Migraine Headache Relief After Transcatheter Closure of Patent Foramen Ovale

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OBJECTIVES
The purpose of this study was to determine the effects of transcatheter patent foramen ovale (PFO) closure on migraine frequency in patients with paradoxical cerebral embolism.

BACKGROUND
The prevalence of migraine headache is higher in cryptogenic stroke patients with PFO than in the general population. Previous studies have suggested that closure of the PFO may reduce migrainous symptoms.

METHODS
Between April 2001 and December 2003, 162 consecutive patients with paradoxical cerebral embolism underwent transcatheter PFO closure for prevention of recurrent cryptogenic stroke or transient ischemic attack. A one-year retrospective analysis of migraine symptoms before and after PFO closure was performed.

RESULTS
Active migraine was present in 35% (57 of 162) of patients, and 68% (39 of 57) experienced migrainous aura; 50 patients were available for analysis at one year. Complete resolution of migraine symptoms occurred in 56% (28 of 50) of patients, and 14% (7 of 50) of patients reported a significant (>50%) reduction in migraine frequency. Patients reported an 80% reduction in the mean number of migraine episodes per month after PFO closure (6.8 ± 9.6 before closure vs. 1.4 ± 3.4 after closure, p < 0.001). Results were independent of completeness of PFO closure at one year.

CONCLUSIONS
In patients with paradoxical cerebral embolism, migraine headaches are more frequent than in the general population, and transcatheter closure of the PFO results in complete resolution or marked reduction in frequency of migraine headache. (J Am Coll Cardiol 2005;45: 493–5) © 2005 by the American College of Cardiology Foundation

Migraine headache is a common, often disabling, condition and represents a significant health care burden. Recent evidence has shown that migraineurs who experience an aura beforehand are twice as likely to have a patent foramen ovale (PFO) (41% to 48%) than the general population (16% to 20%) (1,2). Right-to-left cardiac shunt at rest through a PFO also is more common in migraineurs with aura (15%) than in control patients with PFO who do not experience migraines (0%) (1), suggesting that interatrial communication may play a role in the pathogenesis of migraines.

METHODS
The study was descriptive, correlational, and retrospective. The Western Institutional Review Board approved the

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Statistical analysis. Data are reported as means ± standard deviations. Pearson chi-square, and independent samples t test and paired-samples t tests were used to compare categorical, nominal, and continuous variables, respectively. Early and late follow-up of migraine frequency were compared using a within-subjects repeated-measures analysis of variance. Assumptions of normality and homogeneity of variance were satisfied. The level of significance for all tests was set at 0.05 (two-tailed). Data were analyzed using the Statistical Package for the Social Sciences (version release 11.0.1, SPSS Inc., Chicago, Illinois).

RESULTS
Thirty-five percent (57 of 162) of patients experienced active migraine symptoms at the time of PFO closure and, of these, 68% (39 of 57) had a history of migrainous aura. Table 1 shows that patients with migraine were more likely to be female, and more likely to have a large shunt (>100 embolic tracks using pm-TCD) at rest (p < 0.05) than patients without migraine. There were no significant differences (p = NS) in the baseline characteristics of migraineurs who experienced an aura beforehand (n = 39) and those who did not experience aura (n = 18). Within the migraine group, 7 patients had incomplete follow-up; therefore, 50 migraineurs were included in the final analysis (n = 50).

At a mean duration of follow-up of 37 ± 23 weeks, patients reported significantly fewer migraine episodes/month (6.8 ± 9.6 before closure vs. 1.4 ± 3.4 after closure, p < 0.001). Migraine symptoms were completely relieved in 56% (28 of 50) and significantly (≥50%) reduced in 14% (7 of 50) of patients. Fifteen (30%) patients reported minimal (<50%) or no relief of migraine symptoms. In a subgroup of 21 patients who had serial assessment of migraine frequency at early (18 ± 17 weeks) and late follow-up (40 ± 26 weeks), no significant differences in monthly migraine frequency were found between early (1.6 ± 3.7) and late (1.1 ± 2.6) follow-up (F = 1.69, p = 0.208), suggesting a persistent treatment effect. The degree of migraine relief did not vary according to migraine subtype (Fig. 1). In follow-up, complete PFO closure (≥30 embolic tracks) was successfully achieved in 72% (36/50) of patients. Final closure status did not influence the degree of migraine relief. (chi-square test = 0.18, p = 0.91).

DISCUSSION
This study supports published findings that migraine headache in cryptogenic stroke patients with PFO is more prevalent (35%) than the presence of migraine headache in the general population (12%) (9). Similar to previously published reports of migraine relief after PFO closure (3–5), a significant reduction in overall frequency of migraine headaches was observed, with patients reporting on average an 80% reduction in monthly migraine events.

The significant treatment effect of transcatheter PFO closure on migraine frequency suggests the possibility of a common pathophysiologic substrate for selected patients with migraine and paradoxical embolism. This study is limited, however, by its nonrandomized, uncontrolled design, small sample size, and possibility of recall bias and placebo effect. Although the reported placebo effect in large, randomized trials of migraine prophylaxis (20% to 40%) (10) is significantly lower than the observed treatment effect (70%), it is possible the placement of an intracardiac device may have a more profound placebo effect than medical therapies.

Migraine relief was independent of the completeness of PFO closure, suggesting either a type II error due to insufficient sample-size, an effect based on partial “filtration” of microaggregates, or hypersensitivity of pm-TCD evaluation in quantifying residual shunt. It is possible that some

### Table 1. Baseline Patient and Procedural Characteristics

<table>
<thead>
<tr>
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<th>Nonmigraineurs (n = 105)</th>
<th>Migraineurs (n = 57)</th>
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<tbody>
<tr>
<td><strong>Demographic data</strong></td>
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<tr>
<td>Age (yrs)*</td>
<td>58 ± 17</td>
<td>47 ± 12</td>
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<tr>
<td>Female*</td>
<td>48 (46%)</td>
<td>38 (67%)</td>
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<tr>
<td><strong>Procedural characteristics</strong></td>
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<tr>
<td>Co-existing atrial septal aneurysm†</td>
<td>31 (30%)</td>
<td>14 (25%)</td>
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<tr>
<td>PFO balloon waist size, mm</td>
<td>13.2 ± 3.8</td>
<td>12.9 ± 2.9</td>
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<tr>
<td>Device size, mm</td>
<td>28.7 ± 5.6</td>
<td>27.8 ± 5.4</td>
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<tr>
<td>Closure device type</td>
<td></td>
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<tr>
<td>NMT CardioSEAL</td>
<td>99 (94%)</td>
<td>52 (91%)</td>
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<tr>
<td>AGA Amplatzer</td>
<td>6 (6%)</td>
<td>5 (9%)</td>
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<tr>
<td>Transcranial Doppler data (n = 147)</td>
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<tr>
<td>Large shunt at rest‡</td>
<td>35/95 (37%)</td>
<td>28/52 (54%)</td>
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<tr>
<td>Large shunt at Valsalva‡</td>
<td>82/95 (86%)</td>
<td>50/52 (96%)</td>
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Values are n (%) or mean ± SD. *Significance to p < 0.05. †Protrusion of the interatrial septum with a base width ≥15 mm and mobile excursion ≥10 mm. ‡More than 100 embolic tracks.

PFO = patent foramen ovale.
of the treatment effect could be due to aspirin therapy rather than PFO closure; however, this bias is debatable because 50% (25 of 50) of patients were taking aspirin before PFO closure, and the known effect of aspirin on migraine relief is modest (11). Although the effect of combination aspirin and clopidogrel therapy on migraine frequency has not been established, we observed sustained migraine relief after antiplatelet therapy was discontinued. The consistent observations of this and other studies are provocative and worthy of evaluation with a prospective, randomized trial using objective measures of migraine frequency and severity.

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REFERENCES