

Coronary Angiography and Revascularization Prior to Noncardiac Surgery

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Opinion statement

The role of coronary angiography and revascularization, including percutaneous coronary intervention (PCI) prior to noncardiac surgery remains poorly defined. The goal of preoperative angiography and PCI is improved risk stratification and ideally risk reduction of postoperative cardiovascular events, such as myocardial infarction (MI). By current guidelines, these procedures should be performed sparingly in high-risk stable coronary artery disease (CAD) patients and routinely in patients with acute coronary syndrome (ACS). Anatomic assessment of CAD by routine invasive angiography is discouraged, although noninvasive assessment may soon be possible. As prior trials have failed to show a clear benefit in outcomes, PCI should only be considered in patients with high-risk anatomic features. The ideal management of other anatomic disease discovered by angiography is currently unknown. Limited registry data suggest that PCI is used more frequently than recommended, although the features of these procedures remain poorly elaborated. In patients who do undergo preoperative PCI, careful attention must be paid to patient-specific factors including the nature and urgency of surgery and duration of dual antiplatelet therapy. In summary, substantial evidence gaps warrant further research in this important area.

Scope of the issue: perioperative MI

Perioperative myocardial infarction is a common surgical complication with adverse prognostic implications. The incidence of perioperative MI differs substantially based on the definition and populations studied. Older studies report an incidence ranging from 1 to 4 % of all surgeries [1], although these may be under-estimates, especially given the increasing age of the surgical population and increased sensitivity of modern biomarker assays [2]. The largest recent trial reported an incidence of 5 % using a definition of elevated biomarkers (troponin) and at least one clinical feature (ischemic symptoms, electrocardiographic [ECG] changes, cardiac intervention, or imaging evidence of MI) [3]. Patients with MI had an elevated mortality rate (11.6 vs 2.2 %, $p < 0.001$), and mortality was elevated irrespective of clinical symptoms [3]. Additionally, a large registry recently reported that the elevation of troponins alone, irrespective of ischemic changes, was present in 8 % of adult surgeries and was associated with an increase in 30-day mortality [4]. Only half of these patients would have fulfilled the universal definition of MI. In light of these prognostic implications, the reduction of

postoperative MI has long remained an important goal of perioperative medical care [5••, 6••].

Measures to predict and prevent perioperative MI are challenging because of the distinctive and poorly understood pathogenesis of these events. Postoperative MI appears to represent a heterogeneous interplay between atherosclerotic burden, inflammation, coagulopathy, anemia, fluid shifts, and sympathetic nervous activation (resulting in tachycardia) [2, 7, 8]. The majority of MIs appear to result at least in part from inadequate perfusion in the setting of obstructive CAD and increased metabolic demand (“demand ischemia”) [9]. However, other mechanisms are involved as postoperative MI can occur in the absence of obstructive CAD, as was observed in 28 % of MIs in a recent study [10•]. Acute plaque rupture leading to transmural infarction has generally been thought to be less common in the perioperative setting [2, 7], although this notion has recently been called into question [11]. Overall, pathophysiologic studies have been limited by the asymptomatic nature of many postoperative MIs and the reluctance to proceed to urgent angiography in most symptomatic patients [2].

Preoperative cardiac risk assessment

In light of the aforementioned consequences, cardiac risk assessment has long remained an integral part of the perioperative evaluation [5••, 6••]. The primary goal is to allow the patient, cardiologist, surgeon, and anesthesiologist to more fully integrate cardiac risk into surgical decision-making. A secondary goal is to ideally reduce perioperative events through preoperative risk factor optimization or early identification of physiologically significant coronary disease. Relatedly, a preoperative evaluation occasionally offers an opportunity to identify and address cardiac risk factors in patients who have had limited prior medical care and those with poor effort tolerance.

In order to accomplish these goals, preoperative guidelines recommend a stepwise approach for patients undergoing nonemergent procedures. After the exclusion of acute coronary syndrome, practitioners are recommended to follow a stepwise algorithm incorporating clinical risk scores [1], evaluation of exercise tolerance, and the selective use of noninvasive imaging to detect myocardial ischemia [5••, 6••]. Patients who may be considered for ischemia imaging include those with an elevated (>1 %) predicted perioperative risk of a major adverse cardiovascular event (MACE) [5••] or those undergoing intermediate or high-risk surgery [6••] with uncertain or limited exercise capacity only if the results will impact decision-making or preoperative care. Conversely, routine stress testing before low-risk surgeries is discouraged.

There is extensive (albeit mostly older) literature reporting the prognostic value of stress testing in predicting postoperative MI [12–14]. Greater extent of reversible ischemia detected by myocardial perfusion imaging or stress echocardiography is associated with increased postoperative risk [12]. Conversely, a normal stress test has a high negative predictive value for postoperative events. There are several caveats to this literature, including a lack of randomized or prospective data, a reliance on mostly single-center studies, and an over-sampling of patients undergoing higher risk surgical procedures (such as open vascular or aortic surgery) [5••].

The role of diagnostic angiography in risk assessment

Historically, routine preoperative coronary angiography has been advocated only in the highest risk patients undergoing open vascular surgery. Hertzner and colleagues performed routine preoperative coronary angiography on 139 patients during the 1970s and reported 66 % had advanced or severe CAD, of whom the most severe were referred to preoperative coronary artery bypass grafting (CABG) [15]. However, the clinical relevance of these findings is questionable given contemporary advances in the management of CAD.

A few small studies in recent years have employed routine preoperative diagnostic angiography in selected cohorts. Monaco et al. randomized 208 patients undergoing elective vascular (mostly aortic) surgery with a revised cardiac risk index (RCRI) ≥ 2 to “selective” (performed if a preceding stress test was positive) versus “routine” preoperative angiography [16]. The revascularization rate was higher in the routine compared to the selective cohort (58.1 vs. 40.1 %, $p < 0.01$). In-hospital outcomes did not differ by coronary angiography strategy, although a survival benefit was observed at 4 years. There were several criticisms of this trial including its size and unblinded design, insufficient information on recruitment and randomization, a lack of independent events adjudication, and other methodological issues [5••, 17, 18].

Similarly, Illuminati et al. randomized a cohort of 426 patients for planned carotid endarterectomy to a routine coronary angiography or usual care strategy. Of the patients who underwent routine angiography, 68 (31 %) had obstructive CAD that was treated with PCI and/or CABG [19]. The postoperative cardiac event rate was low; no patients in the routine angiography group had events, while nine patients in the usual care group had events, most of which were silent electrical or troponin changes. After adjustments, routine coronary angiography was the only factor associated with reduced events. In subsequent follow-up of this cohort performed 3.5 years after the surgery, the use of routine angiography remained significantly associated with decreased risk of MI (HR 0.078; 95% CI 0.024–0.256, $p < 0.001$) [20•]. The authors acknowledge that these results may be limited by the unblinded design and limited long-term outcome ascertainment.

Given the relative paucity of data, guidelines state that indications for diagnostic cardiac catheterization are “similar to those identified for the non-operative setting.” [5••, 6••] Routine use of preoperative coronary angiography is discouraged by the American College of Cardiology/American Heart Association (ACC/AHA) guidelines. Although controversial, this recommendation also pertains to candidates for solid organ transplants [21]. In light of the

findings of Illuminati et al. [19], European Society of Cardiology (ESC) guidelines state that routine angiography prior to carotid endarterectomy surgery may be considered (class 2b recommendation) [6••].

Noninvasive approaches to preoperative angiography

Recently, the routine use of cardiac computed tomographic angiography (CCTA) to identify or exclude CAD has been studied in preoperative patients. Ahn et al. retrospectively studied 239 patients who had undergone preoperative CCTA before intermediate-risk surgeries, of whom 8 % had postoperative cardiac events [22]. Notably, 85 % of the patients had a RCRI of ≤ 1 . They found that the addition of CTCA parameters, including a calcium score >113 and the presence of multi-vessel coronary disease, to baseline RCRI improved the prediction of events. The positive predictive value of these features was low (9–18 %), but similar to that reported for myocardial perfusion imaging. Limitations of this study included its retrospective design, possible selection bias, and clinical relevance given the high rate of patients with low clinical risk who received CCTA [23]. As such, preoperative guidelines have not recommended routine CCTA before noncardiac surgery [5••].

Subsequent to the publication of the most recent preoperative guidelines, a larger retrospective analysis was published by Hwang et al. who studied 844 patients with at least one cardiovascular risk factor who had undergone routine CCTA prior to noncardiac surgery [24]. Overall, 3 % of patients had a postoperative event, the mean RCRI was 2, and 20.5 % of patients had an RCRI ≥ 3 . A greater extent of CAD by CCTA was associated with an increased risk of postoperative events. The predictive performance of the RCRI was incrementally improved with the addition of CCTA parameters, with the positive predictive value estimated at 8 % and the negative predictive value at 99 %. However, this study was also limited by its retrospective observational nature, the lack of data regarding post-scan management changes, and possible selection bias [25]. Furthermore, 90 % of patients had moderate or good functional capacity at baseline, raising questions about the necessity of preoperative testing in this cohort [25].

Recently, the first prospective observational study using preoperative CCTA was published by Sheth et al. [10•] In this study, 955 patients undergoing noncardiac surgery with a history of or risk factors for atherosclerosis or a history of congestive heart failure underwent preoperative CCTA. Clinicians were blinded to the results unless left main artery disease was suspected. Overall, 77 % of patients had a RCRI ≤ 1 and postoperative MI or cardiovascular death occurred in 8 % of the total cohort. The authors found that although the CCTA findings were incrementally predictive of postoperative events, they were also nearly five times as likely to inappropriately overestimate the risk among patients who did not have events.

Preoperative PCI—indications and evidence

In response to older retrospective data suggesting a benefit to preoperative revascularization by CABG [26], the Coronary Artery Revascularization Prophylaxis (CARP) trial was performed to study the benefit of coronary artery revascularization or optimal medical therapy in stable

patients prior to planned vascular surgery [27]. The investigators screened 5859 patients, of whom 510 were enrolled and randomized. All patients had at least one vessel with obstructive CAD as confirmed by invasive angiography, although patients with left main artery disease $>50\%$ or left ventricular function $<20\%$ were excluded. Clinically, 49 % of patients had an RCRI ≥ 2 and 62 % underwent preoperative myocardial perfusion imaging. Patients underwent preoperative revascularization by CABG or PCI (depending on local preference). Of note, 4 % of patients randomized to optimal medical therapy subsequently required coronary revascularization before their vascular surgery due to an unstable change in cardiac status. There was no difference in mortality or perioperative myocardial infarction at 2.7 years. Sub-studies of the CARP trial suggested that patients with left main disease (who were not randomized) could potentially benefit from preoperative revascularization [28]. Furthermore, among 109 CARP patients undergoing open abdominal aortic surgery with prior abnormal nuclear stress imaging, preoperative revascularization was associated with reduced events [29]. However, as sub-analyses, these findings should be considered hypothesis-generating rather than definitive [30].

There are no studies specifically studying preoperative PCI in patients presenting with acute coronary syndrome. Retrospective studies suggest that such patients benefit from a revascularization approach prior to surgery. The largest study evaluated 16,478 patients from the years 1999–2004 who had a myocardial infarction and underwent intermediate or high-risk surgeries up to 3 years following the index event [31]. Patients who were revascularized before surgery (11.6 % PTCA, 43.8 % PCI with bare metal stent, 44.6 % CABG) had an approximately 50 % lower rate of reinfarction (5.1 vs. 10.0 %; $p < 0.001$) as well as 30-day (5.2 vs. 11.3 %; $p < 0.001$) and 1-year mortality (18.3 vs. 35.8 %).

In light of these trials and limitations, ACC/AHA and ESC guidelines discourage the use of routine preoperative PCI to reduce perioperative events except in the setting of an acute coronary syndrome [5••, 6••]. Furthermore, the ACC/AHA guidelines state that PCI can also be considered for patients with left main disease whose “comorbidities preclude bypass surgery without undue risk.” [5••] European guidelines, however, state that preoperative revascularization may be considered for patients before high-risk surgery with extensive ischemia on perfusion imaging [6••]. In this setting, the choice of PCI or CABG for revascularization should be based on the urgency of the surgery and anatomic considerations as detailed in the ESC guidelines on myocardial revascularization [32].

Despite these fairly restrictive indications for preoperative PCI, limited registry data suggest a higher real-world use of preoperative PCI. In a Michigan registry of 61,145 PCIs performed between 2002 and 2009, Muthappan et al. reported that 4 % ($n = 2592$) were performed on stable patients prior to “high-risk noncardiac surgery.” [33•] Preoperative PCI patients had a higher burden of comorbidities and were more likely to receive bare metal stents than nonpreoperative PCI patients. Only 3 % of patients had left main disease $\geq 70\%$. After adjustment for baseline variables, peri-procedural outcomes were similar except for increased nephropathy requiring dialysis in the preoperative PCI patients. An

accompanying editorial noted concerns regarding the unchanged incidence of preoperative PCI despite trials (such as CARP) and guidelines to the contrary [30].

Choice of stent and issues of dual antiplatelet therapy

Once a preoperative PCI is contemplated, procedural questions surrounding the choice of stent type and related duration of dual antiplatelet therapy (DAPT) come to the forefront of evaluation. On the one hand, the premature cessation of DAPT is associated with an increased risk of stent thrombosis [34], which often leads to subsequent ACS, need for urgent revascularization and even death [35]. These risks appear to be amplified by the pro-thrombotic postoperative milieu [5••]. On the other hand, continuation of DAPT will likely raise the risk of surgical bleeding [5••], and thus its use may preclude or delay surgery. These tradeoffs are frequently encountered, with recent studies reporting that 4–7 % of patients will undergo major surgery in the year after stent placement [36, 37].

Early studies demonstrated an increased risk of stent thrombosis and postoperative myocardial infarction when DAPT was held for noncardiac surgery in patients who received a bare metal stent (BMS) during the prior 4–6 weeks [38–40]. In contrast, smaller studies reported that balloon angioplasty without stenting could be performed within 2 weeks of surgery with acceptable outcomes, albeit with a higher need for repeat revascularization [41, 42]. On the other hand, drug-eluting stents (DES) generally require 12 months of DAPT to minimize the risk of stent thrombosis [43], although there are data suggesting this duration might be safely shortened to 3–6 months with newer second-generation DES [32].

There is a considerable observational literature regarding postoperative major adverse cardiac events (MACE) in patients with coronary stents, although the findings vary given differences in populations studied [36, 37, 44, 45, 46•, 47]. Overall, the risk of MACE is higher when surgery is performed within 30 days after stent placement and declines after 6 months [47]. The risk of MACE appears to decline differentially by stent type, with reduced risk 6 weeks after BMS and 6 months after DES [45, 46•, 47]. No clear increased MACE risk has been associated with stent type [44, 46•]. These findings should be interpreted cautiously given their observational nature and that the choice of stent is influenced by complex patient-level factors including PCI indication (ACS vs. stable CAD), bleeding risk, comorbidities, and secular trends in interventional cardiology.

The aforementioned literature is reflected in current recommendations regarding DAPT, all of which stress the need to individualize the decision with regards to the PCI indication, coronary lesion location, proposed surgery, and surgical urgency (Table 1) [5••, 6••]. Specifically, both ACC/AHA and ESC guidelines recommend a minimum of 30 days of DAPT after BMS placement, with the continuation of aspirin afterwards. The recommended duration of DAPT after DES is 12 months according to ACC/AHA guidelines, although elective surgery 180 days after DES placement may be considered. ESC guidelines recommend 6 months of DAPT after DES placement, although a range of 3–12 months of DAPT can be considered. However, if the DES was placed for

Table 1. Perioperative PCI and antiplatelet therapy in stented patients—comparison of 2014 ACC/AHA and ESC guidelines

	ACC/AHA Continue aspirin unless surgical contraindication (class 1)	ESC
Balloon angioplasty	Delay surgery for 2 weeks (class 1) Aspirin for 2 weeks	Delay surgery for 2 weeks (class 2a) Aspirin for 2 weeks (class 2a)
BMS	Delay surgery for at least 30 days (class 1) DAPT 4–6 weeks (class I)	Delay surgery 1–3 months (class 2a) DAPT 4 weeks (class 2a)
DES (second generation)	Delay surgery 365 days if possible (Class 1) or 180 days if risk of surgical delay is greater than risk of stent thrombosis (class 2b) DAPT 1 year (class 1)	Delay surgery 6–12 months depending on stent type (class 2a) DAPT 3–12 months (class 2a)

Taken from references [5••, 6••]. *BMS* bare metal stent, *DAPT* dual antiplatelet therapy, *DES* drug-eluting Stent

ACS, the full 12 months of DAPT is recommended [32]. Both guidelines advise a consideration of balloon angioplasty if surgery is very urgently needed. If performed, surgery should be postponed for at least 14 days and aspirin continued during the perioperative period.

In patients who require DAPT cessation for noncardiac surgery, guidelines recommend stopping clopidogrel, or ticagrelor 5 days prior to surgery and prasugrel 7 days prior [32, 43]. Aspirin should be continued in patients with a stent unless absolutely surgically necessary, and DAPT should be reinitiated postoperatively as soon as possible. In situations where DAPT must be discontinued early after a stent (e.g., for urgent surgery), some institutions have employed a “bridging strategy” using intravenous glycoprotein IIb/IIIa inhibitors perioperatively [48]. However, there is no clear evidence to date that this results in improved outcomes or reduced stent thrombosis [49, 50]. Relatedly, the intravenous antiplatelet P2Y₁₂ inhibitor cangrelor has been proposed to be used for bridging high-risk patients before noncardiac surgery. Cangrelor was used in this manner in the BRIDGE trial in patients with ACS or recent stenting awaiting CABG, resulting in greater perioperative platelet inhibition and no difference in major bleeding [51]. However, cangrelor has not yet been studied in patients undergoing noncardiac surgery.

Areas of incomplete knowledge

First, despite its everyday relevance, most data pertaining to this topic are derived from heterogeneous cohorts of both stable and ACS patients. There are relatively few prospective or randomized trials, and none of significant size that have been conducted in the last decade. Most of the literature regarding preoperative evaluation has been performed in the highest risk patients (e.g., vascular surgery) decades ago, and it is unclear how to apply those findings given advances in the fields of surgery and cardiology. Second, there is very limited literature about angiographic findings of preoperative diagnostic angiography, anatomic factors that may influence stenting decisions, or procedural characteristics beyond stent class. Similarly, the role of advanced intravascular

imaging and/or physiologic testing (e.g., fractional flow reserve) has not been examined in this cohort. Additionally, it is unclear whether the same stent characteristics which increase thrombosis risk (e.g., length, stent underexpansion) are similarly deleterious in the postoperative setting. Third, the potential benefit, if any, of complete versus incomplete revascularization with PCI in multi-vessel CAD is unclear. This is of special relevance in light of recent studies of multi-vessel revascularization in ACS [52, 53]. Finally, there are few long-term registry data following patients through a preoperative evaluation, surgery, and postoperative follow-up. Such data would help to establish best practices and quality metrics in this realm.

Conclusion

Coronary angiography and PCI continue to have a role prior to noncardiac surgery, although more research is clearly needed to guide and refine their use. In the absence of specific data, lessons learned from the management of CAD in nonsurgical patients are often applied. However, doing so may be inadequate as the pathophysiology of perioperative MI is likely distinctive. Attention should continue to be paid to preoperative risk assessment, a judicious use of imaging, and prescription of optimal medical therapy in patients with identified CAD. In patients undergoing PCI, a patient- and surgery-specific approach balancing the complex risks and benefits is advocated. Future detailed observational studies, registry data, and randomized trials will help to identify and improve the appropriate use of angiography and revascularization procedures in this setting.

Compliance with Ethical Standards

Conflict of Interest

Joshua Schulman-Marcus, Raymond A. Pashun, and Rajesh V. Swaminathan each declare no potential conflicts of interest.

Dmitriy N. Feldman has served as a consultant/speakers' bureau member for Eli Lilly, Daiichi-Sankyo, Pfizer, Bristol Myers Squibb, and Abbott Vascular. Dr. Feldman is a section editor for Current Treatment Options in Cardiovascular Medicine.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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