

Percutaneous closure of patent foramen ovale to prevent recurrent cerebral embolic events

Interventional procedures guidance
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www.nice.org.uk/guidance/ipg472

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

This guidance replaces IPG109.

1 Recommendations

- 1.1 Evidence on the safety of percutaneous closure of patent foramen ovale to prevent recurrent cerebral embolic events shows serious but infrequent complications. Evidence on its efficacy is adequate. Therefore, this procedure may be used with normal arrangements for clinical governance, consent and audit.
- 1.2 The procedure should only be performed in units with appropriate arrangements for urgent cardiac surgical support in the event of complications.
- 1.3 The National Institute for Cardiovascular Outcomes Research runs the UK Central Cardiac Audit Database (UKCCAD) and clinicians should enter details about all patients undergoing percutaneous closure of patent foramen ovale to prevent recurrent cerebral embolic events onto this database.

2 Indications and current treatments

- 2.1 Before birth, the fetal heart has an opening called the foramen ovale between the right and left atria. This allows blood to bypass the lungs and be directed straight

to the left side of the circulation, supplying blood to the brain and body before it returns to the placenta. The foramen ovale usually closes spontaneously after birth; however, in approximately 1 in 4 people the foramen ovale remains fully or partially open into adulthood. This is then known as patent foramen ovale.

- 2.2 Most people with patent foramen ovale have no ill effects. However, patent foramen ovale increases the risk of blood clots (for example from deep vein thrombosis in the legs) crossing from the right side into the left side of the heart, and from there into the arterial system where they may block blood vessels. If arteries in the brain become blocked, then a stroke or a transient ischaemic attack occurs. This passage of material from the right of the circulation to the left is called paradoxical embolism.
- 2.3 The optimal treatment for patent foramen ovale in patients who have had a thromboembolic event remains undefined. Medical management with anticoagulation (usually warfarin) or antiplatelet therapy (for example aspirin) is commonly used to reduce the risk of further paradoxical thrombus emboli. Surgical closure of patent foramen ovale is sometimes performed as an adjunct to other open-heart surgery, but is rarely done on its own because of associated morbidity.

3 The procedure

- 3.1 Percutaneous closure of patent foramen ovale has been introduced as an option for patients who have had a cerebral embolic event (such as stroke or transient ischaemic attack) and in whom paradoxical embolism through patent foramen ovale is considered to be the cause. It provides an alternative to surgical closure, which is typically considered for patients in whom medical management has failed or for patients in whom anticoagulant or antiplatelet therapy are contraindicated.
- 3.2 Percutaneous closure is performed using local anaesthesia and intravenous sedation, or with the patient under general anaesthesia. A closure device is introduced using a guide wire and delivery sheath through a small incision in the groin into the femoral vein. It is then passed into the heart and across the patent foramen ovale. The closure device is released to close the defect using image

guidance such as echocardiography. Devices of differing design and mechanism are available.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [overview](#).

- 4.1 A randomised controlled trial (RCT) of 980 patients treated by percutaneous patent foramen ovale closure or medical therapy reported rates of stroke of 0.7 and 1.4 per 100 patient-years respectively in the intention-to-treat population ($p=0.08$). An RCT of 909 patients reported that the cumulative incidence of a composite end point of stroke or transient ischaemic attack during 2 years of follow-up, death from any cause during the first 30 days, or death from neurological causes between 31 days and 2 years, was 6% in the percutaneous patent foramen ovale closure group and 7% in the medical therapy group ($p=0.37$). An RCT of 414 patients reported a composite end point of death, non-fatal stroke, transient ischaemic attack or peripheral embolism in 3% (7 out of 204) of patients treated by percutaneous patent foramen ovale closure and 5% (11 out of 210) of patients treated by medical therapy, with a mean follow-up of 4 years ($p=0.34$). A meta-analysis of 58 observational studies (8,185 patients treated by percutaneous patent foramen ovale closure and 2,142 patients treated by medical therapy) reported a pooled incidence of recurrent neurological events of 0.8 (95% confidence interval [CI] 0.5 to 1.1) per 100 person-years for percutaneous patent foramen ovale closure and 4.4 (95% CI 3.2 to 5.6) per 100 person-years for medical therapy.
- 4.2 The RCT of 909 patients treated by percutaneous patent foramen ovale closure or medical therapy reported successful closure at 2-year follow-up in 87% (320 out of 369) of patients who had the procedure. The meta-analysis of 58 observational studies reported a residual shunt immediately after the procedure in 25% (95% CI 17 to 34) of patients; 6% (95% CI 0 to 18) of patients had a residual shunt for more than 12 months.
- 4.3 A UK register reported that 98% (4,133 out of 4,202) of patients treated by

percutaneous patent foramen ovale closure were alive and 2% (69 out of 4,202) of patients were dead at a median follow-up of 3.8 years. Actuarial 5-year and 10-year survival were 98% and 97% respectively.

- 4.4 The specialist advisers listed key efficacy outcomes as reduction in the rate of stroke and systemic emboli, and complete functional closure of the patent foramen ovale.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [overview](#).

- 5.1 The occurrence of any serious adverse event was reported in 23% (numbers not stated), 17% (68 out of 402), and 21% (43 out of 204) of patients treated by percutaneous closure and 22% (numbers not stated), 17% (76 out of 458), and 18% (37 out of 210) of patients treated by medical therapy in the randomised controlled trials (RCTs) of 980, 909, and 414 patients respectively ($p=0.7$, 0.9 and 0.4 respectively).
- 5.2 Death related to the procedure (not further defined) was reported in 0.1% (95% confidence interval [CI] 0 to 0.3) of patients in the meta-analysis of 58 studies (8,185 patients treated by percutaneous patent foramen ovale closure and 2,142 patients treated by medical therapy).
- 5.3 Pericardial effusion or tamponade was reported in 0.3% (95% CI 0 to 0.6) of patients in the meta-analysis of 58 studies. Details of treatment and outcome were not provided.
- 5.4 Perforation of the left atrium and cardiac perforation (not further described) were each reported in 1 patient treated by percutaneous closure in the RCTs of 909 and 980 patients respectively. Vascular surgical repair (not further defined) was reported in 1 patient in the RCT of 909 patients.
- 5.5 Device embolisation or malposition (not further described) was reported in 0.4%

(95% CI 0.2 to 0.7) of patients in the meta-analysis of 58 studies.

- 5.6 Bleeding (described as serious or major) was reported in 3% (10 out of 378) and 0.5% (1 out of 204) of patients treated by percutaneous closure and 1% (4 out of 374, and 3 out of 210) of patients treated by medical therapy in the RCTs of 909 and 414 patients respectively. Major bleeding that was considered to be device- or procedure-related was reported in 0.4% (2 out of 499) of patients treated by percutaneous closure in the RCT of 980 patients.
- 5.7 Air embolism was reported in 0.6% (95% CI 0.2 to 1.0) of patients in the meta-analysis of 58 observation studies (not further described).
- 5.8 Infective or bacterial endocarditis that was considered to be device- or procedure-related was reported in 1 patient in the RCT of 980 patients (no further information was given).
- 5.9 Cardiac thrombus, together with deep vein thrombosis and pulmonary embolism, was detected 4 months after the closure procedure in 1 patient in the RCT of 980 patients.
- 5.10 A fistula between the aortic root and right atrium was described in 1 patient in a case report. There was incomplete patent foramen ovale obliteration with residual shunting in both directions 6 months after the closure procedure. The device was removed through a mini-thoracotomy and the fistula was closed.
- 5.11 Atrial fibrillation was reported in 6% (23 out of 402) of patients treated by percutaneous patent foramen ovale closure and 0.7% (3 out of 458) of patients treated by medical therapy in the RCT of 909 patients ($p < 0.001$). In the closure group, 61% (14 out of 23) of the patients with atrial fibrillation developed it within 30 days of the procedure; atrial fibrillation was transient in 17 patients and persistent in 6 patients. Serious atrial fibrillation (not further defined) was reported in 1% (2 out of 204, and 2 out of 210) of patients in each group in the RCT of 414 patients.
- 5.12 The specialist advisers listed additional adverse events reported in the literature as embolism of clots attached to the device, device erosion, and transient worsening of migraine.

6 Committee comments

- 6.1 The Committee noted that the evidence showed percutaneous closure of patent foramen ovale to be at least as efficacious as medical therapy for preventing recurrent cerebral embolic events, and possibly more efficacious. It considered that use of the procedure, in patients for whom it would be clinically appropriate, should be strongly influenced by patient choice, taking into the consideration the risks and benefits compared with long-term anticoagulant or antiplatelet medication.
- 6.2 The Committee noted that there was variation in the use of adjunctive antiplatelet and anticoagulant medication after the procedure in the published studies. It considered that there are still uncertainties about whether these medications are beneficial and, if so, how long therapy should continue.

7 Further information

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the [overview](#).

Information for patients

NICE has produced [information for the public on this procedure](#). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).