An Electrocardiographic Criterion for Diagnosis of Patent Foramen Ovale Associated With Ischemic Stroke

Hakan Ay, MD; Ferdinando S. Buonanno, MD; Stephen A. Abraham, MD; J. Philip Kistler, MD; Walter J. Koroshetz, MD

Background and Purpose—An M-shaped bifid notch on the ascending branch, or on the zenith, of the R wave in inferior ECG leads (II, III, aVF), so called “crochetage,” is an indicator of ostium secundum atrial septal defects. The pathophysiology underlying this finding remains unknown. A crochetage pattern has not been previously reported in patients with patent foramen ovale (PFO); however, the location of this defect and the secundum atrial septum are similar. The purpose of this study was to determine the prevalence of crochetage in cryptogenic stroke patients with or without PFO.

Methods—A conservative selection scheme was used to identify patients likely to have had PFO-associated strokes (ie, cryptogenic) and to exclude any structural, functional, or vascular heart disease responsible for ECG changes. All patients had a standard 12-lead ECG. The prevalence of crochetage in each group was determined.

Results—Sixty consecutive patients were studied (28 with echo-documented PFO and 32 echo-negative control subjects). The crochetage pattern was present in at least 1 inferior limb lead in 10 of 28 PFO patients (36%) and 3 of 32 control subjects (9%) (P<0.05). The sensitivity and specificity of the crochetage pattern for diagnosis of PFO in cryptogenic stroke cases were 36% and 91%, respectively; positive predictive value was 77%.

Conclusions—The finding of an ECG crochetage pattern may help to identify stroke patients with PFO, may help to streamline their diagnostic workup, and may warrant future studies to determine its value in stratifying stroke risk in patients with PFO. (Stroke. 1998;29:1393-1397.)

Key Words: cerebral ischemia ■ cerebral infarction ■ electrocardiography ■ foramen ovale, patent

Paradoxical embolus through a PFO, a potential channel between the atria, has recently been proposed as a major cause of otherwise cryptogenic embolic stroke.1 The primary, but indirect, evidence rests on the significantly higher prevalence of echocardiographic diagnosis of PFO, especially in young stroke patients without other known causes.1-4 Quick and accurate diagnosis of PFO is important in patients with stroke or TIA to prevent early cerebral or systemic embolic recurrences. However, in common practice, diagnosis of PFO is usually delayed because patients are scheduled for echocardiography days after the onset of stroke. Furthermore, in most centers, transthoracic color Doppler echocardiography is the choice in routine evaluation of stroke patients, but its yield in detecting PFO is very low.5 Moreover, the image quality of color TTE is often degraded during the Valsalva maneuver, a maneuver crucial for creating a right-to-left shunt in those persons without spontaneous shunting. More sensitive, albeit more invasive, techniques such as transesophageal echocardiography or transcranial Doppler ultrasonography are required for the diagnosis of PFO. A readily available indicator of the presence of PFO in stroke patients could streamline the diagnostic evaluation and patient management.

A notched pattern of the R wave, so called “crochetage,” in the inferior limb leads has recently been demonstrated to be associated with ostium secundum-type atrial septal defect (ASD).6 The exact mechanism leading to a crochetage pattern in ASD is not known. Crochetage has not been reported previously in patients with PFO. However, the similar location of PFO and ostium secundum ASD, and the hemodynamic similarities between a large PFO and an ASD, motivated us to investigate the prevalence of crochetage in cryptogenic stroke patients with PFO.

Subjects and Methods

We examined the hospital records of patients admitted between March 1990 and March 1997 with the diagnosis of first-ever ischemic stroke or TIA. The procedures followed were in accordance with institutional guidelines and with the approval of the Institutional Review Board. All patients had clinical symptoms consistent with a specific arterial distribution in the retina, cerebral hemisphere, or brain stem. Symptoms were transient and lasted less than 24 hours in patients with TIA, or longer than 24 hours in those with ischemic stroke. All patients had brain CT or MRI studies compatible with...
their diagnoses. All patients underwent routine laboratory studies (blood chemistries, cell counts), 12 lead ECG, TTE and/or TEE, and noninvasive vascular studies that included duplex carotid Doppler ultrasonography and/or transcranial Doppler sonography. Twenty-four-hour Holter monitoring, conventional cerebral angiography and/or magnetic resonance angiography, and blood tests for hypercoagulable states or immunologic abnormalities were performed only in selected cases in whom no other cause of stroke could be identified.

Our selection process sought to identify a patient cohort most likely to represent PFO-associated strokes and a control group of patients with no identifiable cause of stroke (in other words, a study group of patients with cryptogenic strokes with PFO, and a control group of patients with cryptogenic strokes without PFO). Excluded from our study were: patients with any degree of stenosis or occlusion of a major extracranial or intracranial vessel ipsilateral to the symptomatic side, not only those stenoses that may have caused hemodynamic abnormality but also those that may have served as a source of emboli; patients with small infarctions (less than 15 mm in diameter) in the territory of perforating arteries either associated with 1 of the 4 classic lacunar syndromes (pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, and sensory-motor stroke) or with risk factors for small vessel disease such as diabetes mellitus and hypertension; patients with other rare causes of stroke such as vasculitis, arterial dissection, or complicated migraine; and patients with any structural, functional, or vascular heart disease that might produce ECG changes or that may serve as a source of emboli. In accordance with the latter criterion, we excluded all patients with any history of clinical heart disease, with any ECG abnormality (myocardial ischemia, infarction, atrioventricular or intraventricular conduction block, arrhythmia, pericarditis), or with any echocardiographic (ECHO)—documented cardiac pathology (wall motion abnormality, cardiomyopathy, pericardial effusion or tamponade, segmental left ventricular hypertrophy, ASD, ventricular septal defect, atrial septal aneurysm, or heart valve disease with the exception of mitral valve prolapse.

All patients had a standard 12-lead ECG with a sensitivity of 10 mm/mV and paper speed of 25 mm/s. Crochetage pattern was described as an M-shaped notch on the ascending branch, or at the top of the R wave in inferior limb leads (II, III, and aVF) (Figures 1 and 2); the notching must be persistent in all QRS complexes in an individual lead in a given tracing, or—in the case of multiple tracings—across the various studies. All ECG traces were analyzed with respect to the absence or presence of the crochetage pattern and the number of leads that exhibited notching. Analysis was performed by 2 examiners who were blind to the study groups. Contrast echocardiography studies were performed by injection of 7 mL of saline agitated with 1.0 mL of air into an antecubital vein at rest and with Valsalva maneuver. A PFO was diagnosed if at least 3 microbubbles were seen in the left atrium within 3 cardiac cycles after maximum opacification of the right atrium.

We compared cerebral ischemic lesion size in PFO patients with or without crochetage by assuming that the size of the embolus would be greater in larger infarctions, i.e., involving cortical and subcortical territories of a major intracerebral artery. This type of distribution of infarction referred to the stem or main branch occlusions of the anterior, middle, and posterior cerebral arteries. Infarctions isolated either to cortex or subcortical structures, brain stem, or cerebellum were assumed to be small.

### Results

All data were expressed as mean±SD. Frequency data were given as percentage and the significance was assessed by χ². This was replaced by Fisher’s exact test when a cell frequency was less than 5. Results were considered significant at P<0.05. Agreement between the examiners for identifying a crochetage was evaluated using the κ statistic. A κ value of 1 indicates perfect agreement, whereas 0 indicates only chance agreement. In general, excellent agreement refers to values >0.81, 0.61 to 0.80 indicates good agreement, and values <0.20 indicate poor agreement.

Among a total of 1470 patients with first-ever stroke or TIA, there were 167 patients with cryptogenic strokes; of these, 60 cases fulfilled our conservative eligibility criteria, and comprised 28 cryptogenic stroke patients with PFO and a control group of 32 cryptogenic stroke patients without PFO.

Clinical features of the study patients are summarized in the Table. The mean age was lower in patients with PFO (45.0 versus 52.1 years). The male-female ratio and the clinical type of ischemic attack between groups were not significantly different. The mean number of cardiovascular risk factors (including hypertension, hyperlipidemia, obesity, smoking, and diabetes mellitus) was lower in the PFO group (0.5±0.7 versus 1.0±0.9). There was a difference between the number of TTEs and TEEs performed in each group; TEE examination was performed in 11 patients in the PFO group and in 10 patients in the control group. Moreover, low yield color TTE alone, rather than TEE study with contrast injec-

### Table

<table>
<thead>
<tr>
<th>Selected Abbreviations and Acronyms</th>
<th>Description</th>
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<tr>
<td>ASD</td>
<td>atrial septal defect</td>
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<td>PFO</td>
<td>patent foramen ovale</td>
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<tr>
<td>RBBB</td>
<td>right bundle branch block</td>
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<tr>
<td>TIA</td>
<td>transient ischemic attack</td>
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<tr>
<td>TEE</td>
<td>transesophageal echocardiography</td>
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<td>TTE</td>
<td>transthoracic echocardiography</td>
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**Figure 1.** Examples of ECG tracings of 3 patients with PFO. Evident notching on the ascending limb of the R wave (“crochetage”) in lead III can be noted in patients 1 (top row) and 3 (bottom). Crochetage is seen in lead aVF in patient 2 (middle).

**Figure 2.** Prevalence of crochetage in cryptogenic stroke patients with PFO and in control patients.
Clinical Characteristics of the Study Patients

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>PFO Group</th>
<th>Control Group</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>28</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Age, mean±SD, y</td>
<td>45±16</td>
<td>52±10</td>
<td>0.04</td>
</tr>
<tr>
<td>Sex</td>
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<tr>
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<td></td>
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<tr>
<td>Clinical type</td>
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<tr>
<td>TIA</td>
<td>4</td>
<td>8</td>
<td>0.35</td>
</tr>
<tr>
<td>Stroke</td>
<td>24</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
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<tr>
<td>Color TTE</td>
<td>1</td>
<td>9</td>
<td>0.01</td>
</tr>
<tr>
<td>Contrast TTE and/or TEE</td>
<td>27</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical closure of PFO</td>
<td>4</td>
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In the PFO group, crochetage was noted in 9 patients in only 1 lead, and in 1 patient in 2 leads. Crochetage was present in 6 patients in lead III, in 5 patients in aVf, and in 0 in lead II. In the control group, all 3 patients with crochetage had it in only 1 lead. As defined in the “Materials and Methods,” crochetage was a consistent finding from 1 ECG to the next. A PFO had been ruled out in these 3 patients of the control group (by a TEE in 1, a contrast TTE in 1, and only by a color TTE in 1).

Large (ie, cortical-subcortical) cerebral infarction occurred in 60% of PFO patients with crochetage (6 of 10 cases) but in only 39% (7 of 18) of PFO patients without crochetage. In contrast, small cerebral lesions isolated either to cortical or to subcortical structures, or to the brain stem or cerebellum, tended to be more frequent in PFO patients without crochetage (9 versus 2 cases); however, this difference did not achieve statistical significance (P=0.15).

Although not a primary aim of the present study, we also determined the frequency of incomplete right bundle branch block pattern (incomplete RBBB) (R' or r' in lead V1 or V2 and R' greater than R in V1 and V2 and QRS duration less than 120 milliseconds, or R peak time >50 milliseconds in lead V1 or V2 when QRS duration was <120 milliseconds). There were 4 patients showing incomplete RBBB both in the PFO group and in the control group. Three of 4 patients with the incomplete RBBB pattern in the PFO group, but only 1 in the control group, exhibited the crochetage pattern.

Discussion

The foramen ovale is a channel between the atria that enables passage of blood from the inferior vena cava into the left atrium in fetal life. After birth, pressure changes between the pulmonary and systemic circulations can seal the opening by keeping the valve of the foramen ovale opposed to the ostium secundum septum. However, this is not always the case; autopsy studies demonstrate patency in as many as 35% of adults.8–10 A PFO has the potential to permit passage of emboli from the venous into the arterial circulation.11–15 Lechat et al11 demonstrated an association between PFO and cryptogenic strokes in patients less than 55 years old. The prevalence of PFO was 24% in patients with an identifiable cause for stroke, 40% in patients with no identifiable cause but risk factors, and 54% in patients without identifiable cause or stroke risk factors. Other studies also confirmed a similar association between PFO and otherwise cryptogenic ischemic stroke.16–18 In the present study, our strict inclusion criteria markedly reduced the sample size but minimized contamination of the population with patients who had stroke unrelated to PFO or ECG changes based on other cardiac disease. We excluded all patients with either known or potential cardiac disease.

The actual role of PFO and the variables that determine its role in paradoxical embolism are still not well understood. In addition to risk factors for clotting in the pelvic and leg veins, major determinants might include the size of defect, the degree of right-to-left shunting, direction of current flow in the right heart, range of right-sided heart pressures, and the variable degrees of closure that the valve makes during different periods of the cardiac cycle. Moreover, for paradox-
ical embolism to occur a thrombus in the venous circulation must enter the right atrium and be directed through the foramen while it is open. Many of the parameters that determine passage of thrombus mentioned above are difficult to measure. Currently, the most practical and sensitive diagnostic method is transesophageal contrast echocardiography, which can show the presence of a PFO with approximately 80% sensitivity. Transcranial contrast Doppler sonography is also sensitive in detecting PFO, comparable to that of TEE. However, an echocardiographically documented PFO may be incidental rather than a causative finding. Determining more specific echocardiographic, ECG, and deep venous system characteristics for paradoxical embolus as the cause of stroke would aid in the clinical decision of whether to anticoagulate or to close the PFO.

The ECG pattern of incomplete RBBB has been known as a marker of ASD for at least 40 years; it has been postulated to occur due to selective hypertrophy of the basal portion of the right ventricle or to stretching of the peripheral conduction fibers. Another ECG pattern, independent of incomplete RBBB, in ASD is crochetage: an early M-shaped notch on the R wave of the QRS complex in the inferior limb leads. Crochetage, when present in only 1 lead, has a sensitivity of 73.1%, a specificity of 92.6%, and a positive predictive value of 69% for the diagnosis of ostium secundum ASD, and achieves a specificity of 100% if present in all 3 inferior leads. Heretofore, the pattern has not been associated with any other cardiac conditions, and the pathophysiology is not known; however, it has been reported to disappear from 1 or more leads after surgical closure of the ASD. To the best of our knowledge, no specific ECG pattern has been associated with PFO prior to the current report. Here, we demonstrate a statistically significant increase in the prevalence of a crochetage pattern in the inferior ECG limb leads in patients with PFO and cryptogenic stroke as compared with control patients with cryptogenic stroke without demonstrable PFO. Two blinded examiners detected crochetage in at least 1 inferior ECG lead in 36% of PFO patients as opposed to only 9% of control patients. The low sensitivity suggests that a routine ECG would not be a useful screening test for PFO. However, ECG is an almost uniformly available clinical evaluation tool in all patients with stroke or TIA, principally to rule out other cardiac abnormalities that may serve as potential sources of emboli. Given the high specificity (91%) and moderately high positive predictive value (77%), recognizing a crochetage pattern may increase the clinical suspicion of paradoxical embolism. It may be helpful in streamlining the diagnostic evaluation, especially in a young, otherwise healthy patient with TIA or stroke; for example, within minutes of a patient’s evaluation in the emergency ward, a certain degree of suspicion of PFO-related stroke can be generated, a TEE can be requested with alacrity, and a certain degree of suspicion of PFO-related stroke can be generated, a TEE can be requested with alacrity, and a search for the source of the embolus is initiated with lower extremity ultrasound studies (and magnetic resonance or contrast venography, if necessary). Detection of crochetage does not preclude an echocardiographic study. On the contrary, it may accelerate the clinical arrangements to obtain early echocardiography with techniques more sensitive for PFO (contrast TTE or TEE). Our results may also be helpful in alerting the physician to perform a bedside transcranial Doppler sonography study with contrast injection, if applicable—to take additional precautions, such as filtering all intravenous lines or initiating early anticoagulation.

Heller et al. reported that the presence of crochetage, and the number of leads exhibiting it, correlated both with the degree of left-to-right shunting and with the size of the ASD. It had been previously shown that both the degree of right-to-left shunting and size of the PFO are larger in patients with arterial ischemic events. Our data showed a trend toward larger infarct size in PFO patients with crochetage than in PFO patients without crochetage. Three of 4 patients who were finally referred to surgery for closure of PFO exhibited crochetage. The reason for closure was coexisting fresh deep venous thrombosis in 3 patients and recurrent cerebral embolism with multiple infarctions in 1 patient. Unlike the reports from ASD studies, the crochetage pattern remained unchanged after the closure in each of the 3 patients.

The current study was limited by the relatively small sample size that resulted from very conservative selection criteria. Since patients with any ECG abnormality or a known cardiac disease were excluded, the impact of cardiac conditions on the ECG crochetage pattern remains to be studied. Another limitation of this retrospective study is the diverse methods of investigation used for the diagnosis of PFO. More than 20% of patients in the control group were evaluated only by color TTE. Because of the relatively lower sensitivity of this technique, PFO might have been missed in some cases. However, we suspect that 2 of 3 patients with crochetage in the control group may have had PFO since they did not have a TEE study. It is difficult to arrive at the true predictive value of the crochetage pattern for stroke due to paradoxical embolus without definitive knowledge about the incidence of other causes of stroke in the patients with PFO, specifically in those with and without crochetage.

In conclusion, the finding of a crochetage pattern may serve as a readily available ECG marker to motivate the search for PFO or ASD in patients with stroke or TIA. This study was performed in patients without heart disease or stroke risk factors other than PFO. Future prospective studies are needed to establish the relation of crochetage to PFO in the general population. It will be especially important to determine whether the presence or absence of the crochetage pattern correlates with stroke risk in persons with PFO. The clinically significant hypothesis raised by this study is whether the degree of shunting in patients with PFO correlates with the presence of crochetage, as it does in patients with secundum-type ASD.

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