INTERVENTIONAL/SURGERY

Not yet closed? PFO-migraine link probed in two new studies

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ACC

Atlanta, GA - This year's **American College of Cardiology** (ACC) **2010 Scientific Sessions** marked the four-year anniversary of the disappointing **Migraine Intervention with Starflex Trial** (MIST) results, showing no difference in headache cure between patients who underwent patent foramen ovale (PFO) closure and sham-treated migraineurs.

Amplatzer PFO occluder [Source: AGA Medical]

But the door has never fully slammed shut on the PFO-migraine theory, despite both NMT Medical (the sponsor of MIST) and St Jude Medical pulling the plugs on their respective US trials testing device closure for migraine. One company remains in the game, AGA Medical, which is testing its Amplatzer device in both the US **PREMIUM** trial and the international **PRIMA** trial.

And in fact, at this year's ACC meeting, Italian investigators reported promising effects on migraine following PFO closure using the Amplatzer occluder [**1**]. That news dovetailed with results from a second group of Italians analyzing the effects on migraine with both the Amplatzer and St Jude's Premere device, reported in the March 2010 issue of the *Journal of the American College of Cardiology: Cardiovascular Interventions* [**2**].

At the ACC 2010

In the ACC presentation, **Dr Daniela Trabattoni** (Centro Cardiologico Monzino, Milan, Italy) presented data from a single-center series (May 2000 to September 2009), in which a total of 305 consecutive patients underwent PFO closure following an ischemic event confirmed by brain CT or MRI, followed by confirmation of a PFO. Of the 305, 77 patients (25%) also reported having moderate to severe migraines prior to PFO closure.

Within the first few months, more than one-third of the migraine group reported having no more migraine pain, and 60.5% reported a >50% reduction in migraine duration, frequency, and intensity. Out to a mean of 58 months, 36% of patients reported no more migraine pain, and 55% reported a >50% reduction in duration, frequency, and intensity of migraine attacks; 8% of patients reported no change in migraine occurrence or symptoms.

In this group, PFO closure "resulted in significant mid- and long-term reduction of migraine intensity and frequency in over 80% of patients," Trabattoni concluded. "The role and potential benefits of PFO closure among patients with severe migraine in the absence of previous ischemic events remain questionable and warrant future investigation with appropriately powered and well-designed and executed randomized trials."

To **heart*wire***, Trabattoni emphasized that migraine in and of itself is not an adequate reason for PFO closure. "However, our study, together with previous observations, confirms the positive effect of PFO closure on migraine symptoms in an ischemic setting," she said. "Further evaluations aimed to screen migraineur patients with PFO, highly resistant to drugs, could be of interest in order to better understand which is the best treatment option to follow."

In the literature

Striking findings were also reported in the paper by **Dr Gianluca Rigatelli** (Rovigo General Hospital, Italy) and colleagues in the *Journal of the American College of Cardiology: Cardiovascular Interventions*. Their study enrolled 40 patients with documented large basal shunts and moderate to severe migraines (mean MIDAS score of 35.8) undergoing PFO closure. After a mean of 29.2 months, 100% of patients reported improved migraine symptoms (mean MIDAS score 8.3) and 100% elimination of migraine auras.

Asked by **heart*wire*** why PFO closure seemed to help with migraine in their study while failing to do so in MIST, Rigatelli pointed out that patients in their study were those at a very high risk of paradoxical embolism—a group that was excluded from MIST. "To achieve widespread acceptance, primary percutaneous closure of PFO to treat migraine—a potentially debilitating but nonetheless non-life-threatening condition—must demonstrate a substantial benefit-to-risk ratio," the authors write. "To this end, our findings seem to support primary PFO closure for patients satisfying high-risk clinical and anatomic features for paradoxical embolism."

The best candidates for PFO closure, based on this study, include patients with a large permanent shunt, atrial septal aneurysm, coagulation abnormalities, persistent eustachian valve, and refractory migraine with aura, Rigatelli told **heart*wire***.

He also emphasized that the aim of the study was not to demonstrate clear benefit of PFO closure as a treatment for migraine. "We just wanted to identify some criteria useful to screen patients who would benefit from closure for both migraine and embolism protection," he said. "We believe that this study would be a good basis for further trials: to treat migraine, we should have more than one good reason to put a device in a subject. Good reason enough would be protection from embolism in high-risk patients."

No closer to an answer

In an accompanying editorial [3], **Dr David W Dodick** (Mayo Clinic, Phoenix, AZ) singles out the efforts by Rigatelli et al to define the best group for PFO closure for migraine. "Given the prevalence of migraine in the population, it is critical that only those patients who are highly likely to respond be subjected to an invasive procedure with a potential for serious adverse events," he writes. Unfortunately, he notes, the glacial pace of enrollment has now halted two of the three US trials addressing the PFO-migraine question, and the one remaining probably will not end up illuminating a subgroup that might benefit from closure. On that background, while Rigatelli et al's study "doesn't get us closer to an answer, it keeps the subject open and might guide the selection of subjects for future clinical trials."

Authors of both the ACC presentation and the published paper disclosed having no conflicts of interest. Dodick disclosed being the principal neurology investigator for a patent foramen ovale closure study sponsored by St Jude and also serving as a consultant for Coherex.

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