Drew Ashby, MD; Corey Lyon, DO
University of Colorado Family Medicine Residency, Denver

DEPUTY EDITOR
James J. Stevermer, MD, MSPH
Department of Family and Community Medicine, University of Missouri-Columbia

Should you switch the DAPT agent one month after ACS?

A randomized controlled trial says "Yes," but current guidelines say "No."

PRACTICE CHANGER

Switch to clopidogrel from one of the newer P2Y12 blockers 1 month after an acute coronary event, while continuing aspirin, to decrease bleeding events without increasing the risk of ischemic events.[1]

STRENGTH OF RECOMMENDATION

B: Based on a single randomized controlled trial (RCT).

Cuisset T, Deharo P, Quilici J, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. *Eur Heart J*. 2017;38:3070-3078.

ILLUSTRATIVE CASE

A 60-year-old man is seen in your clinic 30 days after he was hospitalized for acute coronary syndrome (ACS) due to ST-elevation myocardial infarction (STEMI). He underwent percutaneous coronary intervention (PCI) with placement of one stent. He received aspirin and a loading dose of ticagrelor for antiplatelet therapy. He was discharged on dual antiplatelet therapy (DAPT) consisting of daily aspirin and ticagrelor. He asks about the risk of bleeding associated with these medications. Should you recommend any changes?

Platelet inhibition during and after ACS to prevent recurrent ischemic events is a cornerstone of treatment for patients after myocardial infarction (MI).[2] Current American Cardiology Association and European Society of Cardiology guidelines recommend patients with coronary artery disease who have had a recent MI continue DAPT with aspirin and a P2Y12 blocker (ie, clopidogrel, ticlopidine, ticagrelor, prasugrel, or cangrelor) for 12 months following ACS to reduce recurrent ischemia.[2-4]

Studies have shown that using the newer P2Y12 inhibitors (ie, prasugrel and ticagrelor) after PCI leads to a significant reduction in recurrent ischemic events when compared to clopidogrel.[5-7] These data led to a guideline change recommending the use of the newer agents over clopidogrel for 12 months following PCI.[2] Follow-up studies evaluating the newer P2Y12 agents continue to show strong evidence for their use in the first month following PCI, while also demonstrating an increased bleeding risk in the maintenance phase (from 30 days to 12 months post-PCI).[6,7] This increased risk is the basis for the current study, which tested switching from a newer P2Y12 agent to clopidogrel after the initial 30-day period following PCI.

STUDY SUMMARY

Switched DAPT is superior to unchanged DAPT

This open-label RCT (N = 646) examined changing DAPT from aspirin plus a newer P2Y12 blocker (prasugrel or ticagrelor) to a combination of aspirin and clopidogrel after the first month of DAPT post-ACS.[1] Prior to PCI, all patients received a loading dose of ticagrelor 180 mg or prasugrel 60 mg. Subsequently, all patients in the trial took aspirin (75 mg/d) and one of the newer P2Y12 inhibitors (prasugrel 10 mg/d or ticagrelor 90 mg BID) for 1 month. For those enrollees who had

no adverse events after 30 days, half were randomly switched to aspirin and clopidogrel 75 mg/d and the other half remained on aspirin and their newer P2Y12 blocker in a 1:1 ratio. For the next year, researchers examined the composite outcome of cardiovascular death, urgent revascularization, stroke, and major bleeding (as defined by the Bleeding Academic Research Consortium [BARC] classification ≥ Type 2 at 1 year post-ACS).

The average age of the participants was 60 years; 40% had experienced a STEMI and 60% had a non–STEMI. Overall, 43% of patients were prescribed ticagrelor and 57% prasugrel. At 1 year, 86% of the switched DAPT group and 75% of the unchanged DAPT group were still taking their medication. At the 1-year follow-up, the composite outcome was lower in the switched group, compared with the unchanged group (13% vs 26%; hazard ratio [HR] = 0.48; 95% confidence interval [CI], 0.34-0.68; number needed to treat [NNT] = 8).

All bleeding events (ranging from minimal to fatal) were lower in the switched group (9% vs 24%; HR = 0.39; 95% CI, 0.27-0.57; NNT = 7), and bleeding events identified as BARC ≥ Type 2 (defined as needing medical treatment) were also lower in the switched group (4% vs 15%; HR = 0.30, 95% CI, 0.18-0.50; NNT = 9). There were no significant differences in reported recurrent cardiovascular ischemic events (9.3% vs 11.5%; HR = 0.80, 95% CI, 0.50-1.29).

Implementing this practice change is facilitated by the fact that, currently, clopidogrel is less expensive than the newer P2Y12 blockers.

WHAT'S NEW

Fewer bleeding events without an increase in ischemic events

Cardiology guidelines recommend the newer P2Y12 blockers as part of DAPT after ACS, but this trial showed switching to clopidogrel for DAPT after 30 days of treatment lowers bleeding events with no difference in recurrent ischemic events.[2-4]

CAVEATS

Less-than-ideal study methods

This trial was an open-label, unblinded study. The investigators who adjudicated critical events were blinded to the treatment allocation, but some events, such as minor bleeding and medication discontinuation, could be self-reported by patients. In addition, the investigators used a less-than-ideal method (opaque envelopes) to conceal allocation at enrollment.

CHALLENGES TO IMPLEMENTATION

Implementation may require changing a cardiologist's prescription

Implementing this practice change is facilitated by the fact that clopidogrel is currently less expensive than the newer P2Y12 blockers. However, after ACS and PCI treatment, cardiologists usually initiate antiplatelet therapy and may continue to manage patients after discharge. So the family physician (FP) may not be responsible for the DAPT switch initially. Further, switching may necessitate coordination with the cardiologist, as FPs may be hesitant to change cardiologists' prescriptions. Lastly, guidelines currently recommend using the newer P2Y12 blockers for 12 months.[2] JFP

ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.

Copyright © 2019. The Family Physicians Inquiries Network. All rights reserved.

References

1. Cuisset T, Deharo P, Quilici J, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. *Eur Heart J*. 2017;38:3070-3078.
2. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016;68:1082-1115.
3. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33:2569-2619.
4. Roffi M, Patrono C, Collet J-P, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2015;37:267-315.
5. Antman EM, Wiviott SD, Murphy SA, et al. Early and late benefits of prasugrel in patients with acute coronary syndromes undergoing percutaneous coronary intervention. *J Am Coll Cardiol*. 2008;51:2028-2033.
6. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361:1045-1057.
7. Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007;357:2001-2015.