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The Third Generation Carpentier-Edwards Bioprosthesis: Early Results

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The current status of valve replacement was reviewed by analyzing six groups of 100 consecutive patients, each receiving the standard Carpentier-Edwards bioprosthesis, the Starr-Edwards valve or the Björk-Shiley valve in the mitral or aortic position and operated on by the same surgeons in the same institution during an identical time frame. Data were evaluated for valve failure, reoperation, thromboembolism and valve-related deaths. Long-term results up to 9 years showed the superiority of bioprostheses over mechanical valves in terms of valve-related deaths and thromboembolic and anticoagulant complications for a similar rate of valve failure. Persistent drawbacks associated with valvular bioprostheses, namely, transvalvular gradients, limited durability and tissue calcification in young patients, led to continual improvements in valve design and preservation techniques and the development of the third generation Carpentier-Edwards bioprosthesis: the supraanular porcine valve and pericardial valve. The supraanular porcine valve was designed with the aim of decreasing the transvalvular gradient, decreasing turbulence, increasing longevity and decreasing calcification. The pericardial valve was designed with the aim of improving hemodynamics in small-sized orifices, improving mounting techniques to avoid fixation sutures at the commissures, achieving a flexible stent and improving preservation.

Between July 1980 and October 1984, there were 391 supraanular porcine and 61 pericardial valves implanted. The supraanular valves were used for three purposes: isolated aortic, isolated mitral and mitral valve replacement associated with tricuspid anuloplasty. The pericardial valves were used for isolated aortic valve replacement. Short-term results (1 to 4 years) are presented concerning the clinical use of these third generation bioprostheses.

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Since the first glutaraldehyde-preserved biologic valve was introduced in 1968 (1), this method of valve replacement has been widely used because of specific advantages over mechanical valves. Several drawbacks became apparent, however, as the use of the valves became more widespread. Therefore, improvements were introduced leading to a second generation and subsequently a third generation of bioprostheses. The purpose of this paper is to introduce the third generation of the Carpentier-Edwards bioprosthesis by pointing out the research and developmental factors that influenced its design and production and the preliminary results obtained at the Broussais Hospital in Paris during the past 4 years.

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Current Status of Valve Surgery

Two studies by one of us (P.P.) of long-term results obtained with the second generation bioprosthesis are presented. The data compare the standard Carpentier-Edwards bioprosthesis with the Starr-Edwards and Björk-Shiley mechanical valves over a 7 year period between 1974 and 1980 in relation to valve failure, reoperation, thromboembolism and valve-related deaths in six groups of 100 consecutive patients operated on in the same institution by the same surgeons during an identical time frame. We used this approach rather than collating data from various centers, a procedure in which data can be selected to illustrate a particular point of view, because we believe that this protocol is the only scientifically valid one for a retrospective study.

Aortic Valve Replacement

Three groups of 100 consecutive patients with aortic valve replacement were operated on between 1974 and 1978 and underwent long-term evaluation. The duration of follow-up was 5 to 9 years (mean 6). The cumulative follow-up time

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was 1,638 patient-years. During this period, more than 4,500 valves were implanted in our center. Follow-up study was performed from January to April 1984 (2).

Valve failure. In conformance with the Stanford definition, valve failure was defined as encompassing all valve-related complications including confirmed hemodynamic dysfunction, periprosthetic leak, thromboembolism, thrombotic valvular occlusion and endocarditis prompting reoperation or causing death. The incidence of valve failure at the end of 8 years was 20% in the bioprosthesis group, 13% in the Starr-Edwards group and 12% in the Björk-Shiley group. These differences were not statistically significant. However, the 10 cases of valve failure in the bioprosthesis group were responsible for a 20% mortality rate (2 deaths) in contrast to a rate of 73 and 78%, respectively, in the two other groups of prosthetic valve failure.

Reoperation. The actual risk of reoperation at 8 years was 16% in the bioprosthesis group, 5% in the Starr-Edwards group and 2% in the Björk-Shiley group. The difference between the bioprosthesis and the Björk-Shiley group was significant. All cases of valve failure in the bioprosthesis group were gradual and allowed for reoperation, whereas catastrophic events precluding operation were more frequent in the two mechanical prosthesis groups.

Thromboembolism. On an actuarial basis, 95% of patients in the bioprosthesis group were free of thromboembolism at 8 years compared with 81 and 84%, respectively, in the Starr-Edwards and Björk-Shiley groups. This difference was statistically significant, and furthermore, the thromboembolic episodes in the patients with a bioprosthesis were transient whereas patients in the other two groups remained severely disabled after these episodes.

Valve-related deaths. The incidence of valve-related deaths at 8 years was 4% in the bioprosthesis group and 13% in both other groups. There was a statistically significant difference between the bioprosthesis and mechanical valve groups. At least half of the valve-related deaths in the mechanical valve groups were due to thromboembolic complications.

Mitral Valve Replacement

A second, similar study was performed on mitral valve replacement for mitral insufficiency (3). Again the period studied was 1974 to 1978 and three groups of 100 consecutive patients with a bioprosthesis and Starr-Edwards and Björk-Shiley valves were compared. The duration of follow-up was 7 years with a cumulative follow-up time of 2,058 patient-years.

Valve failure. The incidence of valve failure at 7 years was 20% for the bioprosthesis and 21 and 25% for the Starr-Edwards and the Björk-Shiley valves, respectively, but this difference was not statistically significant. At 7 years, only five patients with a bioprosthesis had undergone reoperation for intrinsic alteration of the valve. The most frequent cause of valve failure in the mechanical valve group was a thromboembolic complication.

Reoperation. The actuarial risk of reoperation was 20% in the bioprosthesis group compared with 8% in the other two groups; this difference was not significant. The comparison of reoperation and valve failure underlines the fact that some catastrophic events that did not allow for reoperation occurred in the mechanical valve groups.

Thromboembolism. Of patients with a bioprosthesis, 94% were free of thromboembolic complications at 7 years compared with 70 and 68%, respectively, in the mechanical valve groups; this difference was statistically significant.

Valve-related deaths. The incidence of valve-related deaths was 8% in the bioprosthesis group compared with 18% in each of the two other groups. Although this difference is not significant using the two-tailed t test, it was noted that thromboembolic complications were the main cause of death in the mechanical valve groups. We concluded from these studies that the bioprosthesis was superior to the mechanical valves in terms of valve-related deaths and thromboembolic and anticoagulant complications for a similar rate of valve failure.

The Supraanular Bioprosthesis

In light of such excellent results with the standard Carpentier-Edwards valve, what were the pending problems with this bioprosthesis? There were three: transvalvular gradients with small valve sizes, fatigue lesions (20% at 10 years) and calcification (50% at 4 years in children). For these reasons, the third generation Carpentier-Edwards supraanular valve was developed and tested with the following aims: decreasing the transvalvular gradient, decreasing turbulence around the valve, increasing valve longevity and decreasing the incidence of calcification.

Approach

Because transvalvular gradients result mainly from the impedance caused by the stent and the aortic remnant supporting the cusps, valve design was modified so as to implant the valve in the supraanular position. The concept was to implant the stent and the aortic remnant above rather than inside the anulus of the aortic root so that a larger valve could be used. Only the cusps of the supraanular porcine valve remain exposed to the blood column. Hemodynamics through the valve were also improved by reducing the amount of synthetic material and optimizing sewing anulus design. The supraanular valve was developed according to these specifications and the hemodynamic performance was tested in vitro by comparing the new valve with current aortic valves. Other areas of research focused on 1) optimizing flexibility to decrease loading shock on the commissures

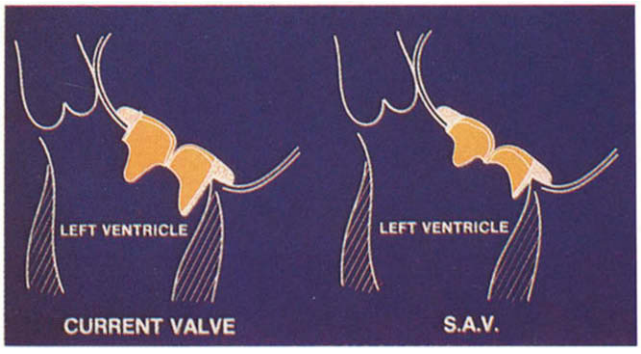
and base of the cusps and to improve hemodynamics, 2) providing a supraanular configuration to allow supraanular positioning of the valve, 3) improving valve design to reduce turbulence, and 4) developing better methods of tissue preservation.

The stent height of the supraanular porcine valve in the mitral position was decreased so as to minimize protrusion into the ventricular cavity and left ventricular outflow tract. The protrusion of the struts over the sewing ring was further decreased in the mitral model by a special configuration of the sewing ring. Strut protrusion over the sewing ring varies from 10 mm for the 25 mm valve to 13 mm for the 35 mm valve, which corresponds to an effective protrusion of 8 to 10 mm within the ventricular cavity if the 2 to 3 mm thickness of the mitral valve anulus is taken into consideration. Comparison between the current model and the supraanular valve shows a 30% decrease in intraventricular protrusion of the current valve (Fig. 1). In vitro hydrodynamics, comparing size 21 valves of the Starr-Edwards, Björk-Shiley, St. Jude Medical and supraanular Carpentier-Edwards types, show a smaller pressure gradient across the supraanular valve at virtually all flow rates with the difference becoming greater as the flow rate increases (Fig. 2).

Tissue Preservation

Improved tissue preservation is important to increase valve longevity. Three areas were selected for improvement: 1) the shipping time, which was decreased to an average of 32 hours under uniform and optimal conditions, 2) fixation of the valves at low compression pressures of 4 mm Hg, and 3) the shipping medium, which was a cold buffered solution with a pH of 7.4 and temperature range of 0 to 6°C. Shipping conditions and handling of the valves have become increasingly difficult in the previous 6 years because of the necessity for commercial laboratories to accommodate an increasing demand. Availability of adequately sized pigs began to be insufficient to cover the needs, which can be 20 times the number of valves produced because of strict criteria in selection and controls. Pig hearts were therefore

Figure 1. The supraanular bioprosthetic valve in the mitral position. Comparison between the current model and the second generation supraanular porcine valve shows a 30% decrease in intraventricular protrusion of the former valve.



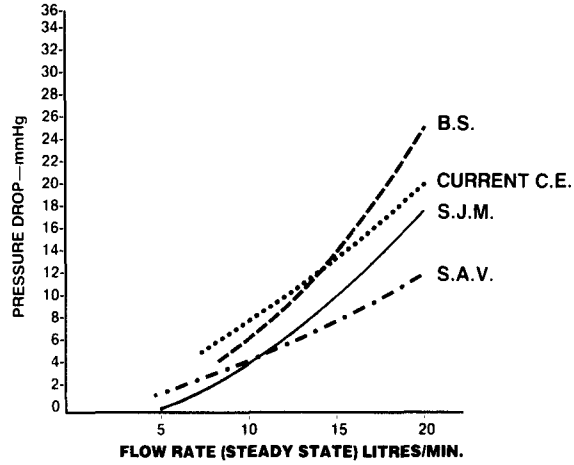


Figure 2. In vitro hydrodynamic comparison of the size 21 Björk-Shiley (B.S.), St. Jude Medical (S.J.M.) and Carpentier-Edwards (C.E.) current and supraanular (S.A.V.) valves.

harvested in countries as far away as the Philippines. Histologic and electron microscopic studies performed on valves that were shipped and processed according to the newer specifications showed that the natural structure of the valvular tissue was preserved. There was no alteration of cell components of the tissues and the crimp of the collagen bundles was preserved. This preservation of histologic structure resulted in improved durability and fewer variations as assessed by in vitro testing of millions of cycles in a pulse duplicator. In earlier models, there was wide variation in durability not only between valves of different laboratories but also between valves from the same laboratory. Fatigue testing of the supraanular valve compared with current porcine valves demonstrated a decreased number of variations and improved average durability (Fig. 3).

Calcification

As shown both experimentally and clinically, calcification results from various factors. Some are associated with the valve itself, such as turbulence, tissue components and technique of preservation, and some are associated with the patient, such as calcium metabolism and the patient's age and diet. Among patient-related factors, only diet could be modified by decreasing calcium intake and this was investigated experimentally by decreasing or increasing calcium intake in animals receiving tissue valve leaflets (4).

Among valve-related factors, turbulence could be decreased by improving valve design, that is, increasing the surface of the valve orifice by the supraanular concept. Tissue components, selection of valves and other valve-related factors were investigated by evaluating the possible influence of age, collagen, source of tissue, dehydration of tissue and stabilization of mucopolysaccharides. Finally, various techniques of preservation were investigated to eliminate or minimize calcification.

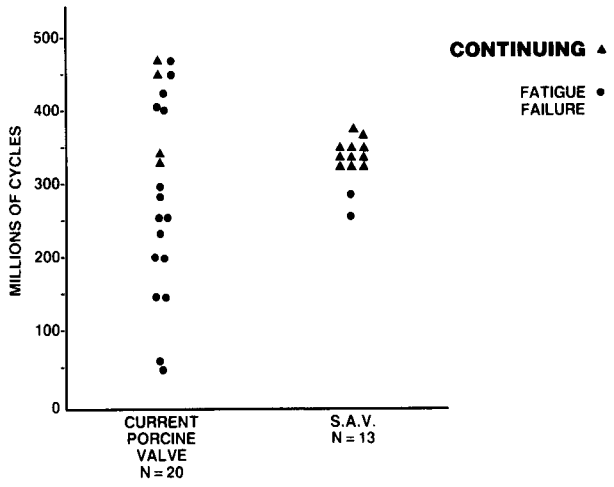


Figure 3. Fatigue testing of the new supraanular valve (S.A.V.) compared with the current porcine valve demonstrates decreased variations and improved average durability, indicating improved preservation in the current model.

Among patient-related factors, it is important to avoid intravenous calcium; we had one case of calcification 1 month after implantation in which an adult died of cardiac failure after having received intravenous injections of calcium gluconate for 15 days. Excess calcium intake through excess consumption of milk or dairy products should be avoided, especially in children. Among tissue-related factors, drying out of leaflet tissue during surgical implantation must absolutely be prevented by permanent irrigation with saline solution because tissue dehydration after exposure to air led to early calcification in the animal model. Other areas continue to be under investigation in tissue preparations, such as the use of magnesium chloride, nonphosphate buffers, surfactant and polymer incorporation to prevent calcification in children, which remains a considerable challenge.

Results

Between July 1980 and October 1984, there were 391 supraanular valves implanted at our institution. They were used for three purposes: isolated aortic, isolated mitral and mitral valve replacement associated with tricuspid anuloplasty.

There were 188 aortic valve replacements with an operative mortality rate of 4.2% (8 cases) and a similar complication rate of 4.2% (8 cases). There were three cases of bleeding that required reoperation. There was one case of cardiac insufficiency and one case of superior vena cava syndrome requiring reoperation. There were no cases of thromboembolism (Table 1).

The isolated mitral valve replacement group comprised 145 patients with an operative mortality rate of 4.1% (6 cases). There were seven cases of bleeding and two cases of perivalvular leak requiring reoperation. There was one case of thromboembolism and one case of cardiac insufficiency (Table 2).

The combined mitral valve replacement and tricuspid anuloplasty group was composed of 58 patients with a 10.3% mortality rate (six cases). Two patients were reoperated on for bleeding, two patients had cardiac insufficiency and one patient developed mediastinitis (Table 3).

Table 2. Results of Mitral Valve Replacement With the Carpentier-Edwards Supraanular Valve in 145 Patients

	Patients (no.)
Operative mortality rate	6 (4.1%)
Perivalvular leak	2 (2)*
Thromboembolism	1
Cardiac insufficiency	1
Miscellaneous	0

*Reoperation.

Pericardial Bioprosthesis

With the problem of the small aortic root in mind, a new pericardial valve was developed with the following aims: 1) improved mounting to eliminate fixation sutures at the commissures, 2) provision of a flexible stent to reduce stress at the commissures and base of the cusps, and 3) better preservation of tissue to improve valve longevity.

Table 1. Results of Aortic Valve Replacement With the Carpentier-Edwards Supraanular Valve in 188 Patients

	Patients (no.)
Operative mortality rate	8 (4.2%)
Perivalvular leak	3 (2)*
Thromboembolism	0
Cardiac insufficiency	1
Miscellaneous	1 (1)*

*Reoperation.

Table 3. Results of Mitral Valve Replacement Plus Tricuspid Anuloplasty With the Carpentier-Edwards Supraanular Valve in 58 Patients

	Patients (no.)
Operative mortality rate	6 (10.3%)
Perivalvular leak	0
Thromboembolism	0
Cardiac insufficiency	2
Miscellaneous	1

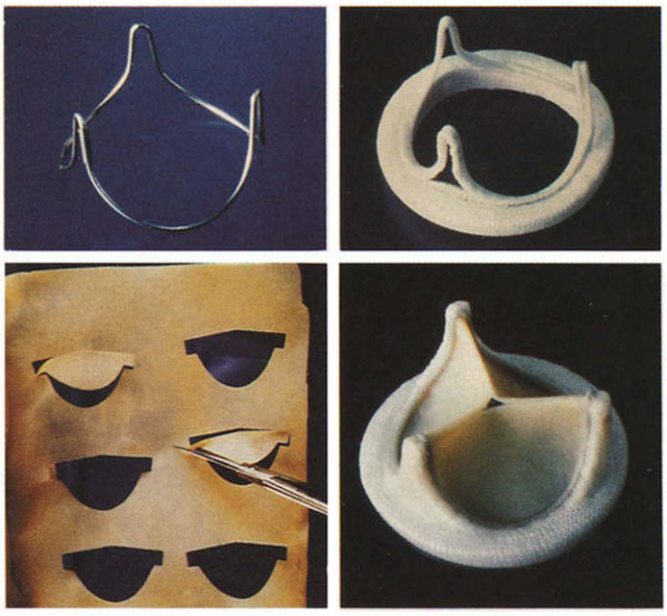


Figure 4. Mounting technique of the pericardial Carpentier-Edwards bioprosthesis (see text).

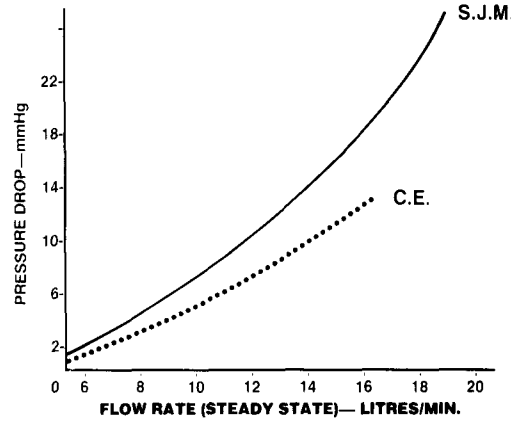
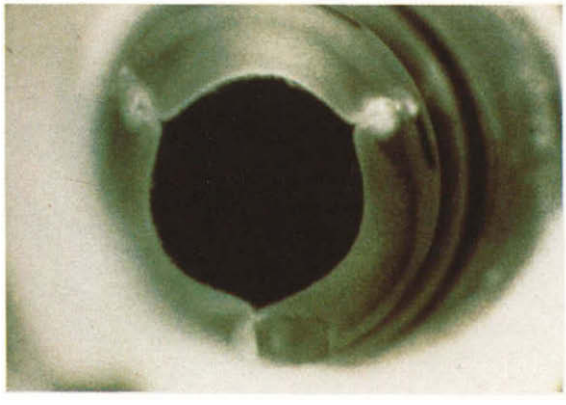


Figure 6. In vitro flow rate of 19 mm St. Jude Medical (S.J.M.) valve and Carpentier-Edwards (C.E.) pericardial valve.

Approach

Improvement in valve design was the object of numerous improvements in the first 10 years. Strut flexibility was an important achievement. However, the use of polypropylene in stent construction led to the phenomenon of strut creep in which the struts became fixed in the valve orifice leading to valve distortion, increased gradients and hemorrhagic anemia. The use of an Elgiloy wire produced a flexible stent, avoiding the creep phenomenon, and improved external/internal ratio by decreasing the thickness of the stent. The stent (Fig. 4, top left) was covered with Teflon as was the sewing ring (Fig. 4, top right). Cusps were cut out of pericardial tissue in appropriate sizes and shapes (Fig. 4, bottom left) and were attached to the stent by sewing them in the supraanular position, except at the commissures where they were drawn into the top of the struts. This procedure eliminated the suture fixation in this area that is present in other valves of the new supraanular type (Fig. 4, bottom right). Comparison with the Ionescu-Shiley current model shows a decrease in strut height and increased internal diameter for valves of the same size. When the valve is compared in a flow tester one can appreciate the greater central orifice (Fig. 5). In vitro testing comparing the valve with the St. Jude Medical valve showed that the in vitro hydrodynamics of the former were better at all flow rates (Fig. 6). In an in vivo study by Cosgrove et al. (5) from the Cleveland Clinic comparing the porcine and pericardial valve, the size 25 pericardial valve demonstrated an advantage in valve orifice area, greatest at low flow, suggesting a more mobile leaflet.

Figure 5. Comparison of Ionescu-Shiley valve (**left**) and Carpentier-Edwards pericardial valve (**right**) in a flow tester showing greater orifice of the pericardial valve. Some distinguishing characteristics of the two valves are: Ionescu-Shiley: 1) rigid stent and orifice, 2) suture at commissure tip, 3) pressure fixed on stent; Carpentier-Edwards: 1) flexible stent and orifice, 2) no commissure suture required, 3) fixed before mounting without pressure.



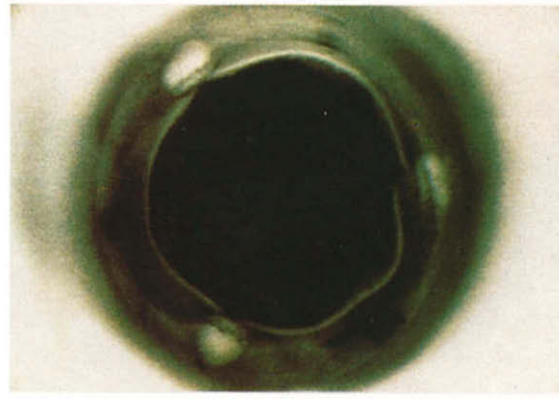


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Table 4. Results of Aortic Valve Replacement With the Carpentier-Edwards Pericardial Valve in 61 Patients

	Patients (no.)
Operative mortality rate	2 (3.2%)
Perivalvular lead	0
Thromboembolism	0
Cardiac insufficiency	0
Miscellaneous	1

Results

The pericardial valve was implanted in 61 patients during the same time period of June 1980 to October 1984 with a mortality rate of 3.2% (2 cases). Three patients were reoperated on for bleeding and one patient developed mediastinitis. There were no cases of perivalvular leak, thromboembolism or cardiac insufficiency (Table 4).

Conclusions

Our current indications for a bioprosthesis are: adults in sinus rhythm, women desiring children, increased risks of anticoagulant agents and patient preference. Contraindications for a bioprosthesis remain in children, patients with renal insufficiency, hyperparathyroidism and early calcification of bioprosthesis (less than 6 years after implantation). Continuing efforts in valve design and preservation are essential if the already excellent results of tissue valves are to be further improved.

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