Can Coronary Blood Flow Velocity Pattern After Primary Percutaneous Transluminal Coronary Angiography Predict Recovery of Regional Left Ventricular Function in Patients With Acute Myocardial Infarction?

Takahiro Kawamoto, MD; Kiyoshi Yoshida, MD; Takashi Akasaka, MD; Takeshi Hozumi, MD; Tsutomu Takagi, MD; Shuichiro Kaji, MD; Yoshiaki Ueda, MD

Background—In the era of primary percutaneous transluminal coronary angioplasty (PTCA), it is important to judge whether myocardium within acute ischemic injury is viable. This study sought to investigate parameters derived from the coronary blood flow velocity spectrum immediately after primary PTCA in patients with acute myocardial infarction and to elucidate the clinical value of coronary blood flow measurement in predicting myocardial viability.

Methods and Results—Using a Doppler guidewire, we measured coronary blood flow velocity after successful completion of primary PTCA in 23 consecutive patients with acute anterior myocardial infarction. Regional wall motion was analyzed to estimate anterior wall motion score index (A-WMSI) by echocardiography before PTCA and 1 month after the onset of symptoms. Average systolic peak velocity (ASV) and deceleration time of diastolic flow velocity (DDT) significantly correlated to 1-month A-WMSI ($r = 0.54, P = 0.007$ and $r = 0.62, P = 0.002$, respectively), and optimal cutoff values to predict viable myocardium (defined as 1-month A-WMSI $\leq 2.0$) were 6.5 cm/s for ASV and 600 ms for DDT (sensitivity = 0.79, specificity = 0.89 and sensitivity = 0.86, specificity = 0.89, respectively). ASV and DDT also correlated weakly to the change in A-WMSI ($r = 0.46, P = 0.03$ and $r = 0.49, P = 0.02$, respectively).

Conclusions—Low ASV and rapid DDT of coronary blood flow spectrum immediately after primary PTCA reflects a greater degree of microvascular damage in the risk area. Analysis of coronary blood flow spectrum immediately after primary PTCA by use of a Doppler guidewire is useful in predicting recovery of regional left ventricular function. (Circulation. 1999;100:339-345.)

Key Words: angioplasty ■ microcirculation ■ myocardial infarction ■ prognosis ■ reperfusion

Percutaneous transluminal coronary angioplasty has been widely performed in cases of acute myocardial infarction (AMI) because of a higher rate of recanalization, better preserved left ventricular function, and a lower rate of complications compared with thrombolysis.1–4 However, patency of the infarct-related coronary artery does not always guarantee salvage of myocardium at risk of ischemia.5 Therefore, the great interest of many cardiologists is in the viability of reperfused myocardium. Assessment of regional myocardial perfusion by contrast echocardiography has revealed a no-reflow phenomenon, which is defined as a lack of enhancement of myocardium by microbubbles despite recanalization of the infarct-related coronary artery5–7; this phenomenon is thought to be established as a result of microvascular damage induced by ischemia. Some studies have shown that the no-reflow segment is not viable,5,8 and it has been shown by use of a Doppler guidewire that the coronary blood flow velocity pattern of no-reflow in patients with reperfused AMI is characterized by the appearance of systolic retrograde flow, diminished systolic antegrade flow, and rapid deceleration of diastolic flow.9 However, the relationship between the coronary blood flow velocity pattern immediately after primary PTCA and the recovery of left ventricular function has not been discussed fully. Therefore, we hypothesized that the degree of reduced systolic antegrade flow or the deceleration time of diastolic flow might reflect the degree of microvascular damage and be predictive of residual myocardial viability. To test this hypothesis, we prospectively compared the coronary blood flow velocity pattern immediately after primary PTCA with use of a Doppler guidewire and the recovery of regional left ventricular wall motion in the risk area assessed by echocardiography in 23 consecutive patients with successfully reperfused anterior AMI.

Methods

Study Population
This study comprised 23 consecutive patients (21 men and 2 women; mean age, 61±10 years; age range, 45 to 75 years) with anterior...
AMI who were successfully recanalized with primary PTCA including rescue stenting within 12 hours after the onset of symptoms. The study inclusion criteria were as follows: (1) first anterior AMI, (2) successful recanalization with primary PTCA (defined as residual stenosis ≤25% visually) within 12 hours after the onset of symptoms, and (3) informed consent to perform primary PTCA and coronary blood flow measurement. The diagnosis of AMI was based on >30 minutes of continuous chest pain, ST elevation >2.0 mm in ≥2 contiguous ECG leads, a >3-fold increase over the normal value in serum creatine kinase, and Thrombolysis In Myocardial Infarction (TIMI) flow grade 0, 1, or 2 at initial coronary angiography. We excluded patients with prior myocardial infarction, those with a cardiac event during follow-up, and those with inadequate recording of coronary flow velocity spectrum or poor echocardiographic image. The study protocol was approved by the ethics committee of Kobe General Hospital. One of the investigators obtained informed consent from all patients before cardiac catheterization.

### Study Protocol

Regional wall motion was examined in the emergency room by use of echocardiography to determine the risk area before angioplasty. All patients received an intravenous bolus injection of 4000 U of heparin before angiography, and a 0.5 mg · kg⁻¹ · min⁻¹ of nitroglycerin was continuously given intravenously soon after establishment of the diagnosis. Intracoronary isosorbide dinitrate (2 mg) was given before coronary angiography. Diagnostic coronary angiography was performed via the femoral approach by use of the Judkins technique. After an additional intravenous or intra-arterial bolus injection of 6000 U of heparin, coronary angioplasty, including rescue stenting, was performed. Stents were deployed by high-pressure implantation techniques. An angiographic criterion of <25% residual stenosis was used to determine the end point of the angioplasty procedure. After successful angioplasty, the guidewire was exchanged for a 0.014-in Doppler guidewire (FloWire; Cardiometrics, Inc). The tip of the Doppler guidewire was placed slightly distal to the culprit lesion, where there was neither a significant stenosis nor a large side branch angiographically, to assess coronary blood flow to the entire area at risk. Phasic coronary blood flow velocity spectrum was recorded on a Super VHS videotape (FloMap; Cardiometrics, Inc) >10 minutes after the last balloon inflation. Serum creatine kinase was measured serially every 3 hours after recanalization until the peak value was obtained. Patients received conventional drug therapy according to individual need, which was determined by the attending physician. The stented patients received anticoagulation with a ticlopidine and aspirin regimen (ticlopidine 100 mg twice a day and aspirin 81 mg twice a day). All patients underwent follow-up echocardiography to examine regional wall motion recovery 1 month after the onset of symptoms.

### Echocardiographic Wall Motion Analysis

The left ventricular wall was divided into 16 segments, and the regional wall motion of each segment was examined and scored according to the American Society of Echocardiography, in which 1 is normal, 1.5 is mild hypokinesis, 2 is hypokinesis, 2.5 is severe hypokinesis, 3 is akinesis, and 4 is dyskinesia. Nine of the 16 segments were determined to be in the vicinity of the left anterior descending coronary artery (LAD), and the anterior wall motion score index (A-WMSI) was calculated as a modification of the wall motion scores in these 9 segments (Figure 1). The change in A-WMSI was also estimated.

### Analysis of Coronary Blood Flow Velocity Spectrum

The coronary blood flow velocity spectrum recorded on a Super VHS videotape was digitized by offline computerized planimetry. The digitized coronary blood flow velocity spectrum provided the following parameters: time-averaged peak velocity (cm/s; APV), average systolic peak velocity (cm/s; ASV), average diastolic peak velocity (cm/s; ADV), maximal peak velocity (cm/s; MPV), and deceleration time of diastolic flow velocity (ms; DDT). Retrograde flow was calculated as a negative value.

---

**Table 1. Patient Characteristics and Clinical Results**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>23</td>
</tr>
<tr>
<td>Age, y</td>
<td>61 ± 10</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>21/2</td>
</tr>
<tr>
<td>Onset to recanalization time, min</td>
<td>250 ± 129</td>
</tr>
<tr>
<td>Segment 6 (%)</td>
<td>17/23 (74)</td>
</tr>
<tr>
<td>%DS before PTCA</td>
<td>89 ± 15</td>
</tr>
<tr>
<td>%DS after PTCA</td>
<td>26 ± 15</td>
</tr>
<tr>
<td>MLD after PTCA, mm</td>
<td>2.4 ± 0.7</td>
</tr>
<tr>
<td>TIMI 3 flow (%)</td>
<td>20/23 (87)</td>
</tr>
<tr>
<td>Peak creatine kinase, IU/L</td>
<td>5116 ± 3849</td>
</tr>
<tr>
<td>Q-wave infarction (%)</td>
<td>19/23 (83)</td>
</tr>
<tr>
<td>A-WMSI on admission</td>
<td>2.49 ± 0.45</td>
</tr>
<tr>
<td>1 month A-WMSI</td>
<td>1.93 ± 0.54</td>
</tr>
</tbody>
</table>

%DS indicates % diameter stenosis and MLD, minimum lumen diameter.

---

**Figure 1.** Diagram of LAD territory. LAX indicates long-axis view; SAX PM, short-axis view at papillary muscle level; 4C, 4-chamber view; 2C, 2-chamber view; Sept, septal; Ant, anterior; Lat, lateral; Post, posterior; and Inf, inferior.
TABLE 2. Comparison Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Viable Myocardium Group (A-WMSI≤2.0)</th>
<th>Nonviable Myocardium Group (A-WMSI&gt;2.0)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>14</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>63±9</td>
<td>58±10</td>
<td>0.23</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>12/2</td>
<td>9/0</td>
<td>0.24</td>
</tr>
<tr>
<td>Onset to recanalization time, min</td>
<td>272±155</td>
<td>216±69</td>
<td>0.32</td>
</tr>
<tr>
<td>Segment 6 (%)</td>
<td>10/14 (71)</td>
<td>7/9 (78)</td>
<td>0.73</td>
</tr>
<tr>
<td>%DS before PTCA</td>
<td>86±17</td>
<td>93±12</td>
<td>0.29</td>
</tr>
<tr>
<td>%DS after PTCA</td>
<td>28±17</td>
<td>24±14</td>
<td>0.59</td>
</tr>
<tr>
<td>TIMI after PTCA, mm</td>
<td>2.2±0.6</td>
<td>2.7±0.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Peak creatine kinase, IU/L</td>
<td>3445±3054</td>
<td>7716±3617</td>
<td>0.006</td>
</tr>
<tr>
<td>A-WMSI on admission</td>
<td>2.37±0.48</td>
<td>2.69±0.35</td>
<td>0.10</td>
</tr>
<tr>
<td>1 month A-WMSI</td>
<td>1.58±0.33</td>
<td>2.48±0.24</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

Analysis of Coronary Angiogram
Percent diameter stenosis and minimum lumen diameter of the culprit lesion were quantitatively analyzed offline by auto edge detection with a validated technique (CMS; Medical Imaging Systems, Inc)14 from a cineangiogram taken before and after primary PTCA. Contrast flow through the infarct-related coronary artery was graded by the standard TIMI flow scale of 0 to 3 from the initial coronary angiogram.15 Collateral flow was graded according to the Rentrop classification of 0 to 3 from the final coronary angiogram.16

Statistics
Results are reported as mean±SD unless otherwise indicated. The difference between A-WMSI before recanalization and A-WMSI at 1 month after symptom onset was evaluated by paired Student’s t test. Comparisons of continuous variables between 2 groups were made by unpaired Student’s t test. The χ² test was used to compare categorical variables. Linear regression analysis was applied to estimate the relation between parameters obtained from coronary blood flow velocity spectrum recordings and 1-month A-WMSI or estimate the relation between parameters obtained from coronary angiography and 1-month A-WMSI or estimate the relation between parameters obtained from coronary angiography and 1-month A-WMSI. Statistical differences were considered significant at a value of P<0.05. The ability of the coronary blood flow parameters to predict viable myocardium was analyzed by use of receiver operating characteristic (ROC) curves, ie, plots of sensitivity versus 1−specificity.17,18

Results
Patient Characteristics and Clinical Results
Thirteen patients (57%) had a history of hypertension, 7 (30%) had diabetes mellitus, 12 (52%) had a cholesterol level >220 mg/dL, and 16 (70%) were smokers. Mean time from the onset of symptoms to coronary reperfusion was 250±129 minutes. Peak creatine kinase level was 5116±3849 IU/L. Nineteen patients developed Q-wave infarction, whereas the other 4 manifested non–Q-wave infarction. There was no clinical, ECG, or enzymatic evidence of reinfarction in any other patient during the 1-month follow-up. In-hospital medications were as follows: nitrate (n=23; 100%), ACE inhibitor (n=19; 83%), β-adrenergic blocking agent (n=14; 61%), calcium antagonist (n=3; 13%), and diuretics (n=3; 13%). (See Table 1.)

Angiographic Results
Primary PTCA, including rescue stenting, was successfully performed in all patients. The culprit lesion was the proximal LAD (segment 6) in 17 patients and mid LAD (segment 7) in 6. Eighteen patients had single-vessel disease, 4 had double-vessel disease, and 1 had triple-vessel disease. No patient showed good collateral flow (Rentrop grade 3), 4 showed fair collateral flow (Rentrop grade 2), and the remaining 19 showed poor or no collateral flow (Rentrop grade 1 or 0) on the initial coronary angiogram. Rescue stenting was performed in 10 patients, and the reasons for rescue stenting were as follows: suboptimal result after repeat balloon inflation (n=5), large dissection (n=2), and haziness or recurrent thrombus (n=3). Percent diameters of stenosis before and after angioplasty were 89±15% and 26±15%, respectively. Minimum lumen diameter after angioplasty was 2.4±0.7 mm. Three patients showed TIMI 2 reflow, and the remaining 20 patients showed TIMI 3 reflow. Only 2 patients had insignificant stenosis distal to the culprit lesion. (See Table 1.)

Baseline and Follow-Up Echocardiography
Baseline and follow-up echocardiography examinations were performed in all 23 patients. A-WMSI decreased significantly from baseline to follow-up (from 2.49±0.45 to 1.93±0.54; P<0.0001; Figure 2), and the change in A-WMSI was 0.56±0.42.

TABLE 3. Parameters of Coronary Flow Velocity Spectrum After Primary PTCA

<table>
<thead>
<tr>
<th></th>
<th>Viable Myocardium Group (A-WMSI≤2.0)</th>
<th>Nonviable Myocardium Group (A-WMSI&gt;2.0)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>APV, cm/s</td>
<td>18±7</td>
<td>18±10</td>
<td>0.96</td>
</tr>
<tr>
<td>ASV, cm/s</td>
<td>12±6</td>
<td>2±8</td>
<td>0.004</td>
</tr>
<tr>
<td>ADV, cm/s</td>
<td>21±8</td>
<td>28±13</td>
<td>0.16</td>
</tr>
<tr>
<td>MPV, cm/s</td>
<td>28±11</td>
<td>56±24</td>
<td>0.0009</td>
</tr>
<tr>
<td>DDT, ms</td>
<td>954±326</td>
<td>470±181</td>
<td>0.0006</td>
</tr>
</tbody>
</table>
Relation Between Coronary Blood Flow Velocity Pattern and Late Results

In accordance with a previous report on low-dose dobutamine echocardiography,13 we defined viable myocardium as 1-month A-WMSI ≤2.00. We divided our patients into 2 groups: viable myocardium group (1-month A-WMSI ≤2.00) and nonviable myocardium group (1-month A-WMSI >2.00). The viable group showed a higher rate of TIMI 3 reflow (14 of 14 versus 6 of 9; P=0.02), a lower peak creatine kinase value (3445±3054 versus 7716±3617 IU/L; P=0.006), and a lower 1-month A-WMSI (1.58±0.33 versus 2.48±0.24; P<0.0001). However, there was no significant difference in baseline characteristics, residual stenosis, or A-WMSI before recanalization (Table 2). Doppler velocimetry data showed significantly higher ASV (12±6 versus 2±8 cm/s; P=0.004), lower MPV (28±11 versus 56±24 cm/s; P=0.0009), and longer DDT (954±326 versus 470±181 ms; P=0.0006) in the viable group compared with the nonviable group (Table 3). Figures 3 and 4 show a typical coronary blood flow velocity spectrum in patients from the viable and nonviable groups, respectively. The coronary blood flow velocity pattern with viable myocardium seems almost normal and that with nonviable myocardium shows reduced ASV caused by systolic retrograde flow and rapid deceleration of diastolic flow velocity. ASV and DDT imme1diately after primary PTCA were compared with 1-month A-WMSI. ASV and DDT significantly correlated with 1-month A-WMSI (y=−8.5x+24.4, r=−0.54, P=0.007 and y=−420x+1576, r=−0.62, P=0.002, respectively; Figure 5), with substantial scatter. On the basis of ROC curve analysis,17,18 optimal cutoff values of 6.5 cm/s for ASV and 600 ms for DDT were chosen to predict viable myocardium (sensitivity=0.79, specificity=0.89 and sensitivity=0.86, specificity=0.89, respectively). There was also a weak correlation between ASV and DDT and the change in A-WMSI (y=9.2x+2.8, r=0.46, P=0.03 and y=428x+524, r=0.49, P=0.02, respectively).

Although stented patients showed significantly lower percent diameter stenosis (17±14% versus 34±13%; P=0.005) and larger minimum lumen diameter (2.7±0.6 versus 2.1±0.6 mm; P=0.03), there was no significant difference in 1-month A-WMSI (1.87±0.59 versus 1.97±0.51; P=NS) or in coronary blood flow parameters (APV, 18±8 versus 17±8 cm/s; ASV, 9±10 versus 7±7 cm/s; ADV, 24±10 versus 23±11 cm/s; DDT, 709±293 versus 808±418 ms; all P=NS) between stented and nonstented patients.

Discussion

We directly measured coronary blood flow velocity after successful primary PTCA and investigated the relationship of the parameters derived from coronary blood flow velocity spectrum at reperfusion and preserved myocardial viability at
late stage. Our major finding was that the higher the ASV and the longer the DDT of the coronary blood flow velocity pattern after primary PTCA, the more the myocardium within a region of acute ischemic injury would recover. We conclude that a low ASV and short DDT can represent characteristics of coronary blood flow with severe microvascular damage, given no significant residual stenosis in the epicardial coronary artery and given that ASV and DDT at reperfusion are predictive of the recovery of regional left ventricular function. To the best of our knowledge, this is the first report to directly compare the coronary blood flow velocity pattern immediately after primary PTCA with the recovery of regional left ventricular function.

**Coronary Blood Flow Velocity Pattern and Microvascular Damage**

In the present study, patients with low ASV showed poorer regional recovery of left ventricular function. Early systolic retrograde flow has previously been reported to be observed frequently in patients with no reflow in case of AMI after successful recanalization. In that previous report, early systolic retrograde flow was explained by an occluded coronary microvasculature, which is thought to cause backflow during systole by contraction of the myocardium. We believe the degree of backflow during systole reflects ASV and that the higher percentage of occluded coronary microvasculature in the infarct-related coronary bed reflects a lower ASV.

**Figure 4.** Coronary blood flow spectrum immediately after recanalization in patient from the nonviable group. Early systolic retrograde flow is dominant, and antegrade flow is decreased. Diastolic peak velocity showed rapid deceleration. In this case, A-WMSI was 3.00 before recanalization and 2.78 1 month after symptom onset. Little functional recovery was seen despite successful recanalization.

**Figure 5.** Comparisons of ASV and DDT with 1-month (1M) A-WMSI. There is a significant correlation between the 2 variables.
Experimental study has demonstrated that microvascular ischemic damage after epicardial coronary artery occlusion affects coronary vascular resistance, and perivascular edema and capillary leukocyte plugging after myocardial ischemia contribute to prevention of full restoration of myocardial perfusion. Short DDT may be explained by an increase in coronary vascular resistance caused by such ischemic microvascular damage. The high ratio of perfused myocardium per functioning coronary microvasculature might reflect the coronary blood flow and would be observed as a short DDT.

Although much better correlation would be expected between ASV, DDT, and the change in A-WMSI, only weak correlations were obtained. This might be related to the fact that good wall motion segments before recanalization, which could be out of the substantial area at risk, were included.

**Coronary Blood Flow and TIMI Flow Grade**

The TIMI study group grading system has been widely used to assess coronary perfusion, and some studies have shown worse outcome with TIMI grade 2 reflow than with TIMI grade 3 reflow. Because the TIMI criterion is based on visual judgment of radiocontrast media runoff in coronary angiography and is thought to be affected by various factors, such as injection speed, injection volume, and diameter and size of the coronary artery, an accurate assessment of coronary blood flow is quite difficult. We demonstrated that more quantitative assessment of coronary blood flow was possible in patients with reperfused AMI by use of a Doppler guidewire, as previously reported.

**Study Limitations**

First, we assumed A-WMSI at 1 month to be an indicator of myocardial viability. This parameter is considered to represent myocardial viability but to be semiquantitative. Further examination should be done in comparison with a single-photon emission CT (SPECT) or PET study to assess the degree of myocardial damage more quantitatively.

Second, the coronary blood flow velocity pattern may alter with the stenosis. In the present study, there was no significant difference in coronary blood flow parameters between stented and nonstented subjects, and therefore the effect of residual stenosis of the epicardial coronary artery should be minimal. The routine use of stents could decrease residual stenosis to almost 0%; thus, the effect of stenosis in the epicardial coronary artery should not be considered.

Third, coronary blood flow measurements were performed 10 minutes after the last balloon inflation in the present study. Some studies have documented that the hyperemic response continues for several hours and that coronary perfusion dynamically alters within a few hours after prolonged coronary occlusion in animals. These dynamic coronary flow changes after reperfused AMI may be the reason for the substantial scatter in plots of ASV and DDT versus 1-month A-WMSI demonstrated in Figure 5. The continuous observation of coronary blood flow alternation for several hours after recanalization could resolve these issues.

**Clinical Implications**

In the present study, we revealed the characteristics of coronary blood flow with effective reperfusion and demonstrated that ASV and DDT after reperfused coronary artery were predictive of the recovery of regional left ventricular function. Analysis of coronary blood flow velocity pattern by use of a Doppler guidewire can be used to predict the regional recovery of left ventricular function at the time of recanalization. This should be helpful in treating patients with reperfused acute myocardial infarction.

**Acknowledgments**

The authors gratefully acknowledge the excellent assistance of all medical personnel of the coronary care unit and catheterization laboratory.

**References**


11. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I, Silverman NH, Tajik AJ. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography: American Society of Echocardiography Committee on Standards, Subcommittee on Quantification of Two-


Can Coronary Blood Flow Velocity Pattern After Primary Percutaneous Transluminal
Coronary Angiography Predict Recovery of Regional Left Ventricular Function in
Patients With Acute Myocardial Infarction?
Takahiro Kawamoto, Kiyoshi Yoshida, Takashī Akasaka, Takeshi Hozumi, Tsutomu Takagi,
Shuichīro Kaji and Yoshiaki Ueda

_Circulation_. 1999;100:339-345
doi: 10.1161/01.CIR.100.4.339
_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/100/4/339

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/