Pressure and Sound Correlates of the Mitral Valve Echocardiogram in Mitral Stenosis

ROSEMARIE SALERNI, M.D., P. SUDHAKAR REDDY, M.D., M. EUGENE SHERMAN, M.D.
JAMES D. O'TOOLE, M.D., DONALD F. LEON, M.D., AND JAMES A. SHAVER, M.D.

SUMMARY The pressure and sound correlates of the mitral valve echocardiogram (MVE) were investigated in 10 patients with mild to moderate mitral stenosis using high fidelity catheter tip micromanometers. Slow and rapid phases of the MVE anterior motion at the time of opening are associated with the slow and rapid phases of the left atrial y descent. The slow MVE motion and the slow y descent begin during isovolumic left ventricular relaxation when left ventricular pressure still exceeds left atrial pressure. The rapid MVE anterior motion and the rapid y descent begin with pressure crossover. Posterior motion of the MVE at the time of closure also occurs in two phases. After the onset of left ventricular pressure rise at end-diastole, a slow posterior motion is associated with a rising left atrial c wave. Rapid posterior motion begins with pressure crossover and is completed near the peak of the c wave. The fall in left atrial pressure during valve opening can be related to movement of the mitral valve away from the left atrium with the fall in left ventricular (LV) pressure. During valve closure, the rising left atrial (LA) pressure can be related to the ascent of the mitral valve toward the left atrium. Both the mitral component of the first heart sound and the opening snap occur at points of maximum MVE excursion and after LV-LA pressure crossover.

ALTHOUGH THE SOUND and pressure correlates in mitral stenosis using high fidelity micromanometer pressures have previously been described,1,2 the valve motion correlates of these parameters have been limited to angiographic studies.34 Since the introduction of echocardiography and the recognition of characteristic patterns of valve motion, this method has been used to study instantaneous valve motion in normal and abnormal states.5 Because of the ease with which the anterior mitral leaflet can be visualized by echocardiography, this structure has been the most extensively studied. The echo pattern has been particularly useful in the evaluation of patients with mitral stenosis.67 Although several investigators have described the relationship of echocardiographic mitral valve motion to the production of heart sounds and murmurs,812 there have been few studies correlating the mitral echocardiogram with hemodynamic events. Recently, investigators have described the pressure and motion correlates of the normal mitral valve echocardiogram in experimental animals.1415 In man, fluid-filled catheter pressures have been used for pressure and motion correlates,16 except in one patient with an atrial septal defect where micromanometer catheters were used.17 This study describes the sound and pressure correlates of echocardiographic mitral valve motion in mitral stenosis using simultaneous high fidelity left atrial (LA) and left ventricular (LV) catheter tip micromanometer pressures recorded with the mitral valve echocardiogram.

Materials and Methods
Ten patients with mitral stenosis were studied during diagnostic cardiac catheterization. Informed consent was obtained from all patients.
TABLE 1. Hemodynamic and Clinical Data—10 Patients with Mitral Stenosis

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Rhythm</th>
<th>PA S/D(m)</th>
<th>LA m</th>
<th>LA-LV Gradient</th>
<th>CO/CI</th>
<th>MVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 20F</td>
<td>NSR</td>
<td>32/14 (22)</td>
<td>9</td>
<td>7</td>
<td>3.47/2.16</td>
<td>1.24</td>
</tr>
<tr>
<td>2 26M</td>
<td>NSR</td>
<td>25/12 (16)</td>
<td>12</td>
<td>10</td>
<td>3.15/2.14</td>
<td>0.8</td>
</tr>
<tr>
<td>3 40F</td>
<td>NSR</td>
<td>24/14 (18)</td>
<td>14</td>
<td>8</td>
<td>4.32/2.48</td>
<td>1.81</td>
</tr>
<tr>
<td>4 23F</td>
<td>NSR</td>
<td>32/16 (23)</td>
<td>17</td>
<td>11</td>
<td>4.56/2.59</td>
<td>1.63</td>
</tr>
<tr>
<td>5 57F</td>
<td>AF</td>
<td>42/18 (28)</td>
<td>23</td>
<td>14</td>
<td>4.86/2.85</td>
<td>1.34</td>
</tr>
<tr>
<td>6 25M</td>
<td>NSR</td>
<td>44/20 (24)</td>
<td>24</td>
<td>17</td>
<td>5.12/2.88</td>
<td>1.18</td>
</tr>
<tr>
<td>7 56F</td>
<td>NSR</td>
<td>32/15 (20)</td>
<td>16</td>
<td>7</td>
<td>4.37/2.44</td>
<td>1.84</td>
</tr>
<tr>
<td>8 44F</td>
<td>AF</td>
<td>40/24 (30)</td>
<td>20</td>
<td>17</td>
<td>3.29/1.88</td>
<td>1.0</td>
</tr>
<tr>
<td>9 49M</td>
<td>AF</td>
<td>36/16 (26)</td>
<td>20</td>
<td>9</td>
<td>3.15/1.66</td>
<td>1.05</td>
</tr>
<tr>
<td>10 47F</td>
<td>AF</td>
<td>28/12 (17)</td>
<td>11</td>
<td>4.5</td>
<td>4.12/2.32</td>
<td>2.07</td>
</tr>
</tbody>
</table>

Abbreviations: NSR = normal sinus rhythm; AF = atrial fibrillation; PA = pulmonary arterial pressure (mm Hg); S = systolic; D = diastolic; m = mean; LA = left atrial pressure; LV = left ventricular pressure; CO = cardiac output (/min); CI = cardiac index (/min/m²); MVA = mitral valve area (cm²).

Clinical and hemodynamic data are summarized in table 1. Seven patients were in sinus rhythm and three in atrial fibrillation. Mild to moderate mitral stenosis was demonstrated with valvular gradients of 5–17 mm Hg and valve areas of 0.8–2.1 cm². All patients underwent right, retrograde and transseptal left heart catheterization using standard technique. Following the diagnostic portion of the hemodynamic study, high fidelity LV pressure was obtained from a retrograde No. 8F Millar Mikrotip catheter. High fidelity LA pressure was obtained from a No. 4F Millar catheter introduced through a No. 9F Ross transseptal catheter. The micromanometer catheters were balanced and calibrated externally on a 0–100 or 0–40 mm Hg scale. Micromanometer and equisensitive fluid catheter pressures were superimposed during slow rates of pressure change to correct for gravitational effects and for reference to zero mm Hg. In two patients, satisfactory gravitational correction was not obtained and, therefore, points of LV-LA pressure crossover were not determined. Internal sound was recorded from the left atrium with an audio output circuitry having a flat response from 40–500 Hz and a roll off of 12 db per octave below 40 Hz. An external phonocardiogram was obtained from a point where the first and second heart sounds and the opening snap could be recorded using Electronics for Medicine microphones at frequency settings of 120–500 Hz. The mitral valve echocardiogram was obtained by standard technique using a Smith Kline Ekoline 20A ultrasonoscope with the 5 in., 2.25 MHz transducer having a 7.5 cm focal length. Simultaneous LA and LV micromanometer pressures, external and internal sound and the mitral valve echogram were recorded on an Electronics for Medicine DR-12 photographic recorder at a paper speed of 100 mm/sec, with time intervals of 20 msec.

The time intervals for the relationships between pressure, sound and motion during mitral valve closure were measured from the onset of the Q wave of the electrocardiogram. These include: 1) Q to the onset of the LV pressure rise, Q-LV; 2) Q to the upstroke of the c wave in the LA pressure, Q-Cu; 3) Q to the c wave peak, Q-Cp; 4) Q to LV-LA pressure crossover, Q-CO; 5) Q to the onset of rapid posterior motion of the anterior mitral leaflet echo, Q-B; 6) Q to the end of rapid posterior echo motion, Q-Ce; 7) Q to the onset of the first high frequency deflection of the mitral component of the first heart sound, Q-M1. Time intervals for mitral valve opening were measured from the first high frequency deflection of the externally recorded aortic component of the second heart sound (A2), and include: 1) A2 to the onset of the rapid phase of the LA y descent, A2-Y; 2) A2 to pressure crossover, A2-CO; 3) A2 to the onset of rapid anterior motion of the anterior mitral leaflet echo, A2-D; 4) A2 to the end of rapid anterior echo motion, A2-E; 5) A2 to the onset of the externally recorded opening snap, A2-OS. The values presented are an average of five beats (table 2).

Results

Mitril Valve Opening

The echocardiogram of the anterior leaflet of the mitral valve at the time of opening shows slow and rapid phases of anterior motion. After the peak of the LA v wave, an initial slow anterior echo motion has an indistinct onset and is accompanied by a gradual fall in LA pressure, the slow y descent (fig. 1). This slow echo motion and pressure fall occur during LV isovolumic relaxation while LV pressure still exceeds LA pressure (fig. 2). At this time, no separation is seen between the anterior and posterior mitral leaflets when both are visualized. Rapid anterior echo motion begins at point D and is accompanied by a rapid y descent in the left atrial pressure. The D point and the onset of the rapid y descent occurs almost simultaneously (within -7 to +2 msec) (table 2). Separation of the leaflets occurs almost simultaneously with the onset of rapid anterior motion of the anterior leaflet echo. The onset of rapid anterior motion of the mitral valve echo precedes pressure crossover by an average of 7 msec (2–12 msec). When the maximum extent of anterior echo motion is reached at the E point, LA pressure significantly ex-
TABLE 2. Pressure, Sound and Echocardiographic Time Intervals*

<table>
<thead>
<tr>
<th></th>
<th>Q-LV</th>
<th>Q-Cu</th>
<th>Q-CO</th>
<th>Q-Cp</th>
<th>Q-B</th>
<th>Q-CE</th>
<th>Q-MI</th>
<th>A+CO</th>
<th>A+D</th>
<th>A+Y</th>
<th>A+OS</th>
<th>A+T</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>51</td>
<td>67</td>
<td>74</td>
<td>70</td>
<td>86</td>
<td>85</td>
<td>78</td>
<td>71</td>
<td>78</td>
<td>100</td>
<td>110</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>47</td>
<td>66</td>
<td>69</td>
<td>72</td>
<td>82</td>
<td>82</td>
<td>58</td>
<td>47</td>
<td>50</td>
<td>82</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>30</td>
<td>40</td>
<td>56</td>
<td>53</td>
<td>67</td>
<td>63</td>
<td>62</td>
<td>50</td>
<td>52</td>
<td>82</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>50</td>
<td>74</td>
<td>77</td>
<td>78</td>
<td>97</td>
<td>98</td>
<td>54</td>
<td>42</td>
<td>42</td>
<td>69</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>44</td>
<td>62</td>
<td>66</td>
<td>64</td>
<td>80</td>
<td>75</td>
<td>37</td>
<td>30</td>
<td>32</td>
<td>63</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>94</td>
<td>107</td>
<td>124</td>
<td>114</td>
<td>130</td>
<td>129</td>
<td>28</td>
<td>25</td>
<td>28</td>
<td>53</td>
<td>55</td>
</tr>
<tr>
<td>7</td>
<td>39</td>
<td>49</td>
<td></td>
<td>80</td>
<td>76</td>
<td>84</td>
<td>90</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>107</td>
<td>97</td>
</tr>
<tr>
<td>8</td>
<td>37</td>
<td>39</td>
<td>63</td>
<td>75</td>
<td>74</td>
<td>91</td>
<td>87</td>
<td>60</td>
<td>56</td>
<td>57</td>
<td>88</td>
<td>87</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>42</td>
<td>66</td>
<td>68</td>
<td>65</td>
<td>82</td>
<td>83</td>
<td>32</td>
<td>30</td>
<td>32</td>
<td>59</td>
<td>56</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>25</td>
<td>—</td>
<td>60</td>
<td>62</td>
<td>76</td>
<td>76</td>
<td>—</td>
<td>—</td>
<td>60</td>
<td>58</td>
<td>89</td>
</tr>
</tbody>
</table>

*Time intervals are in msec.
Abbreviations: For definition of measured intervals, see text.

ceeds LV pressure. The opening snap occurs an average of 23 msec (15–28 msec) after pressure crossover and is coincident with the echo E point (−10 to +3 msec).

Mitral Valve Closure

Posterior motion of the anterior mitral leaflet echogram at the time of mitral valve closure also occurs in two phases. The onset of the slow phase of posterior motion of the anterior mitral leaflet echo is indistinct. This slow phase of echo motion is accompanied by a rise in LA pressure, the c wave (fig. 3). Posterior echo motion and the c wave begin after the onset of LV pressure rise, but when LA pressure still significantly exceeds LV pressure (fig. 4). Rapid posterior motion of the echo at the B point begins with pressure crossover (1–13 msec after). Pressure

**Figure 1.** Simultaneous left atrial (LA) pressure, LA dp/dt and the mitral valve echo (MVE). During valve opening, the slow and rapid phases of anterior echo motion correspond to the slow and rapid phases of the LA y descent. Time lines — 20 msec.
Discussion

Although cineangiography has been used to study the sound and pressure correlates of mitral valve motion in the past, echocardiography has a distinct advantage over this method in several respects: 1) Since it is noninvasive, a study can be performed on subjects in a basal state and can be repeated any number of times. 2) The recording of valve motion is instantaneous and continuous, thus eliminating the cineangiographic film rate as a limitation in the timing of motion events. 3) Valve motion can be studied over many more cardiac cycles. 4) It does not require alteration of physiology by the injection of contrast media or the attachment of radiopaque material to the valve cusps so that they may be seen with cineangiography. At the same time, the limitations inherent in M-mode echocardiography should not be overlooked in the interpretation of data obtained by this method. Some of these limitations include: 1) The "ice pick" nature of a single view from one transducer position may not be representative of motion of the entire valve. 2) The amplitude of valve motion and timing of motion events depends on the angle of the echo beam relative to the motion of the valve, i.e., maximum valve motion is obtained when the leaflet is perpendicular to the echo beam and motion is parallel to it, while motion 90° to the echo beam may not be visualized at all, producing the so called "drop out" phenomenon or showing an apparent slow rate of motion. 3) In time-motion echocardiography, the recorded motion may not solely reflect independent valve leaflet motion, but a combination of leaflet and ring motion. It may also reflect valve motion relative to the echo transducer that is due to movement of the entire heart within the chest cavity.

The results of our study indicate that the initial slow and subsequent rapid anterior motion of the mitral valve noted by echocardiography is closely correlated with changes in the LA pressure. Figure 5 shows a schematic representation of the relationship between pressure, sound and the mitral valve echocardiogram. After A₂ during LV ventricular isovolumic relaxation, the rapidly falling LV pressure may cause descent of the mitral valve into the left ventricle, resulting in a gradual fall in the LA pressure or slow y descent. It can be seen echocardiographically that the mitral valve gradually moves anteriorly or away from the left atrium and into the LV cavity during this time. Studies by Zaky et al.¹⁸ have attributed this to ring motion, which may also explain why, when both leaflets are seen, no separation is noted at this time. With LV-LA pressure crossover, the anterior mitral leaflet echo moves rapidly anteriorly (D-E) accompanied by a rapid y descent in the LA pressure. That the valve is opening at this time is confirmed by separation of the anterior and posterior leaflets seen when both leaflets are visualized. Considering the limits of resolution of the method, the small time interval (7 ± 4 msec) found between pressure crossover and the echo D point may be insignificant.

While these studies were performed in patients with

---

**Figure 2.** Simultaneous equisensitive left atrial (LA) and left ventricular (LV) pressures, the mitral valve echo (MVE) and an external phonocardiogram (EXT PHONO). The onset of rapid anterior echo motion (D) and the rapid y descent in the LA pressure occurs with pressure crossover. The opening snap (OS) is coincident with the echo E point and occurs about 30 msec after pressure crossover.
FIGURE 3. Left atrial (LA) pressure and mitral valve echo (MVE) correlates during valve closure. The c wave rise in LA pressure occurs with the onset of the slow phase of posterior echo motion. Rapid posterior echo motion (B-C) is completed near the peak of the c wave.

FIGURE 4. Simultaneous left atrial (LA) and left ventricular (LV) pressure, the mitral valve echo (MVE), a LA and external phonocardiogram (EXT PHONO) in a patient with mitral stenosis and atrial fibrillation. The onset of posterior echo motion and the LA c wave begin after LV pressure rise. Rapid posterior echo motion (B-C) occurs only after LV-LA pressure crossover.

FIGURE 5. Schematic representation of the relationships between left ventricular (LV) and left atrial (LA) pressure, sound and the mitral valve echocardiogram (MVE). The dashed lines show the points of LV-LA pressure crossover. OS = opening snap.
mitral stenosis, Pohost et al., using fluid-filled catheters in dogs, have shown an interval of 17–33 msec from pressure crossover to the onset of rapid anterior motion (D point) of the mitral valve echo. In addition, Rubenstein et al., using fluid-filled pulmonary capillary wedge and LV pressures in man with normal valves, demonstrated that the echo D point followed pressure crossover by 27–30 msec. These differences may be primarily related to errors in accurately identifying the point of pressure crossover by extrapolation of data obtained from fluid-filled catheters, rather than the normality of the valve. This has been shown by the work of Laniado in dogs with normal valves, using high fidelity pressures, electromagnetic flow probes and both the anterior mitral leaflet echogram and cinefluoroscopy of the valve cusps which had been made radiopaque. Additional studies showed that the valve opening and flow across the mitral valve began with pressure crossover. Additional studies showed that the opening movement of the anterior leaflet echo started simultaneously with the onset of flow across the mitral valve.

The delay of 23 msec (range: 15–28 msec) from pressure crossover to full anterior echo excursion (E point) and the occurrence of the opening snap, however, is significant. These data are in agreement with the cineangiographic findings in mitral stenosis which showed that the y descent of the LA pressure occurred during the descent phase of the mitral valve which terminated 20–35 msec after pressure crossover at the time of the opening snap. Laniado et al. have also shown a delay of 25–40 msec from pressure crossover to full leaflet separation in dogs.

The posterior motion of the mitral valve echo at the time of closure also occurs in two phases, and is correlated with changes in LA pressure. After the onset of LV pressure rise at end-diastole, the mitral valve begins to move toward the left atrium while LA pressure still exceeds LV pressure. Since this movement may be primarily at right angles to the echo beam, it appears as a gradual posterior motion on the echocardiogram. With encroachment on the LA cavity by the upward moving mitral apparatus, there is a rise in LA pressure, the c wave. Once LV-LA pressure crossover occurs, rapid posterior motion of the anterior mitral leaflet echogram begins and the leaflets move into apposition with each other. The small delay (6 ± 5 msec) noted between pressure crossover and the echo B point is within the limits of resolution of this method. The peak of the LA c wave should be related to the mitral valve reaching the full extent of its excursion toward the left atrium at the echocardiographic point C. In some instances, the echocardiographic closure point (C point) occurs after the c wave peak and this discrepancy may be related to the “ice pick” view of the mitral valve obtained by standard echocardiography. Pohost et al. have angiographically demonstrated time differences between the motion patterns of two radiopaque clips placed at different sites on the anterior mitral leaflet free edge. Although the motion pattern of each clip and the anterior mitral leaflet echogram were similar, the timing of each differed.

In all previous angiographic and echocardiographic studies of mitral valve motion, a delay of 15–40 msec has been demonstrated between pressure crossover and complete valve closure. Laniado also showed that flow continued across the mitral valve for 30–40 msec after pressure crossover, indicating that the valve was still open. Our finding of a 15–28 msec delay from pressure crossover, to complete echocardiographic valve closure (point C) is in agreement with these previous observations. The small quantitative differences may be related to the technique of pressure measurement and the pathologic condition of the mitral valve.

Mitril valve opening and closure appears to be a complex series of events which can be defined by echocardiography. This study establishes the relationship between hemodynamic events and the mitral valve motion as depicted by the anterior mitral leaflet echocardiogram in patients with mitral stenosis. We believe that such studies performed in various physiologic and pathologic conditions will contribute significantly to the understanding of the patterns of echocardiographic valvular motion seen in clinical disease states.

References

15. Pohost GM, Dinsmore RE, Rubenstein JJ, O'Keefe DD,
Stroke Volume Calculated from the Mitral Valve Echogram in Patients With and Without Ventricular Dyssynergy

SUSAN RASMUSSEN, R.N., M.S.N., BETTY C. CORYA, M.D., HARVEY FEIGENBAUM, M.D., MARY JO BLACK, B.A., D. EUGENE LOVELACE, B.S., JOHN F. PHILLIPS, M.D., R. JOE NOBLE, M.D., AND SUZANNE B. KNOEBEL, M.D.

SUMMARY A formula was derived for calculating mitral valve stroke volume (MVSV) using the rate of mitral valve (MV) opening (DE slope on the MV echogram), the vertical distance between the mitral leaflet echoes early in diastole (EE), the electrocardiographic PR interval and heart rate. The formula was tested prospectively on 80 consecutive patients from whom 95 simultaneous MV echograms and either thermodilution (45) or Fick (50) cardiac outputs were obtained. Sixteen patients were normal; 54 had coronary artery disease; three had cardiomyopathy; and seven had nonrheumatic mitral regurgitation (MR). Linear regression for stroke volume was \( r = 0.90, SE \pm 0.6 \), and for cardiac output \( r = 0.83, SE \pm 0.5 \) liter for the 73 patients without MR. The presence or absence of ventricular dyssynergy did not alter statistical findings. MVSV consistently overestimated forward stroke volume for the seven patients with MR. This study shows that the MV echogram provides an accurate, widely applicable method for calculating MVSV.

MITRAL VALVE LEAFLET MOTION has been shown to be affected by valve stenosis and prolapse, left ventricular compliance, diastolic pressure, heart rate, and cardiac rhythm. Recordings of the volume of blood flow across the mitral valve in animal studies closely resemble the pattern of mitral valve motion seen echocardiographically. This similarity in motion suggests that the mitral valve echogram reflects blood flow across the valve.

The purpose of this study was to develop and test a clinically applicable method for calculating stroke volume based on information readily available from mitral valve echograms.

Materials and Methods

Patients

Three groups of patients (total number = 96) were included in this study, and 120 cardiac output determinations were made. The first group (A) was the subject of a pilot study and was comprised of 16 patients with coronary artery disease. Twenty-five simultaneous mitral valve echograms and thermodilution cardiac outputs (TDCOs) were performed while the Group A patients were in a coronary care unit. Groups B and C were prospective study groups. Group B represented 30 consecutive patients in a coronary care unit from whom 45 simultaneous mitral echograms and TDCOs were performed. Group C included 50 consecutive patients undergoing cardiac catheterization, including coronary cineangiography and left ventriculography studies, from whom mitral echograms were recorded simultaneously with a Fick cardiac output determination.

Pilot Study: Group A

One technically good mitral valve echogram was selected for each TDCO. In selecting a mitral valve echogram we looked for an echogram in which the DE slope appeared as a continuous echo; tips of both leaflets (EE) were well-defined; and the beat was neither preceded nor followed by a premature complex. The echogram was manually traced on a digital tablet and entered into a Tektronic graphic terminal. A DEC System 10 program was developed to collect the digital coordinates from the tablet. The coor-
Pressure and sound correlates of the mitral valve ecyocardiogram in mitral stenosis.
R Salerni, P S Reddy, M E Sherman, J D O'Toole, D F Leon and J A Shaver

Circulation. 1978;58:119-125
doi: 10.1161/01.CIR.58.1.119

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1978 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/58/1/119.citation

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/