Individualized Duration of Dual Antiplatelet Therapy Guided by Risk Scores
— Ready for Prime Time? —

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In patients undergoing percutaneous coronary intervention (PCI) with stent implantation, dual antiplatelet therapy (DAPT), defined as the combination of aspirin and a P2Y₁₂ inhibitor, is crucial for reducing the risk of stent thrombosis (ST) and recurrent ischemic events.¹ The optimal duration of DAPT after coronary stenting has been the object of extensive investigation.² Prolonged DAPT has been demonstrated to reduce the rate of ST and ischemic recurrence, though increasing the risk of bleeding.³ Conversely, shorter DAPT regimens have been proved to reduce bleeding, but at the cost of decreasing the protection from ischemic recurrence, especially, in patients with acute coronary syndromes (ACS).⁴ In aggregate, results of trials have demonstrated that “a one size fits all” approach is not adequate when selecting the optimal duration of DAPT, thereby mandating individualized treatment strategies aimed at pinpointing the optimal balance between bleeding and thrombotic risks.

As a rule of thumb, current guidelines recommend DAPT for 6 or 12 months after coronary stenting in patients with chronic coronary syndrome or ACS, respectively.⁵ These temporal boundaries, however, are not mandatory because the guidelines also advocate tailoring the duration of DAPT according to the individual’s predicted risk of bleeding and ischemic complications. In daily practice, the classification of patients into different risk categories is not an easy clinical task. Risk scores to support clinical decision-making about the optimal duration of DAPT have been recently developed.⁶ By providing a more objective quantification of the future risk of experiencing an adverse event, a risk score complements clinical judgment, which may prove useful to better define the category of predicted risk in which a patient actually belongs. Two scores have been primarily endorsed by current European guidelines, namely the predicting bleeding complications in patients undergoing stent implantation and subsequent DAPT (PRECISE-DAPT) score and the DAPT score.⁶ The application of the 2 scores is meant to be sequential, with the PRECISE-DAPT score to be used first for assessing the risk of out-of-hospital bleeding and shortening DAPT in patients at high bleeding risk, followed by the use of the DAPT score to assess whether prolonged DAPT beyond 1 year (in patients who have tolerated DAPT) may be beneficial in providing additional ischemic protection while offsetting the increased risk of bleeding portended by prolonged DAPT (Figure). Due to the limited amount of evidence validating their use, guidelines give a Class IIb recommendation (may be considered) for the use of risk scores to evaluate the benefits and risks of different DAPT durations.⁶

In this issue of the Journal, Ji-Yong Jang and co-authors⁷ report the results of a patient-level meta-analysis of 4 randomized clinical trials investigating the prognostic impact of different DAPT durations in patients undergoing PCI. In their study, a total of 5,131 patients who received a 2nd-generation drug-eluting stent were stratified into 3 groups (DAPT duration shorter, longer or consistent with current guideline recommendations) on the basis of bleeding risk, as assessed by the PRECISE-DAPT score, and the duration of DAPT to which they had been randomized. The primary endpoint of the analysis was net adverse clinical events (NACE), a composite of cardiac death, myocardial infarction, ST, stroke or major bleeding. In the entire study cohort, no differences in NACE were observed among the 3 DAPT groups. However, patients in the shorter than recommended DAPT group had a higher risk of ischemic recurrence, primarily driven by higher rates of ischemia-driven target vessel revascularization, while a numerical excess of bleeding was observed in patients who received longer than recommended DAPT. Of note, among the ACS patients, the majority of whom had unstable angina at inclusion, NACE was higher in patients treated with longer than recommended DAPT because of a combined increase in both bleeding and ischemic adverse events. In ACS patients treated with shorter than recommended DAPT, the rate of ischemic complications, but not bleeding, was higher as compared with patients meeting the guideline recommendations for individualized DAPT duration.

The authors have to be commended for undertaking a sophisticated analysis that supports current guidelines’ endorsement of the use of risk scores for individualizing the duration of DAPT after coronary stenting.⁵,⁶ The large sample size, and the randomized nature of DAPT duration...
of following wisely the information provided by the PRECISE-DAPT score for individualizing the duration of DAPT. Indeed, prolonged DAPT in patients at high risk for bleeding, as well as shorter DAPT in patients who may safely tolerate DAPT, are both potential threats to patient safety. The relationship among the risk for ischemic recurrence and the duration of DAPT relative to current recommendations is also an interesting finding that deserves clinical attention. A U-shaped pattern of risk evolution, characterized by higher rates of ischemic events at both the shorter and longer DAPT duration boundaries (relative to the guidelines recommendations), was indeed noticed. Although early withdrawal of anti-ischemic protection explains the negative impact of shorter than recommended DAPT, the consequences of bleeding, eventually resulting in disruption of DAPT and other actionable interventions (i.e., diagnostic or interventional procedures to identify and control bleeding, withdrawal of other cardioprotective medications), may help explain the paradoxical increase of ischemic events with prolonged DAPT. The latter finding adds to the understanding that prolonged DAPT in patients at high risk for bleeding should be avoided (even when features of high ischemic risk coexist), and underline the importance of low bleeding risk as the “sine qua non” of prolonged DAPT.

Figure. Sequential application of risk scores for selecting the optimal duration of DAPT (Right panel) and clinical implications of the duration of DAPT relative to current guidelines recommendations (Left panel). ACS, acute coronary syndrome; CCS, chronic coronary syndrome; DAPT, dual antiplatelet therapy. *1 month may be considered if concerns exist about safety.
In light of the accumulating evidence on the utility of risk scores to guide the duration of DAPT, has the time come for stronger recommendations supporting their clinical use? Probably not yet. To date, the available evidence on the use of risk scores for tailoring DAPT duration comes from retrospective analyses and no prospective studies have been conducted. It also needs to be determined how the use of bleeding risk scores might help in safely guiding the implementation of alternative antiplatelet strategies aimed at reducing the risk of bleeding compared with conventional DAPT (i.e., monotherapy with ticagrelor, de-escalation from more potent P2Y12 inhibitors to clopidogrel). Although further research efforts are needed to provide answers to these questions, given the overly clinical complexity in properly estimating bleeding and ischemic risk, risk scores for guiding DAPT should be currently considered as valuable complements to rigorous clinical judgment and not misunderstood as over-simplistic shortcuts in medical reasoning.

Disclosures
S.J. received institutional research grants, honoraria, and consultancy/advisory board member fees from AstraZeneca; institutional research grant and consultant/advisory board fee from Medtronic; institutional research grants and honoraria from The Medicines Company; consultancy/advisory board member fees from Janssen and Bayer. S.B. has no conflicts of interest to disclose.

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