Performance at 10 years of the CarboMedics 'Top-Hat' valve.
Postclamping time is a predictor of mortality

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Abstract

Objective: The CarboMedics 'Top-Hat' supraannular prosthesis was designed to permit the implantation of a larger prosthesis. We evaluated the outcome at 10 years in patients with this prosthesis. Methods: Between June 1993 and May 2001, 269 patients (average age, 63.9 years) received a CarboMedics 'Top-Hat' supraannular aortic prosthesis. Primary valve replacement was performed on 203 patients (75.5%) and repeat valve replacement on 66 (24.5%). The duration of myocardial ischemia was 70.2 ± 31.4 min, cardiopulmonary bypass 96.1 ± 48.3 min, and postclamping time (time between release of aortic clamp and the end of extracorporeal circulation) 22.1 ± 41.3 min. The mean follow-up was 82.3 ± 17.8 months. Follow-up was 97.6% complete. Results: The hospital mortality was 5.9%. It was 1% when the duration of postclamping time was <15 min, 2.8% between 15 and 29 min, 13.2% between 30 and 44 min, and 26.9% >44 min. In the multivariate analysis, postclamping time, urgent surgery, and body mass index were statistically significant risk factors for hospital mortality. The late mortality was 17.1%. Cardiac-related mortality showed a linearized rate of 18.1% per 1000 patients-year. The Kaplan—Meier estimates for cardiac-related mortality was 75.0% at 10 years. Postclamping time, aortic valve gradient, age over 70 years, and BMI were statistically significant risk factors for cardiac-related late mortality. The incidence of paravalvular leak in the 'Top-Hat' aortic prosthesis was 1.7% per 1000 patients-year. Conclusions: Using the CarboMedics supraannular prosthesis allows implantation of a larger prosthesis without increasing valve-related complications. Postclamping time appears as a strong predictor of both hospital mortality and late cardiac-related death.

1. Introduction

The CarboMedics 'Top-Hat' supraannular prosthesis (introduced in 1993) is a standard valve in which the cuff has been transferred to the inflow level of the valve. As a result, the prosthesis sits above the annulus rather than within it. The valve housing protrudes into the aortic root like a Top-Hat. The satisfactory short- and mid-term clinical performance of the CarboMedics valve has been documented in single-center and multicenter studies [1—3]. In a recent multicenter study in which five institutions pooled their clinical experiences, early outcomes of the 'Top-Hat' valve in this heterogeneous population were similar to those of the standard CarboMedics prosthesis [4]. However, long-term studies in homogeneous clinical series are necessary to confirm these early good results. We have evaluated the outcome at 10 years in patients who received CarboMedics 'Top-Hat' prosthesis at our institution. Those factors that influence early and late results were determined.

2. Materials and methods

Between June 1993 and May 2001, 269 consecutive patients underwent aortic valve replacement with CarboMedics 'Top-Hat' supraannular prosthesis in our institution. During this period, 1648 aortic prostheses were implanted (biological prostheses 580 [35.2%], mechanical prostheses 1068 [64.8%]). Mechanical prostheses included standard CarboMedics in 472 cases, CarboMedics 'Top-Hat' in 269, St. Jude in 180, Sorin in 90, and others in 57.

The group of patients in whom CarboMedics 'Top-Hat' prosthesis was implanted comprised 143 women (53.2%) and 126 men (46.8%) with a mean age of 63.9 years (range, 28—81 years). Fifty patients (18.5%) were in New York Heart Association (NYHA) functional class II, 182 (67.7%) were in class III, and 37 (13.8%) were in class IV. Primary valve replacement was performed on 203 patients (75.5%) and...
repeat valve replacement on 66 (24.5%). A total of 181 patients (67.3%) were in sinus rhythm, 84 (31.2%) had complete arrhythmia caused by atrial fibrillation, and 4 had a pacemaker (1.5%). The mean body surface area was 1.68 ± 0.17 m² (range, 1.28—2.12 m²). The body surface area was lower than 1.60 m² in 90 patients (33.5%), between 1.61 and 1.70 m² in 53 (19.7%), and greater than 1.71 m² in 126 (46.8%).

All patients were investigated preoperatively by means of echo-Doppler, in association with hemodynamic and coronary angiographic examinations in 219 patients (81.4%). The left ventricular ejection fraction calculated by the hemodynamic study (n = 203) (in 16 patients left ventriculography was not performed) or the echocardiographic study (n = 66) ranged between 15% and 78% (average ejection fraction, 50.2 ± 11.7%). The left ventricular ejection fraction was lower than 30% in 17 patients (6.3%).

After completion of preoperative studies, isolated aortic disease was diagnosed in 184 patients (68.4%), aortic and mitral lesions were diagnosed in 70 patients (26%), aortic and tricuspid lesions were diagnosed in 1 patient (0.4%), and triple valve disease was diagnosed in 14 patients (5.2%). Thirty-nine patients (14.5%) had concomitant coronary artery disease and four patients (1.5%) had aneurysmatic dilatation of the ascending aorta.

The cause of the aortic valvulopathy was degenerative or calcific in 142 patients (52.8%), rheumatic in 80 patients (29.7%), active infectious endocarditis in 7 patients (2.6%), and related to previous aortic valve prosthesis in 40 patients (14.9%). In patients with a previously placed prosthesis, operations were performed following structural deterioration of the bioprosthesis in 31 cases, nonstructural dysfunction in 3, prosthetic thrombosis in 1, prosthetic endocarditis in 1, and elective bioprosthesis explantation due to structural deterioration of a mitral bioprosthesis in 4. Among the 204 patients having primary valve replacement, the aortic lesion was pure stenosis or a double lesion with preponderance of stenosis in 163 patients (79.9%) (average aortic valve gradient, 70 ± 28.2 mmHg) and pure insufficiency in 41 patients (20.1%).

### 2.1. Surgery

The operation was performed with standard cardiopulmonary bypass and moderate hypothermia (27—30°C). Myocardial protection was achieved with intermittent blood cardioplegia delivered retrograde, antegrade, or both ways. The cold blood was continuously perfused retrogradely. After aortic valve resection and decalcification of the valve root, both the standard sizer and the supraannular sizer were used in 215 patients (79.9%). The 'Top-Hat' aortic prosthesis was implanted in the supraannular position using non-erecting pledged supported sutures. When implantation of a mechanical prosthesis was indicated (age, need of anticoagulation, or other indications), decision regarding the prosthetic device, including CarboMedics standard, supraannular 'Top-Hat' or other models was left at the discretion of the attending surgeon.

Seventy-three 19-mm prostheses (27.1%), one hundred twenty-nine 21-mm prostheses (47.9%), and sixty-seven 23-mm prostheses (24.9%) were implanted. Seventy patients had associated mitral valve replacement with the CarboMedics standard or OptiForm prosthesis. The posterior leaflet was preserved in all cases, together with the anterior leaflet in 41. Repair of the tricuspid valve (Segmental or De Vega’s annuloplasty) was performed in 15 patients. Associated myocardial revascularization with an average of 1.8 grafts per patient was performed in 39 patients. The ascending aorta was substituted by a tubular graft in three patients, and in one patient a plicature was performed.

The duration of myocardial ischemia was 70.2 ± 31.4 min (range, 28—125 min), cardiopulmonary bypass 96.1 ± 48.3 min (range, 34—369 min), and postclamping time 22.1 ± 41.3 min (range, 2—127 min). Postclamping time was defined as the interval between the release of aortic clamps and the end of extracorporeal circulation. Elective operations were performed in 257 patients (95.5%) and urgent operations in 12 patients (4.5%).

Patients were maintained on a regimen of Coumadin (crystalline warfarin sodium), with a recommended international normalized ratio ranging between 2.5 and 3.5. The ratio was modified according to the individual requirements of each patient during follow-up.

### 2.2. Follow-up

The surviving patients were followed up directly in our outpatient clinic at least once a year during the first postoperative year. Echocardiographic studies were performed at the time of discharge from the hospital and at follow-up. Patients from other reference centers were followed up by their cardiologists. The follow-up data were procured over a 6-month period between May 2004 and October 2004 so that a minimum follow-up period of 3 years was ensured. Information on the 253 patients who were discharged alive from the hospital was obtained through visits in our outpatient clinic in 113 patients (44.7%), contact by telephone in 49 patients (19.4%), contact with the admission department and clinical documentation of the reference hospitals in 37 patients (14.6%), and contact with the reference cardiologist in 25 patients (9.9%). When follow-up was not possible, information on vital status (alive or death) was obtained through the Social Security database (n = 23). Six patients were lost to follow-up. The completeness of follow-up during the closing interval was 97.6%. The mean follow-up was 82.3 ± 17.8 months, ranging from 3 to 11 years. Cumulative follow-up was 1712.7 patient-years.

### 2.3. Statistical analysis

The Patient Analysis and Tracking System database, version 06.02.03 (Dendrite Clinical Systems Inc., Portland, OR, USA), was used. All continuous variables are presented as mean ± standard deviation. Statistical comparison of clinical data was made using the chi-square (χ²) test or Fisher’s exact probability test if any expected cell had less than five cases. Statistical significance was set at p < 0.05. Survival curves were constructed using the Kaplan—Meier estimates and compared with the log-rank test. Factors influencing hospital mortality (i.e., death before 30 days after surgery) were analyzed using multiple logistic regression; its results are expressed as odds ratio (OR) and 95% confidence interval (CI).
Proportional hazards regression (Cox) was used to study the influence of covariates on late mortality, including valve-related mortality, complications, and reoperation; we present its results as hazard ratios. Statistical analyses were performed with the Stata 8/SE (Stata Corporation, College Station, TX, USA) computer program. Patient-prosthesis mismatch was defined as a prosthetic effective orifice area divided by a body surface area lower of less than 0.75 cm$^2$/m$^2$.

3. Results

In the 215 patients in which the orifice area was measured, the mean area was $18.7 \pm 2.3$ mm with the standard sizer compared with $20.9 \pm 2.4$ mm with the supraannular sizer ($p = 0.002$). Echocardiographic studies performed at hospital discharge or during the first follow-up year showed a mean effective orifice area of $1.0 \pm 0.2$ cm$^2$ for the 19-mm prosthesis, $1.4 \pm 0.2$ cm$^2$ for the 21-mm prosthesis, and $1.6 \pm 0.5$ cm$^2$ for the 23-mm prosthesis. Mean body surface areas for the 19-, 21-, and 23-mm prostheses were $1.62 \pm 0.15$ m$^2$, $1.67 \pm 0.15$ m$^2$, and $1.79 \pm 0.16$ m$^2$, respectively. Patient-prosthesis mismatch was documented in 97.3% of patients (71/73) with 19-mm prosthesis, in 54.3% of patients (70/129) with 21-mm prosthesis, and in 3% of patients (2/67) with 23-mm prosthesis. Patients receiving a 19-mm prosthesis were significantly older (mean age, 67.8 ± 10.0 years) than those with a 21-mm prosthesis (63.4 ± 9.0 years) and a 23-mm prosthesis (61.5 ± 9.2 years) ($p < 0.05$).

3.1. Hospital and late mortality

There were 16 hospital deaths with a total mortality of 5.9%. The causes of hospital mortality were cardiac failure ($n = 10$), mediastinitis ($n = 2$), thromboembolism ($n = 1$), hemorrhage ($n = 1$), sepsis ($n = 1$), and arrhythmia ($n = 1$). There were nine hospital deaths in the isolated aortic prosthetic replacement group (9/184; 4.9%) and seven deaths in the combined aortic and mitral and/or tricuspid valve replacement (7/85; 8.2%) ($p = \text{NS}$). The hospital mortality was significantly higher in patients treated with a 19-mm prosthesis (10.9%) compared with patients treated with a 21-mm (3.6%) and 23-mm (3.6%) prostheses ($p < 0.05$). On the other hand, hospital mortality was similar in patients with and without patient-prosthesis mismatch (7.7% [11/143] vs 4% [5/126]; $p = \text{NS}$). Significant predictors of hospital mortality were urgent surgery (OR = 5.85; $p = 0.02$), diabetes mellitus (OR = 3.39, $p = 0.03$), body mass index (BMI) (OR = 1.13 for each kg/m$^2$; $p = 0.025$), preoperative NYHA (OR = 3.16 for each class; $p < 0.001$), duration of myocardial ischemia (OR = 1.18 for each 10 min; $p = 0.01$), duration of cardiopulmonary bypass (OR = 1.15 for each 10 min; $p < 0.001$), and duration of postclamping time (OR = 1.33 for each 10 min; $p < 0.001$). Primary or repeat valve replacement, atrial fibrillation, left ventricular ejection fraction, aortic valve gradient, and associated surgical procedures had no effect on early clinical outcome. A predictive model for hospital mortality obtained by stepwise logistic regression analysis is shown in Table 1. Urgent surgery, BMI, and postclamping time were independent predictors of hospital mortality. Table 2 shows that hospital mortality increased significantly in association with the duration of the postclamping time. Fig. 1 illustrates the probability of death related to the duration of the postclamping time.

There were 46 deaths among 253 perioperative survivors (late mortality, 18.2%). The actuarial survival was 98.4% at 1 year, 95.8% at 5 years, and 64.3% at 10 years (Fig. 2). Causes of death were cardiac in 27 patients with a linearized mortality rate of 18.1% per 1000 patients-year. Cardiac deaths included terminal heart failure ($n = 8$), hemorrhage ($n = 4$), thromboembolism ($n = 2$), mediastinitis ($n = 2$), dehiscence of a mitral prosthesis ($n = 1$), prosthetic endocarditis treated mediically ($n = 1$), myocardial infarction ($n = 1$), and unknown ($n = 8$). The actuarial survival curve for cardiac-related death was 99.2% at 1 year, 91.9% at 5 years, and 75.0% at 10 years (Fig. 3). Risk factors for cardiac-related late death were age (hazard ratio (HR) = 1.06 for each year, 95% CI 1.01—1.17; $p = 0.031$), NYHA (HR = 1.99 for each class, 95% CI 1.04—3.81; $p = 0.037$), aortic gradient (HR = 0.98 for each mmHg, 95% CI 0.96—1.00; $p = 0.036$), duration of myocardial ischemia (HR = 1.13 for each 10 min, 95% CI 0.99—1.28; $p = 0.065$), duration of cardiopulmonary bypass (HR = 1.09 for each 10 min, 95% CI 1.02—1.16; $p < 0.008$), and duration of postclamping time (HR = 1.14 for each 10 min, 95% CI 1.03—1.26; $p < 0.012$). Cardiac-related late mortality was 12.3% (8/63) in patients treated with a 19-mm prosthesis, 9% (11/122) in those treated with a 21-mm prosthesis, and 12.1% in those treated with a 23-mm prosthesis ($p = \text{NS}$). Cardiac-related late mortality was also similar in patients with and without patient-prosthesis mismatch (11.8% [13/132] vs 11.6% [14/121]; $p = \text{NS}$). A predictive model for cardiac-related late mortality obtained by stepwise logistic regression analysis is shown in Table 3. Aortic valve gradient, age over 70 years, and duration of postclamping time were independent risk factors for death of cardiac cause.

Late mortality of noncardiac origin was 7.5% ($n = 19$) with a linearized mortality rate of 13.7% per 1000 patients-year. Causes of death were neoplasms in 9 patients and other causes in 10. The actuarial survival curve for late mortality of

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% confidence interval)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent surgery</td>
<td>9.93 (2.09—47.17)</td>
<td>0.004</td>
</tr>
<tr>
<td>Postclamping time (each 10 min)</td>
<td>1.34 (1.14—1.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (each kg/m$^2$)</td>
<td>1.11 (0.98—1.25)</td>
<td>0.109</td>
</tr>
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Area under the ROC curve = 0.8468.
noncardiac origin was 99.2% at 1 year, 93.4% at 5 years, and 85.6% at 10 years (Fig. 4). Age was the only predictor of mortality (HR = 1.10 for each year, 95% CI 1.03–1.18; \( p = 0.007 \)).

### 3.2. Reoperations

Of the 253 patients who survived the operation, 16 required a reoperation (6.3%) with a linearized reoperation rate of 10.1% per 1000 patients-year. Indications for surgery of the aortic valve included dehiscence of a prosthesis and aneurysm of the ascending aorta in one case, dehiscence of a prostheses and hemolysis in one, and dehiscence of aortic and mitral prosthesis in one. In the remaining 13 patients, reoperations were unrelated to the aortic valve. Indications of surgery included dehiscence of a mitral prosthesis (\( n = 5 \)), progression of mitral regurgitation (\( n = 2 \)), ischemic mitral disease (\( n = 1 \)), occlusion of coronary grafts (\( n = 1 \)), progression of coronary artery disease (\( n = 1 \)), aneurysm of the ascending aorta (\( n = 1 \)), and cardiogenic shock that required ventricular assistance and heart transplantation 24 h after aortic valve replacement (\( n = 1 \)). The actuarial survival curve free from reoperation was 98.4% at 1 year, 97.4% at 5 years, and 70.0% at 10 years.

During the follow-up, one patient had aortic prosthesis-related endocarditis that was treated medically and died, and three patients (1.1%) had dehiscence of the aortic prosthesis and were reoperated, with a linearized incidence of paravalvular leak of 1.7% per 1000 patients-year. Twenty-nine patients (10.8%) had major hemorrhagic episodes that required blood transfusion and/or operation. Hemorrhage was the cause of death in four patients. Ten thromboembolic episodes were recorded (central without sequelae in four, central with sequelae in three, and peripheral in three). Thromboembolism was the cause of death in two patients. The actuarial curve free from thromboembolism was 98.0 ± 0.7% at 1 year, 95.2 ± 1.5% at 5 years, and 94.2 ± 2.1% at 10 years. The actuarial curve free from valve-related complications and mortality was 89.0 ± 1.9% at 1 year, 68.4 ± 4.3% at 5 years, and 36.6 ± 8.7% at 10 years.

At the follow-up closing date, 191 survivors were in NYHA functional class I or II (95.0%), seven survivors were in class III (3.5%), and three survivors were in class IV (1.5%).

### 4. Discussion

The CarboMedics heart valve was introduced for clinical use in 1986 with the peculiarity of the rotatability of the valve after implantation. The usefulness of this novelty in the 80s has been extensively demonstrated in the clinical experience with this prosthesis [5] and outcomes generally comparable with those reported for the St. Jude prosthesis [5—10]. Introduced in 1993, the CarboMedics ‘Top-Hat’ valve is a bileaflet aortic prosthesis designed to be placed in the supraannular position allowing for one or two size...
The concept of patient-prosthesis mismatch defines patients receiving prostheses of smaller sizes than those that would have been adequate according to the body surface area, being defined in most studies as effective orifice area/body surface area of less than 0.7 cm²/m². In this study, although a higher hospital mortality in patients treated with a 19-mm prosthesis was found, prosthetic valve size was not an independent predictor of early or late mortality in the multivariate analysis. In fact, patient-prosthesis mismatch (53% of all cases) was not significantly associated with poor early or late outcome. These findings are in accordance with other studies with a larger number of patients [16,17]. In agreement with these authors, the impact of patient-prosthesis mismatch is mostly noticed in younger patients and in those with high body surface area.

On the other hand, predictors of early and late mortality of cardiac origin identified in the multivariate analysis are consistent with data reported in other studies [18,19]. In contrast, except for the patient’s age, no predictive preoperative risk factor for noncardiac late death was documented. Large databases of morbidity and mortality risk assessment in cardiac surgery allow to discriminate patients at highest risk and, consequently, to adopt preventive measures [20,21]. However, peri- and postoperative factors are more difficult to be controlled. In this respect, we have identified postclamping time as a strong predictor of mortality in aortic valve replacement surgery. As far as we are aware, this factor has not been described and/or analyzed in previous studies on risk factors in surgical cardiac patients. The interval between initiation of extracorporeal circulation and myocardial ischemia (aortic preclamping time) is usually short and used to prepare the administration of the cardioplegic solution. The time elapsed after the release of the aortic clamps to the end of the cardiopulmonary bypass, including the assessment of an adequate electrical rhythm, nonbleeding stitches and vascular anastomoses, warming to normothermia, correct ventilation, and adequate cardiac output, varies according to all these factors. The time to warming to normothermia also varies depending on the policy adopted by each surgeon. Taking into account that preclamping time is short and less variable, postclamping time may be easily calculated by subtracting the duration of cardiopulmonary bypass to the total time of myocardial ischemia. On the other hand, there is always a justifying cause for an extended postclamping time. Prolonged postclamping time indicates
that some problems had occurred, mostly in relation to excessive bleeding or different degrees of cardiac dysfunction. Normal mean postclamping time can be estimated for each type of procedure and surgical strategy. In the present series of 269 patients undergoing aortic valve replacement surgery with or without associated valve procedures (81.8%), the postclamping time averaged 22 min.

When the risk for hospital death is analyzed according to the postclamping time, a direct relationship was observed: the longer the postclamping time, the higher the hospital mortality rate. A postclamping time above the threshold value of 15 min was associated with marked increases in the hospital mortality rate, i.e., 1% for less than 15 min compared with 26.9% for more than 45 min. Moreover, the effect of this variable on early death was apparent in the logistic regression model with an odds ratio of 1.34 for each 10-min interval. Postclamping time as a factor related to poor prognosis is probably a universally perceived concept and may be viewed as the cumulative effect of most preoperative and intraoperative risk factors (e.g., age, poor left ventricular function, complicated surgery, etc.). In this respect, two aspects should be mentioned, on one hand, a prolonged postclamping time leaves little margin for therapeutic maneuver as factors affecting postclamping time are hardly modifiable. On the other hand, analysis of large databases of cardiac surgery (EuroSCORE) may undoubtedly contribute to define the true predictive value of postclamping time. In the present study, postclamping time was also a significant predictor of late death of cardiac cause in the multivariate analysis. This finding has not been previously reported and should be confirmed in future studies. However, it seems reasonable to consider that severe intraoperative complications, such as perioperative myocardial infarction or ventricular dysfunction, may be associated with a higher postoperative morbidity (respiratory distress, renal failure, and other) that may influence on long-term results.

We conclude that in our experience the CarboMedics ‘Top-Hat’ supraannular prosthesis allows implantation of a larger prosthesis without increasing valve-related complications. Postclamping time appears as a strong predictor of both hospital mortality and late cardiac-related death. The prognostic potential of this variable should be confirmed in future studies in different cardiac operations with myocardial ischemia. Low- and high-risk postclamping time cutpoints need to be defined.

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[1] Lundblad R, Hagen OM, Smith G, Kvernebo K. The CarboMedics supraan-


