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.
are associated with significantly lower rates of late and very late stent thrombosis. 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. 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.

**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.

**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. 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.
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. 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. Consequently, there is no effect on all-cause mortality comparing 6 months or less vs 1 year of DAPT. 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, 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-DAPT trial (Safety of 6-month Duration of Dual Antiplatelet Therapy After Acute Coronary Syndrome), 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.

### INTERRUPT DAPT FOR NONCARDIAC SURGERY?

When patients on DAPT after drug-eluting stent PCI need noncardiac surgery, one must...
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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.\textsuperscript{22,23} Given the increased mortality and morbidity associated with bleeding,\textsuperscript{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,\textsuperscript{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 diseases), delaying surgery can be detrimental.\textsuperscript{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.\textsuperscript{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.\textsuperscript{27} More recent observational studies suggest the time frame of increased risk is about 6 months,\textsuperscript{28} and may even be as short as 30 days.\textsuperscript{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.\textsuperscript{6}

If DAPT is interrupted, aspirin should be continued if feasible, as it protects against ischemic events,\textsuperscript{30} and P2Y12 therapy should

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

<table>
<thead>
<tr>
<th>Emergency surgery</th>
<th>Urgent surgery</th>
<th>Elective surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proceed to surgery</td>
<td>Stent implanted ≤ 3 months earlier</td>
<td>Stent implanted ≤ 6 months earlier</td>
</tr>
<tr>
<td>Obtain cardiology consult</td>
<td>Before stopping medications, consult cardiologist</td>
<td>Before stopping medications, consult cardiologist</td>
</tr>
<tr>
<td>Delay procedure</td>
<td>Delay procedure</td>
<td>Delay procedure</td>
</tr>
</tbody>
</table>

- 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
be restarted as soon as possible. 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. 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. 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 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. Notably, some of these trials enrolled patients with first- and second-generation drug-eluting stents, and a subgroup analysis of the DAPT
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trial showed significant attenuation of benefit in those with second-generation drug-eluting stents.\(^3^6\)

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.\(^3^3\) 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.\(^3^7\)

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:

- 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.\(^3^8\) 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.\(^3^9\)

**DISCLOSURES**

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.
REFERENCES


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