A Practice Conundrum: What Is The Optimal Duration of DAPT After PCI?

Improving Outcomes for Patients Undergoing Percutaneous Coronary Intervention

Increasing evidence suggests that eliminating aspirin may be part of the

solution, even among patients with acute coronary syndromes.

Guidelines for patients after percutaneous coronary intervention (PCI) include treatment with dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor to reduce recurrent atherothrombotic events, including stent thrombosis. Prolonged DAPT reduces the risks for ischemic

outcomes but can also elevate bleeding risks, which limits its attractiveness, particularly with more-potent P2Y12 inhibitors. In several recent studies, shortening the duration of DAPT (by reducing the duration of either aspirin or the P2Y12 antagonist) seemed to reduce bleeding complications, but this approach was not tested specifically in patients with acute coronary syndromes

(ACS). Moreover, these studies were underpowered to examine ischemic outcomes. Recent meta-analyses have shed light on the common practice conundrum of determining the optimal duration of dual antiplatelet therapy (DAPT) in patients who undergo percutaneous coronary intervention (PCI). Many studies have looked at the continuation of P2Y12 inhibitor therapy,

but a newer meta-analysis focused on clinical trials that discontinued aspirin therapy and continued P2Y12 inhibitor monotherapy after PCI. A recent network meta-analysis studied different durations of DAPT strategies.

Three research groups have now addressed these issues.

In a manufacturer-funded, open-label trial (Effect of Ticagrelor Monotherapy vs Ticagrelor With Aspirin on Major Bleeding and Cardiovascular Events in Patients With Acute Coronary Syndrome The TICO Randomized Clinical Trial), **(Ref:1)** Kim and colleagues randomized 3056 ACS patients (ST-

segment elevation myocardial infarction [STEMI], 36%; non-STEMI, 33%; unstable angina, 30%) who had undergone successful PCI with an ultrathin-strut, sirolimus-eluting stent to 12 months of DAPT (aspirin plus ticagrelor) or to 3 months of DAPT, followed by 9 months of ticagrelor monotherapy. The 1-year primary composite outcome — major bleeding,

death, MI, stent thrombosis, stroke, or target-vessel revascularization — occurred in 3.9% of the monotherapy group vs. 5.9% of the continued-DAPT group (hazard ratio, 0.66; *P*=0.01, 34% RRR). This benefit was driven predominantly by a reduction in major bleeding (1.7% vs. 3.0%) and nonsignificant trends toward reductions in mortality and other ischemic events.

Benefits were consistent regardless of the type of presenting ACS.

To better understand the impact of aspirin cessation on post-PCI outcomes, O'Donoghue and colleagues **(Ref:2)** conducted a meta-analysis of five randomized trials (N=32,145; ACS, 56%) comparing standard post-PCI DAPT with regimens involving aspirin discontinuation after 1 to 3 months but

continued P2Y12 inhibition (including the study by Kim et al.). In the short-aspirin arm, the P2Y12 inhibitor was ticagrelor or prasugrel in 84% of patients and clopidogrel in 16%. Early aspirin discontinuation was associated with lower risk than extended DAPT for major bleeding (2.0% vs. 3.1%; HR, 0.60, 40% RRR) but not with increases in ischemic outcomes (2.7% and 3.1%; HR,

0.88, RRR:12%) or any individual component. Results were similar in patients presenting with ACS. These findings provide important reassurance that a strategy of discontinuing aspirin may be safer (*ie*, reduce bleeding) and improve risk for MACE after PCI.

This meta-analysis largely represented patients with ST-segment elevation myocardial infarction (STEMI), as only

one trial in the meta-analysis (the TWILIGHT trial) excluded patients with STEMI. The results were consistent – whether patients had acute coronary syndrome (ACS) or STEMI, there was a dramatic reduction in bleeding events without increased risk for cardiovascular events.

Another meta-analysis (Khan et al.), **(Ref:3)** which included 24 randomized

trials (≈79,000 patients), compared extended-term DAPT (>12 months), mid-term DAPT (6 months), and short-term DAPT (<6 months) strategies with the current gold standard of using 12 months of DAPT. Extended-term DAPT was associated with a reduction in risk for myocardial infarction (MI), but the risk for bleeding events was higher, compared with 12 months of DAPT.

Khan's group showed that the best concise DAPT strategy involves discontinuing aspirin rather than the P2Y12 inhibitor. Short-term DAPT followed by P2Y12 inhibitor monotherapy was associated with significantly lower bleeding rates, compared with a short-term DAPT strategy in which the P2Y12 inhibitor was stopped and aspirin was continued.

Compared with ticagrelor, clopidogrel was associated with lower rates of bleeding events. But ticagrelor was associated with lower rates of MACE.

Candidates for long-term P2Y12 inhibitor monotherapy include patients with multiple comorbidities (*eg*, diabetes, hypertension, peripheral arterial disease, renal insufficiency), patients with a history of PCI or MI, patients with

MI at presentation, patients with drug-eluting stents <3 mm in diameter, and patients with a history of vein graft intervention.

The decision to stop aspirin therapy or P2Y12 inhibitor therapy should be based on the individual patient's background and milieu. In most patients, stopping aspirin at 6 months is reasonable, except in complex ACS cases. Emerging

data support discontinuing aspirin and continuing P2Y12 monotherapy.
After 6 months to 1 year of DAPT, the PRECISE-DAPT or DAPT score can be used to predict risk for bleeding. In patients with a PRECISE-DAPT score of ≥25, using a DAPT strategy of longer duration or indefinite P2Y12 monotherapy can be considered, despite the lack of data.

COMMENT

These data add to the existing literature suggesting that initial DAPT with discontinuation of aspirin at 1 to 3 months (and continuation of a P2Y12 inhibitor) might be optimal antiplatelet therapy for patients undergoing PCI with contemporary ultrathin-strut drug-eluting stents, even those presenting with ACS. We must remain

cautious about extrapolating these results to patients treated with clopidogrel and prasugrel, however, since these P2Y12 inhibitors have been studied as monotherapy in only few patients, and genetic polymorphisms can render clopidogrel less effective in 5% to 20% of people. Further studies

demonstrating the safety of this post-PCI approach in STEMI
patients, particularly with non-ultrathin drug-eluting stents, would be helpful.

References:

1: Byeong-Keuk Kim, MD; et al.

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2: O'Donoghue ML, Murphy SA, Sabatine MS. The safety and efficacy of aspirin discontinuation on a

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3: Khan SU, Singh M, Valavoor S, et al. Dual antiplatelet therapy after percutaneous coronary intervention and drug-eluting stents: a systematic review

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