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Evolving field of long-term antithrombotic therapy after percutaneous coronary intervention in patients with atrial fibrillation

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I have following conflicts of interests; however, they are not related to the current work submitted or the manuscript it is referring to.

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Approximately 10% of patients undergoing percutaneous coronary intervention (PCI) are long-term users of oral anticoagulation (OAC) due to atrial fibrillation (AF).[1,2] In recent years, antithrombotic therapy and the management of AF patients after percutaneous coronary intervention have evolved tremendously. Determining the most suitable antithrombotic treatment in this patient subset is based on the assessment of risk factors for recurrent coronary ischemic events in the form of stent thrombosis and denovo lesions, cardioembolic stroke, and bleeding.[2] Dual antiplatelet therapy with aspirin and ADP-receptor blockade is more effective in preventing recurrent coronary ischemic events as compared to anticoagulation only therapy, whereas it is less efficacious in preventing stroke in patients with AF.[3] From this background – based mainly on observational data – triple therapy (OAC plus ADP receptor blocker plus aspirin) became the guideline recommended therapy in AF patients undergoing PCI.[2] However, results of recent clinical trials resulted in two major shifts shaping the landscape of the management of these patients: 1) WOEST and REDUAL-PCI trials with double therapy (OAC plus ADP receptor blocker) reduced major bleeding rate compared to triple therapy; and 2) PIONEER-AF-PCI and AUGUSTUS-PCI trials with non-vitamin K oral antagonist treatments (NOAC) instead of vitamin K oral antagonist treatment as an oral anticoagulant in triple therapy also reduced major bleeds.[4-7] These randomized trials have provided pivotal evidence of the safety benefit of NOACs when compared to vitamin K oral antagonist treatment. It is important to note, however, that these trials were powered for the safety outcome of bleeding and not the ischemic events.

While randomized trials provide the highest standard of evidence in clinical science, they seldom randomize all-comers, and therefore, results may not always be generalizable to all the patients we treat. Moreover, given the variety of possible treatment combinations in these trials,[4-7] not to mention their durations, it is pivotal to have real world data on the topic. In this issue of Journal, Dr Casamira et al shed light into this field by providing real-world comparison data of NOAC vs VKA.[8] They performed an observational retrospective study in two tertiary care hospitals in Spain between 2013-2016. In total, 187 consecutive patients with indication for anticoagulation due to AF from an initial registry of 5,269 patients undergoing PCI were identified. Altogether 45% and 55% of patients were discharged on triple therapy with either NOAC (apixaban, dabigatran or rivaroxaban) or VKA, respectively. Duration of triple therapy was similar and on average 136 days. Safety primary endpoint was the occurrence of major bleeding events as defined by the Bleeding Academic Consortium. At 12 months, the rate of overall bleeding events was significantly lower in the NOAC group than in the VKA group with crude numbers of 12.9% vs 31.4% in NOAC and VKA arms, respectively. Major adverse cardiovascular events occurred in 16.5% of patients treated with NOAC and 22.5% of patients treated with VKA, but given the low sample, no significant differences between groups were noted in this respect. Net clinical benefit defined as a composite of death, myocardial infarction, stent thrombosis, stroke, or major bleeding events occurred in one in five in the NOAC group as compared to roughly one in three in the VKA group.

Results of this real-world data need to be interpreted with its limitations in mind. Patients who received VKA presented with more comorbidities such as hypertension,

dyslipidemia, chronic obstructive pulmonary disease, prior PCI, renal impairment, and higher bleeding risk, whereas those with NOACs showed decreased left ventricular ejection fraction more often. Thus, those who received NOACs had lower risk of events based on their baseline characteristics. Sample size was low and outcome events were not adjudicated. Durations of triple therapy components – OAC, ADP-receptor blocker and aspirin – after triple therapy were not reported. Use of periprocedural antithrombotic treatment was not reported in detail in terms of whether bridging was used. In patients on VKA, the simultaneous low-molecular-weight-heparin use – a quadruple therapy – is especially harmful as shown in a prior report from the prospective AFCAS study.[9] Advantage of NOACs is the relatively rapid onset of action, and therefore, LMWH is useless in this setting as long as the patient can take enteral medication. Moreover, time in therapeutic range was not assessed and poor VKA control may increase the risk of both bleeds and thrombotic events.[10] Despite the limitations, the study findings are in line with the randomized trials.[5-7] To summarize, these data provide signal of lower bleeding rates and similar efficacy of NOAC as compared to VKA in patients with AF undergoing PCI.

Nevertheless, many questions remain unsolved in the management of AF patients undergoing PCI. No comparisons can be made between different NOACs based on the trials published so far. There is also a lack data on the role of aspirin used peri- and immediately post procedurally after PCI in these patients. The risk of stent thrombosis is highest within the first days after PCI and whether a loading dose of aspirin only is adequate to mitigate stent

thrombosis risk is not known. The safe time to switch between NOAC and VKA is another issue.

Therefore, in spite of the progress in the field, many pieces of information remain unaddressed.

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