Bicarbon valve - European multicenter clinical evaluation

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Abstract

Objective: Fifteen collaborating centers in eight countries present their pooled experience with the new Bicarbon® bileaflet valve.

Methods: Between 4/90 and 4/96, 1351 patients, 806 males and 545 females, aged 10 to 83, mean 58.4 ± 12.4, underwent valve implantation. Operations: aortic valve replacement (AVR), 726; mitral valve replacement (MVR), 475; double valve replacement (DVR), 150. Additional procedures: CABG, 211; TV repair, 64; other, 152.

Results: Mortality: 67 early (seven valve related) and 56 late (40 valve related). Valve thrombosis: six obstructive, three non-obstructive; embolism: nine major cerebral, 37 other. Major bleeding: 29. Hemolysis: two clinically significant. Non-structural dysfunction: 24 paravalvular leaks, one leaflet interference. No structural failure! Endocarditis: 24. Reoperation 48: 22 non-structural dysfunctions, 14 endocarditis, seven thrombosis and embolism, five other. Estimated 5-year freedom from valve-related deaths is 97.2% for AVR and 92.4% for MVR; 4-year freedom from valve related deaths for DVR is 90.5%. Mean calculated NYHA improvement is 1.24.

Conclusions: The Bicarbon mechanical prosthesis is well designed, durable, has good hemodynamic features and an acceptably low incidence of complications. © 1998 Elsevier Science B.V. All rights reserved

Keywords: Bicarbon valve; Heart valve replacement; Bileaflet hinged mechanical prosthesis; Results

1. Introduction

Approximately 210,000 patients, worldwide, undergo valve replacement surgery annually [1]. Roughly, two-thirds of this total have mechanical valves implanted.

Accordingly, there is much ongoing investigation related to improving prosthetic valve construction. The development of mechanical valves has been marked by design changes aimed at enhancing safety and efficiency, whilst minimizing deleterious features and complications. Consequently, the bileaflet model, first implanted clinically in 1977, has emerged as today’s prosthesis of preference in many centers [2–6]. The Bicarbon® bileaflet valve (Sorin...
Biomedica, Saluggia, Italy) was introduced in 1990, having been designed to improve durability and hemodynamics and reduce thrombogenicity. Its design is based on two pyrolytic carbon leaflets hinged on a titanium alloy housing coated with a thin carbon layer (Carbofilm®). A clinical investigation trial was programmed to include the experience of 15 predesignated centers** with the object of assessing whether the design criteria have been realized. The collaborating investigative centers pooled the accumulated data related to this new valve archetype in order to report their combined results encompassing 1351 patients undergoing valve implantation surgery over a 6-year period.

2. Materials and methods

Between April 1990 and April 1996, 1351 patients, 806 males and 545 females, aged 10–83 years, mean age 58.4 ± 12.4 years, underwent implantation of one or more Bicarbon valves. All patients included in this study met the accepted criteria for mechanical valve replacement. Those who had implantations of Bicarbon plus another valve type were excluded from the project. Preoperative NYHA classification distribution: 5.2% Class I, 30.9% Class II, 52.9% Class III and 11.0% Class IV.

The etiology of the valve disease in the patient population studied, multiple in some instances, is shown in Table 1. Aortic valve replacement (AVR) was carried out in 726 patients, mitral valve replacement (MVR) in 475 and double valve replacement (DVR) in 150. Valve size distribution was 19–25 mm for AVR and 25–31 mm for MVR in 93% of the patients. Concomitant surgery was performed in 427 instances and comprised CABG in 211 patients (15.6%) tricuspid annuloplasty in 64 (4.7%) and various other procedures in 152 (11.2%). The additional procedures carried out are detailed in Table 2.

Anticoagulants were advised routinely, but there was no uniform protocol; each center followed its usual method. Recommended INR targets were 2.5–3.0 for AVR and 3.0–4.0 for MVR and DVR.

Mortality and morbidity were reported according to established international guidelines [7]. Any event occurring within 30 days of surgery was designated ‘early’. All subsequent events were classified ‘late’.

![Fig. 1. Survival curves including early deaths by implant group.](https://academic.oup.com/ejcts/article-abstract/13/6/685/419051)

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Etiology</th>
<th>AVR n (%)</th>
<th>MVR n (%)</th>
<th>DVR n (%)</th>
<th>Overall n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic</td>
<td>208 (28.7)</td>
<td>200 (42.1)</td>
<td>78 (52)</td>
<td>486 (36.0)</td>
<td></td>
</tr>
<tr>
<td>Degenerative (calcific)</td>
<td>189 (26.3)</td>
<td>0</td>
<td>10 (6.7)</td>
<td>199 (14.7)</td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td>137 (18.9)</td>
<td>9 (1.9)</td>
<td>3 (2.0)</td>
<td>149 (11.0)</td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>0</td>
<td>28 (5.9)</td>
<td>2 (1.2)</td>
<td>30 (2.2)</td>
<td></td>
</tr>
<tr>
<td>Myxomatous</td>
<td>16 (2.2)</td>
<td>55 (11.6)</td>
<td>10 (6.7)</td>
<td>81 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Endocarditic</td>
<td>39 (5.4)</td>
<td>34 (7.2)</td>
<td>15 (10)</td>
<td>88 (6.52)</td>
<td></td>
</tr>
<tr>
<td>Prosthetic dysfunction</td>
<td>51 (7.0)</td>
<td>83 (17.5)</td>
<td>35 (23.3)</td>
<td>169 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>50 (6.7)</td>
<td>50 (10.5)</td>
<td>6 (4.0)</td>
<td>106 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>40 (5.5)</td>
<td>20 (4.2)</td>
<td>10 (6.7)</td>
<td>70 (5.0)</td>
<td></td>
</tr>
</tbody>
</table>

Numbers refer to patients.
The patients discharged from hospital had follow-up examinations at postoperative month 1, 3, 6 and 12 and yearly thereafter. Follow-up closure date was August 1996. Relevant data was obtained by direct physician contact in most cases. Where this was not possible telephone communication or questionnaires were substituted, but this was discouraged. Completeness of follow-up was 98%, 25 patients being untraceable. Mean follow-up was 2.21 ± 1.48 years.

Estimated survival and freedom from event rates were calculated by the Kaplan–Meyer method (confidence limits 95%) [8]. Linearized complication rates were calculated as the number of events per 100 patient-years (%/patient-year). The χ²-test was used for statistical comparison of NYHA class groups. All statistical computations were performed with the PATS (Dendrite Clinical System, Portland, OR) software.

### 3. Results

#### 3.1. Survival and mortality

Thirteen patients (1%) died in the operating room; there were 54 additional early deaths: seven valve related (Table 3). A total of 1284 patients survived surgery and were discharged from hospital. Twenty-five patients were lost to follow-up. Accordingly, 1203 became available for continuing follow-up. There were 56 (4.4%) late deaths, 40 valve related. The cause of death is shown in Table 3.

Estimated survival curves by implant site, including early deaths, may be observed in Fig. 1. It is evident that AVR patients have superior results as compared with MVR and DVR. Overall freedom from death at 5 years is 87.4 ± 1.2%. Fig. 2 depicts freedom from early and late valve related deaths. The best results occurred following AVR, 97.2 ± 1.0% at 5 years. Survival after MVR and DVR was less, 92.4 ± 1.8% and 90.5 ± 3.7% at 5 and 4 years, respectively. Overall freedom from valve related mortality at 5 years is 94.7 ± 1.0%.

The functional capacity of the survivors improved significantly. Whereas the majority of the patients were in Class III or IV before the operation, very few failed to improve to Class I or II postoperatively (Fig. 3). The mean calculated NYHA class improvement is 1.24 (P < 0.05).

<table>
<thead>
<tr>
<th>Concomitant procedures</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>211 (15.6)</td>
</tr>
<tr>
<td>Tricuspid annuloplasty</td>
<td>64 (4.7)</td>
</tr>
<tr>
<td>Aortic root replacement</td>
<td>23 (1.7)</td>
</tr>
<tr>
<td>Aortic root enlargement</td>
<td>14 (1.0)</td>
</tr>
<tr>
<td>Permanent pacing leads</td>
<td>17 (1.2)</td>
</tr>
<tr>
<td>Repair septal defect</td>
<td>10 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td>88 (6.6)</td>
</tr>
</tbody>
</table>

Table 2

![Fig. 2. Freedom from valve-related deaths by implant group.](https://academic.oup.com/ejcts/article-abstract/13/6/685/419051)
3.2. Morbidity

3.2.1. Valve thrombosis

Any thrombosis detected on a valve is included. Nine events occurred, of which six were obstructive and three non-obstructive. Three instances were early events (one obstructive AVR, two non-obstructive MVR) and six cases were late events (four obstructive MVR, one obstructive DVR and one non-obstructive DVR). The aortic obstructive thrombosis manifested itself 23 days after surgery, the patient having refused anticoagulation treatment. She was successfully reoperated and is currently alive. The DVR patient had native valve replacement for endocarditis; after 37 days an obstructive thrombosis occurred. He was reoperated and remains alive. The remaining four obstructive events occurred in MVR patients (from 165 to 394 days after surgery) with imbalanced anticoagulation therapy. Three were reoperated and are alive. The remaining patient died. The three non-obstructive thromboses were detected by echo-Doppler investigation as thrombotic pedicles on the inflow side of the prosthesis. In no case was leaflet entrapment observed. Two instances were early events (MVR), the patients were reoperated and are still alive. The remaining DVR patient was successfully treated by thrombolysis. The overall freedom from valve thrombosis at 5 years is 99.2 ± 0.3%. Freedom from valve thrombosis by implant group is 99.8 ± 0.2% for AVR at 5 years, 98.4 ± 0.6% for MVR at 5 years, 98.4 ± 1.1% for DVR at 4 years (Fig. 4). Linearized rates are reported in Table 4.

3.2.2. Embolism

All events were included, minor with no residua or major with permanent residual deficit. There were 46 events, 18 AVR, 24 MVR, four DVR. Nine patients (one AVR, eight MVR) had major cerebral emboli with extensive brain damage; five of these died (two hospital deaths and three late deaths); the remaining four patients survived the event. Thirty-seven patients suffered other embolic events (17 AVR, 16 MVR, four DVR). These other events include early and late cerebral transient ischemic events without residual deficit and any other peripheral embolic event including myocardial infarction. There were four other

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Early (54)</th>
<th>Late (56)</th>
<th>Total (110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve related</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embolism - major cerebral</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Embolism - other</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Anticoag. related bleeding</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Sudden death</td>
<td>13</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>Unknown/other</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>40</td>
<td>87</td>
</tr>
<tr>
<td>Non valve related</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Cardiac</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Multi organ failure</td>
<td>9</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Renal failure</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Post-op. Bleeding</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Other non cardiac</td>
<td>18</td>
<td>8</td>
<td>26</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>16</td>
<td>63</td>
</tr>
</tbody>
</table>

**Table 3**

Postoperative mortality

**Fig. 3.** Pre-and postoperative NYHA classification.
embolic fatal events: three in-hospital deaths (two MVR, one DVR after myocardial infarction), one late death (a DVR patient with severe paravalvular leak died from cardiac failure after having developed a peripheral embolism). The remaining 28 patients were managed by medical treatment and are currently alive. Freedom from embolic events by implant group is 96.4 ± 0.9% for AVR at 5 years, 93.4 ± 1.4% for MVR at 5 years and 91.5 ± 6.1% for DVR at 4 years (Fig. 5). Linearized rates are reported in Table 4.

3.2.3. Hemolysis (not associated with paravalvular leak)

Raised LDH serum levels have also been reported with this mechanical prosthesis [9]. However, only two clinically significant hemolysis related complications, without paravalvular leaks, were reported in our whole series, both following AVR. Both patients are alive and no reoperation was needed as their hemolysis was no more than moderate LDH < 600, haptoglobin < 10. Linearized rates are reported in Table 4.

3.2.4. Non-structural dysfunction

Twenty-five events were listed: 24 paravalvular leaks and one leaflet impingement by residual chorda. Distribution by valve position was three AVR, 16 MVR and six DVR. The leaflet impingement was in the mitral prosthesis in a DVR patient and required reoperation. Twenty-one additional patients, with hemodynamically significant leak and/or severe hemolysis, were reoperated for correction of the leak. All reoperated patients are long-term survivors. Overall freedom from non-structural dysfunction is 96.7 ± 0.8% at 5 years. Linearized rates are reported in Table 4.

3.2.5. Structural failure

No mechanical or structural failure, whatsoever, has been reported to date.

3.2.6. Bleeding

We itemized all major episodes requiring hospitalization. Twenty-nine episodes were reported: 20 AVR (three early), seven MVR (one early), two DVR. Three MVR patients died late from cerebral hemorrhage. All others survived the event. Freedom (5 years) from bleeding was 95.5 ± 1.0% (overall), 93.8 ± 1.8% for AVR, 97.0 ± 1.3% for MVR and 97.8 ± 1.6% (4 years) for DVR. Linearized rates are reported in Table 4.

3.2.7. Endocarditis

All events, primary or recurring episodes related to preoperative valve infection were included. There were 24 cases (20 primary and four recurrent), 11 AVR, 11 MVR and two DVR. Fourteen cases required reoperation. AVR: three patients alive after medical treatment, one died in hospital and seven were reoperated, of which six are still alive and one died late. MVR: two patients alive after medical treatment, one died in hospital and three died late from sepsis while five were reoperated; three are still alive, one
died during the surgery and one postoperatively. DVR: two patients reoperated; one is still alive and one early death.

Five-year overall freedom from infective endocarditis is 90.9 ± 4.6%. For AVR the figure is 97.7 ± 0.8%, for MVR 90.4 ± 4.7% and for DVR 98.5 ± 1.1% (4 years). Linearized rates are reported in Table 4.

3.2.8. Reoperation

Reoperation was performed in 48 patients: AVR 14, MVR 25, DVR nine. One MVR patient died during the operation, two died in hospital (one MVR and one DVR) and two died late (one AVR, one DVR) (Table 5). The overall estimated 5 years freedom from reoperation is 95.5 ± 0.7%. Fig. 6 shows freedom from reoperation for each valve group: 97.8 ± 0.6% for AVR at 5 years, 93.8 ± 1.2% for MVR at 5 years and 92.2 ± 2.6% for DVR at 4 years (Fig. 5). Linearized rates are reported in Table 4.

4. Discussion

With the advent of extracorporeal circulation for open heart surgery and direct vision of the interior of the human heart, it became obvious that complete valve replacement would be required in many instances. Already in the 1950s, design and manufacture of artificial heart valve substitutes posed a challenge to surgeons and engineers alike. Harken in 1960 and Starr in 1961 initially achieved clinical success with ball and caged valves [10,11]. Subsequently, various models of monodisc valves were developed [12–17]. Most performed unsatisfactorily and were withdrawn from clinical use. The bileaflet principle, originally mooted by Gott and Daggett in 1964, had many theoretical advantages [18]. Kalke et al. refined the concept but were unable to overcome the structural malfunction and thrombogenic problems associated with this type of valve [19]. In 1977,
having modified the design and substituting pyrolitic carbon leaflets and housing, the St. Jude Medical valve was introduced for patient evaluation [20]. Intermediate and long-term results established the clinical domination of this model [5,21,22] and provoked competitors, working on similar principles, to produce superior, more efficient archetypes with the object of offering the patient a better and safer prosthesis.

The Bicarbon valve, a third generation bileaflet mechanical prosthesis, has many unique design features aimed at raising the merit of such appliances. The curved leaflets are made from solid pyrolitic carbon deposited onto a graphite core; the streamlined metal housing is made from titanium alloy coated with a thin film of pyrolitic carbon. The innovative hinge design permits movement of the leaflets by rolling and not by sliding, usual in other models, exposing all the hinge surfaces to continuous washout throughout the cardiac cycle. The leaflets have been geometrically designed to produce balanced partition blood flow through the valve orifice, resulting in less turbulent, more physiologic streaming and lower overall Reynolds shear stress levels [23]. The valve has a composite, fabric biocompatible sewing ring coated, too, with Carbofilm so that all the surfaces exposed to the blood are covered with non-thrombogenic material [24]. The housing is rotatable within the sewing ring. The net result was a potentially durable creation with minimal thrombogenicity and hemolysis and improved hemodynamic performance.

To evaluate the clinical performance of the Bicarbon a multicenter European prospective trial was programmed. The aim was to register a basic core of 1200–1500 implants in a central data base and to continuously follow-up on this cohort over as long a period as possible. The 15 selected centers committed to complete follow-up and to provision of accurate, updated information as and when requested. Such a multicenter investigation in predesignated locations has the distinct advantage of rapidly achieving significant numbers in heterogeneous patient populations. The input has the distinct advantage of rapidly achieving significant numbers in heterogeneous patient populations. The 15 selected centers committed to complete follow-up and to provision of accurate, updated information as and when requested. Such a multicenter investigation in predesignated locations has the distinct advantage of rapidly achieving significant numbers in heterogeneous patient populations. The input has the distinct advantage of rapidly achieving significant numbers in heterogeneous patient populations. The input has the distinct advantage of rapidly achieving significant numbers in heterogeneous patient populations.

The overall mortality, early and late, in our patients is marginally better than that occurring in other somewhat smaller series reporting results with Bileaflet valves [2,4–6,21,22]. Overall freedom from valve related death at 5 years is gratifyingly high (Fig. 2).

Five of the nine thrombotic events, one AVR and four MVR, were related to inadequate anticoagulant therapy. As with other bileaflets, patients require lifelong, well-controlled anticoagulation. In the mitral area, neglect of such therapy may prove particularly hazardous. Lysis of the thrombus may be attempted in carefully chosen cases and was effective in one of our patients. If this method fails reoperation is indicated. In our series surgery was successful in all seven cases so managed. The only patient who died was not referred for either lytic or operative treatment. The overall freedom from valve thrombosis is very satisfactory (Fig. 4). Of the 46 embolic events reported, nine were major cerebral emboli, of which five died. The remaining four patients were left with significant neurological deficit. The incidence of thromboembolic events occurring in patients with Bicarbon valves corresponds with those reported for other currently used bileaflet valves – St. Jude Medical and CarboMedics [2,4,6,21,22]. Linearized rates for the above complications are very similar to ours even though early events were excluded from their calculations [4]. Recently introduced trials of very early lytic therapy in patients with thrombotic major cerebrovascular accidents offer the hope of significant improvement in the outcome of this dreaded complication. Additional improvements in Bileaflet valve design need to be developed to further minimize this problem.

All mechanical valves are known to promote subclinical hemolysis, easily compensated for by healthy bone marrow [25]. Clinically significant hemolysis is not a major problem with normally functioning bileaflet prostheses. Decompen- sated chronic hemolytic anemia is rare and is most commonly associated with accelerated destruction of erythrocytes caused by chronic paravalvular leak. Reoperation may be necessary if hemolysis remains severe enough to require repeated transfusions over a prolonged period, despite medical therapy. Hemolysis is not a serious problem with the Bicarbon valve, the multicenter study experience producing only two instances of clinically significant hemolysis, of moderate degree only, in patients without paravalvular leak. Di Salvo and Walesby reported mildly elevated mean lactic acid dehydrogenase levels and normal haptoglobin parameters in patients with Bicarbon prostheses [9].

Non-structural dysfunction is for practical purposes a complication not caused by intrinsic valve malfunction. Paravalvular leaks result mainly from a combination of two factors: heavily calcified, distorted native valve annuli and deficiencies in suturing technique. Twenty-two of the 25 of the cases in our series were reoperated and all survived (Table 5).

No structural or mechanical failure has been reported in our cumulative experience! This finding confirms the strength and durability of the materials used for both the housing and the disc and the efficacy of the hinge mechanism.
All major bleeds were anticoagulant related. Inevitably, in a large patient group treated at home with anticoagulants aimed at achieving INR levels of 2.5 to 4.0, isolated incidences of serious bleeding must be expected. Three late deaths from this complication succumbed from extensive intracranial hemorrhage.

The diagnosis of infective endocarditis was clinical in some patients, blood cultures being negative. Aortic and mitral valves were equally affected and 14 cases required reoperation. This manifestation remains a serious complication with significant mortality. Similar results have been reported in other large series of CarboMedics and St. Jude Medical bileaflet valve implantations [14,21].

Results of all reoperations, irrespective of cause, in 48 patients in this series were excellent except for those with infective endocarditis where mortality was 28.5% contrasted with 3% for those reoperated for other reasons. Hemodynamic performance of the Bicarbon has been reported previously using non-invasive techniques [26–29]. These investigations showed good hemodynamics for Bicarbon valves in the aortic and mitral positions, comparing favorably with the St. Jude Medical prostheses.

5. Conclusions

The new Bicarbon model appears to have fulfilled most of its expectations. Its hemodynamic profile is at least as good, if not better, than other bileaflet prostheses. No structural failure has been reported to date. Complications are acceptably low, comparable with similar type valves.

References