Are we ready to withdraw acetylsalicylic acid after complex percutaneous coronary intervention?

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Dual antiplatelet therapy (DAPT) with acetylsalicylic acid (ASA) and a P2Y12 receptor inhibitor is the cornerstone treatment both in patients with acute coronary syndromes (ACS) and in those undergoing percutaneous coronary intervention (PCI). At the beginning of the drug-eluting stent (DES) era, stent thrombosis (ST) emerged as the most relevant complication, and therefore more powerful P2Y12 inhibition and DAPT prolongation were recommended [1, 2].

With technological refinements, newer thinner-strut DES now show dramatically improved safety profiles compared with their ancestors [3]. The increased safety of third generation DES has encouraged the treatment of complex lesions in older and more fragile patients, in whom the bleeding risk still carries relevant prognostic implications [4].

For the definition of the complex PCI, we commonly refer to the so-called “Giustino’s criteria” [5]: either 3 vessel or ≥ 3 lesions treated, ≥ 3 stents implanted, bifurcation with 2 stents, total stent length > 60 mm or treatment of a chronic total occlusion, with most of the ischemic risk driven by double bifurcation stenting. In the setting of bifurcation PCI, a single “provisional” stenting is currently recommended by the European Bifurcation Club (EBC) consensus document [6], but careful planning is mandatory, as the ischemic risk is heightened when the second stent is placed in “bail-out”, beyond the planned strategy [7].

In addition, the identification of high bleeding risk (HBR) patients [8, 9] has become crucial to define the DAPT strategy [10]. In HBR patients, the overlap between ischemic and bleeding features is common and therefore the evaluation of the net clinical benefit of DAPT duration becomes tricky. Costa et al. [11] documented that those patients enrolled in the PRECISE-DAPT study who underwent complex PCI had a higher risk of ischemic events, but benefitted from long-term DAPT only if HBR features were not present. In order to obtain an optimal balancing between the ischemic and the thrombotic risk, a modulation of antithrombotic strategy has been proposed, with an initial DAPT period to reduce the ST risk during the phase of strut endothelialization, followed by long-term antiplatelet monotherapy with either ASA or a P2Y12 receptor inhibitor to contain the bleeding risk [12]. In the subgroup of patients with complex lesions...
enrolled in the TWILIGHT trial, Dangas et al. [13] showed that, after 3-month DAPT, continuation of ticagrelor monotherapy was associated with a lower incidence of bleeding without increasing the risk of ischemic events compared with continuing DAPT.

The multicentric, randomized, open-label SMART-CHOICE trial [14] enrolled 2,993 patients — with ACS in 60% of cases — undergoing PCI with second generation DES in Korea to receive 12-month DAPT vs. 3-month DAPT followed by P2Y₁₂ monotherapy (mostly clopidogrel). At 12 months of follow-up, shorter DAPT followed by P2Y₁₂ monotherapy was non-inferior to 12-month DAPT for the primary endpoint of major adverse cardiac and cerebrovascular events, with a lower rate of bleeding events expressed as Bleeding Academic Research Consortium (BARC) bleeding type 2–5. In the current issue of the Cardiology Journal, Roh et al. [15] performed a post-hoc analysis of the SMART-CHOICE trial among the 498 patients who underwent complex PCI, with intravascular ultrasound guidance used in 31.5% of cases. Similarly to the TWILIGHT trial, also in the SMART-CHOICE complex, the P2Y₁₂ inhibitor monotherapy showed adverse event rates comparable to the DAPT group.

Two recent meta-analyses [16, 17] showed that shorter DAPT regimens followed by P2Y₁₂ monotherapy appear safe in containing bleeding events, without a significant increase in ischemic risk among unselected patients.

Looking ahead, complex PCI undoubtedly deserves careful planning, with single stenting recommended in bifurcations, and when double stenting is needed, imaging becomes vital to optimize strut overlapping and reduce the risk of strut malapposition. In this view, the EBC proposed a modulated DAPT duration strategy according to clinical presentation, HBR, stenting strategy and the use of intraprocedural imaging [18].

At present, the optimal DAPT duration after complex PCI is still under debate. ASA-free strategies, in light of the limited evidence, cannot be routinely recommended and should be restricted to selected patients. A meaningful approach should take into account both clinical and procedural risk variables (Fig. 1).

In the nearest future, without doubt we will witness several trials focusing various de-escalation antiplatelet therapeutic approaches after PCI or ACS [19].

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**Figure 1.** Decisional algorithm proposed for antiplatelet duration after complex percutaneous coronary intervention (PCI); ACS — acute coronary syndrome; ARC — Academic Research Consortium; ASA — acetylsalicylic acid; HBR — high-bleeding risk; DAPT — dual antiplatelet therapy; PRECISE-DAPT — PREdicting bleeding Complications in patients undergoing stent Implantation and Subsequent Dual AntiPlatelet Therapy. Bleeding risk stratification according to PRECISE-DAPT score and ARC-HBR score is defined as a 1-year risk of a BARC (bleeding ARC) type 3 or 5 ≥ 4% or of intracranial hemorrhage ≥ 1%.
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