Transcatheter closure versus medical therapy of patent foramen ovale and presumed paradoxical thromboemboli

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CRD summary
This review assessed transcatheter closure and medical therapy for patent foramen ovale. The authors concluded that transcatheter closure may prevent a substantial number of recurrent strokes, but definitive conclusions were not possible because of methodological limitations and a lack of comparability between the studies of these treatments. The authors' cautious conclusions correctly reflect the poor-quality studies on this topic.

Authors' objectives
To assess and compare transcatheter closure and medical therapy for patent foramen ovale.

Searching
MEDLINE was searched from 1985 to July 2003; the search terms were stated. Additional articles were searched for in the reference lists of retrieved studies. Articles published in English and foreign language journals were eligible. Unpublished studies were not sought.

Study selection
Study designs of evaluations included in the review
Studies with at least 10 patients per cohort, and with a mean duration of follow-up of 12 months, were eligible for inclusion. The mean duration of follow-up ranged from 12 to 47 months for transcatheter closure, and from 13 to 43 months for medical therapy.

Specific interventions included in the review
Studies of transcatheter closure of foramen ovale or medical therapy were eligible for inclusion. The included studies used a variety of transcatheter devices (further details were given in the report) and used different antiplatelet or anticoagulant regimens after surgery. The latter included aspirin, with or without clopidogrel or ticlopidine, or ticlopidine alone.

Participants included in the review
Studies in patients with patent foramen ovale who had had a previous thromboembolic event were eligible for inclusion. All of the participants in the included studies had presumed paradoxical emboli associated with patent foramen ovale. The patients ranged in age from a mean of 40 to 50 years in transcatheter closure studies, and from 36 to 58 years in medical therapy studies. The proportion of male patients varied from 30 to 66% in transcatheter studies, and from 53 to 60% in medical therapy studies. A higher proportion of patients had risk factors for atherosclerosis in medical therapy studies than in transcatheter studies, while previous multiple cerebrovascular events were more common in transcatheter closure studies than in medical therapy studies.

Outcomes assessed in the review
Studies that assessed neurologic thromboembolic events (transient ischaemic attack (TIA), stroke or non-cerebrovascular systemic embolism), or reported or presented sufficient data to calculate actuarial freedom from recurrent neurologic events at 1 year, were eligible for inclusion.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The extracted data included: the number of patients with major and minor complications of transcatheter closure; the number of patients with a recurrent event of TIA, stroke and noncerebrovascular systemic embolism; and the number of these events at 1-year for both transcatheter closure and medical therapy. Attempts were made to exclude duplicate data. Four studies with potentially overlapping populations were excluded.

**Methods of synthesis**
How were the studies combined?
The rate of major and minor complications was calculated for studies of transcatheter closure. The incidence range of stroke or TIA events was reported separately for studies of transcatheter closure and medical therapy.

How were differences between studies investigated?
A regression analysis was performed to investigate the relationship between the incidence of stroke or TIA and age for transcatheter closure and for medical therapy studies, and the relationship between the incidence of stroke or TIA and complete closure of patent foramen ovale at 6 months.

**Results of the review**
Sixteen studies (n=2,250) were included. There were 6 retrospective and 4 prospective studies of transcatheter closure (1,355 patients) and 3 retrospective and 3 prospective studies of medical therapy (895 patients).

**Complications after transcatheter device closure.**
Minor complications were reported in 7.9% of the patients and major complications in 1.5%. Major complications included death, haemorrhage requiring blood transfusion, cardiac tamponade, need for surgical intervention and massive fatal pulmonary emboli. Minor complications included bleeding not requiring transfusion, periprocedural atrial arrhythmias, transient atrioventricular node block, device arm fractures (25, 31), device embolisation with successful catheter retrieval, asymptomatic device thrombosis, need for recatheterisation, symptomatic air embolism, transient ST-segment elevation, arteriovenous fistula formation and femoral haematoma.

**Recurrent events for transcatheter device closure and medical therapy.**
The incidence of stroke or TIA ranged from 3.8 to 12% at 1 year with medical therapy, and from 0 to 4.9% after transcatheter closure. Seven of the 10 studies of transcatheter closure reported rates of 1.7% or less. There was a trend towards an increasing incidence of recurrent events with increasing mean age for both transcatheter closure and medical therapy studies. There was no apparent correlation between stroke or TIA and complete closure of patent foramen ovale at 6 months in studies of transcatheter device closure.

**Authors’ conclusions**
Transcatheter closure may prevent a substantial number of recurrent strokes, but definitive conclusions could not be reached because of a lack of comparability between studies of transcatheter closure and medical therapy. Randomised controlled trials (RCTs) are required.

**CRD commentary**
The review question was clear in terms of the study design, intervention, participants and outcomes. The search strategy was limited to one electronic database and reference lists of identified studies, thus the possibility of publication bias is highly likely. Attempts were made to limit language bias. The methods used to select the studies and extract the data were not described, and it is not known whether any efforts were made to reduce errors and bias. Validity was not
formally assessed, although some methodological limitations of the studies were discussed in the text.

Adequate details of the included studies were given. Given the considerable clinical heterogeneity among the studies identified, it was appropriate to report the range of event rates. The authors appropriately considered the limitations in study design and differences across the studies. Consequently, the authors’ cautious conclusions correctly reflect the poor quality of studies on this topic.

One of the authors has participated in trials of transcatheter devices and medical therapy, and has received expenses from pharmaceutical and manufacturing companies.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that RCTs are required to examine the benefits of transcatheter closure of patent foramen ovale, to define the subgroups most likely to benefit, and to assess the cost-effectiveness of this technology.

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