Antithrombotic therapy in atrial fibrillation and stent implantation: treatment or threats by the use of triple or dual antithrombotic therapy

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Atrial fibrillation (AF) is associated with increased risk of stroke and thromboembolism, and thus oral anticoagulation (OAC) therapy is indicated in patients considered at moderate-to-high risk. The net clinical benefit favors anticoagulation for almost all AF patients with the exception of those at very low risk of ischaemic stroke, with a CHA2DS2-VASc score of 0 (1, 2). When the CHA2DS2-VASc score is applied to many AF populations, the percentage of patients with an indication for OAC is increased, as high as 94% (3–5). Based on the results of a real-world nationwide cohort study of patients with non-valvular AF, the net clinical benefit was clearly in favor of VKA treatment in AF patients with increased risk of stroke/thromboembolism, regardless of bleeding risk estimation (as assessed by the HAS-BLED risk score) (1, 2, 6).

Nearly 10% of patients with acute coronary syndrome (ACS) have AF (7). Anti-coagulated patients with AF presenting with an ACS or with chronic ischaemic heart disease undergoing percutaneous coronary intervention (PCI) with stent implantation represent a complex management cohort, especially from the concomitant use of dual antiplatelet therapy required after stent implantation, leading to triple therapy (TT). In these patients, one has to balance the risk of stroke (from AF), recurrent cardiac ischemia (if ACS), stent thrombosis and serious bleeding. The latter is clearly multifactorial, and can have important prognostic implications (8). Nonetheless, there is lack of robust evidence for TT use, as most of available information are based on small, single-centre and retrospectively analysed cohorts.

Two recent expert consensus documents recommend TT in patients with AF presenting with ACS or those undergoing stenting, including OAC plus aspirin 100 mg per day and clopidogrel 75 mg per day in the short term, followed by therapy with OAC plus a single antiplatelet drug (aspirin or clopidogrel), and OAC alone if stable after one year from the index event (9, 10). Many similarities are evident between European and North American practice (11).

In the September issue in Thrombosis and Haemostasis, Bernard et al. provided us with valuable information on the benefit of OAC in patients with AF undergoing coronary stent implantation (12). Based on a study population of 8,962 unselected patients with AF, the authors studied 417 patients who underwent stent implantation. They conclude that OAC was independently associated with decreased risk of subsequent composite end-point.

These French data confirm a previous Spanish study with a similar design, supporting the protective role of OAC (13). The findings by Bernard et al also support the potential risk of using drug-eluting stents (DES) in this population (14). Although the authors recognised the presence of a common management protocol, only 23% of patients received OAC at discharge. Importantly, the OAC indication was not associated with the assessed risk of stroke or bleeding in patients. These data reflect the reality of the clinical management of these patients in the ‘real world’, with elderly subjects and high prevalence of important comorbidities, and expected high risk of complications during the follow-up.

This year, renewed interest into the optimal treatment of the antithrombotic treatment is evident (15, 16). In a Danish nationwide cohort of patients with AF and stenting, the authors raise the possibility that even short-term TT is hazardous with regard to bleeding risk, without a safe therapeutic window (15) as also reported by others. Indeed, it is recognised that TT increases the risk of bleeding (15, 17, 18). In the modest-sized WOEST randomised trial, the primary endpoint (all bleeding) was largely driven by minor bleeds – also, not all participants had AF (69%) – and there were patients with radial (vs femoral) and acute (vs elective) procedures (16). Moreover, the duration of TT (12 months) was prolonged when compared to recent recommendations (9, 10), which also might have influenced bleeding rates. Also, there was scarce use of proton pump inhibitors and it is uncertain if the increase in mortality noted in this small trial was related to cessation of antithrombotic therapy when bleeding occurred. Bleeding is clearly multifactorial, as highlighted by the European consensus document (8) and in this population, renal impairment could be an important ‘driver’ of bleeds (19).

Based on the available evidence, including the findings of the study by Bernard et al. (12), when TT is indicated we should perhaps try to have the shortest possible
time exposed to such a regimen. Indeed, the key message as recommended by the consensus documents (9, 10), is to shorten the period of TT (i.e. when dual antiplatelet therapy is added to OAC), limiting the duration of TT as much as possible based on clinical scenario, type of stent, and bleeding risk (e.g. as assessed by use of the HAS-BLED score [20]). The duration of TT is mainly determined by two variables: the clinical setting (ACS or elective coronary intervention; non-modifiable variable) and the type of stent (bare metal stent or DES; modifiable variable) (21). Since the benefit of double antiplatelet therapy in patients with ACS is mainly obtained during the first few months, the type of stent may also in ACS patients be the most important variable influencing duration of TT. With DES of the third generation including also polymer-free DES and bioabsorbable vascular scaffolds the risk of stent thrombosis has diminished (22–24) and shorter durations of combination antithrombotic therapy might, therefore, become clinical routine, a hypothesis that has to be proven by ongoing and future investigations.

New oral anticoagulant drugs offer new possibilities, and indeed a reduction of bleeding episodes are expected (25, 26), eventually also in combination with dual antiplatelet therapy. First moderate recommendations to use one of the new oral anticoagulants during TT instead of VKAs come from the North American consensus document (10), but ongoing updates of this and the European document might be stricter in such recommendations. However, until new recommendations are published and results of the ongoing trials in this field become available, clinicians should follow the current guidelines (27), assess the thrombotic and bleeding risk in every of our patient and tailor a carefully antithrombotic regimen in every individual patient, as part of our holistic management in these patients (28).

Conflicts of interest
Dr. Marín has received research grants from and served in the speakers bureau of Bayer, Boehringer-Ingelheim and Pfizer. Dr. Huber has served in the speakers bureau of Bayer, Boehringer-Ingelheim, Daiichi-Sankyo, Bristol Myers/Squibb and Pfizer. Professor Lip has served as a consultant for Bayer, Astellas, Merck, Astra-Zeneca, Sanofi-Aventis, Aryx, Portola, Biotoric, and Boehringer-Ingelheim and has been on the speaker bureau for Bayer, Boehringer-Ingelheim, and Sanofi-Aventis.

References