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Management of antiplatelet therapy in patients with coronary stents undergoing noncardiac surgery: association with adverse events

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Abstract

Background: Perioperative discontinuation of antiplatelet therapy (APT) in patients with coronary stents has been associated with major adverse cardiac events. Our aim was to analyse the perioperative management of APT in such patients and its relationship to the incidence of major adverse cardiac and cerebrovascular events (MACCE) and major bleeding events (MBE) in noncardiac surgery.

Methods: We completed a prospective multicentre observational study of patients with coronary stents undergoing noncardiac surgery in 11 hospitals in Spain. The main objectives were to record perioperative events and prospectively analyse the management of APT, and to assess whether the different preoperative APT regimens were associated with MACCE and MBE.

Results: Of 432 surgical procedures studied, 15% experienced a perioperative MACCE and 37% a MBE. Overall mortality was 3.0%. Presurgical APT was prescribed in 95% of procedures, and was preoperatively discontinued in 15%. Surgery was urgent or emergent in 22% of patients, 31% were ASA IV, and 38% had a Revised Cardiac Risk Index of IV. MACCE were related to recent myocardial infarction (P=0.038), chronic kidney disease (P<0.001), insulin-dependent diabetes (P=0.006) and no preoperative APT (P=0.018). MBE also increased MACCE risk (P<0.001). We found statin therapy (P=0.049) and obesity (P=0.016) to be protective factors for MACCE.

Conclusions: Patients with coronary stents undergoing noncardiac surgery suffer a high incidence of perioperative adverse events, even with perioperative APT. Major adverse cardiac and cerebrovascular events are mainly related to previous medical conditions and perioperative major bleeingn events. Our findings should be treated with caution when applied to an elective surgery population.

Clinical trial registration: NCT01171612.

Keywords: antiplatelet agents; cardiovascular system/complications; perioperative period/complications

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Editor's key points

- The association of discontinuation of preoperative antiplatelet therapy with major bleeding, cardiac and cerebrovascular events was assessed in a multicentre prospective observational study.
- Of the 432 subjects with coronary stents undergoing noncardiac surgery, 15% had an adverse event and 3% died.
- Patients with coronary stents undergoing noncardiac surgery appear to be at high risk for adverse events even when receiving perioperative antiplatelet therapy.

Percutaneous coronary intervention (PCI) with stent implantation has become the most frequent therapeutic revascularization procedure in patients with coronary artery disease (CAD). Dual antiplatelet therapy (APT) with aspirin and P2Y12 inhibitors are needed to prevent or reduce stent thrombosis until stent endothelialisation, which takes between one to 12 months, depending on the type of stent and its indication.[1,2]

Premature discontinuation of dual APT has been identified in several observational studies as the most important predictive factor for stent thrombosis.[3] A common reason for discontinuing APT is the need for noncardiac surgery, estimated to be required during the first yr post-implantation by nearly 5% of patients with bare metal stents (BMS),[4] and by 4.4% to 7% of patients with drug eluting stents (DES).[5] Moreover, a review of the incidence of adverse events after noncardiac surgery found stent thrombosis rates from 0% to 18% in patients with BMS, and from 0% to 7% in patients with DES.[6] Although it is rightly assumed that there is an increased risk of bleeding in the setting of noncardiac surgery in patients under APT, the actual incidence is unclear, as studies report varying rates, in part as a result of different bleeding endpoint definitions.[6]

Currently available clinical practice guidelines recommend delaying elective surgery in patients who require dual APT up to at least four weeks after BMS, and up to six months to one yr after DES implantation whenever possible.[7–12] This is supported by a systematic review of the literature showing that the rate of perioperative major cardiac events in patients with DES is higher when performed during the first yr post-implantation than afterwards (0%-18% us 0%–12%, respectively).[13] The incremental risk of adverse cardiac events after noncardiac surgery among post-stent patients is highest in the initial six months after implantation and stabilizes at 1% after this period.[14] In the event that the surgery cannot be postponed beyond the recommended time for dual APT, there is no general consensus on the optimal time for the discontinuation of dual APT preoperatively.

Guidelines on perioperative APT management in patients with coronary stents assess the risk of stent thrombosis *vs* the risk of surgical bleeding.[7–9] When stopping dual APT is mandatory because of the risk of surgical bleeding in patients in whom the risk of stent thrombosis is high, i.v. bridging therapy with glycoprotein IIb-IIIa inhibitors has been described.[8] According to the 2006 recommendations of the French Society of Anesthesiology and Intensive Care, if withdrawal of antiplatelet agents is necessary, substitution with flurbiprofen (a reversible inhibitor of cyclo-oxygenase with a short half-life) or therapeutic doses of heparin may be indicated,[15] however, randomized clinical trials have revealed conflicting results.[16]

In surgery with low or intermediate risk of bleeding, guidelines recommend stopping clopidogrel and continuing aspirin during the perioperative period for patients on dual APT and switching to aspirin for patients on clopidogrel monotherapy.[9] Unfortunately, the level of evidence from clinical trials is limited, and these recommendations are mainly based on expert opinion. Therefore, there is a need for well-designed prospective studies to guide physicians on optimal APT management in patients with coronary stents undergoing surgery.[10]

The main objectives of the present study were to prospectively analyse the actual practice of APT management in patients with coronary stents undergoing noncardiac surgery and to assess whether the different perioperative APT regimens are associated with major adverse cardiovascular and cerebrovascular events (MACCE) and major bleeding events (MBE).

Methods

This was a prospective observational multicentre study carried out at 11 hospitals in Catalonia (ClinicalTrials.gov identifier NCT01171612). The protocol was approved by the appropriate Ethics Review Committee (CEIC 2009560) and conducted in accordance with the Declaration of Helsinki. All participants or their legal guardians provided written informed consent before enrolment. All patients fulfilling the inclusion criteria were consecutively recruited from January 2010 to April 2012.

Participants

We recruited all patients aged ≥18yr with coronary stents undergoing scheduled or emergency noncardiac surgery requiring hospital admission for at least 24 h. All enrolled subjects received general, neuraxial, peripheral nerve block or local anaesthesia and sedation. Exclusion criteria were patients with previous coronary artery bypass graft in an artery with a previous stent, outpatient surgery, pregnant women, and obstetric procedures.

Variables and data collection

We collected patient data and potential preoperative risk factors for MACCE, which included the presence of active cardiac conditions (unstable coronary syndromes; decompensated heart failure; significant arrhythmias; severe valvular disease), clinical risk factors (history of CAD, chronic kidney disease, congestive heart failure, diabetes mellitus [DM] or cerebrovascular disease), and other minor predictors of ischaemic disease (age>70 yr, abnormal electrocardiogram [ECG], non-sinus rhythm, or hypertension). We also collected data concerning the PCI and main features of the stent (type and number of stents, date of implantation). In subjects with more than one stent, we took into consideration the most recently implanted stent to analyse the time interval between implantation and surgery. Data on preoperative pharmacological treatments and data related to the ongoing surgical procedure were also obtained.

The prescribed APT regimen was recorded throughout hospital admission and at 30 and 90 days after surgery. The analysis of preoperative APT withdrawal was done by recording the date of the last dose of APT and the date of surgery. We defined complete withdrawal of APT as the total