Role of the sinuses of Valsalva on the opening of the aortic valve

Giuseppe Pisani, MS,^a Raffaele Scaffa, MD,^b Ornella Ieropoli, PhD,^c Edoardo M. Dell'Amico, MS,^c Daniele Maselli, MD,^b Umberto Morbiducci, PhD,^a and Ruggero De Paulis, MD^b

Objective: The present in vitro study was designed to ascertain whether the presence of sinuses of Valsalva in the aortic root were able to regulate the valve effective orifice area and modulate the gradient across the valve independently from root compliance.

Methods: Four different root configurations were prepared. Of the 4, 2 were silicon configurations with the same compliance, 1 with and 1 without sinuses of Valsalva, in which a 25-mm Solo stentless aortic valve was sutured inside. The other 2 configurations were obtained by substituting the upper part of the root with a straight Dacron graft or with a Valsalva graft in a remodeling fashion to reproduce the surgical situation. All roots were mounted in a pulse duplicator to measure the pressure decrease across the valve and effective orifice area at different cardiac outputs.

Results: With increasing cardiac output up to 7 L/min, an increase in the pressure decrease across the valve was evident in both configurations without sinuses of Valsalva (7.90 ± 1.7 and $11 \text{ mm Hg} \pm 0.1 \text{ mm Hg}$, respectively) but not in those with sinuses (2.87 ± 0.5 and $2.42 \text{ mm Hg} \pm 0.5 \text{ mm Hg}$). Similarly, with increasing cardiac output, the effective orifice area increased significantly only in the roots with sinuses (5.13 ± 0.5 and 5.47 ± 0.5 vs 3.06 ± 0.3 and $2.50 \text{ cm}^2 \pm 0.02 \text{ cm}^2$, respectively).

Conclusions: When the cardiac output is increased to greater than the resting physiologic values, the presence of sinuses of Valsalva, independently of root compliance, prevents an increase in the pressure decrease across the valve by way of an increase of the effective orifice area. (J Thorac Cardiovasc Surg 2013;145:999-1003)

The role played by the sinuses of Valsalva in regulating smooth and progressive closure of the aortic valve is well known. Vortex structures forming in the sinuses soon after systole has begun are of paramount importance in modulating the leaflet movements, ensuring synchronous, homogeneous, and stress-free leaflet closure. Little is known whether the sinuses might also be important in regulating valve opening and therefore in optimizing ventricular ejection. Our studies,¹ as well as those of other groups,² using echocardiography have shown that in the absence of sinuses of Valsalva, the aortic valve opening velocity was altered, implying that the presence of sinuses is also important during systole. Furthermore, the importance of root compliance in ensuring normal leaflet movements is also known. In the presence of a stiff root, the dynamic of the leaflets is altered and somehow mimics that seen in the absence of sinuses.³ The present study was designed to ascertain the role played by sinuses of Valsalva in regulating aortic valve opening independently from the root compliance.

METHODS

Two molds of sintered resin with a diameter of 25 mm, 1 with and 1 without sinuses of Valsalva, were prepared. The maximum diameter at the sinuses was 35 mm. Two silicon roots were then obtained by dipping the 2 molds into a liquid silicon solution. Each immersion left a thin layer of silicon on the mold. Usually, 30 immersions were required to obtain a wall thickness of $1.3 \text{ mm} \pm 0.3 \text{ mm}$ with compliance of 3% to 4%. The computation of the compliance of the silicon roots was conducted according to the Food and Drug Administration "Replacement Heart Valve Guidance."⁴ A Stentless Solo (Sorin Biomedica, Saluggia, Italy), 25-mm pericardial valve was sutured inside each 1 of the 2 roots with a technique similar to the standard surgical technique using 4-0 polyester sutures and taking care to obtain perfect valve geometry and smooth pericardial tissue apposition with the silicon wall. Thus, 2 silicon configurations were obtained: silicon-straight and silicon-Valsalva. The final configuration showed a perfect fit between the valve and root (Figure 1). Another 2 roots with and without sinuses were then prepared in a similar manner and 2 other Solo valves were sutured inside. Next, the upper part of the silicon root was cut, following the crescent shape of the valve and replaced by suturing in its place a straight or Valsalva (Terumo Vascutek, Renfrewshire, UK) Dacron graft using the classic remodeling technique to reproduce the typical surgical situation. Two hybrid configurations were therefore obtained: hybrid-straight and hybrid-Valsalva (Figure 2). All testing of the 4 roots, 2 silicon and 2 hybrid, both with and without sinuses of Valsalva, was conducted using a Vivitro System pulse duplicator (Vivitro System, Victoria, British Columbia, Canada).⁵ The 4 assembled models of aortic root and valve were installed in the aortic position of the pulse duplicator for the hydrodynamic test. A complementary (nontest) valve, the CarboMedics Prosthetic Heart Valve (29 mm; CarboMedics, Austin, Tex), was installed in the mitral position. The simulation conditions included 4 different cardiac output (CO) values (ie, 2, 3.5, 5, and 7 L/min) at a pulse rate of 70 beats/min and a mean aortic pressure of 100 mm Hg. The test fluid used was saline (density, 1000 kg/m^3 ; dynamic viscosity, 10^{-3} Pa/s). The 4 configurations were tested in different conditions. Hydrodynamic tests on the silicon-Valsalva and silicon-straight configurations were performed by

From the Department of Mechanics,^a Politecnico di Torino, Turin, Italy; Department of Cardiac Surgery,^b European Hospital, Rome, Italy; and Sorin Biomedica,^c Saluggia, Italy.

Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication Jan 9, 2012; revisions received Feb 5, 2012; accepted for publication March 20, 2012; available ahead of print April 16, 2012.

Address for reprints: Ruggero De Paulis, MD, Department of Cardiac Surgery, European Hospital, Via Portuense 700, Rome 00149, Italy (E-mail: depauli@tin.it). 0022-5223/\$36.00

Copyright © 2013 by The American Association for Thoracic Surgery
doi:10.1016/j.jtcvs.2012.03.060

Abbreviations and Acronyms

CO = cardiac output

EOA = effective orifice area

partially filling the housing aortic chamber with saline solution, mimicking the physiologic-like compliance of the construct. This experimental setting aimed at investigating the behavior of the valve in the presence of the Valsalva sinuses when aortic compliance is ensured. In contrast, the hybrid-Valsalva and hybrid-straight configurations were tested without forcing compliant behavior on the constructs (by filling with saline solution the housing aortic chamber). The rationale for this second setting was to investigate the behavior of the valve in the presence of differently shaped commercial grafts. A dedicated software control system was used to drive and control the mock circulatory system (ViviTest, ViVro Systems). This allowed us to obtain and analyze the physiologic flow and pressure waveforms within the in vitro simulator. Technically, the analog aortic, ventricular, and mitral pressure signals were acquired using 3 pressure transducers (Utah Medical Products, Salt Lake City, Utah). The volumetric flow rates in the aortic and mitral positions were acquired using an electromagnetic flow meter system incorporating Carolina Medical probes (Carolina Medical Electronics, East Bend, NC). A sample rate of 500 Hz was considered appropriate. Analog signals were acquired using a 12-bit analog I/O resolution A/D board (KPCI-3101; Keithley Instruments, Cleveland, Ohio). The hydrodynamic performance of the assembled models of aortic root and valve was evaluated in terms of the aortic transvalvular pressure decrease and the effective orifice area (EOA), calculated using the well-established Gorlin formula, where Q is the volumetric aortic flow rate. Data are presented as the mean $\pm$ standard deviation, as obtained, for each simulated flow rate, from 3 independent experimental sessions.

RESULTS

The pressure decrease across the valve and EOA at each CO value is shown in Figure 3 and 4 for the silicon and hybrid configurations, respectively.

Pressure Decrease

In both silicon root configurations (Figure 3, *Left*), the pressure decreases across the valve were comparable at a CO of 2, 3.5, and 5 L/min (2.57 ± 0.41 , 2.05 ± 0.50 , and $2.10 \text{ mm Hg} \pm 0.60 \text{ mm Hg}$ vs 1.32 ± 0.34 , 1.51 ± 0.68 , and $2.65 \text{ mm Hg} \pm 0.44 \text{ mm Hg}$, respectively). However, when the CO was increased to 7 L/min, the pressure decrease markedly increased in the silicon roots without sinuses ($7.90 \text{ mm Hg} \pm 1.77 \text{ mm Hg}$) but not in the roots with sinuses ($2.87 \text{ mm Hg} \pm 0.53 \text{ mm Hg}$). Similarly, in both hybrid root configurations (Figure 3, *Right*) the pressure decreases were comparable at 2, 3.5, and 5 L/min (1.20 ± 0.47 , 1.26 ± 0.21 , and $1.83 \text{ mm Hg} \pm 0.15 \text{ mm Hg}$ vs 1.09 ± 0.03 , 1.63 ± 0.12 , and $4.16 \text{ mm Hg} \pm 0.37 \text{ mm Hg}$, respectively). Also, for the hybrid root configurations, when the CO was increased to 7 L/min, the pressure decrease remained low in the presence of sinuses ($2.42 \text{ mm Hg} \pm 0.5 \text{ mm Hg}$) but markedly increased in the absence of sinuses ($11 \text{ mm Hg} \pm 0.1 \text{ mm Hg}$).

Effective Orifice Area

Paralleling the results in pressure decrease, the EOA was comparable in all 4 root configurations at lower CO, but they were significantly larger at 7 L/min only in both configurations with sinuses (5.13 ± 0.5 and 5.47 ± 0.5 for the silicon and hybrid root, respectively; Figure 4).

DISCUSSION

The 3 anatomic pouches located immediately above the aortic valve were described in the 17th century by the Italian anatomist Antonio Maria Pini, who termed them the “Valsalva,” from the location of his grandfather’s family castle. Although from that day onward, they have always been termed the “sinuses of Valsalva,” it was Leonardo da Vinci, who many years before had described, depicted, and explained in detail their shape and function. The greatness of Leonardo da Vinci in understanding the anatomy of the aortic valve has been celebrated by Robicsek⁶ in a historical article. Recently, we have also reported how much Leonardo da Vinci had understood the modern concepts of the function of the aortic valve—from the generation of vortices and their importance in smooth valve closure, to the cusp’s surface of coaptation, to a stunning description of leaflet histology.⁷ In the modern era, the experiments of Bellhouse and Bellhouse⁸ in the early 1970s methodically demonstrated the role of the sinuses in generating vortices to prevent the leaflet from affecting the aortic wall and in regulating aortic valve closure. All subsequent studies have always focused on the role played by the sinuses during the diastolic phase⁹ and even more so after various types of valve-sparing procedures entered the surgical arena. In the past 10 years, a large number of studies have demonstrated the problem related to a lack of sinuses of Valsalva or, in contrast, the benefit of their reconstruction during surgery of the aortic root.^{10,11} All studies, whether in vitro¹² or with the use of transesophageal echocardiography^{1,2} or contrast phase magnetic resonance imaging,¹³ have invariably shown the positive effect of the sinuses in regulating leaflet dynamics during the cardiac cycle and even in modulating coronary flow.¹⁴ However, very little has been reported on the role played by the sinuses, if any, during systole. Because the sinuses are located on the aortic side, very similar to an extension of the aortic leaflet into the aortic wall, their role has always been considered almost exclusively in diastole. The function of the sinuses in systole has always been considered marginal, and most studies considered the cusp motion during the cardiac cycle, just as an increase in valve opening velocity is reported every time the aortic root is reconstructed in the absence of the sinuses.^{1,2} In this experimental setting, we were able to show how the sinuses of Valsalva are also important in modulating the relative obstruction of flow present in the outflow tract of the left ventricle every time an increase in CO is present.

FIGURE 1. The 2 root configurations with (*left*) and without (*right*) sinuses created out of silicon with the same compliance. The conduit diameter was 25 mm and the stentless valve size was 25 mm in both cases. The maximum diameter at the sinuses was 35 mm.

This is secondary to an increase in the opening of the aortic valve area (Figure 5) that is possible only in the presence of the sinuses. Thus, the presence of sinuses of Valsalva appears to guarantee a progressive increase in the valve area and therefore an absence of gradient every time the CO is greatly increased such as during intense physical exertion. In the absence of sinuses, the aortic valve appears to be progressively more obstructive to flow when the CO increases. Although this aspect might not be clinically relevant, it is undoubtedly evident that under conditions of maximal effort the presence of the sinuses helps the heart to be more efficient and reduce energy losses. It is also generally accepted that the normal compliance of the root is extremely important in ensuring normal leaflet dynamics. Root expansion during systole is particularly important in the leaflet-free margins remaining distended and flat during their opening. In the absence of compliance, the leaflets have less space when traveling from their close to their full opening position, and, as a consequence, their free margin will show wrinkles and folds that might potentially contribute

to an accelerated rate of failure. The progressive loss of elasticity in the aortic wall with advancing age, even more evident in patients with hypertension or atherosclerosis, is considered a cause that contributes to progressive leaflet degeneration resulting in valve stenosis.¹⁵ Furthermore, because the leaflet movements inside a rigid and stiff root are somehow similar to those recorded in the absence of sinuses, it is evident how reconstructing an aortic root using nonelastic material such as Dacron and without providing neosinuses, might double the causes of suboptimal leaflet function. However, the data from the present study have shown that the presence of sinuses, independently of root compliance, is important in augmenting the aortic valve area and minimizing flow obstruction when the CO increases. When the CO was increased from 5 L/min to 7 L/min in the 2 study groups without sinuses, the mean gradient significantly increased and the EOA did not change or decreased slightly. In contrast, when the sinuses were present, and the CO was increased, the mean gradient did not change and the EOA progressively increased in both groups. This finding indicates that the presence of sinuses is important in modulating hemodynamics during systole. This information is important, in particular because it indicates that in patients who have undergone aortic root reconstruction, for whom root compliance is, by definition, markedly reduced or lost, the presence of the sinuses maintains normal systolic performance. This aspect gives more strength to our conclusion that the presence of sinuses of normal shape and dimensions might eventually compensate for the lack of root compliance. Combining the results of the present study with the known effects of the root compliance on leaflet movements and stress, it is likely that the presence of compliance is important for normal leaflet dynamics, in term of smooth leaflet movement and wrinkle-free cusp opening. Also, the presence of sinuses guarantees hemodynamic efficiency, even in the presence of increased CO. Although the clinical relevance of this finding might not be very important, because the maximum mean gradient at 7 L/min of CO was 8 mm Hg to 10 mm Hg, it helps in

FIGURE 2. The 2 root hybrid configurations with (*left*) and without (*right*) sinuses created out of silicon in which the upper part was cut out following the valve contours and substituted with a straight graft or a Valsalva Dacron graft. Both conduit diameters were 26 mm.

FIGURE 3. Diagram of pressure decrease across the valve in the Valsalva silicon and straight silicon configurations (*left*) and in the Valsalva-hybrid and straight-hybrid configurations (*right*). When the cardiac output (CO) increased from 5 L/min to 7 L/min, an increase in the pressure decrease only occurred in the roots without sinuses. Note that no marked difference was present within each group with the same root configuration.

our understanding of how normal anatomy is functional to normal physiologic functions and another method by which the efficiency of the heart is maintained in conditions of an increased workload such as strenuous sport activity. In contrast to our findings, Sripathi and colleagues¹⁶ with a numeric simulation using finite element analysis showed that the root compliance contributes to the ability of the normal valve to increase its EOA in response to increased physiologic demands. To obtain this finding, they had to apply a difference in pressure across the valve of 8 mm Hg before an increase in EOA became apparent. They concluded that such pressure was needed for obtaining backward leaflet bending against the root as the main contributor to the increase in EOA. However, by definition, finite element modeling uses static models and is usually used to measure stress. When more complex and dynamic condition are evaluated, such as when mimicking an increase in CO output, a fluid–structure interaction would be the minimum requirement to draw sound conclusions. Their experiment has simply demonstrated that by applying a greater pressure on its ventricular surface, the leaflet can bend backward and this is more evident in the presence of a compliant root. Therefore, the applied pressure is used as a surrogate for the gradient and the consequent deduction might not be accurate. Finally, the same simulation was not repeated in

a straight root to rule out that it was the presence of sinuses that allowed a greater valve opening. In our experimental setting, the increase in pressure gradient generated by an increase in CO was inversely related to the EOA, just as in the actual clinical situation, and this was further confirmed by the direct recording of a larger anatomic area (Figure 5). In conclusion, although the root compliance is extremely important in the mechanism of valve opening through the well-known “pull and release” mechanism, and, again, it regulates the leaflets smooth opening by accommodating the excess of their free edge, it appears that the presence of sinuses plays an important and probably additive role in allowing a progressive increase in valve opening necessary to avoid an increase of gradient across the valve. Although it would require additional studies, this phenomenon could be explained by a progressive reduction of pressure inside the sinuses (induced by the vortices) by increased flow across the valve. This lower pressure beyond the leaflets explains how the leaflet can reach and maintain a wider opening area. In contrast, in the absence of sinuses and eddy currents, this mechanism cannot take place.

Study Limitations

Stentless pericardial valves were used for the present study; therefore, we could not determine whether the

FIGURE 4. Diagram of effective orifice area (EOA) in the Valsalva-silicon and straight-silicon configurations (*left*) and in the Valsalva-hybrid and straight-hybrid configurations (*right*). When the cardiac output (CO) increased from 5 to 7 L/min, an increase in the EOA was only present in the roots with sinuses. Note that no marked difference was present within each group with the same root configuration.

FIGURE 5. Direct visualization of valve operating condition inside a root with and without sinuses (hybrid configurations) at a cardiac output of 7 L/min. A larger opening area was evident in the valve inserted in a root with sinuses.

same findings would also apply to normal living valves. However, independently of the different manufacturing of pericardial valves that could influence better cusp movement, all pericardial valves have greater inertia than the natural living valve. Because the same valve type and size were used for all the experiments, we believe the valve material might have a small influence on the whole experiment and results. Similarly, the same experiment could have been performed using smaller valve sizes to verify whether the same

results were also present at different diameters. However, because the roots were molded according to the valve size to a perfect fit, we would not have expected significant differences. Finally, because of the difficulties in constructing a hybrid configuration to a silicon-molded root using the reimplantation technique, we exclusively used the remodeling type of valve-sparing procedures. We therefore could not determine whether this finding would also apply to the reimplantation type of valve-sparing procedure in which stabilization of the annulus is present.

References

1. De Paulis R, de Matteis GM, Nardi P, Scaffa R, Bassano C, Chiariello L. Analysis of valve motion after the reimplantation type of valve-sparing procedure (David I) with a new aortic root conduit. *Ann Thorac Surg.* 2002;74:53-7.
2. Leyh RG, Schmidtke C, Sievers HH, Yacoub MH. Opening and closing characteristics of the aortic valve after different types of valve-preserving surgery. *Circulation.* 1999;100:2153-60.
3. Robicsek F, Thubrikar MJ. Are we implanting half valves? The role of sinus wall compliance in aortic valve function. *Ann Thorac Surg.* 1999;67:597.
4. Food and Drug Administration Replacement Heart Valve Guidance, version 4.1. October 14, 1994.
5. Scotten LN, Walker DK, Dutton JW. Modified Gorlin equation for the diagnosis of mixed aortic valve pathology. *J Heart Valve Dis.* 2002;11:360-8.
6. Robicsek F. Leonardo da Vinci and the sinuses of Valsalva. *Ann Thorac Surg.* 1999;52:328-35.
7. Morea M, De Paulis R. "Il buso" (the orifice): how much did Leonardo know of the aortic valve? *J Cardiovasc Med.* 2007;8:399-403.
8. Bellhouse BJ, Bellhouse FH. Mechanism of closure of the aortic valve. *Nature.* 1968;217:86-7.
9. Thubrikar MJ, Nolan SP, Aouad J, Deck D. Stress sharing between the sinus and leaflets of canine aortic valve. *Ann Thorac Surg.* 1986;42:434-40.
10. Kunzelman KS, Grande KJ, David TE, Cochran RP, Verrier ED. Aortic root and valve relationships: impact on surgical repair. *J Thorac Cardiovasc Surg.* 1994;107:162-70.
11. Miller DC. Valve-sparing aortic root replacement in patients with the Marfan syndrome. *J Thorac Cardiovasc Surg.* 2003;125:773-8.
12. Fries R, Graeter T, Aicher D, Reul H, Schmitz C, Böhm M, et al. In vitro comparison of aortic valve movement after valve-preserving aortic replacement. *J Thorac Cardiovasc Surg.* 2006;132:32-7.
13. Kvitting JPE, Ebbens T, Wigström L, Engvall J, Olin CL, Bolger AF. Flow patterns in the aortic root and the aorta studied with time-resolved, 3-dimensional, phase-contrast magnetic resonance imaging: implications for aortic valve-sparing surgery. *J Thorac Cardiovasc Surg.* 2004;127:1602-7.
14. De Paulis R, Tomai F, Bertoldo F, Ghini AS, Scaffa R, Nardi P, et al. Coronary flow characteristics after a Bentall procedure with and without sinuses of Valsalva. *Eur J Cardiothorac Surg.* 2004;26:66-72.
15. Robicsek F, Thubrikar MJ, Fokin AA. Cause of degenerative disease of the tri-leaflet aortic valve: review of subject and presentation of a new theory. *Ann Thorac Surg.* 2002;73:1346-54.
16. Sripathi VC, Kumar RK, Balakrishnan KR. Further insights into normal aortic valve function: role of a compliant aortic root on leaflet opening and valve orifice area. *Ann Thorac Surg.* 2004;77:844-51.