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The sunset of triple antithrombotic therapy for atrial fibrillation patients

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The management of atrial fibrillation (AF) in patients who have undergone percutaneous coronary intervention (PCI) is challenging. Oral anticoagulation is indicated in patients with AF for the primary and secondary prevention of stroke and systemic embolism, whereas dual antiplatelet therapy (DAPT) combining aspirin plus a $P2Y_{12}$ inhibitor, is indicated in patients who are undergoing PCI with stent implantation for the prevention of thrombotic complications. Thus, the use of the triple antithrombotic therapy, including the combination of an anticoagulant plus DAPT, has been empirically used in clinical practice after PCI in patients with AF requiring oral anticoagulation. Although this triple antithrombotic therapy may minimize the risk of cerebrovascular and coronary ischaemic events, it also has the potential to cause harm in a relevant proportion of patients. Indeed, compared with oral anticoagulation therapy alone, the addition of DAPT to an oral anticoagulant agent is associated with at least a three-fold increase in fatal and non-fatal bleeding complications.[1,2] Thus patients treated with a triple antithrombotic therapy should be considered at high risk of bleeding, prompting the implementation of strategies to minimize this risk. Accordingly, European and North American consensus documents and guidelines, in principle, have recommended a duration of triple therapy for the shortest time necessary. However, shortening the course of triple therapy does not appear to substantially reduce bleeding, as shown in the ISAR-TRIPLE trial, where no significant difference in the rates of overall major bleeding was observed between 6-week and 6-month triple therapy, peaked within the first 30 days of initiation of triple therapy.[3] Therefore, an alternative strategy to reduce bleeding risk may be to drop out one antiplatelet agent from the triple combination, thus composing a dual antithrombotic therapy.

The most updated recommendations regarding the management of antithrombotic therapy in patients with AF who undergo PCI can be found within the recent European guidelines focused on DAPT, which were released in 2017 after the PIONEER AF-PCI trial.[3] This document provides the following main recommendations on triple or dual therapy:

- triple therapy with aspirin, clopidogrel, and oral anticoagulation should be considered for 1 month, irrespective of the type of stent used (Class IIa);
- longer duration of triple therapy up to 6 months should be considered in patients with high ischaemic risk due to an acute coronary syndrome or other anatomical/procedural characteristics that outweigh the bleeding risk (Class IIa); and
- dual therapy with clopidogrel 75 mg/day and oral anticoagulant should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk (Class IIa).

Therefore, according to the guidelines triple therapy should be used routinely, and dual therapy should be restricted to selected patients with high bleeding risk. The RE-DUAL PCI trial provides further consistent evidence on the net clinical benefit of dual therapy, which should give cardiologists confidence to drop aspirin in case of higher bleeding risk. However, even after RE-DUAL PCI trial results, short triple therapy including the combination of aspirin, clopidogrel, and a non-vitamin K oral anticoagulant, should still remain a choice, especially in patients with high thrombotic risk, such as those treated for myocardial infarction or those undergoing complex PCI.

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