Leidraad PFO-sluiting

Guideline for the Closure of Patent Foramen Ovale

NEDERLANDSE VERENIGING VOOR CARDIOLOGIE

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Inhoud

Introduction

The board of the Netherlands Society of Cardiology appointed a committee to establish a consensus statement on the closure of patent foramen ovale (PFO). The board has been asked by the Ministry of Health, Welfare and Sports to give a recommendation on the indications and performance of PFO closure after the Healthcare Inspectorate advised the Ministry on the concentration of care in congenital heart disease in 2009 in which closure of PFO's was not included, but was assumed to be related to the percutaneous closure of atrial septal defects. One of the recommendations of the Inspectorate was to establish national guidelines on PFO closure.
The committee consisted of interventional cardiologists, imaging cardiologists, and a neurologist on behalf of the Netherlands Society of Neurology.

Authors and Committee

Committee members from the Netherlands Society of Cardiology:
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PFO and stroke

About a third of ischemic cerebral vascular accidents is cryptogenic, meaning that no cause could be found after thorough neurological and vascular analysis[1]. Retrospective studies have suggested an association between the presence of cryptogenic stroke and the presence of a patent open foramen ovale[2,3,4]. This association is strongest in younger patients and if an additional atrial septal aneurysm (ASA) is present[5,6]. PFO prevalence in the general population is 20-30% and decreases with age. However, the presence of PFO does not lead to an increased risk of stroke in the general population[7,8, 9]. In observational studies the risk of recurrent stroke in patients with a recent TIA or minor ischemic stroke and a PFO or ASA was increased only in patients with PFO and ASA $\leq$ 55 years[10,11,12,13]
Right-to-left shunting of trombo-embolic material via the PFO is the pathophysiological mechanism through which the presence of PFO is associated with ischemic stroke and transient ischemic accident. Certain clinical events increase the risk[1,14]. Closure of PFO would therefore be a logical way to reduce the risk of recurrent strokes in addition to medical therapy.

The literature contains many reports on the effects of percutaneous closure of PFO[15]. These retrospective studies mainly show a benefit of closure of PFO over medical therapy alone, but methodological issues like non randomisation or selection bias flaw many. Several meta-analyses show conflicting efficacy of PFO closure in the prevention of stroke.
Until now, three prospective randomized controlled trials have shown that PFO closure in patients with ischemic cryptogenic stroke is not superior to medical therapy[16,17,18]. A post hoc subgroup analysis of the RESPECT trial showed that in patients aged < 45 years, in patients with substantial right-to-left shunting and in patients using acetylsalicylic acid only PFO closure was better than medical therapy[18]. After per-protocol and as-treated analysis PFO closure also seemed superior to medical therapy[18]. Device type (Amplatzer device versus Starflex device) might play a role in PFO-closure efficacy[19]. Several meta-analyses using these three randomized trial data show conflicting results as to the statistical significance of the treatment efficacy. A recent meta-analysis using individual patient data found among 2,303 patients that closure was not significantly associated with the primary composite outcome (recurrent stroke, transient ischemic attack and death), but the difference became significant after covariate adjustment[20]. In this study the recurrence rate of stroke was low (0.98 per 100 patient-years in both arms). Incidence of atrial fibrillation during follow-up was 2-3 times higher in the device closure group and might be the unrecognized ethology of the index stroke, stressing the need for a thorough diagnostic work-up before classifying the index event as cryptogenic stroke.

Taking these results into consideration it might be that certain patients might profit from PFO device closure. The Risk of Paradoxical Embolism score (RoPE) is a score that is based on a model study using data from 12 different studies[21]. This score can estimate the PFO attributable stroke risk based on age, absence of classical risk factors for atherosclerosis and the presence of cortical infarction[21,22]. The maximum score is 10 (i.e. young, no risk factors, cortical infarction) and the minimum score is 0 (elderly, risk factors, no cortical infarction).
A RoPE score $=$ 6 has been associated with PFO attributable risk of 62% (95% confidence interval 54-68%) and a 2 year risk of stroke recurrence of 8%. A score $=$ 8 denotes a PFO attributable risk of 84% (confidence interval 79-87%) and a 2 year risk of stroke recurrence

of 6%. As the RoPE score has not yet been validated in another cohort, it can be assumed that the PFO attributable risk at a certain score in the prospective population will be lower and it might be more appropriate to use RoPE $\geq$ 8 for risk stratification, the RoPE score can help with the selection of patients, who will benefit from percutaneous PFO closure.

Recommendations concerning the percutaneous closure of a persistent open foramen ovale in cryptogenic stroke

Class III level of evidence A
Closure of a persistent foramen ovale is NOT beneficial in ***unselected*** patients with transient ischemic attack or cryptogenic stroke

Class IIa level of evidence A
Closure of a persistent foramen ovale should be considered in patients with transient ischemic attack or cryptogenic stroke and a ROPE score $\geq$ 8* (evidence C) and at least one clinical riskfactor**

Class IIb level of evidence A
Closure of a persistent foramen ovale may be considered in patients with transient ischemic attack or cryptogenic stroke and having a ROPE score $\geq$ 6* (evidence C) and at least one clinical riskfactor**

*RoPE score, *risk of paradoxical embolism-score*: absence of a history of hypertension (1 point), absence of a history of diabetes mellitus (1 point), absence of a history of stroke or TIA (1 point), nonsmoker (1 point), presence of cortical lesion on imaging (1 point), the patient is aged 18-29 years (5 points) or aged 30-39 years (4 points) or aged 40-49 years (3 points) or 50-59 years (2 points) or 60-69 years (1 point) or $\geq$ 70 years (0 points)

**clinical risk factors: large shunt, atrial septal aneurysm, multiple ischemic lesions on CT or MR, recurrent clinical events, history of deep venous thrombosis, pulmonary embolism and/or thrombophilia, Valsalva-associated embolic events, ischemic event on arousal, long travel/immobilization associated event or simultaneous systemic and pulmonary event.

PFO and scuba diving

Decompression illness is one of the risks of professional and recreational diving. After too fast ascent from high pressure depth inert gases (i.e. nitrogen) dissolved in tissues and blood under high pressure will come out of solution and form gas-bubbles. Although the incidence of decompression sickness is rare, estimated at 2.8 cases per 10,000 dives, with the risk 2.6 times greater for males than for females, the presence of PFO might lead to venous bubbles entering the arterial circulation causing cerebral or myocardial infarction[23,24,25]. Recurrent neurological decompression illness was associated with the presence of a large shunt and the lack of using a more conservative diving approach[26]. Prevention of decompression illness is possible through proper decompression procedures and prevention of arterial gas embolism by closure of the PFO[27].

Recommendations concerning the percutaneous closure of a persistent open foramen ovale in scuba diving*

Class IIb level of evidence C

Closure of a persistent foramen ovale with large right-to-left shunt might be considered in divers.

*Currently the working group on cardiology and sports is preparing a guideline on diving

PFO and ortho-deoxy platypnea

Ortho-deoxy platypnea is a syndrome, in which dyspnoea and oxygen desaturation of blood occurs in upright position and resolves in the prone position [28,29]. It can be due to right-to-left shunting intracardiac shunting through a PFO, pulmonary vascular shunting of ventilation-perfusion mismatch due to pulmonary parenchymal disease. In cases with PFO most are patients with additional pulmonary diseases such as pneumonectomy, pulmonary embolism, other chronic lung diseases or aortic root disease. Closure of PFO in the absence of pulmonary hypertension, either by surgery or by percutaneous closure has been reported to be effective[30].

Recommendations concerning the percutaneous closure of a persistent open foramen ovale in ortho-deoxy platypnea

Class Ia level of evidence C

Closure of a persistent foramen ovale is recommended in symptomatic patients with ortho-deoxy platypnea syndrome without pulmonary hypertension.

Conclusion

This committee of the Netherlands Society of Cardiology for the formulation of a consensus statement concerning percutaneous closure of PFO, considering the evidence available at present, acknowledges the potential clinical benefit of percutaneous closure for the prevention of recurrent embolic stroke in selected patients. The nature of the stroke needs to be documented and careful evaluation and exclusion of other potential causes of stroke, especially paroxysmal atrial fibrillation, is strongly recommended. In young patients, in the absence of other potential risk factors for stroke, percutaneous PFO closure can be considered. The RoPE score may be used for documenting the likelihood of a causal relationship of the PFO and for establishing an indication for percutaneous closure. This procedure should only be performed in highly experienced centres by experienced teams. This consensus statement committee will monitor the literature and will evaluate these recommendations when new scientific evidence mandates revision.

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