

EDITORIAL COMMENT

# Coronary Stents and Risk for Noncardiac Surgery

## Much Ado About Something, Nothing, or DAPT?\*

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The topic of duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) has been gaining increasing interest in recent years. On one hand, the impact of DAPT cessation may be modest and very heterogeneous, bound to the circumstances under which it occurred (1). On the other hand, extended DAPT with aspirin and either clopidogrel, prasugrel, or ticagrelor beyond 1 year after a drug-eluting stent (DES), compared with aspirin monotherapy, may be beneficial and associated with reduced risks of stent thrombosis and major adverse cardiovascular and cerebrovascular events (MACCEs), albeit at the expense of increased bleeding (2). Even so, newer contemporary DES platforms may allow for “early” discontinuation of DAPT in appropriately selected patients (3). Current international guidelines suggest 6 to 12 months of DAPT after a DES, and 1 month of DAPT after a bare-metal stent (BMS) (4,5).

In this issue of the *Journal*, Mahmoud et al. (6) join this evolving, vibrant discussion about the duration of DAPT by examining outcomes after noncardiac surgery (NCS) in stented and nonstented patients. Although the focus shifts away from DAPT and the study examines whether there is an independent association between coronary stenting and noncardiac surgery, outcomes in patients who have received a stent are inextricably bound to the status of their

DAPT. Unfortunately, data on antiplatelet therapy use is lacking in this study. The authors conducted a retrospective analysis of 24,313 NCSs performed in 22,853 unique patients from 2006 through 2011. Of these cases, 1,120 (4.6%) included patients with an intracoronary stent. Thirty-day post-operative occurrence of MACCEs occurred in 3.7% of patients with a stent and 1.5% of patients without a stent ( $p < 0.001$ ).

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The risk of MACCE was dependent on time from stenting to NCS with substantially elevated risk in the first year after stenting (adjusted odds ratio [aOR]: 2.59; 95% confidence interval [CI]: 1.36 to 4.94), but not thereafter (aOR: 0.89; 95% CI: 0.59 to 1.36). The authors acknowledge that detailed stent-related data was often missing; furthermore, during the study period (2006 to 2011), contemporary stent platforms would have been used infrequently. Such newer-generation stent platforms account for the majority of current implants and may safely allow for shorter duration of DAPT after intracoronary stenting (3). Thus, data from this analysis may not be generalizable to contemporary PCI practice patterns.

Another key finding was that increased risk of MACCE was observed in patients undergoing NCS 6 to 12 months after implantation of BMS (aOR: 4.1; 95% CI: 1.49 to 11.91) but not DES (aOR: 1.03; 95% CI: 0.22 to 4.78). The authors propose that this finding may warrant reconsideration of current international guidelines, which suggest a delay in elective NCS of only 1 month after BMS implantation. We would urge caution about this suggestion and rather encourage more scrutiny into the circumstances that may have motivated a patient to receive a BMS. Although the current study does not allow for such a detailed analysis, the cohort receiving BMS may be fundamentally different and higher risk than that receiving a DES.

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The authors conducted an angiographic review and emphasize that most perioperative myocardial infarctions represented de novo lesions or type 2 myocardial infarctions with supply/demand imbalance; the primary mechanism was not stent thrombosis, although the number of total events was only 14. If the BMS and DES populations are considered separately, it is possible that the BMS patients may have had comorbidities (e.g., anemia, chronic renal insufficiency) rendering them more susceptible to such mechanisms of perioperative myocardial infarction. On balance, it would be premature to recalibrate current guidelines on the basis of this finding without better characterization of differences between the BMS and DES populations.

In a related vein, the authors provided limited data on the context in which patients required surgery. Again, purely speculative, those patients with an increased tendency for bleeding may have received BMS and bleeding may have created a need for NCS and/or interruption of DAPT. The context in which DAPT cessation occurs has been shown to be critically important. Mehran et al. (1) conducted the PARIS (Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients) Registry, a prospective observational study of >5,000 patients in which categories of DAPT cessation were pre-defined as physician-recommended discontinuation, brief interruption (for surgery), or disruption (related to noncompliance or bleeding). Compared with those on DAPT, the adjusted hazard ratio for major adverse cardiovascular events due to interruption was 1.41 (95% CI: 0.94 to 2.12;  $p = 0.10$ ) and to disruption was 1.50 (95% CI: 1.14 to 1.97;  $p = 0.004$ ). Although the authors report the percentage of patients requiring emergency surgery in both stented and nonstented groups, more elaborate information on the context in which an NCS occurred may help to understand the adverse outcomes that occurred and whether the BMS group was a more “primed” substrate for such events.

By drawing attention to the independent association between MACCE and NCS, the authors re-focus attention on medical therapy alone as a treatment option for appropriately selected patients with stable coronary artery disease (7). It is noteworthy that while the exclusion of patients with recent myocardial infarction attenuated the risk of death (aOR: 3.00;

95% CI: 0.93 to 9.67;  $p = 0.0067$ ), it did not have the same effect on MACCE (aOR: 3.05; 95% CI: 1.15 to 8.08;  $p = 0.025$ ) in the first 6 months after stent implantation. Risk (perhaps leading to the selection of BMS in the first place) may beget risk (increased risk once the BMS is implanted) in patients with BMS, and a more suitable approach may be one that is appropriately conservative, provided there is not an acute coronary syndrome.

To summarize, Mahmoud et al. (6) provide an important contribution to the dialogue on patients with a history of intracoronary stent undergoing NCS. Distinct from most other studies that it follows, this analysis contains a control group and establishes prior coronary stent implantation as an independent risk factor associated with MACCE in those undergoing NCS. Such a finding is a reminder that a conservative approach with optimal medical therapy alone may be most appropriate in select patients without an acute coronary syndrome. Key findings from this analysis are that risk for MACCE is time dependent, substantially elevated in the year after stenting and not thereafter, and that increased risk of MACCE and bleeding after 1 month is not limited to only those with DES. The analysis is restricted by limited data on stent types used and the context in which NCS occurred and also by lacking data on antiplatelet therapy. Contemporary, newer, second-generation stent platforms may not be associated with the same risk of adverse outcomes and may allow for safe discontinuation of DAPT within 6 months of PCI in select patients. Although the authors showed an increased risk of MACCE in patients undergoing NCS 6 to 12 months after implantation of BMS but not DES, such a finding should not necessarily prompt re-evaluation of current guidelines without understanding the contexts in which BMS was chosen and NCS was required. As in all clinical research, we should be cautious about making strong inferences about therapy in observational registries where hidden biases could make it just as possible that it is much ado about nothing as it is much ado something.

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