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Post-PCI Antithrombotic Treatment With High Bleeding Risk*

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Antiplatelet therapy after percutaneous coronary intervention (PCI) is as old as the procedure itself. However, the duration of dual antiplatelet therapy (DAPT) with aspirin and an adenosine receptor antagonist (clopidogrel, ticagrelor, or prasugrel), the use of single antiplatelet therapy (SAPT) with 1 antiplatelet agent, or the use of no antiplatelet therapy in patients on chronic oral anticoagulation yields as many treatment permutations on post-PCI treatment as there are studies addressing this question.

It is not surprising that there is a sense of confusion. Undertreatment risks stent thrombosis, myocardial infarction, and a high risk of death, whereas overtreatment risks major bleeding, possible cessation of antithrombotics, and a high risk of death from bleeding or myocardial infarction. Trying to define the patient at high risk of thrombosis from the patient at high risk of bleeding is difficult, because risk factors for both tend to overlap.[1]

Increasingly, the risk of major bleeding is viewed as an important factor in determining the post-PCI antithrombotic regimen. To some extent this is a result of the newer generations of drug-eluting stents, which have lowered the risk of thrombotic complications after PCI.[2] Arguably, post-PCI antithrombotic regimens are based on balancing bleeding and thrombotic risk,[3] but are longer DAPT regimens needed for patients with high bleeding risk having PCI for an acute coronary syndrome?

MASTER DAPT STUDY

In this issue of the *Journal of the American College of Cardiology*, Smits et al[4] use a subgroup analysis of the MASTER DAPT (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen) study[5] to address this question in patients with high bleeding risk

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and a prior myocardial infarction (95% of this subgroup had an acute coronary syndrome at the index PCI). The MASTER DAPT study was an open label study of patients with high bleeding risk who had completed DAPT for 1 month after PCI without a thrombotic complication.

At 1 month, subjects were randomized to an abbreviated antiplatelet regimen of SAPT for a further 11 months (or 6 months if they were on an oral anticoagulant) vs a standard antiplatelet regimen of at least a further 2 to 11 months of DAPT. Most of the abbreviated SAPT group used aspirin or clopidogrel, whereas in the standard antiplatelet group virtually all patients were taking aspirin and 79% were on clopidogrel.[5] The definition of high bleeding risk incorporated a number of risk factors shared by the Academic Research Consortium High Bleeding Risk score[6] and the PRECISE-DAPT (PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy) score.[7] Patients with in-stent restenosis or stent thrombosis were excluded.

The co-primary outcomes 12 months after PCI were net adverse clinical outcomes (NACE) including all-cause death, myocardial infarction, stroke, or Bleeding Academic Research Consortium 3 or 5 bleeding events,[6] and major adverse cardiac and cerebral events, which was NACE without the bleeding events. The authors show that in patients with prior myocardial infarction, the abbreviated antiplatelet regimen had NACE (HR: 0.83; 95% CI: 0.61–1.12) and major adverse cardiac event (HR: 0.86; 95% CI: 0.62–1.19) similar to the standard antiplatelet regimen. Combined endpoints improve the power of a study, but pooling component endpoints across studies can provide insights into the balance of bleeding and thrombotic risk.

META-ANALYSES

Compared with standard DAPT regimens, meta-analyses of short-DAPT followed by SAPT show less bleeding with no difference in death or myocardial infarction, but possibly higher risks of stent thrombosis.[8,9] Fortunately, stent thrombosis is a rare complication with the newer generation drug-eluting stents,[2] and may be offset by lower risks of myocardial infarction and death due to avoidance of major bleeding with the short-DAPT to SAPT regimens.[6]

SHORT-DAPT VS PREMATURE CESSATION OF DAPT

In contrast to predetermined prescribed shorter durations of DAPT, premature cessation of DAPT due to frailty, poor social support, or poor medical adherence is strongly related to mortality and adverse cardiovascular outcomes both soon after PCI and for years later.[10] These observations do not inform the value of short-DAPT regimens, but rather reflect the high risks of adverse outcomes related to inequalities in our society and the provision of health services that are only recently becoming the focus of health care policy.[11] These are just as powerful determinants of health care outcomes as the avid debate of DAPT duration.

THE PATIENT WITH HIGH BLEEDING RISK

This tradeoff of major bleeding and thrombotic events is likely more important in patients with high bleeding risk who were the focus of MASTER DAPT[5] and TWILIGHT (Ticagrelor with Aspirin or Alone in High-Risk Patients after Coronary Intervention).[12] Several scores identify characteristics of the patient with high bleeding risk after PCI,[6,7] and include older age, chronic kidney disease, prior bleeding events, use of oral anticoagulants, and PCI for myocardial infarction.

However, the current subgroup analysis by Smits et al[4] suggests that short-DAPT of 1 month followed by SAPT is an acceptable regimen in patients with high bleeding risk and recent myocardial infarction. This is supported by a subgroup analysis of patients with myocardial infarction having PCI in the TWILIGHT study with ticagrelor monotherapy[13] and the RE-DUAL (Evaluation of Dual Therapy With Dabigatran vs Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting) study with dabigatran and clopidogrel or ticagrelor compared with warfarin and DAPT.[14] The one outlier is the acute coronary syndrome subgroup of the STOP DAPT 2 (Short and Optimal Duration of Dual Antiplatelet Therapy-2) study, in which clopidogrel monotherapy after short-DAPT did not meet noninferiority to a standard duration DAPT.[15] Although many subjects with a recent myocardial infarct in this subgroup analysis of MASTER DAPT were on this regimen, this SAPT regimen may be better suited to patients with PCI for stable coronary syndromes.

For patients requiring full-dose oral anticoagulants, the 4 pivotal trials of antithrombotic therapy strongly favor a direct oral anticoagulant over warfarin and suggest that SAPT may start from 1 week to 1 month after PCI depending on thrombotic risk, and 1 year after PCI many patients may de-escalate further to oral anticoagulation and no antiplatelet therapy.[3]

The MASTER DAPT investigators should be congratulated for this important contribution to the PCI field. This study, combined with the weight of other similar trials, points to shorter DAPT regimens and preferably SAPT in patients at high bleeding risk who have completed a month of DAPT without adverse thrombotic events, even in those with recent myocardial infarction.

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