Direct oral anticoagulants after percutaneous patent foramen ovale (PFO) closure

A Call for Caution

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Direct Oral Anticoagulants After Percutaneous Patent Foramen Ovale (PFO) Closure: A Call for Caution

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Conflict of interest: Drs Ann Bovin and Henrik Vase have nothing to disclose. Prof. Jens Erik Nielsen-Kudsk has been a consultant for Gore Medical and a Proctor and Investigator for Boston Scientific and Abbott. Erik Lerkevang Grove has no conflicts related to this manuscript, but reports the following general COIs: He has received speaker honoraria or consultancy fees from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer, MSD, Mundipharma, Portola Pharmaceuticals, and Roche. He is an investigator in the SATELLITE and FLAVOUR studies (AstraZeneca) and has received minor unrestricted research grants from Boehringer Ingelheim

Patient: Female, 45-year-old
Final Diagnosis: Intracardiac device thrombosis
Symptoms: —
Medication: Direct oral anticoagulants, rivaroxaban
Clinical Procedure: Patent foramen ovale (PFO) closure
Specialty: Cardiology

Objective: Unusual or unexpected effect of treatment
Background: Transient atrial fibrillation (AF) following percutaneous patent foramen ovale (PFO) closure is common. Anticoagulation therapy should be considered in selected cases of prolonged AF after PFO closure, but guidelines do not provide clear recommendations on indication or choice of anticoagulant therapy for patients with post-procedural AF.

Case Report: A 45-year-old woman presented with cryptogenic stroke verified by magnetic resonance imaging (MRI). Echocardiography revealed a PFO, which was closed percutaneously using a Gore septal occluder (25 mm). She was discharged on aspirin monotherapy (75 mg oral daily) according to institutional standard. Three weeks later, she presented with atrial fibrillation (AF). A direct oral anticoagulant (DOAC) (rivaroxaban 20 mg once daily) was initiated and aspirin was discontinued. After 4 months of follow-up, a routine echocardiography revealed large thrombi attached to both sides of the PFO occluder.

Conclusions: DOACs may be ineffective in preventing thrombus formation on device surfaces. Until more evidence has been provided, we suggest that DOACs are not routinely used for stroke prevention in patients following PFO closure or similar procedures within the first 3 months after device implantation.

MeSH Keywords: Anticoagulants • Atrial Fibrillation • Foramen Ovale • Thrombosis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/922467
**Background**

Closure of PFO in patients with cryptogenic stroke reduces recurrence rates [1–3], but AF is detected in 4.6–6.6% within the first weeks after the procedure [2,4]. Such AF episodes are usually of short duration, likely due to tissue irritation or inflammation caused by the occluder, and resolve spontaneously with time after the procedure. Oral antiplatelet therapy with aspirin alone or a combination of aspirin and clopidogrel is the recommended post-procedural treatment regimen [5]. Guidelines do not provide recommendations on indication and choice of anticoagulant therapy for patients who develop post-procedural AF. DOACs are increasingly used for stroke prevention in atrial fibrillation [6] but have not been tested in patients with newly inserted closure devices. Device thrombosis is relatively rare, reported in only 1.7% of such patients [7]. We report a case of device thrombosis on a newly inserted PFO occluder device during ongoing DOAC treatment, and we call for caution with these patients.

**Case Report**

A 45-year-old white woman presented with a cryptogenic stroke verified by magnetic resonance imaging (MRI) of the brain. She was previously healthy and had no prior vascular disease. No cardiovascular hazards or risk factors were identified. Screening for thrombophilia was negative, and 7 days of Holter monitoring did not reveal cardiac arrhythmias. Echocardiography, however, revealed a patent foramen ovale (PFO). The PFO was closed percutaneously using a Gore septal occluder (25 mm) with optimal positioning and without immediate complications. She was discharged on oral antiplatelet therapy with aspirin (75 mg daily) as monotherapy according to our institutional standard. The optimal type, combination, and duration of antithrombotic therapy after PFO closure is currently unknown. Most expert centers use aspirin in combination with clopidogrel for 1–3 months, followed by antiplatelet monotherapy [5], and the benefit of adding clopidogrel to aspirin has been questioned [6]. In the REDUCE trial, clopidogrel was used in addition to aspirin for only 3 days after the procedure [2]. Instructions for use for the Gore septal occluder and the Amplatzer PFO occluder recommend post-procedural antiplatelet treatment without any specification of type or combination. In our institution, with a volume of more than 800 PFO and ASD closures, we have only seen 5 cases of device thrombosis in patients receiving aspirin alone.

Three weeks later, our patient presented with atrial fibrillation (AF). Treatment with a direct oral anticoagulant (DOAC) (rivaroxaban 20 mg once daily) was initiated, and at the same time aspirin was discontinued, and she was discharged. At follow-up 4 months later, a routine echocardiography revealed large thrombi attached to both the right and left disc of the PFO occluder (Figure 1, Video 1). DOAC was discontinued and the antithrombotic treatment was switched to warfarin combined with aspirin, and partial thrombus resolution was seen another 4 months later. Due to incomplete thrombus resolution at 1-year follow-up, warfarin was replaced by low-molecular-weight heparin administered subcutaneously, resulting in thrombus resolution 3 months later. The patient is asymptomatic now and did not have thromboembolic complications in the course after device implantation.

**Figure 1.** Transesophageal echocardiography displaying the interatrial septum and the large thrombi attached to the Gore septal occluder on the right and the left atrial discs.

**Video 1.** Transesophageal echocardiography displaying the interatrial septum and the large thrombi attached to the Gore septal occluder on the right and the left atrial discs.
**Discussion**

Few studies have investigated the ability of DOACs to prevent thrombosis in patients with implanted devices. The RE-ALIGN study compared dabigatran to warfarin in patients with mechanical heart valve prostheses, but the study was prematurely stopped due to excess of bleeding and thrombotic events [8]. More recently, the GALILEO trial of rivaroxaban after transcatheter aortic valve insertion was stopped early due to patient harm [9,10]. It has been hypothesized that foreign artificial materials implanted in the heart, such as valve prostheses and possibly also occluder devices, may trigger the tissue pathway of coagulation on the artificial surface, a pathway that is unaffected by DOACs [8]. Such a mechanism could potentially lead to device thrombosis. After 3 months, the fabric membrane of a PFO occluder is thought to be covered by ingrowth of endocardial tissue [11].

**Conclusions**

While awaiting more evidence of the efficacy and safety of DOACs in patients with implanted devices, we suggest that DOACs should not be routinely prescribed in patients with a newly implanted PFO occluder device.

**Conflict of interest**

Dr. Ann Bovin and Henrik Vase have nothing to disclose. Prof. Jens Erik Nielsen-Kudsk has been a consultant for Gore Medical and a Proctor and Investigator for Boston Scientific and Abbott. Erik Lerkevang Grove has no conflicts related to this manuscript, but reports the following general COIs: He has received speaker honoraria or consultancy fees from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer, MSD, Mundipharma, Portola Pharmaceuticals, and Roche. He is an investigator in the SATELLITE and FLAVOUR studies (AstraZeneca) and has received minor unrestricted research grants from Boehringer Ingelheim.

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