Electrocardiographic Left Atrial Abnormalities and Risk of Ischemic Stroke

Shun Kohsaka, MD; Robert R. Sciacca, EngScD; Kenichi Sugioka, MD; Ralph L. Sacco, MD; Shunichi Homma, MD, FACC; Marco R. Di Tullio, MD

Background and Purpose—We evaluated the association between electrocardiographic left atrial abnormality (ECG-LAA) and ischemic stroke, especially whether ECG-LAA provides additional prognostic information to that provided by echocardiography.

Methods—A population-based, case-control study included 146 patients with first ischemic stroke and 195 age-, gender-, and race/ethnicity-matched community control subjects. ECG-LAA was defined as either P-wave duration >120 ms or P-terminal force in precordial lead V1 (PTFV1) >40 mV·ms.

Results—PTFV1 >40 mV·ms was associated with ischemic stroke after adjustment for other stroke risk factors (odds ratio [OR], 2.32; 95% CI, 1.29 to 4.18). The association remained significant after adding echocardiographic left atrial diameter to the model (OR, 2.31; 95% CI, 1.28 to 4.17). PTFV1 was independently associated with stroke in patients in the upper half of echocardiographically determined left ventricular mass (adjusted OR, 4.5; 95% CI, 2.20 to 9.15) but not in those in the lower half (OR, 0.58; 95% CI, 0.20 to 1.65; P=0.0008).

Conclusions—ECG-LAA can supplement 2D echocardiography in assessing the risk of ischemic stroke, especially in subjects with increased left ventricular mass. (Stroke. 2005;36:2481-2483.)

Key Words: echocardiography • electrocardiography • risk factors • stroke

Left atrial (LA) enlargement is a risk factor for ischemic stroke.1,2 LA anteroposterior diameter by 2D echocardiography (Echo-LAE) is commonly used for evaluating the LA size but has limitations related to the LA irregular geometry and physical constraints imposed by the spine and sternum. In clinical studies, Echo-LAE provided contradictory results as a predictor for ischemic stroke. For chronic atrial fibrillation, Echo-LAE was of no value for predicting thromboembolism,3 whereas LA size was a main predictor of stroke.4 Reasons for these conflicting data remain unclear.

Assessment of electrocardiographic LA abnormality (ECC-LAA) is a noninvasive and universally available method. ECG-LAA is observed in the setting of hypertensive heart disease5 and is known to reflect increases in left ventricular (LV) filling pressure and the consequent remodeling process.6 Reliable ECC-LAA criteria might offer a simple and inexpensive way to predict the risk of ischemic stroke in addition to echocardiographic LA assessment.

Methods
Patients were drawn from the Northern Manhattan Stroke Study (NOMASS), a community-based epidemiological study for assessing stroke incidence, risk factors, and prognosis in the multiethnic population of northern Manhattan.7 From June 1993 through December 1996, 234 patients (>39 years of age) with computed tomography- or MRI-confirmed first-time ischemic stroke and 286 stroke-free controls were recruited. A total of 88 stroke patients and 91 control subjects were excluded because of absence of native P-waves on the ECG (eg, atrial fibrillation, pacemaker rhythm), leaving 146 stroke patients and 195 control subjects.

Echocardiographic and electrocardiographic studies were interpreted blinded to case-control status and other clinical characteristics. Interobserver and intraobserver variability for variables measured ranged between 8% and 10%. LA enlargement was defined as (1) a P-wave duration in limb leads >120 ms, and (2) an area subtended by the terminal negative component of a biphasic P-wave in precordial lead V1 (PTFV1) >40 mV·ms.8 The area for PTFV1 was calculated by multiplication of the duration and depth of the waveform. LA diameter was measured by 2D transthoracic echocardiography at the level of the aortic valve and normalized by the subject’s body surface area. Values for normalized LA diameters were divided into quartiles, with the highest quartile considered LA enlargement.

Univariate and multivariate logistic regression analysis was used to test the association between ECG-LAA and ischemic stroke. Multivariate analysis was used to determine the odds ratio (OR) for ECG-LAA and ischemic stroke after adjusting for established stroke risk factors. Echocardiographically determined LA index (continuous variable) was included in a second multivariate model to determine whether the association of ECG-LAA and ischemic stroke was independent of echocardiographic measurements. Echocardiographically derived LV mass index (continuous variable) was also included in the model.

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From the Departments of Medicine (R.R.S., K.S., S.H., M.R.DiT.) and Neurology (R.L.S.), Columbia-Presbyterian Medical Center, New York, NY; and the Department of Cardiology (S.K.), Texas Heart Institute and Baylor College of Medicine, Houston.
Correspondence to Marco R. Di Tullio, MD, Professor of Clinical Medicine, Associate Director, Adult Echocardiography Laboratory, Columbia University Medical Center, PH3-342, 622 W 168th St, New York, NY 10032. E-mail md42@columbia.edu
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**Results**

Demographics and measured echocardiographic parameters are shown in Table 1. For stroke patients, ECG-LAA assessed by the P-wave interval was noted in 2.7% and by PTFV1 in 54%. The sensitivity and specificity of PTFV1 was 54% and 62%, with the likelihood ratio for a positive and negative test of 1.4 and 0.8, respectively. The positive and negative predictive values were 51% and 64%, respectively. The stroke risk associated with Echo-LAE and ECG-LAA is reported in Table 2. Among the ECG-LAA criteria studied, PTFV1 was found to be associated with stroke in multivariate analysis (OR, 2.35; 95% CI, 1.29 to 4.18). The association remained significant after adjustment for Echo-LAE (OR, 2.31; 95% CI, 1.28 to 1.65). A highly significant interaction between PTFV1 and LV mass on the stroke risk was observed ($P=0.0008$).

The effect of PTFV1 on stroke risk was strongly dependent on LV mass. After adjustment for other stroke risk factors, a strong increase in stroke risk with PTFV1 was observed only in subjects in the 2 highest quartiles of LV mass index (Figure). The adjusted OR for stroke in subjects in the upper half of LV mass distribution was 4.5 (95% CI, 2.20 to 9.15), whereas for those in the lower half, it was 0.58 (95% CI, 0.20 to 1.65). A highly significant interaction between PTFV1 and LV mass on the stroke risk was observed ($P=0.0008$).

**Discussion**

The finding that ECG-LAA is related to ischemic stroke is new and of interest. Although sensitivity and specificity of ECG-LAA for stroke diagnosis were modest, the strength of the association between ECG-LAA and ischemic stroke was of a similar magnitude to that of Echo-LAE and stroke. Moreover, the association between PTFV1 and stroke remained significant even after adjusting for the presence of Echo-LAE, which suggests that ECG-LAA may be used to supplement the role of Echo-LAE for assessing the risk of ischemic stroke. Because Echo-LAE measurements carry certain limitations because of irregular LA geometry, ECG-LAA, which reflects global electrophysiological changes secondary to atrial remodeling, could overcome these limitations.

Of all criteria for LA abnormality, PTFV1 is the most commonly used and consistent. Therefore, it is not entirely surprising that PTFV1 was more sensitive than a wide P-wave for predicting ischemic stroke. However, ECG patterns that reflect a change in LA morphology can be secondary to multiple factors, including electrical remodeling and other

**TABLE 1. Demographics, Stroke Risk Factors, and Echocardiographic Parameters**

<table>
<thead>
<tr>
<th>Demographic matching criteria</th>
<th>Stroke Patients (n=146)</th>
<th>Control Subjects (n=195)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69.5±11.0</td>
<td>67.6±11.3</td>
<td>0.13</td>
</tr>
<tr>
<td>Male (%)</td>
<td>70 (48.0)</td>
<td>87 (44.6)</td>
<td>0.54</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>42 (28.8)</td>
<td>58 (29.7)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>78 (53.4)</td>
<td>97 (49.7)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>22 (15.1)</td>
<td>39 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Stroke risk factors (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>98 (67.1)</td>
<td>99 (50.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes</td>
<td>52 (35.6)</td>
<td>25 (12.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>34 (24.6)</td>
<td>35 (18.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>53 (36.6)</td>
<td>86 (44.1)</td>
<td>0.16</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>44 (30.1)</td>
<td>36 (18.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>15 (10.3)</td>
<td>8 (4.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>LVH (echocardiographic)</td>
<td>72 (50.7)</td>
<td>48 (25.5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**TABLE 2. Risk of Ischemic Stroke for Various Echocardiographic and Electrocardiographic Criteria for LA Enlargement and Abnormality**

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted for Stroke Risk Factors</th>
<th>Adjusted for Stroke Risk Factors and Echo-LAE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>$P$ Value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Echo-LAE</td>
<td>2.95 (1.50–5.79)</td>
<td>0.002</td>
<td>1.98 (0.74–5.24)</td>
</tr>
<tr>
<td>P-wave &gt;120 ms</td>
<td>1.35 (0.33–5.47)</td>
<td>0.68</td>
<td>2.13 (0.38–11.86)</td>
</tr>
<tr>
<td>PTFV1 &gt;40 ms-mm</td>
<td>1.89 (1.22–2.92)</td>
<td>0.004</td>
<td>2.35 (1.29–4.18)</td>
</tr>
</tbody>
</table>
pathological changes, and might not be attributable to a change in size.\textsuperscript{9} The electrophysiological effects of stroke itself can be a potential confounder as well.

LA size is significantly associated with LV mass, and any condition causing LV hypertrophy (LVH) may produce Echo-LAE as a secondary phenomenon. The association between PTFV\textsubscript{1} and stroke in our study was limited to subjects with increased LV mass, and a strong interaction was noted. We reported previously on the influence of LVH on the association between LA size and stroke, especially in women.\textsuperscript{2} The relationship between ECG LVH and echo-calculated LV mass for risk of ischemic stroke has also been demonstrated.\textsuperscript{10} The present data suggest that a simple ECG-derived parameter of LA abnormality may help refine the prediction of stroke risk in subjects with increased LV mass. LA abnormality, and possibly an associated tendency to develop atrial arrhythmias, might also be involved in the explanation of the well-known association of LVH with stroke.

**Conclusions**

A PTFV\textsubscript{1} $>$40 ms-mm is strongly and independently associated with ischemic stroke in subjects in the upper half of echocardiographic LV mass distribution. Additional studies are necessary to define the complex factors linking LV mass, LA size, and LA electrical abnormalities to ischemic stroke.

**Acknowledgments**

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**References**

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http://stroke.ahajournals.org/content/36/11/2481