Although largely based on expert opinion and limited by paucity of data, current guidelines recommend that elective surgery after percutaneous coronary intervention (PCI) with implantation of a drug-eluting stent should be delayed until completion of 1 year of dual antiplatelet therapy (APT) to avoid the risk of adverse cardiac events. Recent data have challenged this recommendation, and timing of surgery beyond 6 months after stent implantation may not affect the risk for adverse outcomes in those undergoing noncardiac surgery. In this issue of Circulation: Cardiovascular Interventions, Tokushige et al\(^1\) in a retrospective analysis of the Coronary Revascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) PCI/coronary artery bypass grafting (CABG) registry cohort 2, now add to the evidence describing outcomes in patients undergoing noncardiac surgery after coronary revascularization.\(^3\)

**Noncardiac Surgery After Coronary Revascularization**  
**More Contemporary Evidence Needed**

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Consecutive patients were enrolled in the CREDO-Kyoto PCI/CABG registry cohort 2 after first coronary revascularization among 26 centers in Japan between January 2005 and December 2007. In this analysis, the authors compared the incidence and outcomes of surgical procedures between the PCI and CABG groups. Timing of surgery from the time of coronary revascularization was classified as early (within 42 days) and late (beyond 42 days). Primary ischemic (death or myocardial infarction) and primary bleeding (moderate or severe bleeding by the Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded coronary arteries classification) outcomes were assessed at 30 days after the PCI procedure.

Perhaps, as expected, surgical procedures were performed more frequently after CABG than after PCI (cumulative 3-year incidence, 27% versus 22%; unadjusted \(\text{P}<0.0001\)). This observation was largely dominated by a cumulative incidence of surgical procedures that was significantly higher after CABG than after PCI within the first 6 months; the difference did not meet statistical significance after 6 months.

And, unfortunately, the authors were not able to distinguish those surgical procedures scheduled before coronary revascularization from those needed after coronary revascularization. We speculate that there may have been a bias toward CABG in patients scheduled for noncardiac surgical procedures in advance of revascularization to obviate the need for APT after PCI. In adjusted analyses, the risk of previous CABG relative to previous PCI for the primary ischemic outcome was not significant (hazard ratio, 0.97; 95% confidence interval [CI], 0.47–1.89; \(\text{P}=0.9\)); previous CABG relative to previous PCI was associated with lower bleeding risk, however (hazard ratio, 0.36; 95% CI, 0.12–0.87; \(\text{P}=0.02\)). Although these results may add to our confidence for the safety of noncardiac surgery after coronary revascularization either through CABG or PCI, there are limitations to this descriptive study. First, the recommended antiplatelet regimen (APT) was aspirin (≥81 mg once daily) indefinitely after both PCI and CABG and thienopyridine with ticlopidine or clopidogrel for ≥1 month after bare metal stent implantation and for ≥3 months after drug-eluting stent implantation. More than 90% of patients given a thienopyridine were treated with ticlopidine, the use of which is limited by sometimes fatal blood dyscrasias and which has largely been supplanted by other antiplatelet therapies.\(^4\) The antiplatelet regimen used, then, may not be representative of contemporary clinical practice. Second, there were important differences in baseline characteristics of patients undergoing PCI versus CABG; in particular, the incidence of emergency coronary revascularization in the PCI group was 39% when compared with 9.2% in the CABG group (\(\text{P}<0.0001\)). Although there were no differences in the primary ischemic end point, this significant difference should be noted. In a post hoc analysis of the CREDO-Kyoto PCI/CABG Registry Cohort-2, Tokushige et al\(^5\) demonstrated the effect of initial acute myocardial infarction presentation on the outcome of surgical procedures after coronary stent implantation; the cumulative incidence of death, myocardial infarction, and stent thrombosis at 30 days were significantly higher in the early group (surgery within 42 days) than in the late group (beyond 42 days) in the acute myocardial infarction stratum (18.4% versus 2.6%; \(\text{P}<0.0001\)) but not in the non–acute myocardial infarction stratum. Third, as the authors acknowledge, the current analysis did not provide information on the urgency of the surgical procedures, a variable that has been shown to be independently predictive of outcome.\(^2\) Fourth, the number of events, particularly for the bleeding outcome, were small (7 events in the CABG group and 60 in the PCI group). In adjusted subgroup analyses comparing early versus late surgery, there...
was no difference in risk of ischemic events between the PCI and CABG groups in those patients who underwent early surgery. Although the lower risk of previous CABG relative to previous PCI for bleeding remained significant in those undergoing early surgery (hazard ratio, 0.13; 95% CI, 0.01–0.76; \( P = 0.02 \)), the total number of events was small (2 in the CABG group versus 22 in the PCI group), reflected by the wide CI. Fifth, even though it is reported that 56% of patients in the PCI group received a drug-eluting stent, the effect of type of stent on the bleeding and ischemic outcomes is not evident from this study.

Notwithstanding these limitations, Tokushige et al.\(^5\)\(^6\) present an important analysis that seems to corroborate a recurring message in the literature, that the risks of noncardiac surgery after coronary revascularization and early interruption of dual APT may be overstated in current guidelines. In a retrospective cohort study of nearly 42,000 patients undergoing noncardiac surgery within 2 years of coronary stent placement, Hawn et al.\(^2\) reported that the 3 factors most strongly associated with major adverse cardiovascular events were nonelective surgical admission (adjusted odds ratio, 4.77; 95% CI, 4.07–5.59), myocardial infarction in the preceding 6 months (adjusted odds ratio, 2.63; 95% CI, 2.32–2.98), and revised cardiac risk index >2 (adjusted odds ratio, 2.13; 95% CI, 1.85–2.44). After 6 months of stent implantation, neither stent type nor timing of surgery was associated with adverse outcomes; continuation of dual APT after 6 months did not assuage the risk for major adverse cardiovascular events. Furthermore, multiple randomized trials have examined different durations of dual APT after PCI. Prolonged therapy with dual APT does not necessarily confer protection from ischemic events and may accentuate bleeding.\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\) Such observations are a signal that shorter duration of dual APT may be acceptable in appropriately selected patients and may safely allow for elective, noncardiac surgery in advance of 1 year after PCI with a drug-eluting stent. A caveat is that these randomized trials examined the duration of dual antiplatelet therapy with clopidogrel specifically. There are limited data on the optimal duration of therapy with the novel antiplatelet therapies prasugrel or ticagrelor, both of which have been shown to be effective and safe in those patients presenting with acute coronary syndrome.\(^11\)\(^12\) Current recommendations for duration of therapy with one of these P2Y\(_{12}\) receptor antagonists are based on experience with clopidogrel; future studies should investigate the risks of these new antiplatelet therapies in patients undergoing noncardiac surgery.

Although Tokushige et al.\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\) take a step forward in elucidating the risks associated with noncardiac surgery after coronary revascularization, future studies should examine these hazards with contemporary APT and modern, newer-generation drug-eluting stents. Such studies that more closely parallel current practice will help inform decision making on the perioperative management of patients with recent coronary revascularization undergoing noncardiac surgery. We would not be surprised if an update to current guidelines suggests a shorter duration of dual APT after PCI in appropriately selected patients who receive second-generation drug-eluting stents. An individual patient’s cardiac substrate and the context/urgency with which a surgery/procedure is performed are important elements that should complement an overall assessment of risk. The bulk of recommendations for patients with recent coronary revascularization undergoing noncardiac surgery is largely based on expert opinion, and studies like that conducted by Tokushige et al.\(^5\)\(^6\) but more generalizable to contemporary practice, are needed to create a larger evidence base to guide care.

Disclosures

None.

References


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