Aortic Valve Replacement With the Freestyle Stentless Bioprosthesis
Five-Year Experience

Kwok L. Yun, MD; Colleen F. Sintek, MD; Alden D. Fletcher, MD; Thomas A. Pfeffer, MD; Gary S. Kochamba, MD; Manly R. Hyde, MD; Jesus O. Torpoco, MD; Siavosh Khonsari, MD

Background—Stentless aortic valves were designed to provide a more physiological flow pattern and lower transvalvular gradient, which may have an important bearing on postoperative left ventricular function and remodeling. In this study, we prospectively analyzed the 5-year clinical results with the Freestyle valve (Medtronic, Inc) and its hemodynamic performance by serial echocardiography.

Methods and Results—Between January 1993 and August 1997, 95 patients with a mean age of 75 years underwent aortic valve replacement with the Freestyle prosthesis. Sixty-four percent of patients received valves ≥23 mm, and 37% had concomitant coronary artery bypass grafting. Average follow-up was 44±18 months (mean±SD), and echocardiography was performed preoperatively, at discharge, at 3 to 6 months, and annually thereafter. The 30-day operative mortality rate was 3%, with an overall actuarial survival rate of 80±6% (mean±SEM) at 5 years. Of the 10 late deaths, only 2 were cardiac related, thereby yielding a freedom from cardiac mortality of 94±3% after 5 years. No patient required reoperation on the aortic valve for any reason, including structural degeneration, nonstructural dysfunction, or prosthetic valve endocarditis. There were 9 thromboembolic and 3 anticoagulant-related bleeding events, none of which was fatal. The actuarial freedom from valve-related morbidity and mortality was 79±4% at 5 years. Hemodynamically, the mean transvalvular gradient significantly decreased after valve replacement and was reduced further by 41% by 6 months with a corresponding increase in effective orifice area. Left ventricular mass index fell to 75% of the preoperative value by 2 years.

Conclusions—The Freestyle stentless valve can be implanted safely in the elderly with excellent midterm clinical results. It has superb hemodynamics in terms of residual transvalvular gradient, effective orifice area, and regression of left ventricular hypertrophy. (Circulation. 1999;100[suppl II]:II-17–II-23.)

Key Words: valves ■ hemodynamics ■ echocardiography ■ survival

Despite >30 years of investigations and clinical applications, the ideal aortic valve substitute remains elusive. Although conventional stented bioprostheses avoid the hazards of embolization and anticoagulation, the rigid stent design increases the likelihood of structural failure and reoperation.1-2 Furthermore, the obstructive nature of the stent leads to a nonphysiological flow pattern and residual pressure gradient,3 which may have an important bearing on postoperative left ventricular function and clinical outcome.4,5 particularly in small valves. Although the aortic homograft, first introduced by Ross6 in 1962, is an excellent alternative to the stented biologic prosthesis in terms of performance,7,8 its clinical use is severely restricted by its limited availability.

Another option is the stentless aortic xenograft, which was first introduced into the clinical arena by Binet and associates9 in 1965 and O’Brien and Clareborough10 in 1966. Despite excellent initial results, early enthusiasm waned because of premature structural deterioration as a consequence of the poor preservation methods. This concept of using the aortic root as a physiological stent for the valve prosthesis was revived by David et al11 in 1987 when they initiated a new trial using a stentless porcine aortic valve. Since then, several stentless bioprosthetic valves have been introduced by various manufacturers with reports of superior hemodynamics and excellent clinical outcome by several major centers.12-19

Since 1993, our institution has been 1 of the study centers in the United States for the Freestyle aortic root bioprosthesis (Medtronic, Inc). Initial results for the first 64 patients were reported previously.19 In the present study, we prospectively evaluated the hemodynamic performance of the Freestyle valve by serial echocardiography and the clinical outcome of 95 patients in the last 5 years.

Methods

Between January 1993 and August 1997, 95 patients underwent aortic valve replacement (AVR) with the Freestyle aortic root...
prosthesis. All candidates for bioprosthetic aortic valve implantation were considered for the Freestyle valve. Those requiring concomitant procedures other than coronary revascularization were excluded. The study cohort was part of a multicenter trial for the Medtronic Freestyle stentless xenograft, and the protocol was approved by the investigational review board of our institution.

All patients were followed up prospectively with serial echocardiography performed preoperatively, at discharge, at 3 to 6 months, at 1 year, and annually thereafter. Mean values for each echocardiographic measurement were derived from 3 consecutive heart beats in patients in sinus rhythm and from 5 beats in those in atrial fibrillation or a VVI pacemaker. The effective orifice area (EOA) of the aortic valve was calculated by the continuity equation, and the mean transvalvular gradient at rest was derived from the simplified Bernoulli equation accounting for the flow velocity across the left ventricular outflow tract. Left ventricular mass was calculated according to Devereux and Reichek and then indexed to body surface area (LVMI). Echocardiographic classification of aortic insufficiency (AI) was in accordance with the criteria described by Perry and associates.

Selected preoperative patient characteristics are summarized in Table 1. The surgical procedure consists of a modified subcoronary technique, which has been described previously and remained relatively constant throughout the study period. Pertinent intraoperative variables, including aortic cross-clamp time, cardiopulmonary bypass time, and valve sizes, are listed in Table 2. Typically, warfarin therapy was continued for 3 months unless there was a major contraindication to anticoagulation. Follow-up was 98% complete and averaged 44 ± 18 months (4162 patient-months).

Morbid and fatal valve-related events were categorized as structural valve deterioration, nonstructural valve dysfunction, thromboembolism, anticoagulant-related hemorrhage, prosthetic valve endocarditis, reoperation, valve-related mortality, and all valve-related morbidity and mortality (VRMM), according to the framework devised by the American Association for Thoracic Surgery and the Society for Thoracic Surgeons ad hoc committee.

![Figure 1](image_url) Overall actuarial survival estimates for all patients.
Statistical Analysis

Variability of continuous data is expressed as ±SD and that of important ratios as ±70% confidence limits. Repeated-measures ANOVA was used to detect any significant changes in mean transvalvular gradient across the aortic valve prosthesis, EOA, and LVMI over time. If statistically significant, Student’s paired t test was then performed, with Bonferroni’s method used to correct for multiple comparisons. Actuarial life table data were calculated by the Cutler-Ederer method. The actuarial estimates were used to describe the time-related event-free rates from death and other valve-related complications, and the variability of these estimates is indicated by ±SEM. The actuarial curves were compared with the use of the log-rank or Wilcoxon test. A 2-tailed value of $P < 0.05$ was considered statistically significant.

Results

Operative Mortality and Late Survival Rates

The 30-day operative mortality rate was 3±2% (in-hospital mortality rate, 2±2%), with no death being directly valve related. One patient with associated coronary artery disease sustained a right ventricular infarct and died on postoperative day 2. Another patient had sudden death on postoperative day 6, which was most likely related to an arrhythmic event. Postmortem examination revealed only the presence of coronary artery disease but no evidence of myocardial infarction. The suture lines on the Freestyle bioprosthesis were intact, and the valve was well positioned. The last death occurred after discharge on postoperative day 14. The patient had been readmitted to another hospital and treated for pleural effusions. She developed hypotension and could not be resuscitated. Autopsy demonstrated evidence of bilateral adrenal hemorrhage, suggesting possible adrenal insufficiency, which possibly could have contributed to the patient’s death. Six patients required permanent pacemakers; 4 patients had tachycardia-bradycardia syndrome, and the other 2 developed complete heart block.

The overall actuarial survival rates were 96±2% and 80±6% after 1 and 5 years, respectively (Figure 1). The causes of late deaths, determined by autopsies, death certificates, hospital records, and family communications, are listed in Table 3. Of the 10 late deaths, only 2 were cardiac related. One patient suffered a fatal myocardial infarction 4 years after AVR, and another had sudden death 6 months after hospital discharge. When noncardiac deaths were excluded, freedom from cardiac mortality was 96±2% and 94±3% after 1 and 5 years, respectively (Figure 2). At last follow-up, 98% of patients were in NYHA class I or II, with a mean of 1.17±0.43 (versus 3.02±0.7 preoperatively, $P = 0.001$).

Valve-Related Complications

During follow-up, there was no single incidence of structural degeneration or nonstructural dysfunction as indicated by clinical examination or echocardiographic evaluation. Five patients presented with spiking fever at 2, 4, 4½, 9, and 11 months postoperatively. Blood cultures were positive with coagulase-negative Staphylococcus epidermis in 3 patients and Enterococcus in another patient, and 1 patient had no growth on blood cultures. Although no vegetations were seen on echocardiography and the Freestyle valves were functioning normally, all patients were treated empirically for presumed prosthetic valve endocarditis with a 6-week course of intravenous antibiotics and have subsequently done well. Consequently, the estimated freedom from reoperation at 5 years is 100%.

The actuarial estimates of freedom from thromboembolism were 93±3% and 91±3% at 1 and 5 years, respectively. There were 9 documented thromboembolic events, none of which was fatal. Of these, 5 occurred in the perioperative

<table>
<thead>
<tr>
<th>TABLE 3. Causes of Late Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic carcinoma</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Complications of peripheral vascular disease</td>
</tr>
<tr>
<td>Renal failure</td>
</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Sudden death</td>
</tr>
</tbody>
</table>

Values are number of patients.
period (3 strokes and 2 transient ischemic attacks). During follow-up, there were 2 strokes and 2 transient ischemic attacks at 9 and 16 months and at 7 months and 5 years, respectively. Two of the patients had developed atrial arrhythmias close to the time of the events.

A total of 3 patients developed a clinically important anticoagulant-related bleeding event. One patient required vagotomy and pyloroplasty for a bleeding ulcer 9 days after surgery. Another patient had an upper gastrointestinal hemorrhage on postoperative day 18 that resolved with conservative treatment. The third patient developed melena and coffee-ground emesis 4 months postoperatively and required readmission and medical management. Estimated freedom from anticoagulant-related hemorrhage at 1 and 5 years was 97±2%.

All VRMM
Twenty-two patients fell into this composite category, which included all morbid and fatal events that were clearly or possibly valve related (including all 30-day operative deaths and late cardiac mortality). As shown in Figure 3, the 1- and 5-year actuarial estimates of freedom from valve-related morbidity and mortality were 82±4% and 79±4%, respectively.

Valve Hemodynamics and Left Ventricular Mass
The mean aortic transvalvular gradient and EOA according to valve size and for all patients preoperatively, at discharge, at 6 months, and at yearly intervals up to 4 years are summarized in Tables 4 and 5, respectively. Because of the small number of echocardiograms available at 5 years (n=3) and the relatively fewer patients in the 19-, 25-, and 27-mm valve categories, repeated-measures ANOVA was performed only for all patients combined regardless of valve sizes and up to 4 years. As shown, mean transvalvular gradient decreased significantly after AVR and was reduced further by 41% at 3 to 6 months. Thereafter, the gradient remained relatively stable. Correspondingly, there was a significant increase in EOA in the immediate postoperative period and again at 3 to 6 months.

As shown in Table 6, LVMI had fallen by 8.3% by the time of hospital discharge. By 2 years, this figure was further reduced to 75% of the preoperative value. However, at the 3- and 4-year follow-ups, there was an increase in LVMI toward that measured during the 3- to 6-month study; nevertheless, this was still significantly lower than before surgery.

At the time of discharge, 71 patients (76%) had no AI, 12 patients (13%) had trace AI, and 9 patients (10%) had 1+ or mild AI. During follow-up, prosthetic valve incompetence resolved in 4 of the 9 patients with 1+ AI, whereas 8 patients with no or trace regurgitation progressed to mild insufficiency. Interestingly, of the 13 patients with 1+ AI during follow-up, 6 had received 27-mm valves.

### TABLE 4. Changes in Mean Aortic Transvalvular Gradient According to Valve Size

<table>
<thead>
<tr>
<th>Size, mm</th>
<th>Preoperative</th>
<th>Discharge</th>
<th>3–6 mo</th>
<th>1 y</th>
<th>2 y</th>
<th>3 y</th>
<th>4 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>52.7±7.4</td>
<td>17.9±4.1</td>
<td>14.0±5.2</td>
<td>12.9±2.5</td>
<td>14.0±3.4</td>
<td>12.3±4.4</td>
<td>11.3±1.6</td>
</tr>
<tr>
<td>21</td>
<td>58.4±17.2</td>
<td>15.4±9.0</td>
<td>8.9±4.5</td>
<td>9.7±5.3</td>
<td>8.5±4.6</td>
<td>6.3±2.9</td>
<td>6.7±3.4</td>
</tr>
<tr>
<td>23</td>
<td>48.5±18.1</td>
<td>12.9±4.6</td>
<td>7.6±2.7</td>
<td>7.6±4.1</td>
<td>6.4±3.4</td>
<td>4.7±2.0</td>
<td>2.9±2.3</td>
</tr>
<tr>
<td>25</td>
<td>42.9±13.8</td>
<td>10.3±5.5</td>
<td>6.5±2.7</td>
<td>4.3±2.6</td>
<td>4.6±2.2</td>
<td>3.8±2.0</td>
<td>3.7±2.6</td>
</tr>
<tr>
<td>27</td>
<td>46.7±23.6</td>
<td>10.8±5.2</td>
<td>5.1±2.6</td>
<td>4.4±2.3</td>
<td>4.3±3.0</td>
<td>4.4±3.2</td>
<td>6.0±4.2</td>
</tr>
<tr>
<td>Total*</td>
<td>50.5±18.2</td>
<td>13.0±6.5</td>
<td>7.6±4.2†</td>
<td>7.3±4.6†</td>
<td>7.0±4.5†</td>
<td>5.5±3.6†</td>
<td>5.7±3.9†</td>
</tr>
</tbody>
</table>

*Values are mm Hg (mean±SD).

*P=0.0001 by repeated-measures ANOVA; †P<0.05 vs preoperative; ‡P<0.05 vs discharge.
Clinical Outcome

The Freestyle stentless valve was designed to have superior hemodynamic performance compared to the standard stented porcine or bovine pericardial bioprostheses. Despite the relative greater complexity of implantation and longer aortic cross-clamp time compared with stented aortic valves, we have demonstrated that AVR with the Freestyle xenograft can be performed safely in the elderly population with a low operative mortality rate of 3%. This figure is comparable to those previously reported in other large series involving the use of stentless aortic prostheses. Furthermore, none of the perioperative deaths was directly valve related. The 1-year actuarial survival rate of 96% compares favorably to the 88% reported by Westaby and associates at the John Radcliffe Hospital in Oxford, United Kingdom, 1 of the centers with vast experience using the Freestyle valve. Similar short-term results have been reported with the Prima Edwards, Toronto SPV, and Biocor PSB stentless xenografts. At 5 years, the actuarial survival rate had declined to 80%. Although commendable, this figure is lower than that for the Toronto SPV valve (93% at 5 years) as reported by David and colleagues. However, there are substantial differences between the 2 study populations. The patients in the present series were older (mean age, 75 versus 62 years), were in a higher preoperative NYHA functional class (87% versus 51% in NYHA class III or IV), and received smaller valves (mean size, 23.2 versus 26.5 mm). However, different sizing methodologies between manufacturers may account for the valve size discrepancy. Of the 10 late deaths, only 2 were cardiac related, yielding a freedom from cardiac death at 5 years of 94%, including perioperative deaths. This is comparable to a later case-match study reported by the same group, in which the 8-year late freedom from cardiac mortality (excluding operative deaths) after 43 months of follow-up was 95%.

There were no cases of structural valve degeneration or nonstructural valve dysfunction as indicated by clinical symptoms or serial echocardiographic evaluations. Although 5 individuals developed fever and positive blood cultures within the first year, a definitive diagnosis of prosthetic valve endocarditis could not be documented by echocardiography. All patients were treated successfully with a 6-week course of intravenous antibiotics. Thus, repeated AVR had not been required with the Freestyle valve in our follow-up. These figures are comparable to the 10-year experience with the Toronto SPV stentless valve recently reported by David and associates. It should be noted that there were 4 incidences of primary tissue degeneration with the Toronto SPV valve after the first 5 years, yielding an actuarial freedom from structural valve degeneration of 85% at 9 years. It is possible that we may encounter some structural failures in the next 5 years.

There were 5 early and 4 late neurological events. Three perioperative episodes occurred early in our experience when anticoagulants were not routinely administered after AVR with the Freestyle valve. Stroke occurred postoperatively in 2 patients with known carotid atherosclerotic occlusive disease. Another 2 patients who sustained late transient ischemic attacks had developed new-onset atrial arrhythmias before their events. Thus, it is unclear whether these 4 episodes were directly valve related. The number of anticoagulant-related hemorrhages was relatively low and occurred early during a time of frequent adjustment of anticoagulant dosage. As expected, most episodes of anticoagulant-related hemorrhage and thromboembolism occurred within the first year, possibly reflecting the time required for healing and endothelialization of the suture lines.

To evaluate the overall clinical performance of the Freestyle bioprosthesis, actuarial estimates of freedom from

### TABLE 5. Changes in EOA According to Valve Size

<table>
<thead>
<tr>
<th>Size, mm</th>
<th>Preoperative</th>
<th>Discharge</th>
<th>3–6 mo</th>
<th>1 y</th>
<th>2 y</th>
<th>3 y</th>
<th>4 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>0.59±0.08</td>
<td>1.07±0.23</td>
<td>1.19±0.19</td>
<td>1.29±0.19</td>
<td>1.16±0.14</td>
<td>1.29±0.34</td>
<td>1.09±0.27</td>
</tr>
<tr>
<td>21</td>
<td>0.57±0.19</td>
<td>1.33±0.35</td>
<td>1.54±0.38</td>
<td>1.46±0.32</td>
<td>1.61±0.38</td>
<td>1.59±0.53</td>
<td>1.57±0.38</td>
</tr>
<tr>
<td>23</td>
<td>0.78±0.30</td>
<td>1.44±0.26</td>
<td>1.76±0.31</td>
<td>1.79±0.33</td>
<td>1.85±0.44</td>
<td>1.96±0.33</td>
<td>2.16±0.65</td>
</tr>
<tr>
<td>25</td>
<td>0.86±0.55</td>
<td>1.76±0.45</td>
<td>2.24±0.67</td>
<td>2.34±0.69</td>
<td>2.21±0.46</td>
<td>2.25±0.57</td>
<td>2.38±1.17</td>
</tr>
<tr>
<td>27</td>
<td>1.09±0.79</td>
<td>1.94±0.55</td>
<td>2.59±0.66</td>
<td>2.67±0.75</td>
<td>2.73±0.88</td>
<td>2.67±0.67</td>
<td>2.70±0.73</td>
</tr>
<tr>
<td>Total*</td>
<td>0.79±0.48</td>
<td>1.54±0.47†</td>
<td>1.89±0.63‡‡</td>
<td>1.94±0.69‡‡</td>
<td>1.96±0.70††‡</td>
<td>2.07±0.69††‡</td>
<td>2.15±0.91††‡</td>
</tr>
</tbody>
</table>

Values are cm² (mean±SD).

*P=0.0001 by repeated-measures ANOVA; †P<0.05 vs discharge.

### TABLE 6. Changes in LVMI According to Valve Size

<table>
<thead>
<tr>
<th>Size, mm</th>
<th>Preoperative</th>
<th>Discharge</th>
<th>3–6 mo</th>
<th>1 y</th>
<th>2 y</th>
<th>3 y</th>
<th>4 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>100±35</td>
<td>97±15</td>
<td>90±34</td>
<td>82±19</td>
<td>81±23</td>
<td>87±20</td>
<td>81±36</td>
</tr>
<tr>
<td>21</td>
<td>117±25</td>
<td>101±20</td>
<td>92±22</td>
<td>78±31</td>
<td>87±26</td>
<td>96±18</td>
<td>96±21</td>
</tr>
<tr>
<td>23</td>
<td>125±33</td>
<td>113±33</td>
<td>101±36</td>
<td>98±26</td>
<td>97±28</td>
<td>87±25</td>
<td>105±14</td>
</tr>
<tr>
<td>25</td>
<td>128±37</td>
<td>116±19</td>
<td>110±32</td>
<td>93±30</td>
<td>97±26</td>
<td>134±58</td>
<td>107±30</td>
</tr>
<tr>
<td>27</td>
<td>123±32</td>
<td>121±39</td>
<td>97±35</td>
<td>80±14</td>
<td>88±17</td>
<td>95±30</td>
<td>98±25</td>
</tr>
<tr>
<td>Total*</td>
<td>121±32</td>
<td>110±28†‡</td>
<td>98±31†‡</td>
<td>87±26†‡</td>
<td>91±25†‡</td>
<td>97±33†‡</td>
<td>99±25†‡</td>
</tr>
</tbody>
</table>

Values are g/m² (mean±SD).

*P=0.0001 by repeated-measures ANOVA; †P<0.05 vs preoperative; ‡P<0.05 vs discharge.
VRMM were calculated. At 5 years, the freedom rate was 79%, which compares favorably to a study from New York University Medical Center of a similar-age patient cohort after AVR with conventional stented aortic prostheses (61% freedom from VRMM at 5 years). Additionally, we have taken a conservative estimate of VRMM by including events that may not have been directly valve related.

**Hemodynamics**

Clinical reports have demonstrated that the residual transprosthetic pressure gradient after AVR for aortic stenosis is a major risk factor for impaired left ventricular diastolic dysfunction and incomplete regression of left ventricular hypertrophy postoperatively.\(^4\)\(^5\)\(^30\) This, in turn, has important implications in terms of late onset of congestive heart failure and fatal arrhythmia events. The Freestyle stentless xenograft was designed to simulate the superior hemodynamics of the cryopreserved aortic allograft compared with the conventional stented bioprosthesis.\(^6\)\(^7\)

In this series, the mean transvalvular gradient for all patients decreased significantly after AVR. This was reduced by another 41% in the first 3 to 6 months but remained stable thereafter. The explanation for this initial improvement is unclear but is probably related to resolution of tissue edema secondary to surgical trauma and reabsorption of any thrombus between the native aortic root and the bioprosthesis. As a result, there was a corresponding increase in EOA at 3 to 6 months compared with the time of discharge. These findings corroborate those previously noted by other investigators.\(^12\)\(^15\)\(^26\)\(^27\)\(^31\)–\(^33\) When the data are tabulated according to valve size, the mean transvalvular gradient and EOA are similar to those reported for the Toronto SPV valve\(^15\)\(^26\)\(^27\) but compare favorably to the Biocor\(^31\) and Prima\(^13\)\(^16\) stentless prostheses.

In terms of ventricular remodeling, there was a significant reduction of 8.3% in LVMi by the time of discharge. In a prospective study of 57 patients at Sunnybrook Health Science Center, Christakis and associates\(^48\) demonstrated a 9.8% decrease in echocardiographically measured LVMi 4 days after isolated AVR. In this series, LVMi continued to decrease by another 18% by 2 years. However, there was an upswing at the 3- and 4-year study. This finding is in agreement with that reported by Westaby and colleagues\(^12\) of 200 patients who underwent AVR with the Freestyle stentless valve. The reason for this is probably multifactorial, but it may partially be related other coexisting morbidities, such as hypertension (68% of patients).

Finally, we did not observe any significant AI or progression of trivial regurgitation during late follow-up. It is interesting to note that 6 of 13 patients with mild AI had received 27-mm valves. Whether this is of any significance is unclear and requires further echocardiographic follow-up.

In summary, this prospective analysis demonstrates that the Freestyle stentless valve can be implanted safely with excellent midterm clinical results. It has superb hemodynamics in terms of residual transvalvular gradient, EOA, and regression of left ventricular hypertrophy. It is a valuable alternative for those with a small aortic root, particularly in the elderly patient. The question of durability compared with conventional stented bioprostheses remains unanswered and requires longer follow-up.

**References**


Aortic Valve Replacement With the Freestyle Stentless Bioprosthesis: Five-Year Experience
Kwok L. Yun, Colleen F. Sintek, Alden D. Fletcher, Thomas A. Pfeffer, Gary S. Kochamba, Manly R. Hyde, Jesus O. Torpoco and Siavosh Khonsari

Circulation. 1999;100:II-17-II-23
doi: 10.1161/01.CIR.100.suppl_2.II-17

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/100/suppl_2/II-17

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/