Title: Patent Foramen Ovale Closure and Migraine: Clinical Benefit and Harm

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Research questions:

1. What is the evidence that percutaneous closure of the patent foramen ovale (PFO) results in an improvement in migraines?

2. What is the clinical benefit and harm associated with percutaneous closure of the PFO for migraines?

Methods:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 2, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. The search results were limited to articles published between 2003 and April 2008, and English language publications only. Filters were applied to limit the retrieval to HTAs, systematic reviews, clinical trials and observational studies. Internet links are provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Due to the large volume of observational studies and narrative reviews identified and to the publication of recent meta-analyses, the observational studies and narrative reviews included in this report were limited to those published between 2007-2008.

Results:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs) and observational studies.
Due to the large volume of observational studies identified, the observational studies included in the main body of the report were limited to those that specifically studied migraines; whereas the Appendix contains those observational studies that provide harms information about the procedure but that did not study migraines.

The literature search identified one health technology assessment, two meta-analyses, one randomized controlled trial, one non-randomized controlled trial, and numerous observational studies.

**Overall summary of findings**

**Clinical benefit of PFO closure for migraines:**

Only one RCT was identified on the effects of percutaneous closure of the patent foramen ovale (PFO) for treating migraines. The trial randomized 147 migraine sufferers into either the PFO closure with the STARFlex implant or the sham procedure group. The study found that there was no statistically significant difference in the primary endpoint of migraine cessation between the groups (3 people in each group experienced cessation). In addition, secondary endpoints were not achieved. The implant group experienced more procedural serious adverse events and all events were transient.

One non-randomized controlled clinical trial has been conducted on the effects of percutaneous PFO closure on migraine symptoms and medications. The trial involved 169 subjects, divided into 3 groups: PFO treated with percutaneous closure (Closed PFO, n = 41), PFO with no intervention (Open PFO, n = 63), and patients without PFO (Controls, n = 65). The study found that after 90 days, there was a highly significant reduction in migraine frequency in the Closed PFO group (83%) compared with the Open PFO (0%) and control (10%) groups. The study results also demonstrated a statistically significant reduction in migraine severity and MIDAS scores (measuring the impact of migraines on quality of life) in the PFO closure group compared to the other two groups.

Two meta-analyses have been conducted on percutaneous PFO closure and migraines. However, neither of these included the RCT above because it was published recently (2008). The first meta-analysis suggested an improvement of migraine with PFO closure, but recognized that the grade of evidence was low. The second meta-analysis in patients who had previously experienced a stroke found that PFO closure resulted in an improvement or cure of migraine in 72% of patients. The authors acknowledged the limitations and drawbacks.

Numerous observational studies were identified; 5 of which were published recently (2007-2008). Two of these recent observational studies found that over 85% of patients had significant improvement in migraines after percutaneous PFO closure, and another study found that over 60% of patients had improvement in migraines after percutaneous PFO closure. In another study, all 10 patients studied experienced resolution of migraines after percutaneous PFO closure. One study analyzed migraines that developed following percutaneous PFO closure.

**Clinical harm of PFO closure (not specific to migraines):**

One health technology assessment on percutaneous PFO closure for the prevention of cerebral embolic stroke was published in 2004. This report found the rate of major complications ranged from 0-10% with an annual incidence of 1.5%, and the rate of minor complications ranged from...
0-24% with an annual incidence of 7.9%. The HTA Specialist Advisors noted that serious adverse events were uncommon and potentially included device embolization, thromboembolism on or from the device, and pericardial diffusion. Other mild side effects included migraine, minor arrhythmias and local bruising at the catheter puncture site, but these were mainly of a transitory nature. The HTA also noted that different devices have different potential problems and therefore, they should not be considered as one.

A more recent (2007) narrative review discussed further safety information on percutaneous PFO closure. Additional safety information is included in the Appendix.
References summarized:

Health technology assessments


Systematic reviews and meta-analyses


Randomized controlled trials


Non-randomized clinical trials


Observational studies


Appendix – Further information:

Horizon scanning reports


Review articles


**Observational studies**


**Medical device alerts**


**Additional references**


