Long-Term Clinical and Hemodynamic Performance of the Hancock II Versus the Perimount Aortic Bioprostheses

Vincent Chan, MD, MPH; Alexander Kulik, MD, MPH; Anthony Tran, BSc; Paul Hendry, MD; Roy Masters, MD; Thierry G. Mesana, MD, PhD; Marc Ruel, MD, MPH

Background—The Medtronic Hancock II and the Carpentier-Edwards Perimount are among the world’s most commonly used aortic bioprostheses. However, a direct comparison of their clinical performance is lacking. To minimize biases inherent to between-center comparisons, we examined these prostheses within a large, contemporary, single-center cohort.

Methods and Results—Between 1990 and 2007, 1659 patients (mean age, 73.1±9.3 years) underwent aortic valve replacement with either the Hancock II (N=1021) or the Perimount (N=638). Patients were prospectively followed-up with serial clinic visits and echocardiograms for up to 16 years (mean, 5.0±3.3 years). There was no significant difference in aortic root size preoperatively (P=0.7). Aortic root enlargement was more commonly performed with the Perimount (P<0.001), and the manufacturer valve size of the implanted prosthesis was larger with the Hancock II (P<0.001). Postoperatively, peak and mean transprosthesis gradients were higher for the Hancock II (32.7±0.7 and 16.0±0.3 mm Hg, respectively) than for the Perimount (24.9±0.7 and 13.4±0.4 mm Hg, respectively; P<0.001). However, no difference in left ventricular mass regression was observed at late follow-up (P=0.9). Unadjusted 10-year survival was 59.4±2.4% for the Hancock II and 70.2±3.8% for the Perimount (P=0.07). Multivariable predictors of survival did not include prosthesis type (P=0.2).

Conclusions—For the same manufacturer valve size, the Perimount is larger, which may warrant enlarging the aortic root more often, and it is associated with better hemodynamics than the Hancock II. These differences do not impact survival or left ventricular mass regression, and the long-term clinical performances of the Hancock II and Perimount bioprostheses are equivalent. (Circulation. 2010;122[Suppl 1]:S10–S16.)

Key Words: echocardiography ■ surgery ■ survival ■ valves

The Medtronic Hancock II and the Carpentier-Edwards Perimount are among the world’s most commonly used aortic bioprostheses. Observational studies from North America and Europe have reported excellent clinical outcomes after aortic valve replacement (AVR) with either the Hancock II or the Perimount,1–7

The Medtronic Hancock II offers 10- and 15-year survival ranging from 63% to 67% and 35% to 47%, respectively.1–4 The Perimount performs similarly, with 10- and 15-year survival ranging from 53% to 69% and 35% to 68%, respectively.5–7 Reported freedom from structural valve deterioration, reoperation, prosthetic valve endocarditis, and thromboembolism are favorable after AVR with either the Hancock II or the Perimount.1–7

Of those studies that have included sizeable cohorts, most have involved multiple centers. Variability in perioperative and postoperative management therefore may have influenced long-term outcomes. Despite the widespread use of both the Hancock II and the Perimount aortic bioprostheses, no direct comparison of these valves has yet been made available.

Questions regarding the hemodynamic performance of these 2 bioprostheses also remain. The Perimount has been suggested to confer improved hemodynamics compared to other contemporary bioprostheses. Data supporting this, however, are scarce and limited to early follow-up.8

Therefore, we performed an observational study involving 1659 patients who underwent AVR with either the Medtronic Hancock II or the Carpentier-Edwards Perimount bioprosthesis. To minimize information and selection biases inherent to between-center comparisons, we examined these prostheses within a large, contemporary, single-center cohort in which patients received similar perioperative and postoperative care. The objective of this study was to longitudinally evaluate the performance of these 2 heart valves with respect to survival, valve-related complications (ie, freedom from reoperation, structural valve deterioration, and endocarditis), and hemodynamic performance at late follow-up.
Materials and Methods

Funding Support and Ethics Approval
Medtronic and Edwards Lifesciences provided unrestricted financial support to the University of Ottawa Heart Institute Valve Clinic. The University of Ottawa Heart Institute has existing ethics approval from its institutional research ethics board to anonymously gather, analyze, and publish data that are prospectively collected before and after heart valve replacement. As such, individual patient consent was waived.

Patient Population
Between 1990 and 2007, 1659 patients underwent first-time AVR with either the Hancock II (N=1021) or the Perimount bioprosthesis (N=638) at the University of Ottawa Heart Institute. Patients who required redo-sternotomy or concomitant valve surgery are not included in this analysis. The decision to implant a given prosthesis after another was determined by the operating surgeon in a nonrandomized fashion. Baseline patient characteristics are described in Table 1.

Surgical Technique
Standard surgical technique included use of median sternotomy, cardiopulmonary bypass, blood or crystalloid cardioplegia, and mild systemic hypothermia (32°C–34°C). Implantation of the Hancock II or the Perimount in the aortic position was performed with braided sutures, either pledged or nonpledged. Aortic root enlargement was performed at the time of root closure or during implantation according to techniques reported by Nicks et al10 and Manouguian et al11 by using either autologous pericardium or a Hemashield (Boston Scientific) patch.11 The distribution of prostheses implanted according to labeled manufacturer size is shown in Figure 1.

Follow-Up
All patients who underwent valve replacement in this series were prospectively followed-up at the University of Ottawa Heart Valve Clinic. Additional clinical information and echocardiographic data were collected retrospectively. This included annual assessments for the occurrence of prosthesis-related complications according to the Guidelines for Reporting Mortality and Morbidity after Cardiac Valve Interventions.12–14 Follow-up was obtained through clinic visits and telephone interviews. Total follow-up was for 5.0±3.3 years and was 93.8% (1556/1659) complete. No postoperative follow-up was available for the remaining 6.2% of patients. The mean follow-up for the Hancock II prosthesis was 5.6 years (95% confidence interval, 5.3–5.8 years) and the mean follow-up for the Perimount prosthesis was 3.9 years (95% confidence interval, 3.7–4.1 years).

Echocardiographic Assessment
Patients had an echocardiogram preoperatively to measure cardiac dimensions, transvalvular pressure gradients, and valve regurgitation severity as recommended by the American Society of Echocardiography.13–15 Patients underwent regular follow-up transthoracic echocardiograms at their first annual visit and subsequently as clinically indicated. Left ventricle (LV) mass was calculated via the equation: LV mass (g)=0.80[(1.04)(posterior wall thickness+LV end-diastolic diameter+septal wall thickness)−LV end-diastolic diameter3]1/6, as recommended per American Society of Echocardiography guidelines.13–15 Indexed LV mass was calculated by dividing LV mass by each patient’s body surface area. Published reference effective orifice area values were used for the Hancock II and Perimount in determining the presence of patient–prosthesis mismatch.16–18 Indexed effective orifice area was calculated by dividing the effective orifice area of a given prosthesis by each patient’s body surface area.

Statistical Analysis
Data were imported and analyzed in Stata 10.1. Baseline categorical characteristics were compared between patients receiving either the Medtronic Hancock II or the Carpentier-Edward Perimount aortic bioprosthesis by using a χ² test or Fisher exact test. Ordinal variables were compared by using a Wilcoxon rank-sum test. Continuous variables were assessed by using a Student t test when normally distributed and the Wilcoxon rank-sum test when data were skewed.

The Kaplan-Meier method was used to assess survival, in addition to freedom from reoperation, structural valve deterioration, and

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<th>Table 1. Patient and Operative Characteristics</th>
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<td>Age (years)</td>
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<td>Atrial fibrillation*</td>
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<td>Body surface area (m²)</td>
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<td>Female</td>
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<td>NYHA III/IV</td>
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<td>LV grade†</td>
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<td>I</td>
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<td>III</td>
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<td>IV</td>
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<tr>
<td>Etiology of aortic valve disease</td>
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<td>Regurgitation‡</td>
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<td>Stenosis§</td>
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<td>Aortic root size¶</td>
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<td>Aortic prosthesis size</td>
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<td>Aortic root enlargement**</td>
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<td>Anoxia time (minutes)</td>
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<td>CPB time (minutes)</td>
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<td>Concomitant CABG</td>
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<tr>
<td>0</td>
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<td>1</td>
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<tr>
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<td>≥3</td>
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<td>Indexed effective orifice area area</td>
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<td>≥0.65 cm²/m²</td>
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<td>0.65–0.85 cm²/m²</td>
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<td>≥0.85 cm²/m²</td>
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<td>30-day mortality</td>
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*Includes permanent and paroxysmal atrial fibrillation preoperatively.
†LV Class I=ejection fraction >50%.
Class II=ejection fraction 35%–50%.
Class III=ejection fraction 20%–34%.
Class IV=ejection fraction <20%.
‡Defined as the presence of aortic insufficiency ≥2+. Preoperatively.
§Defined as the presence of aortic stenosis at least moderate in severity preoperatively.
¶Technique based on methods described by Nicks et al10 and Manouguian et al11 by using either autologous pericardium or a Hemashield (Boston Scientific) patch.11 The distribution of prostheses implanted according to labeled manufacturer size is shown in Figure 1.
∥Calculated with the Wilcoxon rank-sum test.
△Measured echocardiographically.
endocarditis.\textsuperscript{12} Risk factors associated with survival were determined by using a Cox proportional hazards model. The proportional hazards assumption was verified by testing Schoenfeld residuals and built by incorporating variables with \( P < 0.10 \) on log-rank testing; patient and operative characteristics that differed between prosthesis groups, and previously described risk factors associated with survival for patients undergoing AVR.\textsuperscript{19} All covariates were entered into the final model simultaneously. Multivariable modeling was not performed for the outcome of reoperation given the low number of events.

Postoperative transprosthesis gradients and changes in postoperative left ventricle mass were compared between aortic bioprostheses by using a Student \( t \) test. Subanalyses were conducted according to aortic size and aortic pathology. These comparisons were subject to the Bonferroni correction.

**Results**

**Preoperative and Operative Characteristics**

Table 1 outlines the preoperative and operative characteristics of patients implanted with either the Medtronic Hancock II or the Carpentier-Edwards Perimount aortic bioprosthesis. Patients in the Perimount group were more likely to be female and to have atrial fibrillation preoperatively compared to patients in the Hancock II group. Although aortic root sizes were not significantly different, the implanted prosthesis size was smaller for the Perimount, and aortic root enlargement was performed more often than in patients receiving the Hancock II. Patients in the Perimount group had larger indexed effective orifice area measurements.

**Survival**

Unadjusted 5- and 10-year survival was 82.8\%±1.4\% and 59.4\%±2.4\% with the Hancock II, and 87.7\%±1.7\% and 70.2\%±3.8\% with the Perimount prosthesis (\( P = 0.07 \); Figure 2). In total, 291 deaths occurred in patients in the Hancock II group, whereas 94 deaths occurred in the Perimount prosthesis group. Overall, 77 deaths were valve-related (64 Hancock II and 13 Perimount) and 168 deaths were not valve-related (127 Hancock II and 41 Perimount). The cause of the remaining 140 deaths was unknown.

Univariate risk factors associated with survival included age, concomitant coronary artery bypass graft, gender, and preoperative New York Heart Association functional class (Table 2). Notably, prosthesis type was not associated with survival on univariate (hazard ratio [HR] 0.8 Perimount vs Hancock II; 95\% confidence interval [CI] 0.6–1.0; \( P = 0.07 \)) or multivariable analysis (HR, 0.8 Perimount vs Hancock II; 95\% CI, 0.6–1.1; \( P = 0.2 \); Table 3). Significant risk factors associated with survival on multivariable analysis included age, concomitant coronary artery bypass graft, gender, and preoperative New York Heart Association class.

**Figure 1.** Prostheses implanted based on labeled manufacturer size and bioprosthesis type. Implanted Perimount sizes ranged from 19 to 31, whereas Hancock II sizes ranged from 21 to 31. The number of prostheses implanted is shown at the top of each bar.

**Figure 2.** Unadjusted survival. This figure depicts survival from all causes of death. A total of 291 deaths were observed among Hancock II patients, and 94 deaths were observed among Perimount patients.
Table 2. Univariate Risk Factors Associated With Survival

<table>
<thead>
<tr>
<th>Age (per increasing year)</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
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<tbody>
<tr>
<td>Concomitant CABG*</td>
<td>1.5</td>
<td>1.2–1.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Female</td>
<td>0.7</td>
<td>0.6–0.9</td>
<td>0.02</td>
</tr>
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<td>Preoperative NYHA III-IV</td>
<td>1.7</td>
<td>1.4–2.1</td>
<td>&lt;0.001</td>
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</table>

Nonsignificant covariates
- Aortic root enlargement: 0.8 (0.4–1.4; 0.4)
- Aortic prosthesis size: 1.0 (0.9–1.0; 0.2)
- Indexed effective orifice area: 1.0 (0.8–1.3; 0.9)
- Perimount prosthesis: 0.8 (0.6–1.0; 0.07)
- Preoperative atrial fibrillation: 1.0 (0.4–2.6; 0.9)
- Preoperative LV function (per increasing grade): 1.2 (0.8–2.0; 0.4)
- Surgeon¶: 0.5–1.1¶ 0.2–2.0¶ 0.1¶
- Year of surgery (per later year): 1.0 0.9–1.0 0.1

*Entered into model as a dichotomous variable.
†Calculated based on published effective orifice area values.
‡Includes permanent and paroxysmal atrial fibrillation.
§LV Class I—ejection fraction >50%.
Class II—ejection fraction 35%–50%.
Class III—ejection fraction 20%–34%.
Class IV—ejection fraction <20%.
¶Eleven surgeons (A–K) implanted the aortic valve bioprostheses of the patients in this study. Each surgeon and aortic bioprostheses type were included in a Cox model assessing overall survival. The range of hazard ratios for all surgeons (A–K) is the one reported in the Table, along with the range of 95% CI. The reported P is the lowest one of all surgeons. No surgeon was associated with a statistically significant effect on survival.

Valve-Related Reoperation, Structural Valve Deterioration, and Endocarditis

Figure 3 depicts the freedom from reoperation for patients receiving either the Hancock II or the Perimount. Ten-year freedom from reoperation was 97.0% ± 1.2% and 99.6% ± 0.4% for the Hancock II and Perimount, respectively (P = 0.2). In total, 11 reoperations (Hancock II, 10; Perimount, 1) occurred in this cohort.

Structural valve deterioration (Hancock II, 97.5% ± 1.1%; Perimount, 97.2% ± 1.9% at 10 years; P = 0.6) and prosthetic valve endocarditis (Hancock II, 99.3% ± 0.3%; Perimount, 98.3% ± 1.2% at 10 years; P = 0.7) were also not different between valve types.

Table 3. Multivariable Risk Factors Associated With Survival

<table>
<thead>
<tr>
<th>Age (per increasing year)</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concomitant CABG*</td>
<td>1.3</td>
<td>1.0–1.6</td>
<td>0.03</td>
</tr>
<tr>
<td>Female</td>
<td>0.7</td>
<td>0.6–0.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Preoperative NYHA III-IV</td>
<td>1.6</td>
<td>1.3–2.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Nonsignificant covariates
- Aortic root enlargement: 0.8 (0.4–1.5; 0.5)
- Perimount prosthesis: 0.8 (0.6–1.1; 0.2)
- Preoperative atrial fibrillation: 1.0 (0.3–3.2; 0.9)
- Year of surgery (per later year): 1.0 1.0–1.0 0.5

Similar results were observed when patients were subanalyzed according to aortic prosthesis implant size or preoperative aortic valve pathology (Figure 5). In patients who received an aortic bioprosthesis of size ≥21, mean transprosthetic gradients were higher with the Hancock II (19.2 ± 8.1 vs 14.6 ± 5.6 mm Hg; P < 0.001), although no difference in indexed LV mass regression was observed (13.2 ± 8.2 vs 20.0 ± 5.0 g/m²; P = 0.5; Figure 5). In patients who received an aortic bioprosthesis of size ≥23, mean transprosthesis gradients were again higher with the Hancock II (15.4 ± 6.5 vs 12.7 ± 6.7 mm Hg; P < 0.001), although no difference in indexed LV mass regression was observed (18.6 ± 4.3 vs 18.1 ± 3.6 g/m²; P = 0.9; Figure 5).

Indexed LV mass regression also was not significantly different between the Hancock II vs the Perimount among patients with preoperative aortic stenosis (14.6 ± 3.7 vs 19.6 ± 2.9 g/m²; P = 0.3) or aortic insufficiency (38.2 ± 11.8 vs 35.6 ± 5.9 g/m²; P = 0.9), despite lower mean transprosthesis gradients with the Perimount (Figure 4).

Discussion

To minimize information and selection biases inherent to between-center comparisons, we performed an observational study involving a large, contemporary, single-center cohort who underwent AVR with either the Medtronic Hancock II or the Carpentier-Edwards Perimount. We compared patients who underwent first-time AVR with either of these 2 aortic bioprostheses with respect to survival, valve-related complications, namely reoperation, structural valve deterioration, and endocarditis, and hemodynamic performance at late follow-up.

The preoperative demographics of this study cohort were similar to other studies that have described outcomes after AVR with either the Hancock II or the Perimount.1–7 In the present study, patients receiving the Perimount were more likely to be in atrial fibrillation preoperatively and to be female compared to patients receiving the Hancock II. However, mean preoperative aortic root diameter was similar
between the Perimount and Hancock II groups. Notwithstanding, patients in the Perimount group generally received a valve of smaller manufacturer size, and they were more likely to undergo concomitant aortic root enlargement at the time of AVR.

Prosthesis type was not associated with unadjusted survival (Figure 2). When adjusting for differences in preoperative and operative characteristics, prosthesis type also was not associated with survival (Table 3). Significant risk factors associated with survival included age, concomitant coronary artery bypass graft, gender, and preoperative New York Heart Association functional class; all of which support our previous findings regarding predictors of survival after AVR.19,20 Female gender was associated with improved survival; this finding adds to the relatively scarce literature describing outcomes after valve replacement with respect to gender.20

Notably, aortic root enlargement and indexed effective orifice area were not predictive of survival. This may relate to several factors. First, severe mismatch (indexed effective orifice area <0.65 cm²/m²) was not common in this patient population. Second, aortic mismatch impacts survival in patients with LV dysfunction;21,22 however, the majority of patients in this study had preserved LV function. And third, among patients with moderate mismatch (indexed effective orifice area between 0.65 and 0.85 cm²/m²), only 4 were younger than 70 years of age and either with a body mass index <30 kg/m² or with impaired LV function.22 We have also previously shown that aortic root enlargement may be performed safely in patients with small aortic roots.11 In that study, patients with small aortic roots undergoing enlargement received larger prostheses and had improved hemodynamics in follow-up; however, no difference in long-term survival was observed.11

The Hancock II and Perimount also were not different in terms of valve-related complications. Freedom from reoperation, structural valve deterioration, and prosthetic valve endocarditis were in accordance with previously published noncomparative data.1–7

One of the findings of this study was that transprosthesis gradients were persistently higher with the Hancock II relative to the Perimount. However, these higher gradients were not associated with any difference in LV mass regression. The echocardiographic assessments of LV mass regression were made during later follow-up when ventricular remodeling after AVR is likely complete.23,24 Similar results were also observed when patients were stratified according to

![Figure 3. Freedom from reoperation. Ten reoperations were observed among Hancock II patients and 1 reoperation was observed among Perimount patients.](http://circ.ahajournals.org/)

<table>
<thead>
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<th>Number of patients at risk</th>
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<tr>
<td>Hancock II</td>
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<td>Perimount</td>
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aortic prosthesis size and preoperative aortic pathology. Our finding that the Perimount prosthesis is larger than that of the Hancock II at a given labeled size is in keeping with previously published in vivo data.

Limitations
This was a nonrandomized study; therefore, patients receiving the Hancock II and Perimount differed in regard to a variety of preoperative characteristics. Known confounders were controlled via multivariable modeling; however, the possibility exists that unmeasured confounders may have influenced outcomes. A randomized comparison would be ideal; however, such a study is unlikely to be performed. Because in vivo effective orifice area measurements were not available for all patients, reference values were used. Postoperative hypertension and medical therapy, which may impact late LV mass regression, also were not described for this cohort. Overall, although no difference in survival was observed between the Hancock II and Perimount, it is possible that a difference might be observed with larger patient numbers or longer follow-up. The causes of death were not known for a proportion of patients in this study; therefore, the conclusions of the study can only be extended to that of all-cause survival.

Conclusions
For the same manufacturer valve size, the Perimount is larger, which may necessitate enlarging the aortic root more often, and it is associated with better hemodynamics than the Hancock II. Nevertheless, with minimization of biases and confounders, the long-term clinical performances of the Hancock II and Perimount bioprostheses are equivalent.

Disclosures
Dr Ruel is on the speakers’ bureau of Medtronic. Dr Ruel also receives a research grant from Edwards Lifesciences.

References
6. Neville PH, Aupart MR, Diemont FF, Sirinelli AL, Lemoine EM, Marchand MA. Carpentier-Edwards pericardial bioprosthesis in aortic or

Figure 5. Transprosthesis gradients and left ventricle mass regression according to aortic valve size and pathology. Preoperative aortic stenosis (AS) refers to the presence of at least moderate AS on preoperative echocardiography, whereas preoperative aortic insufficiency (AI) refers to the presence of AI ≥2+ on preoperative echocardiography. The definitions of preoperative AS and AI were not mutually exclusive; therefore, patients may be counted in both groups. Echocardiographic measurements were made for 132 patients with aortic size ≤21 (Hancock II, 46; Perimount, 86), 472 patients with aortic size ≥23 (Hancock II, 316; Perimount, 156), 270 patients with AS (Hancock II, 154; Perimount, 116), and 61 patients with AI (Hancock II, 39; Perimount 22).


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