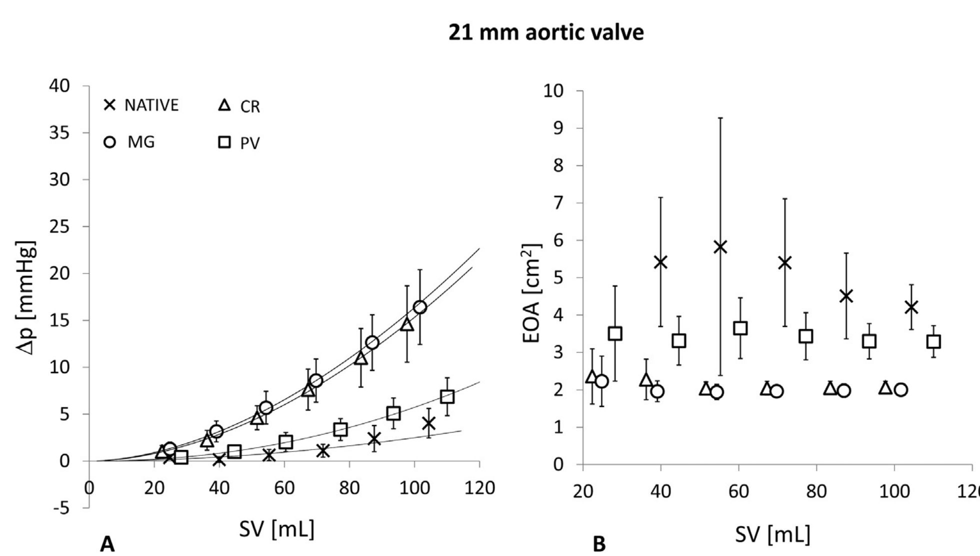
Fig 1. *(A) Mean pressure drops and (B) EOAs with confidence intervals for 19-mm aortic valves. "X" indicates native valve; triangles, Crown valve; circles, Magna valve; and squares, Perceval valve. (CR = Crown valve; EOA = effective orifice area; MG = Magna valve; PV = Perceval valve; SV = stroke volume.)*



volumes for a 19-mm native aortic annulus (ie, 40 mL and 60 mL, respectively). Probably, the presence of the very thin stent, in which the pericardial leaflets are not strictly bonded to the stent itself, allowed the valve to function as a stentless valve. Furthermore, being an expandable prosthesis, the internal diameter can adapt in size, to a certain extent, to that of the ventricular-arterial junction, with a benefit in terms of fluid dynamic performance. In contrast, a standard stented valve has a fixed internal diameter, specific for each type and size of valve. Moreover, the inflow shape and prosthesis-annulus interaction in the PV avoid any abrupt geometric discontinuity between the LVOT and native annulus and the prosthesis ring, carrying the flow from the LVOT into the valve, with less flow disturbance and reduced loss of mechanical energy compared with a classic stented prosthesis.

It is worthwhile to note that due to its structural characteristics, the sutureless feature [10], and the standardized sizing strategy, the sutureless valve might provide a more reproducible and therefore less surgeon-dependent fluid dynamic performance, as illustrated by the narrow confidence intervals shown in Figure 1. The PV potentially possesses the fluid dynamic characteristics of a stentless valve, because the leaflets are not firmly bounded to a stiff, bulky stent. Instead, the stent is thin, leaving the leaflets to move freely, resulting in pressure drop as low as transcatheter aortic valves [15, 16], and consequently, a lower incidence of patient-prosthesis mismatch, even in small aortic annuli, and avoiding its potential negative clinical consequences [3, 4, 6]. Never-theless, the low incidence of patient-prosthesis mismatch can be achieved with a complex surgical procedure, such

Fig 2. *(A) Mean pressure drops and (B) EOAs with confidence intervals for 21-mm aortic valves. "X" indicates native valve; triangles, Crown valve; circles, Magna valve; and squares, Perrceval Valve. (CR = Crown valve; EOA = effective orifice area; MG = Magna valve; PV = Perceval valve; SV = stroke volume.)*



as aortic annulus enlargement or stentless valve implantation, which need longer cross-clamp times.

The CR valve has structural characteristics that are similar to its predecessor (ie, the MitroFlow). Aware of the conservative sizing strategy reported for the MitroFlow valve [17] and the misleading effect of the labeled size on valve comparison and selection, we compared the bioprostheses according to their corresponding aortic annulus size. In the 19-mm aortic root, both CR 21 (external diameter, 24 mm) and MG 19 (external diameter, 24 mm) fit the aortic annulus size and were then implanted and compared. Thus, we did not test a CR valve with a labeled size of 19, which fits a native annulus with a diameter of less than 19 mm. The CR 19 should be used only in rare cases (ie, in less than 1% of patients) with an annulus size of 18 mm or less [9, 18].

Our experimental findings show that the CR valve performed slightly better than the MG valve, with a greater difference with the 19-mm annulus size. Even though the internal diameter of the CR valve is smaller than that of the MG valve, its lower gradient may be explained by the presence of the pericardium outside the stent posts, which allows optimal exploitation of the internal diameter area. In this regard, prostheses with pericardium outside the stent posts currently represent the pinnacle in the evolution of such stents in hydrodynamic terms [14], but provide a performance that is still far lower than that of a native valve because of the bulky stent [3]. The MG bioprosthesis represents a point of reference in the bioprosthesis field, because it is the evolution of a valve that has shown excellent durability [19]. In our study, as expected, it provided a good fluid dynamic performance.

Study Limitations

The internal diameter of the sutureless valve used in this study adapts to the size of the native annulus. This valve was implanted in an isolated passive aortic root. That might have induced an enlargement of the prostheses diameters during the systole, with respect to real in vivo scenarios, for two reasons. The isolated aortic root did not encompass the surrounding tissues that are present in a whole heart and that could affect root dilation; and the explanted root does not encompass the contracting muscular component. Regarding this last point, it should be considered that the literature reports aortic root enlargement during systole. Results reported in this work allows for reliable comparisons among the tested prostheses, because they had been tested in extremely repeatable conditions in the in vitro setup. Nonetheless, the absolute values of the reported quantities could not replicate clinical data owing to different working conditions and measurement techniques. Another possible limitation could be the continuous suture technique adopted for implanting the stented bioprostheses. Even though this type of suture does not gather tissue beneath the prosthesis, the possible shrinking of the LVOT might have had an impact on energetic terms such as energy loss and pressure drop.

Conclusion

In small aortic annuli, all of the valves tested provided good fluid dynamic performance. In particular, the pressure drop for the sutureless bioprosthesis was the lowest and was somewhat close to the performance of a native aortic valve as tested in our experimental setup. The sutureless approach therefore could represent an interesting evolution in the bioprostheses field from the hemodynamics perspective.

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