To the Editor: A relatively high percentage of residual shunting was present 6 months after patent foramen ovale (PFO) closure using a bioabsorbable device (1). The presence of moderate to severe residual shunt might increase the risk of cryptogenic stroke (2,3). Despite the fact that the device is currently off the market, many patients were treated worldwide, and little is known about the long-term efficacy and safety. We report the long-term safety and efficacy of the bioabsorbable device used for percutaneous PFO closure.

As reported previously, between November 2007 and January 2009, all consecutive patients who underwent a percutaneous closure of a symptomatic PFO with a bioabsorbable device (Biotar, NMT Medical, Boston, Massachusetts) were included (1). Intracardiac echocardiography was used during most procedures.

After discharge, routine follow-up was scheduled at 1, 6, 12, and 24 months, using contrast transthoracic echocardiography (cTTE). The residual shunt rate was classified as none, minimal, moderate, and severe, as described previously (1).

Continuous variables with normal distribution are presented as mean ± SD. Residual shunt sizes at different time points were compared using the Wilcoxon signed rank test. Univariate statistical analysis, using a Cox proportional hazards model, was used to identify risk factors for residual shunting and adverse events after PFO closure. All statistical analyses were performed using SPSS software version 17.0 (SAS Institute, Cary, North Carolina).

Percutaneous PFO closure with the bioabsorbable device was performed in 62 consecutive patients (55% women; mean age: 47.7 ± 11.8 years). Ninety-four percent of the patients had experienced a cryptogenic stroke or transient ischemic attack (TIA) and were referred by a neurologist. Eight patients (12.9%) had a history of supraventricular tachycardia (SVT).

These data were previously reported (1). In summary, device implantation was successful in 60 patients (96.8%), and there were complications in 2 patients (3.2%). A minimal vascular surgical intervention was needed to retrieve the device at the femoral vein in both. A small groin hematoma was present in 6 patients (9.7%).

There were no procedure-related deaths, major adverse cardiac events, or stroke between discharge and 2-year follow-up. In 7 patients (11.3%), new SVTs were diagnosed in the first month after closure, and 1 (1.6%) was diagnosed between 1- and 6-month follow-up. Patients with known rhythm disorders did not report an increase in SVT episodes after PFO closure. A TIA occurred in 2 patients, both within the first year after closure. No device-related complications or recurrent ischemic cerebral events occurred between 12- and 24-month follow-up.

One day after closure, a residual shunt was present in 60% (36 of 60 patients): minimal in 31.7%, moderate in 20%, and severe in 8.3% of patients. At 12-month follow-up, in total, 25% of patients (14 of 56 patients) had a residual shunt: minimal in 17.9%, moderate in 5.4%, and severe in 1.8% (p = 0.76 compared with 6-month follow-up as reported previously) (1). The 4 patients missing from this follow-up had no residual shunt at 6 months. At 24-month follow-up, 30.9% (17 of 55 patients) had a residual shunt (21.8% minimal, 9.1% moderate, and 0.0% severe; p = 0.37) compared with 12-month follow-up. At 24-month follow-up, cTTE was not performed in 4 patients, and 1 patient was lost to follow-up. Three of these 4 patients were the same as described at 12-month follow-up. The other 2 patients had no residual shunt at 12-month follow-up. All these patients had no new symptoms or complications at 24-month follow-up. Between 12- and 24-month follow-up, the residual shunt size remained the same in 8 patients and both increased and decreased by 1 level in 1 patient. Three patients with a minimal residual shunt at 12-month follow-up had no shunt at 24-month follow-up. However, 6 patients without a shunt at 12-month follow-up experienced a minimal residual shunt at 24-month follow-up. No predictors of residual shunt could be identified. Efficacy data are shown in Figure 1.

The bioabsorbable device has a high residual shunt rate of 30%, even 2 years after closure. This implies that this device was insufficient for percutaneous closure of a PFO, and long-term follow-up seems to be necessary.
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REFERENCES


Letters to the Editor

P2Y12-Based Platelet Function Assays Should be Complemented With Cyclooxygenase-Dependent Testing in Framing the Therapeutic Windows for Dual Antiplatelet Therapy

We read with interest the paper by Cuisset et al. (1) on the subject of very low on-treatment platelet reactivity (VLTPR) as a measure of hyper-response to thienopyridines. The efficacy of platelet inhibition as evaluated by vasodilator-stimulated phosphoprotein (VASP) phosphorylation flow cytometry assay was used as a predictor of non-access site-related bleeding events. The absence of information regarding the periprocedural use of aspirin and the related cyclooxygenase–dependent platelet inhibitory response is a major drawback of the present study (1). Dual antiplatelet therapy, capitalizing on different pathways of platelet inhibition, has been paramount in improving outcomes in patients with acute coronary syndromes within both the low- and high-risk strata (2). It is unclear from the study by Cuisset et al. (1) whether their utilization of different thienopyridine protocols had any impact on aspirin administration or dosing. We believe that this omission compromises the robustness of the presented data. By disregarding the variability in the individual responsiveness to aspirin, the authors have assumed that all patients had a similar level of platelet inhibition before exposure to thienopyridines. By adhering to this assumption, the authors have negated the independent contribution of aspirin response as a confounding variable in their clinical outcomes trial. The acknowledged widespread variability in aspirin-induced platelet inhibition may have influenced both the incidence of ischemic and bleeding events (3,4). The cumulative effect of dual antiplatelet therapy is achieved by compounding 2 different mechanisms of anti-aggregation. It stands to reason, therefore, that strategies designed to delineate the therapeutic window of antiplatelet therapy need to be more comprehensive than the one presented in the current study, which focused solely on P2Y12 platelet receptor activity. They would need to incorporate platelet function testing exploring all drug-specific pathways of platelet inhibition implemented in an individual patient. This point is underscored by the very low sensitivity of the VLTPR dichotomization threshold of the platelet reactivity index VASP. The proposed marker performs sufficiently in isolating patients who are unlikely to suffer a bleeding event. Conversely, its sensitivity of 17% is clearly inadequate in identifying patients who are prone to bleeding. The authors demonstrated that patients with VLTPR did not have a lower thrombotic adverse event rate compared with those remaining within the targeted therapeutic window. This information coupled with the high negative predictive value of the platelet reactivity index VASP threshold is interesting and warrants further validation. Another issue worth looking into stems from the authors’ decision to exclude patients with a known bleeding diathesis (1). Although the rationale for selecting a homogenous patient population is clear, in doing so the authors have excluded high-risk patients who are likely to gain the greatest benefit from individualized antiplatelet therapy management. The aforementioned caveats notwithstanding, the authors are to be congratulated on highlighting the importance of documenting interpatient variability in response to antiplatelet therapy, which is the foundation of subsequent individual tailoring of platelet inhibition.

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