Response to Letter by Giardini and Donti

Response:

We appreciate the interest of Drs Giardini and Donti in our work. While we agree that the deposit of fibrin at the interface between blood and the device is one of the mechanisms for shunt abolition after transcatheter closure of patent foramen ovale (PFO) with the Amplatzer PFO occluder, we question their affirmation that this process would always be within the physiological limits. If this were the case, we would wonder why most of the groups performing such procedures have prescribed some type of antithrombotic therapy (usually aspirin) for at least several months after device implantation even in cases without residual shunt at the end of the procedure. There is no doubt that the concern regarding potential thromboembolic complications related to the implementation of a prosthesis at the atrial level has prompted the medical community to recommend the use of antithrombotic therapy after transcatheter PFO closure from the very beginning. In fact, half of the patients included in our study exhibited an activation of the coagulation system above the normal limits 1 week after PFO closure and in 15% of them the markers of coagulation activation remained abnormally high 1 month after device implantation. Cases of device thrombosis have been reported for all types of commercially available PFO closure devices, including the Amplatzer PFO device, clearly suggesting that the process of “physiological device thrombosis” can become exacerbated and pathological in some cases. Thus, it seems appropriate to control the PFO closure device thrombotic process with some kind of antithrombotic therapy, at least up to the completion of device endothelialization. While it is true that no cases of device thrombosis was observed using transosophageal echocardiography in our study, it must be borne in mind that the presence of an identifiable thrombus is not needed to show abnormal and clinically relevant activation of the coagulation system, as it has been extensively demonstrated in diseases such as atrial fibrillation for which anticoagulant therapy has been shown to be effective in preventing thromboembolic events. Furthermore, the study was not powered to demonstrate a relationship between enhanced thrombogenesis and thrombus formation or clinical events. We also differ from Drs Giardini and Donti in that we were not surprised at the lack of relationship between the degree of coagulation activation and device size, because most (88%) of the patients received a 25-mm PFO occluder device and the larger (35-mm) PFO device was used in only 3 patients. However, we also failed to demonstrate any relationship between device size and the degree of coagulation activation in a previous study using the Amplatzer atrial septal occluder device, suggesting that differences of a few millimeters in device size might not play an important role in the individual detectable response of the hemostatic system to atrial device implantation. Even though there seems to be consensus about the need for antithrombotic treatment after PFO closure, no studies have yet determined the most appropriate antithrombotic treatment after transcatheter closure of PFO or the duration of such therapy. Thus, the choice and duration of antithrombotic treatment after PFO closure has evolved empirically, with aspirin for at least 6 months the therapy most frequently used. However, thromboembolic events and device thrombosis continue to occur under aspirin therapy within the months after PFO closure and this has prompted some clinicians to add, again empirically, another antiplatelet agent, clopidogrel, on top of aspirin for a few months. As a preliminary step toward determining the optimal type and timing of antithrombotic therapy for such patients, our mechanistic study evaluated the hemostatic effects of the implantation of a PFO closure device at the atrial level, and showed that transient enhanced activation of the coagulation system was the main effect associated with the procedure, with no detectable effect on platelet activation. While our results provide a mechanistic rationale for short-term anticoagulation in such cases we never stated that on the basis of these results anticoagulant therapy must henceforth be established as the antithrombotic treatment after PFO closure. As emphasized throughout the article, our results reinforce the importance of performing out prospective and adequately powered randomized trials to determine the most appropriate and cost-effective antithrombotic therapy after PFO closure. At a time when transcatheter PFO closure might become a standard treatment for patients with cryptogenic stroke, we must put all efforts into reducing the potential iatrogenic complications related to such a procedure. Making the type and duration of antithrombotic therapy after the procedure an evidence-based decision will be a major step in this direction.

Disclosures

None.

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