Travis M. Howard, MD
Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH

Umesh N. Khot, MD
Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH; Clinical Assistant Professor, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH

Dual antiplatelet therapy after percutaneous coronary intervention: Personalize the duration

ABSTRACT

The recommended duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention with a drug-eluting stent has changed from 1 year for all to a more personalized approach based on the patient's risks of ischemia and bleeding. The trend is toward shorter treatment in view of lower rates of late and very late stent thrombosis with newer drug-eluting stents and the risk of bleeding with DAPT. But some patients at high risk of ischemic events and low risk of bleeding may benefit from longer treatment.

KEY POINTS

A shorter duration of DAPT (< 12 months) is favored for patients at high risk of bleeding or low risk of ischemia, or both.

DAPT for 12 months or more should be considered for patients at high risk of ischemic events (eg, due to prior myocardial infarction) and at low risk of bleeding.

For patients on DAPT who need noncardiac surgery, 3 factors should be considered: risk of bleeding if surgery is performed while the patient continues DAPT; risk of stent thrombosis if DAPT is interrupted; and consequences of delaying surgery. For some, a bridging protocol can be used.

DUAL ANTIPLATELET THERAPY (DAPT) with aspirin and a P2Y12 inhibitor after a percutaneous intervention (PCI) is one of the most commonly prescribed therapies in cardiovascular medicine. However, treatment strategies have evolved as our understanding of stent thrombosis has deepened and stents have improved, leading to uncertainty, even among cardiologists, about how to best manage DAPT.

This article reviews current guidelines on the duration of therapy and perioperative management of DAPT after PCI (**Table 1**).

■ BEYOND THE RIGID 1-YEAR RECOMMENDATION

Bare-metal stents, developed to keep an artery open after angioplasty, were associated with stent thrombosis and restenosis, requiring repeat revascularization in many patients.[1] The risk of stent thrombosis was found to be mitigated by aspirin and 1 month of ticlopidine, sparking the initial enthusiasm for DAPT as we know it today.[2]

Drug-eluting stents were subsequently developed to reduce the risk of stent restenosis.[1] However, concerns about late and very late stent thrombosis with first-generation drug-eluting stents precipitated the need for longer DAPT. Trials at the time assessed 1 year of therapy, and when it was found to be effective, it became the reference duration of DAPT after drug-eluting stent placement, regardless of the clinical presentation at the time of PCI.[3,4]

Second-generation drug-eluting stents have better polymers and smaller struts and

TABLE 1

Dual antiplatelet therapy (DAPT) after percutaneous coronary intervention with a drug-eluting stent

Initial DAPT duration

The rigid 1-year recommendation for initial DAPT duration has been revised, and the optimal duration is now defined by balancing risk of bleeding vs avoiding future ischemic events

In patients with high bleeding risk or low ischemic risk, or both, shorter durations of DAPT are favored; in those with low bleeding risk or high ischemic risk, or both, longer durations of DAPT are favored

Perioperative management of DAPT for noncardiac surgery

Consider: Risk of bleeding during surgery while on DAPT
Risk of stent thrombosis
Consequences of delaying surgery

Avoid surgery while patient is on DAPT unless emergent or bleeding risk is minimal

Risk of stent thrombosis is highest initially and decreases over time but is never zero. If possible, delay surgery for at least 3 months and ideally for 6 months

If DAPT is interrupted, continue aspirin, as it protect against stent thrombosis

Consider bridging with intravenous antiplatelet agents if the risk of stent thrombosis is particularly high and surgery cannot be delayed

Long-term DAPT (> 12 months)

Appraise the risks and benefits for the individual patient

Consider in patients at high risk of future ischemic events (eg, patients who have had prior myocardial infarction) and low bleeding risk

are associated with significantly lower rates of late and very late stent thrombosis.[1] These improvements propelled the use of drug-eluting stents rather than bare-metal stents, and they became the predominantly placed stent, even in patients for whom the duration of DAPT must be shorter.[5] However, increased bleeding with prolonged DAPT remained a major drawback, so an extensive evaluation of DAPT duration was undertaken. Knowing how long and under what conditions to continue DAPT after drug-eluting stent PCI is critical for best managing these patients.

Shorter DAPT for some patients

The 2016 American College of Cardiology and American Heart Association (ACC/

AHA)[6] guidelines and the 2017 European Society of Cardiology (ESC)[7] guidelines provide the most recent updates on DAPT management. Despite subtle differences, their overall message is the same. The rigid recommendation for 1 year of DAPT after PCI with a drug-eluting stent irrespective of indication has been revised, and a new paradigm has been introduced. DAPT duration is now determined by balancing risk of future ischemic events against bleeding (**Figure 1**).

For patients with an acute coronary syndrome treated with a drug-eluting stent, at least 12 months of DAPT is recommended. However, just 6 months can be considered for those with high bleeding risk.

For patients with stable ischemic heart disease treated with a drug-eluting a stent, at least 6 months of DAPT with clopidogrel is recommended, but just 3 months can be considered for those at high bleeding risk, or even just 1 month if 3 months of DAPT poses safety concerns.

These guidelines were based on multiple randomized controlled trials over the previous decade that compared 6 months or less of DAPT with longer durations after PCI with a drug-eluting stent.[8–14] Meta-analyses of these trials demonstrated that in an all-comers population, regardless of PCI indication and underlying comorbidities, shorter durations of DAPT decrease bleeding at the expense of increased ischemic events, eg, stent thrombosis and myocardial infarction.[15–17] Further exploration of the data behind this conclusion illuminates the intricacies of DAPT management and provides the foundation for the current guidelines.

■ BALANCING RISKS

Bleeding risk from DAPT is directly proportional to the length of therapy, with longer periods leading to increased bleeding events and higher rates of noncardiovascular mortality.[15] On the other hand, the reduction of ischemic events from DAPT is greatest in the first few weeks due to protection from early stent thrombosis. Over time, the benefit from protection against stent thrombosis decreases, and the predominant advantage of DAPT shifts to protection from spontaneous myocardial infarction, ie, from plaque rupture at sites remote from the stented index lesion.[18]
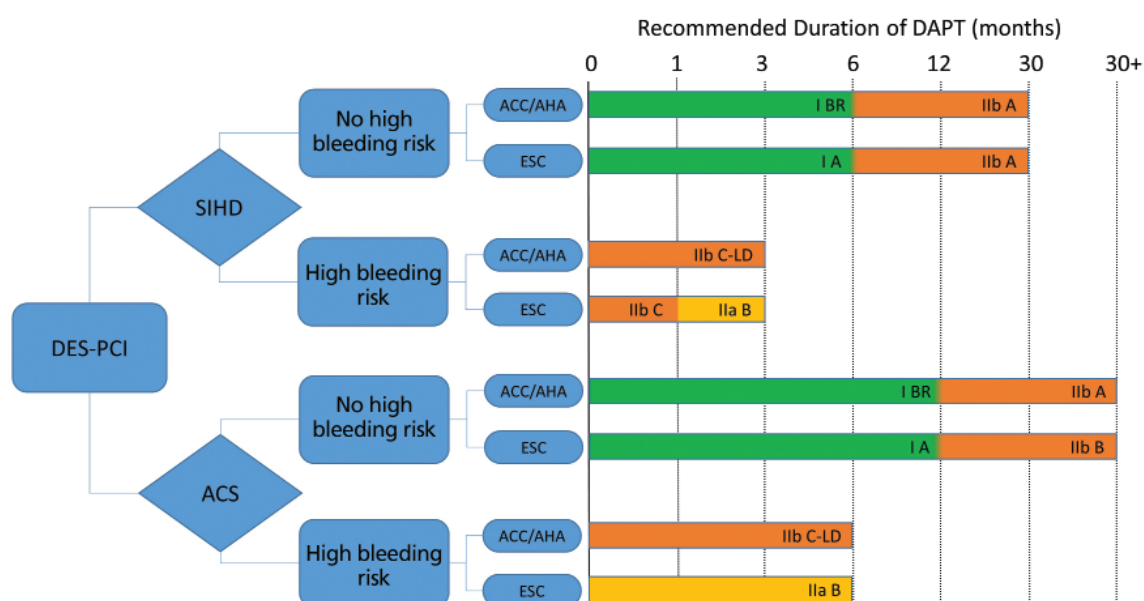
Figure 1. Recommended duration of dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stents. Class of recommendation and level of evidence: class I, benefit much greater than risk; class II, benefit greater than risk, with conflicting evidence or opinion; class IIa, weight of evidence or opinion is in favor of usefulness; class IIb, usefulness is less well established. Level of evidence: A, from multiple randomized clinical trials; B or BR, from one or more randomized trials; C or C-LD, from nonrandomized observational studies.

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; ESC = European Society of Cardiology; PCI = percutaneous coronary intervention; SIHD = stable ischemic heart disease

Information from references 6 and 7.

Despite the reduction of stent thrombosis and myocardial infarction with persistent DAPT, cardiac mortality rates are the same with 6 months or less of therapy compared with longer durations.[15] This is likely due to the declining mortality risk of stent thrombosis over time and the inclusion of smaller myocardial infarctions with less prognostic relevance in trial end points.[19] Consequently, there is no effect on all-cause mortality comparing 6 months or less vs 1 year of DAPT.[15] Thus, it can be reasoned that patients at high risk of bleeding, low risk of ischemic events, or both, may benefit from a shorter duration of DAPT, and those at low risk of bleeding, high risk of ischemic events, or both, may benefit from a longer duration.

Although no study has exclusively focused on patients with stable ischemic heart disease who received drug-eluting stents, subgroup analyses demonstrate that they are at much lower risk of stent thrombosis and myocardial infarction,[20] hence the adequacy of DAPT for 6 months according to the most recent guidelines. The recommendations for patients with an acute coronary syndrome and high bleeding risk are based on the same logic. They were supported in the 2018 SMART-DATE trial (Safety of 6-month Duration of Dual Antiplatelet Therapy After Acute Coronary Syndrome),[21] which demonstrated a higher risk of myocardial infarction in patients with acute coronary syndrome who received DAPT for 6 months compared with 12 or more months. But no difference was found in all-cause mortality with longer DAPT due to the higher incidence of bleeding.

Treatment has evolved, leading to uncertainty about how to best manage DAPT

■ INTERRUPT DAPT FOR NONCARDIAC SURGERY?

When patients on DAPT after drug-eluting stent PCI need noncardiac surgery, one must

Assess:
Urgency of surgery
Bleeding risk
Timing of coronary stent

Emergency surgery

Proceed to surgery
Obtain cardiology consult

Urgent surgery

Stent implanted ≤ 3 months earlier

Delay procedure

Stent implanted 3–6 months earlier

Before stopping medications, consult cardiologist

Stent implanted > 6 months earlier

Elective surgery

Stent implanted ≤ 6 months earlier

Delay procedure

Stent implanted > 6 months earlier

High bleeding risk
Cannot take aspirin
Cannot delay procedure

Before stopping medications, consult cardiologist

Proceed to surgery
Continue aspirin 81 mg daily including procedure day
Hold clopidogrel, ticagrelor 5 days before surgery
Hold prasugrel 7 days before surgery
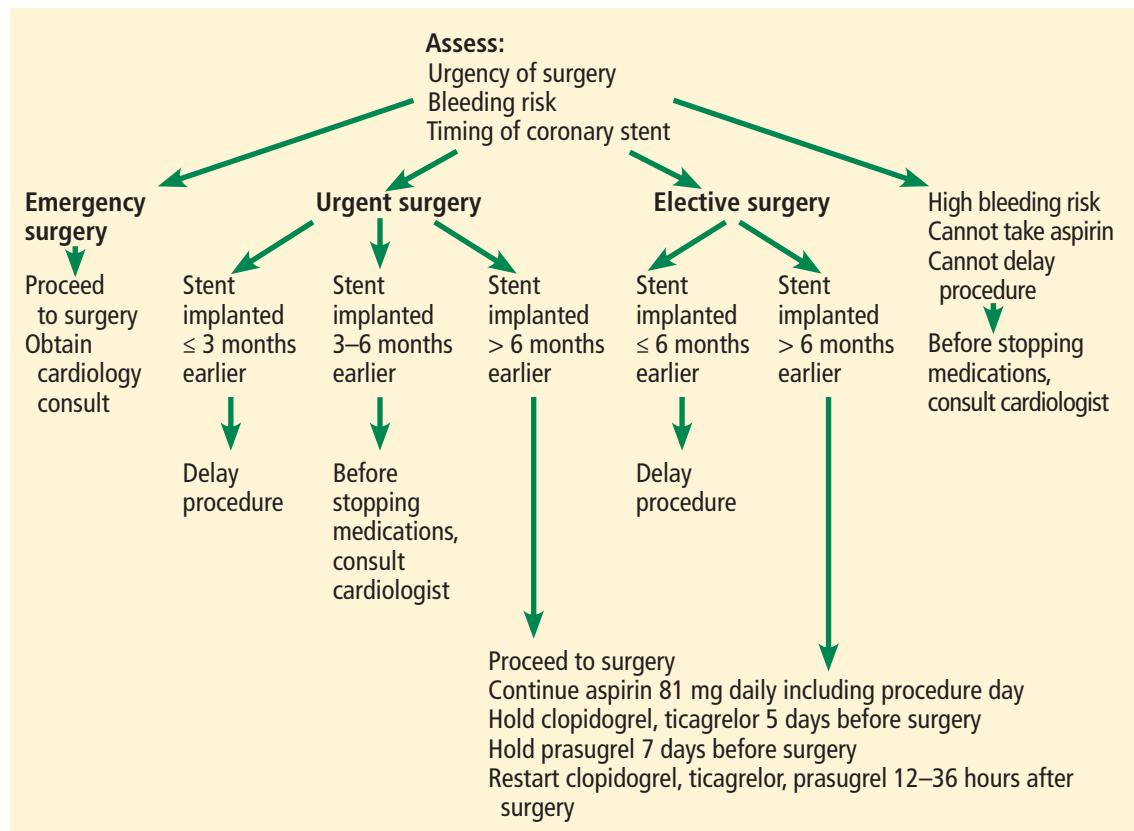Restart clopidogrel, ticagrelor, prasugrel 12–36 hours after surgery

Figure 2. Guidelines for preoperative management of patients with coronary stents undergoing noncardiac surgery.

DAPT duration is now determined by balancing risk of ischemia vs risk of bleeding

consider:
- The risk of bleeding from surgery if DAPT is continued
- The risk of stent thrombosis if DAPT is interrupted
- The consequences of delaying surgery.

These are complicated questions but can be approached in a disciplined manner.

The risk of bleeding during surgery is higher for a patient on antiplatelet therapy.[22,23] Given the increased mortality and morbidity associated with bleeding,[24] antiplatelet therapy should be minimized before surgery unless it can be performed with minimal bleeding risk while on DAPT. However, because DAPT significantly reduces the risk of stent thrombosis, and interruption of DAPT after stent placement is one of the strongest risk factors for stent thrombosis,[6] the tension between the risks of bleeding and stent thrombosis must be balanced. When possible, this dilemma can be solved by delaying surgery. However, in many situations (eg, for malignant and vascular dis-

eases), delaying surgery can be detrimental.[25,26]

Multiple observational studies have tried to determine a time frame after stenting when the risk of DAPT interruption is low enough for patients to undergo surgery.[27–29] Older observational studies based on bare-metal stents and mostly first-generation drug-eluting stents found that the risk of stent-related thrombotic complications is highest in the first 4 to 6 weeks but continues to be elevated for at least 1 year.[27] More recent observational studies suggest the time frame of increased risk is about 6 months,[28] and may even be as short as 30 days.[29]

Based on these data, Cleveland Clinic uses the approach shown in **Figure 2**. Developed by a multidisciplinary team of specialists, the algorithm balances the risks of bleeding, stent thrombosis, and delaying surgery and is similar to the one in the ACC/AHA guidelines.[6]

If DAPT is interrupted, aspirin should be continued if feasible, as it protects against ischemic events,[30] and P2Y12 therapy should

Patient with coronary stent needs noncardiac surgery

Can take aspirin

Can't take aspirin

Has bare metal stent

Has drug-eluting stent

Very high risk

Consult interventional cardiologist

Stent implanted ≤ 6 weeks earlier

Stent implanted > 6 weeks earlier

Stent implanted ≤ 3 months earlier

Stent implanted 3–6 months earlier

Hold aspirin for 7 days before surgery

Bridge

No bridge

Bridge

Any high-risk features?
Left main artery
Proximal left anterior descending artery
Bifurcation
Chronic renal insufficiency stage 4 or 5

Bridge if bare metal stent implanted ≤ 6 weeks or drug-eluting stent implanted ≤ 6 months earlier

Restart aspirin 12 hours after procedure

Perioperative protocol (can take aspirin)
Continue aspirin 81 mg daily including procedure day
Hold clopidogrel, ticagrelor 5 days before surgery
Hold prasugrel 7 days before surgery
Restart clopidogrel, ticagrelor, prasugrel 12–36 hours after surgery

Yes: Bridge

No: No bridge

Restart clopidogrel, ticagrelor, prasugrel 12–36 hours after surgery

If bridging, admit to hospital in cardiology service;
Begin tirofiban 2 days after stopping dual antiplatelet therapy with
    0.1 µg/kg/min intravenously
    (reduce dose by 50% if creatinine clearance is < 60 mL/min);
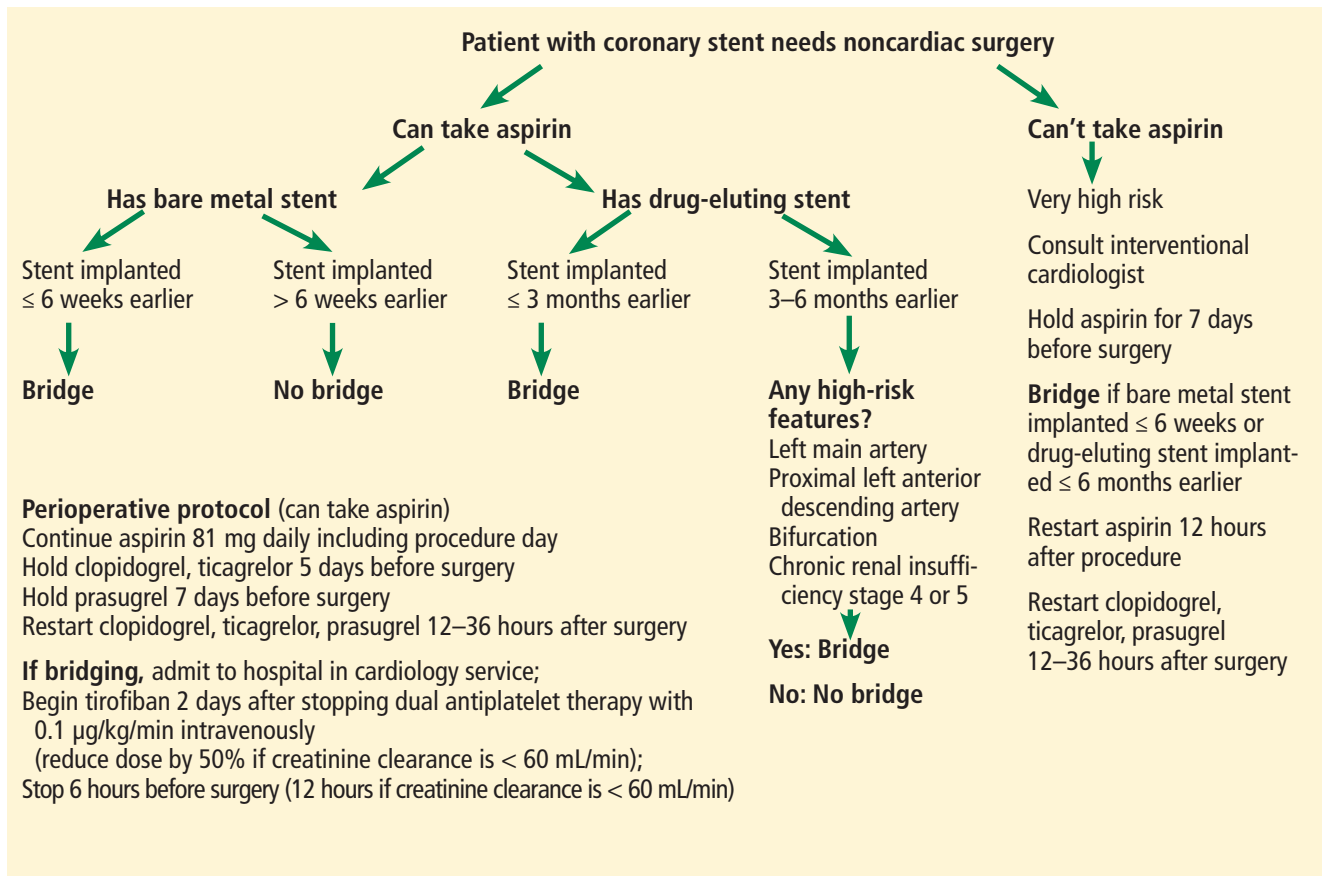Stop 6 hours before surgery (12 hours if creatinine clearance is < 60 mL/min)

Figure 3. Guidelines for bridging before surgery in patients with prior coronary stent.

be restarted as soon as possible.[6,7] If the risk of stent thrombosis is particularly high and surgery cannot be delayed, it should be performed in hospitals where heart catheterization is readily available, and bridging with intravenous antiplatelet agents should be considered.[6,7] Our approach to intravenous antiplatelet bridging is shown in **Figure 3**.

■ WHO NEEDS LONGER DAPT?

Whether DAPT is beneficial for longer than 12 months has been debated for many years. After the first-generation drug-eluting stents were introduced and 12 months was subsequently identified as the standard DAPT duration, multiple trials have investigated whether extending DAPT further would be useful.[8,11,17,31–33] As for determining whether shorter DAPT duration could be indicated, risk of future ischemic events was balanced against bleeding.

The first and largest study to investigate this question[18] found that in patients who completed 12 months of DAPT after PCI without suffering an ischemic or bleeding event, continuing DAPT for 18 additional months reduced myocardial infarction and stent thrombosis rates but increased major bleeding and mortality compared with patients taking aspirin and placebo. The increase in mortality was driven by noncardiovascular causes. Subgroup analysis found that in patients with a prior myocardial infarction, the reduction in ischemic events was most pronounced and survival was greatest, although overall mortality was still neutral in this population. Subsequent meta-analyses of this and other randomized controlled trials comparing more than 12 months of DAPT and shorter durations demonstrated similar findings.[34,35] Notably, some of these trials enrolled patients with first- and second-generation drug-eluting stents, and a subgroup analysis of the DAPT

trial showed significant attenuation of benefit in those with second-generation drug-eluting stents.[36]

Attention subsequently turned to prolonged DAPT in patients with a prior myocardial infarction. The PEGASUS TIMI 54 trial (Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared With Placebo on a Background of Aspirin–Thrombolysis in Myocardial Infarction 54) tested prolonged DAPT in patients who had a myocardial infarction in the previous 1 to 3 years.[33] It found a reduction in most ischemic end points but no effect on the rate of all-cause mortality. These results were confirmed in a meta-analysis of the PEGASUS trial plus subgroups from 4 additional randomized controlled trials.[37]

Based on these findings, clinical decision-making surrounding more than 12 months of DAPT therapy requires an individualized appraisal of the risk and benefits. As discussed previously, with safer, newer-generation drug-eluting stents, the largest benefit of long-term DAPT is reduction of spontaneous myocardial infarction. This highlights the shift from local stent-related protection of early DAPT to systemic protection with longer therapy.

Bottom line. Long-term DAPT should only be considered in patients with a prior myocardial infarction who are at high risk of recurrence and low risk of bleeding (class of recommendation IIb).[6,7] The PRECISE-DAPT score and the DAPT score can be used to help determine if a patient may benefit from prolonged therapy.[7]

The PRECISE-DAPT score (**www.precisedaptscore.com**) is based on the patient's:
- Hemoglobin level
- White blood cell count
- Age
- Creatinine clearance rate
- History of bleeding.

The DAPT score (**http://tools.acc.org/daptriskapp/#!/content/calculator/**) is based on the following:

> **Bleeding risk from DAPT is directly proportional to the length of therapy**

- Age
- Cigarette smoking
- Diabetes mellitus
- Myocardial infarction
- Prior PCI or prior myocardial infarction
- Paclitaxel-eluting stent
- Stent diameter less than 3 mm
- Congestive heart failure or left ventricular ejection fraction less than 30%
- Placement of a stent in a vein graft.

In patients who discontinue P2Y12 inhibitors, current recommendations are to continue aspirin indefinitely for cardiac protection. However, as noted below, this is an area of active research to identify the best option to ensure protection from cardiovascular risk while reducing the risk of bleeding.

■ FUTURE DIRECTIONS

In the future, DAPT management will likely continue to focus on defining the optimal level of platelet inhibition at various stages of post-PCI and tailoring therapy appropriately. Since much of the data underpinning current guidelines on DAPT management was accrued from observational studies with first- and second-generation drug-eluting stents, future guidelines will likely accept even shorter durations of DAPT for most patients, and provide considerations for P2Y12 monotherapy.

The recently published TWILIGHT (Ticagrelor With or Without Aspirin in High-Risk Patients After Coronary Intervention) trial emphasizes this model.[38] Patients at high risk of bleeding and ischemic events who completed 3 months of DAPT were randomized to continue DAPT or receive ticagrelor monotherapy for 12 months. Bleeding rates were significantly lower in the monotherapy group without a statistically significant increase in ischemic events. A 2020 meta-analysis of multiple similar trials confirmed these findings.[39] ■

■ DISCLOSURES

■ REFERENCES

1. **Iqbal J, Gunn J, Serruys PW**. Coronary stents: historical development, current status and future directions. Br Med Bull 2013; 106:193–211. doi:10.1093/bmb/ldt009

2. **Schömig A, Neumann FJ, Kastrati A, et al**. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 1996; 334(17):1084–1089. doi:10.1056/NEJM199604253341702

3. **Fox KA, Mehta SR, Peters R, et al**. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) Trial. Circulation 2004; 110(10):1202–1208. doi:10.1161/01.CIR.0000140675.85342.1B

4. **Steinhubl SR, Berger PB, Mann JT 3rd, et al**. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA 2002; 288(19):2411–2420. doi:10.1001/jama.288.19.2411

5. **Valgimigli M, Patialiakas A, Thury A, et al**. Zotarolimus-eluting versus bare-metal stents in uncertain drug-eluting stent candidates. J Am Coll Cardiol 2015; 65(8):805–815. doi:10.1016/j.jacc.2014.11.053

6. **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 Thorac Cardiovasc Surg 2016; 152(5):1243–1275. doi:10.1016/j.jtcvs.2016.07.044

7. **Valgimigli M, Bueno H, Byrne RA, et al**. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2018; 39(3):213–260. doi:10.1093/eurheartj/ehx419

8. **Gilard M, Barragan P, Noryani AAL, et al**. 6- versus 24-month dual antiplatelet therapy after implantation of drug-eluting stents in patients nonresistant to aspirin: the randomized, multicenter ITALIC trial. J Am Coll Cardiol 2015; 65(8):777–786. doi:10.1016/j.jacc.2014.11.008

9. **Colombo A, Chieffo A, Frasheri A, et al**. Second-generation drug-eluting stent implantation followed by 6- versus 12-month dual antiplatelet therapy: the SECURITY randomized clinical trial. J Am Coll Cardiol 2014; 64(20):2086–2097. doi:10.1016/j.jacc.2014.09.008

10. **Feres F, Costa RA, Abizaid A, et al**. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: the OPTIMIZE randomized trial. JAMA 2013; 310(23):2510–2522. doi:10.1001/jama.2013.282183

11. **Costa F, Vranckx P, Leonardi S, et al**. Impact of clinical presentation on ischaemic and bleeding outcomes in patients receiving 6- or 24-month duration of dual-antiplatelet therapy after stent implantation: a pre-specified analysis from the PRODIGY (Prolonging Dual-Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia) trial. Eur Heart J 2015; 36(20):1242–1251. doi:10.1093/eurheartj/ehv038

12. **Gwon HC, Hahn JY, Park KW, et al**. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. Circulation 2012; 125(3):505–513. doi:10.1161/CIRCULATIONAHA.111.059022

13. **Kim BK, Hong MK, Shin DH, et al**. A new strategy for discontinuation of dual antiplatelet therapy: the RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation). J Am Coll Cardiol 2012; 60(15):1340–1348. doi:10.1016/j.jacc.2012.06.043

14. **Schulz-Schüpke S, Byrne RA, Ten Berg JM, et al**. ISAR-SAFE: a randomized, double-blind, placebo-controlled trial of 6 vs 12 months of clopidogrel therapy after drug-eluting stenting. Eur Heart J 2015; 36(20):1252–1263. doi:10.1093/eurheartj/ehu523

15. **Palmerini T, Benedetto U, Bacchi-Reggiani L, et al**. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. Lancet 2015; 385(9985):2371–2382. doi:10.1016/S0140-6736(15)60263-X

16. **Navarese EP, Andreotti F, Schulze V, et al**. Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug eluting stents: meta-analysis of randomised controlled trials. BMJ 2015; 350:h1618. doi:10.1136/bmj.h1618

17. **Giustino G, Baber U, Sartori S, et al**. Duration of dual antiplatelet therapy after drug-eluting stent implantation: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol 2015; 65(13):1298–1310. doi:10.1016/j.jacc.2015.01.039

18. **Mauri L, Kereiakes DJ, Yeh RW, et al**. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014; 371(23):2155–2166. doi:10.1056/NEJMoa1409312

19. **Claessen BE, Henriques JP, Jaffer FA, Mehran R, Piek JJ, Dangas GD**. Stent thrombosis: a clinical perspective. JACC Cardiovasc Interv 2014; 7(10):1081–1092. doi:10.1016/j.jcin.2014.05.016

20. **Yeh RW, Kereiakes DJ, Steg PG, et al**. Benefits and risks of extended duration dual antiplatelet therapy after PCI in patients with and without acute myocardial infarction. J Am Coll Cardiol 2015; 65(20):2211–2221. doi:10.1016/j.jacc.2015.03.003

21. **Hahn JY, Song YB, Oh JH, et al**. 6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial. Lancet 2018; 391(10127):1274–1284. doi:10.1016/S0140-6736(18)30493-8

22. **Devereaux PJ, Mrkobrada M, Sessler DI, et al**. Aspirin in patients undergoing noncardiac surgery. N Engl J Med 2014; 370(16):1494–1503. doi:10.1056/NEJMoa1401105

23. **Rodriguez A, Guilera N, Mases A, et al**. Management of antiplatelet therapy in patients with coronary stents undergoing noncardiac surgery: association with adverse events. Br J Anaesth 2018; 120(1):67–76. doi:10.1016/j.bja.2017.11.012

24. **Glance LG, Dick AW, Mukamel DB, et al**. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. Anesthesiology 2011; 114(2):283–292. doi:10.1097/ALN.0b013e3182054d06

25. **Krupski WC, Nehler MR, Whitehill TA, Lawson RC, Strecker PK, Hiatt WR**. Negative impact of cardiac evaluation before vascular surgery. Vasc Med 2000; 5(1):3–9. doi:10.1177/1358836X0000500102

26. **Khorana AA, Tullio K, Elson P, et al**. Time to initial cancer treatment in the United States and association with survival over time: an observational study. PLoS One 2019; 14(3):e0213209. doi:10.1371/journal.pone.0213209

27. **van Werkum JW, Heestermans AA, Zomer AC, et al**. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol 2009; 53(16):1399–1409. doi:10.1016/j.jacc.2008.12.055

28. **Hawn MT, Graham LA, Richman JS, Itani KM, Henderson WG, Maddox TM**. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. JAMA 2013; 310(14):1462–1472. doi:10.1001/jama.2013.278787

29. **Egholm G, Kristensen SD, Thim T, et al**. Risk associated with surgery within 12 months after coronary drug-eluting stent implantation. J Am Coll Cardiol 2016; 68(24):2622–2632. doi:10.1016/j.jacc.2016.09.967

30. **Eisenberg MJ, Richard PR, Libersan D, Filion KB**. Safety of short-term discontinuation of antiplatelet therapy in patients with drug-eluting stents. Circulation 2009; 119(12):1634–1642. doi:10.1161/CIRCULATIONAHA.108.813667

31. **Lee CW, Ahn JM, Park DW, et al**. Optimal duration of dual antiplatelet therapy after drug-eluting stent implantation: a randomized, controlled trial. Circulation 2014; 129(3):304–312. doi:10.1161/CIRCULATIONAHA.113.003303

32. **Collet JP, Silvain J, Barthélémy O, et al**. Dual-antiplatelet treatment beyond 1 year after drug-eluting stent implantation (ARCTIC-Interruption): a randomised trial. Lancet 2014; 384(9954):1577–1585.

doi:10.1016/S0140-6736(14)60612-7

33. **Bonaca MP, Bhatt DL, Cohen M, et al**. Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med 2015; 372(19):1791–1800. doi:10.1056/NEJMoa1500857

34. **Bittl JA, Baber U, Bradley SM, Wijeysundera DN**. Duration of dual antiplatelet therapy: a systematic review for the 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(10):1116–1139. doi:10.1016/j.jacc.2016.03.512

35. **Khan SU, Singh M, Valavoor S, et al**. Dual antiplatelet therapy after percutaneous coronary intervention and drug-eluting stents: a systematic review and network meta-analysis. Circulation 2020; 142(15):1425–1436. doi:10.1161/CIRCULATIONAHA.120.046308

36. **Hermiller JB, Krucoff MW, Kereiakes DJ, et al**. Benefits and risks of extended dual antiplatelet therapy after everolimus-eluting stents.

JACC Cardiovasc Interv 2016; 9(2):138–147. doi:10.1016/j.jcin.2015.10.001

37. **Udell JA, Bonaca MP, Collet JP, et al**. Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. Eur Heart J 2016; 37(4):390–399. doi:10.1093/eurheartj/ehv443

38. **Mehran R, Baber U, Sharma SK, et al**. Ticagrelor with or without aspirin in high-risk patients after PCI. N Engl J Med 2019; 381(21):2032–2042. doi:10.1056/NEJMoa1908419

39. **Khan SU, Singh M, Valavoor S, et al**. Dual antiplatelet therapy after percutaneous coronary intervention and drug-eluting stents: a systematic review and network meta-analysis. Circulation 2020; 142(15):1425–1436. doi:10.1161/CIRCULATIONAHA.120.046308

Address: Umesh N. Khot, MD, Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, J2-4, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; khotu@ccf.org