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EDITORIAL

Dual-Antiplatelet Therapy After Percutaneous Coronary Intervention: How Short Is Too Short?

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Dual-antiplatelet therapy (DAPT) is recommended after percutaneous coronary intervention (PCI) for patients presenting with chronic coronary syndrome as well as acute coronary syndrome.[1] However, optimal duration of DAPT is a matter of debate. On the one hand, ischemic risk, especially early after PCI, is high and should be reduced by DAPT. On the other hand, DAPT goes in line with an enhanced risk for bleeding events. Especially in patients with further comorbidities or at advanced age, bleeding risk is substantially increased.[2,3] For a long time, reduction of ischemic events was the main aspect of DAPT. However, this changed substantially as bleeding is recognized as a relevant factor with impact on hard outcome end points, such as death. The relevance of bleeding is underlined by recent randomized controlled trials. In PEGASUS-TIMI 54, for example, a DAPT regimen with ticagrelor led to no reduction of all-cause death, although rate of myocardial infarction was reduced.[4] In contrast, the COMPASS (Cardiovascular Outcomes for People Using Anticoagulation Strategies) trial revealed a reduction in death from any cause without a significant decrease of myocardial infarction.[5] Preventing ischemic events, like myocardial infarction, is still the main purpose of DAPT. However, reduction of bleeding events, which also contribute to hard end points, like all-cause death, is a major challenge for the upcoming years. Recent guidelines recommend DAPT for 12 months after acute coronary syndrome with ST-segment–elevation myocardial infarction[6] and non–ST-segment–elevation myocardial infarction. However, in patients presenting with non–ST-segment–elevation myocardial infarction, shorter duration of DAPT may be considered in patients with high or very high bleeding risk.[7] After PCI in patients presenting with chronic coronary syndrome, DAPT duration of 6 months is recommended. However, shortening to at least 1 month or extension up to ≥12 months is also supported by the guidelines in dependence of ischemic and bleeding risk.[1]

See Article by Kinlay et al.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Kinlay et al evaluated real-world data from the Veterans Affairs Healthcare System for duration of DAPT and long-term outcomes.[8] Particularly noteworthy is the long follow-up of up to 13 years. However, as excellently pointed out by the authors, the focus is mainly on the outcome within 2 years after index PCI, because the relevance of the DAPT duration for the long-term outcome of several years is questionable. Their major findings were as

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follows: (1) a discontinuation of DAPT before 9 months after PCI was associated with an increased risk for death (cardiovascular and noncardiovascular) and (2) discontinuation after 9 months lead to reduced rates of bleeding, cardiac death, and myocardial infarction. Reduced bleeding rates are logical after discontinuation of DAPT. However, reduced risk for myocardial infarction is surprising, and the reason for this remains unclear. Maybe the patients with discontinuation after 9 months of DAPT had a lower baseline ischemic risk in comparison to the patients with continuation of DAPT, leading to a higher event rate in this group.

Unfortunately, patients with death within 14 days after PCI were excluded from the study to focus on long-term outcome of DAPT duration. However, as we learned from the AUGUSTUS (Open-Label, 2×2 Factorial, Randomized, Controlled Clinical Trial to Evaluate the Safety of Apixaban versus Vitamin K Antagonist and Aspirin versus Aspirin Placebo in Patients With Atrial Fibrillation and Acute Coronary Syndrome and/or Percutaneous Coronary Intervention) trial, this early phase after PCI is the crucial key for avoiding severe ischemic complications with DAPT, even in addition to long-term anticoagulation.[9] This led to the recommendation to add DAPT to oral anticoagulation at least for the length of hospital stay or 1 week before changing the regimen to oral anticoagulation plus clopidogrel.[7]

There is an effort to investigate newer regimens with shorter DAPT to reduce the risk of bleeding without increasing the risk of ischemia. For patients with acute coronary syndrome, SMART-DATE (6-Month Versus 12-Month or Longer Dual Antiplatelet Therapy After Percutaneous Coronary Intervention in Patients With Acute Coronary Syndrome) revealed an increase in myocardial infarction for patients with 6 months of DAPT in comparison to 12 months. However, this trial was performed in an Asian cohort, and about 80% of all patients received clopidogrel as P2Y12 inhibitor.[10] PEGASUS-TIMI 54 and the DAPT study even revealed benefits on ischemic end points for a prolonged DAPT over 1 year. However, bleeding risk increased as expected.[11,12] Furthermore, short DAPT duration with following ticagrelor monotherapy is an emerging regimen. Two studies with 1 and 3 months of DAPT demonstrated no increased risk for ischemic end point, whereas bleeding rate significantly decreased.[13,14] These successful trials already led to inclusion of such regimens into recent guideline.[1,7]

One point to consider in any case is that a large proportion of the patients in the study of Kinlay et al was men.[8] To date, there are no differentiated recommendations for DAPT duration between men and women. Traditionally, female sex has been considered a risk factor for bleeding. However, the Academic Research Consortium for high bleeding risk published a proposal to identify patients with high bleeding risk undergoing PCI. In this proposal, female sex was not addressed as a risk factor for bleeding.[15] The performance of this risk score was confirmed by real-world data, which showed an increase in access-site bleeding in female patients but not overall bleeding in a 1-year follow-up.[16] Nevertheless, female patients are mostly underrepresented in randomized controlled trials, which limits meaningfulness of data for both sexes.

Besides traditional antiplatelet agents, the COMPASS trial revealed beneficial effects for a dual pathway inhibition with acetylsalicylic acid and rivaroxaban (2.5 mg 2 times a day) in patients with chronic coronary syndrome.[5] Subsequently, in patients after PCI, a dual pathway inhibition led to decreased rate of major adverse cardiovascular events, death, and stroke, but not myocardial infarction, and an increased rate of bleeding events.[17] The mechanism behind these findings is unclear to date. Beside anti-inflammatory properties,[18] rivaroxaban was also shown to inhibit platelet aggregation, which may contribute further to the risk reduction in COMPASS.[19]

To date, optimal antithrombotic regimens after PCI are not known for a broad range of patients. However, current guidelines allow an individual approach, supporting different regimens and duration of DAPT in dependence of ischemic and bleeding risk. Nevertheless, new trials are urgently needed to improve treatment after PCI, especially for the bleeding risk. Kinlay et al provide important information on the impact of DAPT duration on ischemic and bleeding end points, supporting a short DAPT duration.[8]

ARTICLE INFORMATION

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Disclosures

None.

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