Effect of Valve Deformity on Results and Mitral Regurgitation After Inoue Balloon Commissurotomy

Ted Feldman, MD; John D. Carroll, MD; Jeffrey M. Isner, MD; Robert J. Chisholm, MD; David R. Holmes, MD; Ali Massumi, MD; Augusto D. Pichard, MD; Howard C. Herrmann, MD; Simon H. Stertzer, MD; William W. O'Neill, MD; Gerald Dorros, MD; Ponnambalam Sundram, MD; Thomas M. Bashore, MD; K. Ramaswamy, MD; Lisa S. Jones, RN; and Kanji Inoue, MD

Background. The effect of valve deformity and patient age adversely affect the results of percutaneous transvenous mitral commissurotomy (PTMC) with conventional balloons.

Methods and Results. These factors were characterized after PTMC with the Inoue balloon. The increases in mitral valve area and mitral regurgitation after the procedure were evaluated comparing echocardiographic score of 8 or less versus more than 8, age of less than 60 versus age of 60 years or more, and age of less than 70 versus age of 70 years or more. One hundred sixty-two patients (mean age, 52±14 years) were studied. For the entire group, mitral valve area increased from 1.0 to 1.8 cm² (p<0.001). Valve area increased from 1.0±0.3 to 1.8±0.6 cm² in patients with echocardiographic score of 8 or less (n=102) and from 1.0±0.3 to 1.7±0.5 cm² with echocardiographic score of more than 8 (n=44). Patients less than 60 years old (n=104) had increases in valve area from 1.0±0.3 to 1.8±0.6 cm² versus 1.0±0.4 to 1.8±0.6 cm² for those 60 years old or older (n=50) (p=NS). There was no significant difference in resultant valve area when the age division was increased to less than 70 versus 70 years or more. Similarly, the percentage of patients with 2+ or greater increase in mitral regurgitation was not different for those with higher than for those with lower echocardiographic scores (4% versus 12%, p=NS), age of less than 60 versus age of 60 years or more (10% versus 10%, p=NS), or age of less than 70 versus age of 70 or more years (9% versus 18%, p=NS). Valve replacement for mitral regurgitation was performed in four patients (one emergency), all with echocardiographic scores of less than 8.

Conclusions. Age and extent of valve deformity do not have significant effects on acute results of PTMC using the Inoue balloon. Unique balloon geometry or the controlled, stepwise balloon sizing may explain these acceptable acute results in patients with more-deformed valves. (Circulation 1992;85:180–187)

Although percutaneous transvenous mitral commissurotomy (PTMC) was first performed in 1982 using the Inoue balloon catheter,1 it is only recently that this device has had widespread use in North America. Until recently, balloons designed for peripheral arterial angioplasty were modified and then used for mitral valve dilatation. The first PTMC procedures in the United States involved a single balloon and had resultant valve areas between 1.0 and 1.5 cm².2–4 To achieve greater valve areas, a second balloon was passed across the atrial septum and inflated with the first.5–12 The results of both...
double-balloon catheter valvuloplasty and surgical commissurotomy have been less optimal in patients with severe valve apparatus deformity. Patients with thin, pliable leaflets and no evidence of significant subvalvar disease have been considered ideal for commissurotomy, whereas those with thickened, calcified, rigid leaflets and severe subvalvar thickening have been treated with valve replacement.

The Inoue balloon catheter is a novel single-balloon device constructed of latex with a nylon mesh to limit its inflated size and shape. In contrast to single or double conventional balloons, this device has a unique geometry. The importance of balloon characteristics, such as shape, for the outcome of balloon valvotomy, especially when significant valve deformity is present, is not known. The present report describes results of the Inoue PTMC device both in general and with respect to the influence of the degree of valve deformity on the immediate results of the procedure.

Methods

Patients

One hundred sixty-two patients underwent catheterization for PTMC. Thirty-four were male, and 128 were female. Seventy-six percent were caucasian, 10% were black, 5% were Hispanic, 5% were oriental, and 3% were other racial groups. Mean patient age was 52±14 years. Fifteen percent of patients were of New York Heart Association functional class IV, 57% were of class III, 26% were of class II, and 2% were of class I. The class IV patients tended to be older with a mean age of 58±17 years (p=NS).

Inclusion criteria included symptomatic mitral stenosis, mitral valve area of 1.5 cm² or less, and informed consent. Exclusions included mitral regurgitation of more than 2+4 on left ventriculography, associated significant aortic stenosis or regurgitation, active endocarditis, or contraindications to transseptal puncture (e.g., left atrial thrombus). All patients gave informed consent according to protocols approved by each contributing center's institutional review board.

Mitral Valve Echocardiographic Scoring

Patients were categorized as having more or less severe valvar and subvalvar disease according to an echocardiographic scoring system currently in common use. Leaflet rigidity, leaflet thickening, leaflet calcification, and subvalvar thickening were each stratified from 0 to 4, with 4 representing the most diseased condition. Higher scores indicated more severe disease, and a maximum score of 16 was possible. All centers participating in this investigation used the same scoring system.

Valve Dilatation

All patients had two-dimensional and Doppler echocardiography, coronary arteriography, and left ventriculography performed before PTMC. Mitral valve dilatation was accomplished via the transeptal antegrade approach. Transeptal puncture was performed with a Ross or Brockenbrough needle and a Mullin sheath introduced from the right femoral vein. Baseline hemodynamic and cardiac output determinations were recorded. Cardiac output was determined by the Fick method in 31% of patients, thermodilution in 66%, and green dye curves in 3%. Maximal nominal inflated balloon diameter was selected according to the patient's height (26-mm balloon for patients 160 cm or less, 28-mm balloon for patients 160–180 cm, and 30-mm balloon for patients more than 180 cm). The balloon size was calibrated using test inflations before insertion into the patient. Inflations with small volumes of dilute contrast could thus be made beginning at a balloon diameter 3–4 mm smaller than nominal. A specially designed 175-cm-long, 0.025-in.-diameter spring-tip guide wire was then passed through the Mullin sheath into the left atrium. The Mullin sheath was removed over the wire, and a 14F dilator was advanced over the guide wire and through the atrial septum to enlarge the passage. The Inoue balloon catheter, in its elongated and low profile configuration, was then exchanged for the dilator and advanced across the interatrial septum and into the left atrium. The distal portion of the balloon was inflated with a small volume of dilute contrast; this ensures that it will not pass among chordal structures during passage from the left atrium to the left ventricle. With the aid of a preformed stylet, the balloon was manipulated into the left ventricle (Figure 1). With the balloon in the left ventricle, the distal portion of the balloon was inflated with a large syringe attached to the proximal portion of the catheter outside of the femoral vein, and the balloon was withdrawn to fit against the mitral valve. The remainder of the balloon was then inflated, causing enlargement of the mitral orifice (Figure 1). Finally, the balloon was deflated. The entire cycle of inflation, positioning, and deflation lasted approximately 5–10 seconds. The first inflation was performed to a balloon diameter of 3–4 mm less than nominal, followed by successive inflations by 0.5–2-mm increments to the maximum balloon diameter. After each balloon inflation, the balloon catheter was withdrawn into the left atrium, and the transmitral gradient was immediately reassessed. A color Doppler examination, auscultation, examination of the left atrial pressure waveform, and, on occasion, left ventriculography were repeated to evaluate any change in mitral regurgitation. If the transvalvular gradient persisted and no increase in mitral regurgitation was observed, another balloon inflation was performed to a balloon diameter 0.5–2 mm larger. This stepwise process was repeated until the mitral gradient was reduced as much as possible without a significant increase in mitral regurgitation.

After valvuloplasty, hemodynamic measurements and cardiac output determination were repeated. Gradient and cardiac outputs were measured with the catheter in place across the interatrial septum.
1 to 4. Oximetry and color Doppler examinations were performed to evaluate presence or absence of left-to-right intracardiac shunting from the transeptal passage of catheters. Oximetric evidence of a shunt with a Qp-to-Qs ratio of more than or equal to 1:2:1 was considered significant.

Statistical comparisons between groups of patients were made using an unpaired t test. Multiple comparisons were made with the Bonferroni correction. A value of p<0.05 was considered significant. All data are presented as mean±SD.

**Results**

The PTMC procedure was successfully completed in 154 of 162 patients (95%). Hemodynamic evaluation for the group of 154 patients showed a decrease in mean left atrial pressure from 24±7 to 18±7 mm Hg (p<0.001), an increase in cardiac output from 4.1±1.3 to 4.5±1.4 l/min (p<0.001), a decline in mean transmitral gradient from 14.3±6.0 to 5.9±3.2 mm Hg (p<0.001), and an increase in mitral valve area from 1.0±0.3 to 1.8±0.6 cm² (p<0.001).

Before PTMC, 24% of patients had a mitral valve area of less than 0.8 cm², 54% had an area of less than 1.0 cm², and 79% had an area of less than 1.2 cm². After dilatation, 69% of patients had a resultant valve area of 1.5 cm² or more, and 78% had an area of more than 1.2 cm².

Table 1 shows patients with echocardiographic scores of 8 or less compared with those with echocardiographic scores of more than 8. Echocardiographic scores were available in 146 patients; those with higher echocardiographic scores were significantly older. There were no significant differences in the pre-PTMC valve area, post-PTMC valve area, or percent increase in valve area after the procedure (Figure 2). Echocardiographic scores may have some subjectivity despite the well-developed scoring system used. Therefore, patients were also divided by age. The correlation between echocardiographic score and age was 0.52 (p<0.01) (Figure 3). Table 2 shows the comparisons of those less than 60 with those 60 years old or older and those less than 70 with those 70 years old or older. Patients more than 60 years old had a significantly higher mean echocardiographic score. In addition, they had a higher inci-

<table>
<thead>
<tr>
<th>Table I. Comparisons of Patients by Echocardiographic Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiographic score</td>
</tr>
<tr>
<td>≤8 (n=102)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Atrial fibrillation (n)</td>
</tr>
<tr>
<td>MVA before dilatation (cm²)</td>
</tr>
<tr>
<td>MVA after dilatation (cm²)</td>
</tr>
<tr>
<td>MVA increase (%)</td>
</tr>
<tr>
<td>Increase MR ≥2+ (n)</td>
</tr>
</tbody>
</table>

MVA, mitral valve area; MR, mitral regurgitation.

Withdrawal of the catheter before these measurements could result in a spurious mitral valve area calculation in patients with catheter-related atrial septal defect of any size. Left ventriculography was performed to evaluate any change in mitral regurgitation compared with that before PTMC. The degree of mitral regurgitation was graded on a scale of from

**FIGURE 1. Cineangiograms. After balloon catheter is positioned in left atrium, distal half is inflated and floated across valve into left ventricle. Device is pulled back until mitral valve is engaged (top panel). Proximal portion of balloon is inflated, creating "figure 8" or dumbbell shape, which "locks" into valve orifice (middle panel). Center of balloon is then fully inflated (bottom panel). Note calcification in anterior mitral valve leaflet (arrows) and asymmetric inflation of distal portion of balloon in middle panel, denoting significant valve deformity.**
dence of atrial fibrillation. There were no differences in pre- or post-PTMC valve areas or percent increase in valve area after PTMC (Figure 2). When the age comparison was increased to age less than 70 versus age of 70 years old or older, there still was no difference in resultant mitral valve area or increase in mitral valve area (Table 2). Patients more than 70 years old had higher New York Heart Association functional class and a mean age of 78±6 years.

In addition, when echocardiographic score and age were considered as continuous variables, there were weak correlation coefficients between the increase in mitral valve area and echocardiographic score ($r=-0.04$) and between the increase in mitral valve area and age ($r=-0.16$) (Figure 4).

Valve deformity has also adversely affected the occurrence of mitral regurgitation after mitral commissurotomy. Ninety-two percent of patients in this series had 0 or 1+/4 mitral regurgitation before PTMC, and 77% had 0 or 1+ mitral regurgitation after dilatation (Table 3). Sixty-six percent had no increase in mitral regurgitation, and 22% had an increase of one grade. Eleven percent had an increase of two or more grades. In one of these patients, emergency mitral valve replacement was necessary; in three others, valve replacement was performed weeks after the procedure.

When patients with echocardiographic scores of 8 or less were compared with those with scores of more than 8, there was no significant difference in the number of
TABLE 2. Comparisons of Patients by Age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Echocardiographic score</th>
<th>NYHA class</th>
<th>Atrial fibrillation (n)</th>
<th>MVA before dilatation (cm²)</th>
<th>MVA after dilatation (cm²)</th>
<th>MVA increase (%)</th>
<th>Increase MR ≥2+ (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60 (n=104)</td>
<td>6.3±2.2</td>
<td>2.8±0.7</td>
<td>28% (29)</td>
<td>1.0±0.3</td>
<td>1.8±0.6</td>
<td>93±69</td>
<td>10% (10)</td>
</tr>
<tr>
<td>≥60 (n=50)</td>
<td>8.5±3.0</td>
<td>3.0±0.7</td>
<td>68% (34)</td>
<td>1.0±0.4</td>
<td>1.8±0.6</td>
<td>82±60</td>
<td>10% (5)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>&lt;70 (n=137)</td>
<td>6.6±2.5</td>
<td>2.8±0.7</td>
<td>35% (48)</td>
<td>1.0±0.3</td>
<td>1.8±0.6</td>
<td>91±68</td>
<td>9% (12)</td>
</tr>
<tr>
<td>≥70 (n=17)</td>
<td>10.0±2.8</td>
<td>3.3±0.6</td>
<td>88% (15)</td>
<td>0.9±0.3</td>
<td>1.6±0.6</td>
<td>78±46</td>
<td>18% (3)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>&lt;0.006</td>
<td>&lt;0.0001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association; MVA, mitral valve area; MR, mitral regurgitation.

patients with an increase in mitral regurgitation of two or more grades (Table 1). Patients 60 years old or older did not have a greater incidence of increased mitral regurgitation by two or more grades than those less than 60 years old (Table 2). Similarly, patients 70 years old or older did not have a greater incidence of increased mitral regurgitation by two or more grades than those less than 70 years old (Table 2).

Because the Inoue balloon is sized by maximum inflated diameter and dilatations are performed in a stepwise manner, beginning with a diameter less than maximum, the balloon size and number of inflations were compared for patients who did and did not have an increase of 2+ or more in mitral regurgitation.

There were no differences in balloon size (Table 4), number of balloons overinflated (to a diameter greater than nominal maximum) or underinflated during the procedure, or number of balloon inflations. Because inflations were done in a stepwise manner beginning with a small diameter and because gradient, cardiac output, and changes in mitral regurgitation are evaluated after each inflation, the procedure was terminated if a significant increase in mitral regurgitation occurred before adequate valve dilatation was accomplished. The resultant valve area and percent increase in area in the patients who developed 2+ or greater mitral regurgitation are therefore smaller. In the group with less mitral regurgitation, it is possible that the larger number of patients in whom balloons were overinflated reflects the operator’s willingness to pursue a better reduction in gradient as long as no increase in mitral regurgitation occurs. The small group size of patients with a large increase in mitral regurgitation makes these comparisons difficult.

Significant complications are listed in Table 5. The valve could not be crossed in four patients. There were no hospital deaths; one patient was thought to have had a transient ischemic attack. Three patients required vascular repair at the site used for arterial catheter access. One patient with prior coronary bypass surgery had circumflex occlusion 1 hour after PTMC and was recanalized using direct coronary angioplasty. Two patients had cardiac perforation—one during transeptal puncture (requiring no specific therapy) and the second during balloon inflations (treated successfully with pericardiocentesis). Two patients had ventricular fibrillation requiring DC shock, and two developed rapid atrial fibrillation requiring cardioversion. Atrial septal defects of 1.2:1 or greater were reported in 10 patients and were more than 1.5:1 in three patients (mean, 1.61±0.53). As noted earlier, four patients developed severe mitral regurgitation, one requiring emergency mitral valve replacement.

Discussion

Although PTMC was first introduced by Inoue in Japan in 1982,1 it is only recently that the Inoue device has had widespread use in North America. The PTMC technique using this device differs substantially from the variety of techniques using single or double peripheral arterial balloons to accomplish percutaneous valve dilatation. Conventional single balloons large enough to cause adequate valve enlargement have a large profile that may make cross-
ing the atrial septum difficult. These balloons also have a very slow inflation-deflation cycle. The use of two smaller conventional balloons in combination requires either double atrial septal punctures or passage of two balloons and catheter shafts through a single atrial puncture. In addition, it is sometimes difficult to negotiate two balloons across the mitral valve simultaneously, and they may be unstable in the valve orifice when inflated. Conventional balloons also require the insertion of a guide wire across the mitral orifice into the left ventricle with significant resultant ventricular ectopy.

In contrast, the Inoue balloon, even in inflated diameters up to 30 mm, is stretched and made more slender before passage across the atrial septum with a less-prominent deflated profile. The device is guided across the mitral valve without the aid of a guide wire and thus does not require the presence of a wire in the ventricle. Flotation of the balloon across the valve may make this portion of the procedure simpler. The balloon also is self-positioning. After the distal one third of the balloon is inflated in the left ventricle, it is pulled back snugly against the valve orifice. The proximal portion is then inflated, creating a dumbbell or “figure 8” configuration; only then, when the balloon is positioned in the valve orifice, is the middle portion of the balloon inflated with resulting valve dilatation (Figure 1). These technical differences result in a simpler procedure using the Inoue balloon compared with conventional double balloons. However, the relative ease of use is not by itself adequate. The present report demonstrates that this balloon device has acceptable acute hemodynamic results in patients considered ideal for commissurotomy as well as in those with more severe valvular deformities.

Most patients undergoing double-balloon mitral dilatation have mean resultant valve areas between 1.8 and 2.4 cm$^2$. Nobuyoshi et al$^{20}$ reported an increase in valve area from 1.4±0.4 to 2.0±0.5 cm$^2$ in a series of 106 patients using the Inoue balloon, and Chen et al$^{27}$ reported an increase in valve area from 1.1±0.3 to 2.0±0.4 cm$^2$ in 71 patients with the Inoue device. Mean patient ages in the latter two studies were 53±11 and 34±8 years, respectively. Hung et al$^{28}$ described an increase in mitral valve area from 1.0±0.3 to 2.0±0.7 cm$^2$ in 219 patients (mean age, 43 years). In the present study, mean valve area increased from 1.0 to 1.8 cm$^2$ in a population with a mean age of 52±14 years.

The influence of the extent of valve deformity on the outcome of mitral commissurotomy has been well characterized. A prominent opening snap and the absence of fluoroscopic calcification have been the traditional guidelines for patient selection for surgical commissurotomy. Even then, an intraoperative decision regarding valve replacement is made. Similarly, the early results of PTMC have not been as good in patients with more-deformed valves. Palacios et al$^{29}$ found the postdilatation valve area to be significantly lower in patients with greater valve deformities.

Use of an echocardiographic scoring system to evaluate valve deformity as an aid to patient selection has become a common practice. Two-dimensional echocardiographic characterization of valve leaflet mobility, subvalvular thickening, leaflet thickening,
and calcification allows for stratification of each of these variables on a scale of from 1 to 4. Therefore, valves with very little deformity have low scores, whereas those with severe deformity have high scores. In the study by Palacios et al,29 patients with scores of 8 or less demonstrated an increase in mitral valve area from 0.9 to 1.9 cm². Those with scores of more than 8 had an increase from 0.9 to 1.6 cm² using double-balloon technique. The lesser impact of valve deformity on the results of PTMC with the Inoue device may be related to the unique geometry of the balloon. It is also possible that the lower inflated pressures achieved by this device contribute to the results in more-deformed valves.30,31

The occurrence of mitral regurgitation after PTMC has not been as clearly influenced by the presence of subvalvular disease.32 In the present study, the majority of patients had 0 or 1+ mitral regurgitation both before and after PTMC. An increase of 2+ or greater mitral regurgitation was noted in 16 of 162 patients (10%). Fourteen of these patients had an echocardiographic score of 8 or less (Table 3), and 10 were less than 60 years old (Table 2). Thus, the incidence of mitral regurgitation does not appear to be greater among patients with more severe valve deformity after PTMC. Interestingly, three patients were judged to have a decrease by one grade in mitral regurgitation after PTMC. Although it is likely that differences in loading conditions and ventriculographic technique account for the difference in observed mitral regurgitation, it is also possible that commissurotomy for there to be better coaptation of the valve leaflets and a decrease in degree of regurgitation.

The relation between PTMC outcomes and the degree of valve deformity is in large part dependent on the accuracy of assessment of the valve characteristics. The echocardiographic score is well described and currently represents the most common standard for evaluation of leaflet deformity and subvalvular disease. However, this index requires some subjective evaluation. The echocardiographic scores reported by this group of investigators represent the spectrum of interpretation seen in a variety of centers. Assuming that greater valvular involvement occurs with age, the use of age to segregate patients is another manner in which the degree of valve deformity may be considered. Patients under age 60 had significantly lower echocardiographic scores than those over age 60, which is in keeping with the expected progression of valve deformity as age increases. Patients over age 70 had echocardiographic scores greater than those over age 60 and similar to those of patients with scores of more than 8. In addition, they had significantly higher New York Heart Association functional class. There still was no difference in the resultant mitral area or in the increase in mitral area among these older patients. Because the findings in patients separated by age parallel those when patients are separated by echocardiographic scores, the limitations of the subjective echocardiographic score are not likely to influence the interpretation of these results.

Although the immediate results of dilatation with the Inoue device among patients with significant valve deformity appear to be acceptable, the long-term durability of dilatation for these patients remains to be determined. It is likely that restenosis will occur with a higher frequency among patients with severe valve deformities.33 The definition of success after PTMC may be better characterized by long-term clinical status than by any arbitrary immediate post-PTMC valve area. In addition, success may be defined differently for patients ideally suited for commissurotomy than for those unsuitable for valve surgery and poorly suited for PTMC. The occurrence of restenosis and the functional results of dilatation may be more related to valve characteristics34 whereas the early results may be influenced by balloon characteristics.30

It is remarkable that significant increases of 2+ or more in mitral regurgitation occurred almost entirely in patients with low echocardiographic scores (Table 3). As has been suggested previously, the worsening of regurgitation may depend on localized changes in very specific portions of the mitral leaflets or chordae tendinea that cannot be characterized by a description of the degree of overall valve deformity.32 Not only was echocardiographic score not clearly associated with changes in mitral regurgitation in the present study, but in addition the number of balloons that were overinflated and the number of balloon inflations (Table 4) were no different in patients with severe valve deformity. The occurrence of mitral regurgitation during valvuloplasty appears to be an unpredictable event and may even be more common in younger patients with less-deformed valves. One important consideration is that by using stepwise inflations with the Inoue balloon catheter and evaluating mitral regurgitation with color Doppler after each inflation, it is possible to stop before mitral regurgitation becomes even worse.35 Although the appearance of late restenosis appears significantly related to the degree of valve deformity, neither the immediate results of balloon dilatation nor the occurrence of mitral regurgitation appears to be as clearly related.

**Study Limitations**

Echocardiographic scores were reported by each investigating center independently. These evaluations were unblinded and represent a variety of institutions. It is likely that differences in scoring occurred among different investigators. Stratification by age was used as an additional method with which to assess the degree of valve deformity. As seen in Figure 3, there is a significant correlation between age and echocardiographic score.

It is important to emphasize that the results reported here reflect immediate post-PTMC outcome. The durability of valvotomy is not likely to be different than that with other forms of commissurotomy and will require long-term evaluation.
References
34. Vahanian A, Michel PL, Jung B, Cormier B, Roger V, Acaj C: Should balloon valvotomy be performed for severely calcified mitral stenosis (abstract)? Circulation 1990;82(suppl III):III-79

Key WORDS • mitral stenosis • valvuloplasty • Inoue balloon • percutaneous transvenous mitral commissurotomy
Effect of valve deformity on results and mitral regurgitation after Inoue balloon commissurotomy.
T Feldman, J D Carroll, J M Isner, R J Chisholm, D R Holmes, A Massumi, A D Pichard, H C Herrmann, S H Stertzer and W W O'Neill

Circulation. 1992;85:180-187
doi: 10.1161/01.CIR.85.1.180
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 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/85/1/180

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/