Mitral Valve Repair in Rheumatic Disease
The Flexible Solution

J.M. Bernal, MD; J.M. Rabasa, MD; F.G. Vilchez, MD; J.C. Cagigas, MD; J.M. Revuelta, MD

Background. Mitral valve repair in rheumatic disease is technically more difficult, and there is little information on the long-term stability of this technique.

Methods and Results. From January 1975 to December 1990, 327 patients underwent mitral valve repair with the Duran flexible ring annuloplasty for rheumatic valve disease. Mean age was 45.4±12.6 years (range, 23 to 73 years). The techniques used for valve repair include a Duran flexible ring annuloplasty in all cases, commissurotomy in 272 (83.2%), papillary muscle splitting in 171 (52.3%), and subvalvular apparatus repair in 59 patients (18.0%). One hundred one patients required associated tricuspid valve surgery (30.8%). Hospital mortality was 3.36%, being lower for patients with isolated mitral valve repair (2.7%) than those with mitrotricuspid surgery (4.9%). Mean follow-up was 8.6 years (range, 1 to 17 years) and was 96.5% completed. Thirty-four patients required reoperation for severe mitral insufficiency in 12, mitral restenosis in 18, and aortic valve disease in 4. The actuarial curve free from reoperation for mitral cause at 16 years is 89.9±3.2%. Late mortality occurred in 42 patients (13.2%). Actuarial survival curve at 16 years is 84.0±3.2% for isolated mitral valve repair and 64.6±6.7% for mitrotricuspid patients.

Conclusions. Mitral valve reconstruction with Duran flexible ring annuloplasty in rheumatic valve disease entails a low hospital mortality with satisfactory long-term clinical results. (Circulation. 1993;88[part 1]:1746-1753.)

Key Words • mitral valve • surgery

Mitral valve repair represents a better alternative than valve replacement, as previously described,1,3 in terms of a higher survival rate and a significant reduction in mitral valve–related complications. However, the variety of reconstructive techniques4–6 together with the mixed patient population series studied and a certain “mystery” created around this technically demanding surgery have significantly limited the widespread use of this beneficial surgical treatment. On the other hand, long-term studies proving the stability of these techniques are scare. This moved us to analyze our experience in patients with rheumatic disease who underwent mitral valve repair with the Duran flexible ring annuloplasty.

Methods

Patient Selection

From January 1975 to December 1990, 327 patients with rheumatic mitral or mitrotricuspid valve disease underwent mitral reconstructive surgery at our institution. Patients with pure mitral stenosis treated by isolated open mitral commissurotomy and those with associated aortic valve surgery were excluded from this retrospective study.

Indications for valve repair mainly depend on the preoperative echo-Doppler study. Patients with mitral insufficiency and those with a significant regurgitant jet detected intraoperatively after commissurotomy were selected for valve repair with a Duran ring. Patients with predominant stenosis and extensive fibrosis or calcification of the leaflets or subvalvular apparatus required mitral valve replacement.

This group was made up of 69 men (21.1%) and 258 women (78.9%) with a mean age of 45.4±12.6 years (range, 23 to 73 years). Twenty patients (6.1%) had a previous mitral valve operation (6 open and 14 closed mitral commissurotomies). One patient had a previous percutaneous mitral valvuloplasty. At the time of surgery, 8 patients were in New York Heart Association (NYHA) functional class I (2.5%), 108 in class II (33.0%), 180 in class III (55.0%), and 31 in class IV (9.5%).

One hundred seven patients had a previous thromboembolic accident (32.7%), and 75 patients (22.9%) were on thromboembolic prophylaxis with coumadin. Cardiac rhythm was atrial fibrillation in 239 patients (73.1%) and sinus rhythm in the remaining 88 patients (26.9%).

Mitral valve and left ventricular functions were preoperatively and postoperatively studied by echo-Doppler in 175 patients at our institution, with a mean interval of 8.1 years. Postoperative mitral valve area was determined using the half-pressure time method10 and the grade of mitral regurgitation following the criteria by Spain et al.11 Left ventricular function was calculated by means of the method described by Theichholz et al.12 Echocardiographic study was important in selecting patients for valve repair, particularly when the subvalvular apparatus was not significantly affected and flexibility of the leaflets and the chordae tendineae was...
preserved, but the surgical assessment was always the determinant.

The mitral valve disease consisted of mixed lesion with predominant stenosis in 149 patients (45.6%), with predominant insufficiency in 89 patients (27.2%), and pure insufficiency in 89 patients (27.2%). One hundred one patients had an associated tricuspid valve disease (30.8%), consisting of functional insufficiency in 55 patients (54.5%) and organic lesion in 46 patients (45.5%).

Surgical Technique and Valve Repair

Surgical techniques used for valve repair have already been described.5,13-16 Mitral valve findings are described in Table 1. The mitral annulus size was assessed by measuring the intertrigonal zone that represents one third of the total annular size. The mitral annulus was found to be dilated in 263 patients (80.4%). The commissures were fused in 184 patients (56.2%) and calcified in 10 (3.0%). The mitral leaflets were affected in 67 patients (20.5%), and the subvalvular apparatus was affected in 124 patients (37.9%).

Predominant annular dilatation was found in 30 patients (9.2%). The leaflet lesion was the main pathological finding: commissural fusion or calcification in 86 (26.3%) and leaflet retraction in 24 patients (7.3%). Subvalvular apparatus as predominant lesion was found in 187 patients (57.2%): prolapse in 54 patients (16.5%) and chordal tendineous restricted motion in 133 (40.7%) (Table 2).

Type of technique used for mitral valve repair is shown in Table 3. Annular dilatation presented in 263 cases (80.4%) and was treated by Duran flexible ring annuloplasty, like those patients with other reconstructive techniques (n=59) in whom the flexible ring was implanted to support the valve repair. Flexible ring sizes were 31 mm in 152 patients (46.5%), 29 mm in 123 (37.6%), 27 mm in 32 (9.8%), and 33 mm in 20 (6.1%). Duran ring sizes corresponded to the measured intertrigonal distance, a fibrose zone of the mitral annulus attached to the aortic root that is not distensible as the remaining annulus.25 The intertrigonal distance is easily demonstrated by looping one of the medial chordae of the anterior leaflet and pooling on it; two furrows will form a point to the location of the anterior and posterior trigones. Pathology of the subvalvular apparatus was determined by echocardiographic study and cardiac catheterization.

Associated tricuspid valve repair was required in 101 patients (30.8%) (Table 4): flexible ring annuloplasty in 85 patients, De Vega’s annuloplasty in 11, segmental annuloplasty in 2, commissurotomy in 33, and valve replacement (Hancock I porcine valve) in 3 patients.

Thromboembolic Prophylaxis

Patients in sinus rhythm received dipyridamole and aspirin for the first 3 postoperative months (n=101). Those patients on atrial fibrillation received coumadin for 3 months (n=182) and permanently when a giant left atrium or massive thrombus was found (n=33).

Follow-up

All surviving patients received 3- and 6-month follow-up after surgery and then annual follow-up until the end of the follow-up in December 1991. The follow-up data were procured in a 6-month period (June through December 1991). The patients were followed directly in our outpatient clinic (n=175) or through direct contact with their cardiologists (n=130).

### Table 1. Anatomic Lesions in the Mitral Valve

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annular dilatation</td>
<td>263</td>
<td>80.4</td>
</tr>
<tr>
<td>Commissural fusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>106</td>
<td>32.4</td>
</tr>
<tr>
<td>Severe</td>
<td>43</td>
<td>13.1</td>
</tr>
<tr>
<td>Commissural calcification</td>
<td>10</td>
<td>3.0</td>
</tr>
<tr>
<td>Leaflet retraction</td>
<td>26</td>
<td>7.9</td>
</tr>
<tr>
<td>Leaflet calcification</td>
<td>41</td>
<td>12.5</td>
</tr>
<tr>
<td>Chordal elongation</td>
<td>41</td>
<td>12.5</td>
</tr>
<tr>
<td>Chordal rupture</td>
<td>13</td>
<td>3.9</td>
</tr>
<tr>
<td>Subvalvular apparatus fusion</td>
<td>70</td>
<td>21.4</td>
</tr>
</tbody>
</table>

### Table 2. Functional Lesions in the Mitral Valve

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predominant annular dilatation</td>
<td>30</td>
<td>9.2</td>
</tr>
<tr>
<td>Predominant leaflet lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commissural fusion/calcification</td>
<td>86</td>
<td>26.3</td>
</tr>
<tr>
<td>Leaflet retraction</td>
<td>24</td>
<td>7.3</td>
</tr>
<tr>
<td>Predominant subvalvular apparatus lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leaflet prolapse</td>
<td>54</td>
<td>16.5</td>
</tr>
<tr>
<td>Restricted motion</td>
<td>133</td>
<td>40.7</td>
</tr>
</tbody>
</table>

### Table 3. Surgical Techniques for Mitral Valve Repair

<table>
<thead>
<tr>
<th>Technique</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annular repair: flexible ring annuloplasty</td>
<td>327</td>
<td>100</td>
</tr>
<tr>
<td>Leaflet repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commissurotomy</td>
<td>272</td>
<td>83.2</td>
</tr>
<tr>
<td>Leaflet resection</td>
<td>5</td>
<td>1.5</td>
</tr>
<tr>
<td>Subvalvular apparatus repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chordae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenestration</td>
<td>16</td>
<td>4.9</td>
</tr>
<tr>
<td>Shortening</td>
<td>36</td>
<td>10.9</td>
</tr>
<tr>
<td>Replacement</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Transposition</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Resection</td>
<td>3</td>
<td>0.9</td>
</tr>
<tr>
<td>Papillary muscle splitting</td>
<td>171</td>
<td>52.1</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>(2.55 techniques per patient)</td>
</tr>
</tbody>
</table>
Eleven patients were lost to follow-up in the first 2 postoperative years, and follow-up was 96.5% complete. The average follow-up was 8.6 years (range, 1 to 17 years), with a cumulative follow-up of 2716 patients per year.

The values are expressed by means of the average and standard deviation. \( \chi^2 \) and Student’s \( t \) test were used to analyze the significance between variables. Actuarial curves were obtained by the life-table method.

**Results**

Hospital mortality occurred in 11 patients (3.36%). The cause of death was heart failure in 8 patients, respiratory insufficiency in 2, and hemorrhage in 1. Thirty-one patients (9.5%) presented with postoperative cardiac failure requiring some type of pharmacologic or mechanical support. Hospital mortality for the 226 patients undergoing isolated mitral surgery was 2.7% (6 of 226), and it was 4.9% (5 of 101) \( (P=.06) \) for patients with mitrotricuspid surgery.

Postoperative complications immediately after surgery consisted of bleeding requiring reexploration in 9 patients (2.7%) and perioperative major arrhythmias in 7 patients (2.1%).

Of the 316 surviving patients, 42 died during the late follow-up (13.2%). The causes of death were heart failure in 19 patients, cerebrovascular accident in 3, mesenteric embolism in 1, sudden death in 2, hepatic disease in 2, sepsis in 2, malignant disease in 1, pancreatitis in 1, reoperation in 1, and unknown in 10 patients. Late mortality for the patients who underwent isolated mitral surgery was 23 patients (10.4%), and it was 19 patients (19.8%) \( (P=.05) \) for mitrotricuspid surgery. Higher mortality associated with the tricuspid disease was mainly due to pulmonary hypertension \( (n=75) \) and poor left ventricular function \( (n=32) \). The actuarial survival curve at 16 years is 78.1±3.1% (Fig 1A). Hazard function for death is shown in Fig 1B. For the group of 226 patients who underwent isolated mitral repair surgery, the actuarial survival curve at 16 years is 84.0±3.2%, whereas for the group with mitrotricuspid surgery, it is 64.6±6.7% \( (P=.02) \) (Fig 2).

**Reoperation**

Thirty-four patients have required a valve reoperation after an interval of 70.3±53.8 months. In 30 patients, the reoperation was necessary for mitral dysfunction and in 4 for an aortic valve disease. There were 10 early reoperations (within 2 years) and 24 late reoperations. The causes of reoperation were severe mitral insufficiency in 10 patients (8 early and 2 late), stenosis in 18 (all of them late), and an infective endocarditis in 2. Causes of reoperation are shown in Table 5. In all cases, the prosthetic ring was fully endothelialized and without thrombi, except for 4 patients who showed a ring dehiscence. A new flexible ring annuloplasty was performed in 2 patients, and a valve replacement was performed in 28. Mortality at reoperation occurred in 1 patient (2.9%). Actuarial curve free from reoperation at 16 years for mitral structural deterioration is 89.9±3.2% (Fig 3A). Hazard function for mitral structural deterioration is shown in Fig 3B.

**Thromboembolism**

Thirty-eight thromboembolic events occurred in this series, 12 peripheral and 26 central (15 transient, 10 with permanent neurologic impairment, and 1 patient died). The actuarial curve free from thromboembolism at 16 years is 79.2±3.2% (Fig 4A). The hazard function for thromboembolism is shown in Fig 4B.

One hundred twenty-seven patients with high thromboembolic risk factors (giant left atrium, left atrial thrombus, and previous thromboembolic event) suffered 19 thromboembolic episodes (15.0%) during the follow-up. Actuarial curve free from thromboembolism at 16 years is 65.7±10.7%. The remaining patients without risk factors have had 19 thromboembolic epi-

<table>
<thead>
<tr>
<th>Valve repair</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commissurotomy</td>
<td>33</td>
</tr>
<tr>
<td>Flexible ring annuloplasty</td>
<td>85</td>
</tr>
<tr>
<td>De Vega annuloplasty</td>
<td>11</td>
</tr>
<tr>
<td>Segmental annuloplasty</td>
<td>2</td>
</tr>
<tr>
<td>Valve replacement</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>101</td>
</tr>
</tbody>
</table>

**TABLE 4. Tricuspid Valve Surgery**
sodes (9.5%) \( P \leq 0.01 \), and the actuarial curve free from thromboembolism at 16 years is 88.6\pm2.7\% \( (P=0.02) \) (Fig 5).

**Infective Endocarditis**

Two patients had infective endocarditis in the later stages of the follow-up. Both of them were reoperated on, and a valve replacement was carried out without mortality.

**Anticoagulant-Related Complications**

Of the patients who received postoperative coumadin, either temporary \( (n=182) \) or permanent \( (n=33) \), or following a thromboembolic episode, anticoagulant complications have occurred in five patients.

**Valve-Related Complications**

The actuarial curve free from valve-related complications (hospital and late mortalities, reoperation, infective endocarditis, thromboembolism, and anticoagulant-related complications) is 59.2\pm3.2\% at 16 years (Fig 6A). Hazard function for valve-related complications is shown in Fig 6B.

**Patient Status**

Two hundred sixty-three patients have been followed; at the end of this study, 59.7\% are in the NYHA functional class I \( (n=157) \), 33.1\% in class II \( (n=87) \), and 7.2\% in class III \( (n=19) \).

**Valve Function**

Of the 263 surviving patients who were followed, 233 still have their originally repaired mitral valve (88.6\%). The valve function has been studied by clinical examination and echo-Doppler in 175 patients followed directly at our institution (Table 6). The left ventricular function was normal in 90.6\% of the patients, and the systolic and diastolic diameters of the left ventricle were normal in 91.4\% and 89.7\%, respectively. The diameter of the left atrium was enlarged in 94.5\% of the patients studied. The calculated mitral area was within normal limits in 85.3\% of the patients, and mild residual mitral stenosis was detected in 14.7\%. Mild residual mitral regurgitation was found in 20\%, and moderate was found in 1.2\%. Echocardiographic study demonstrated that the left ventricular ejection fraction improved significantly after surgery, particularly at long-term follow-up, since preoperative mean ejection fraction was 55.1\pm7.3\% (32\% to 69\%) and postoperative was 61.4\pm9.7\% (39\% to 73\%).

**Discussion**

Since the 1970s, reconstructive surgery of the mitral valve was implanted definitively after the pioneering work of Carpentier.\(^4\) Since then, clinical experience has shown that this conservative surgery involves minor hospital mortality and more satisfactory long-term clinical results.\(^5\)-\(^7\) There have been few clinical series reported analyzing a homogeneous patient population with the same valve etiology, and it has been pointed out that the repair in rheumatic valve disease is technically more difficult and less stable than in a degenerative lesion,\(^8\)-\(^10\) so we retrospectively studied our 16-year experience exclusively in patients with rheumatic mitral valve disease.

A careful analysis of the anatomic and functional mitral valve lesion is necessary to ensure that each one is repaired. Lesions of the subvalvular apparatus were not uncommon in this series (57.2\%).

Mitral valve reconstructive surgery without annuloplasty entails a high incidence of early failures.\(^2\) In our series, all patients received Duran flexible ring annuloplasty to repair the annular dilatation (80.4\%), to reinforce the annulus, or to increase the leaflet coaptation (19.6\%).

Flexible ring annuloplasties\(^23\),\(^24\) were introduced based on the principles of mitral valve reconstruction introduced by Carpentier,\(^22\) particularly after the dis-
covery of the three-dimensional continuous movements of the valve annulus. This author recognizes the importance of the mitral annular function, calling his ring “semirigid,” which indicates a certain tendency to flexibility.

It has been claimed, as a criticism of flexible rings, that Carpentier’s rigid ring restores a normal systolic configuration with the characteristic 3:4 ratio between the anteroposterior and transverse diameters. However, this normal orifice can be observed only during surgery with the heart at rest or in necropsy. Mitral annulus changes continuously during the cardiac cycle and plays a role in left ventricular function. For that reason, a rigid annuloplasty could never maintain the annular physiology. Annuloplasty with the Duran flexible ring and other second-generation rings reduces the abnormally dilated annulus, allowing the threedimensional configuration of the mitral valve. The clinical demonstration of the importance of this was recently described by David et al., showing that patients who underwent a Duran flexible ring annuloplasty presented significantly better left ventricular performance and left ventricular systolic function in the early postoperative period than those undergoing Carpentier rigid ring annuloplasty. In an experimental study with a porcine mitral valve, Van Rijk-Zwikker et al. demonstrated that Duran flexible ring annuloplasty interferes less with valvular function and filling of the basal part of the left ventricle than does a Carpentier rigid ring. They suggested that these results could have only a limited clinical significance but can be a determinant in patients with impaired left ventricular function.

A consequence of preserving the left ventricular function is a reduction of the hospital mortality (3.3%), even lower in patients undergoing isolated mitral valve reconstruction (2.7%). These values contrast with those reported with Carpentier’s ring (5.3%) and for mitral replacement (5% to 8%). The results obtained in our study are similar to those reported for the isolated open mitral commissurotomy, indicating that mitral reconstruction in the rheumatic valve disease does not represent an additional risk regarding the mitral commissurotomy. The echo-Doppler study performed after an average 10-year follow-up showed that 90.6% of the patients have normal left ventricular function.

Long-term survival has been satisfactory, significantly better in the isolated mitral valve repair group than in the mitrotricuspid surgery group (84.0±3.2% versus 64.6±6.7% at 16 years) (P=.03). These values also compare favorably with those reported with Carpentier rigid ring annuloplasty.

Since in our series the etiology of the mitral valvular lesion was rheumatic in all cases and the patient population was young (mean age, 45.4 years), the incidence of mitral structural deterioration is considered low, as only 30 patients (9.4%) were reoperated for that cause, a figure similar to that reported for the isolated open mitral commissurotomy.

Hazard function for reoperation show two points in time with a higher incidence of reoperation: during the first 2 postoperative years and 10 years after surgery. Early reoperations (n=10) were necessary for an error of indication or technical failures. The predictability of the mitral reconstructive techniques (10 early failures among 327 patients; 3%) has been very satisfactory. This value is comparable to that of the open mitral commissurotomy and slightly better than those of other techniques of mitral repair. At the present time, the routine use of peroperative transesophageal

echo-Doppler allows detection of most of the early failures and correction during surgery. Another group of patients (n=18) were reoperated later as a progres-

FIG 5. Actuarial curve free from thromboembolism for patients without preoperative thromboembolic risk (no TE risk) and for patients with thromboembolic risk (TE risk) at 16 years.


sion of the valve disease. The actuarial curve free from reoperation for mitral structural deterioration at 16 years is 89.9±3.2%, which is similar to that reported for
open mitral commissurotomy. Deloche et al. presented an actuarial curve free from reoperation at 13 years that was lower than 80% in a series of patients with rheumatic valve disease who underwent mitral valve repair with Carpentier rigid ring, as another study showed worse results in terms of long-term incidence of mitral structural deterioration compared with our series. However, these findings are difficult to relate exclusively with the type of the prosthetic ring used.

Left ventricular outflow obstruction with the rigid ring has never been observed with the flexible annuloplasties.

Thromboembolism represents the main complication after surgery. Thirty-eight patients suffered from a thromboembolism episode throughout follow-up (11.6%). The thromboembolic hazard curve shows that the incidence of this complication was higher 10 years after surgery, coinciding with the reoperation hazard curve. The postoperative thromboembolism is related to the etiology of the valve lesion, the existence of preoperative risk factors, and the use of thromboembolic prophylaxis. Patients with rheumatic disease have a higher incidence of thromboembolism than do those with degenerative or ischemic pathology. Long-term studies in patients undergoing isolated open mitral commissurotomy show actuarial curves free from thromboembolism similar to that of our study. In our series, it can be noticed that the presence of preoperative risk factors was high (75%). The actuarial curve free from thromboembolism was significantly worse in the group of patients with preoperative high-risk factors than in those without them. However, 215 patients were in atrial fibrillation postoperatively, and in only 33 patients was it initially decided to administer coumadin permanently. This fact could be an additional reason for such a high incidence of thromboembolic events, since by changing the anticoagulation policy we significantly reduced the embolic complications.

Postoperative clinical results have been satisfactory, since 92.8% of the patients are in NYHA functional class I-II and leading an active normal life. Left ventricular and mitral valve functions also were satisfactory long-term after surgery. Significant residual mitral regurgitation was detected in only 1.2% of patients. Cardiac function and the incidence of mitral regurgitation compare favorably with the data reported for Carpentier rigid ring annuloplasty.

We conclude that mitral valve reconstructive surgery with Duran flexible ring annuloplasty for rheumatic disease can be carried out with very satisfactory early and long-term results, and it allows improvement of left ventricular function. These results also demonstrated the stability of this surgery, since only a reduced number of patients required reoperation for mitral structural deterioration.

Acknowledgments

We are indebted to Dr Carlos G. Duran for his important active surgical participation in this series. We express our sincere appreciation to Mrs Charo Sanchez for her secretarial assistance.

References


Mitral valve repair in rheumatic disease. The flexible solution.
J M Bernal, J M Rabasa, F G Vilchez, J C Cagigas and J M Revuelta

Circulation. 1993;88:1746-1753
doi: 10.1161/01.CIR.88.4.1746
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1993 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/88/4/1746

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/