EuroIntervention 2014;10:38-46

Perioperative management of antiplatelet therapy in patients with coronary stents undergoing cardiac and non-cardiac surgery: a consensus document from Italian cardiological, surgical and anaesthesiological societies

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The authors' affiliations and also the accompanying supplementary data can be found in the online version of this paper at the following website: http://www.pcronline.com/eurointervention/72nd_issue/8

KEYWORDS

- antiplatelet therapy
- aspirin
- coronary artery disease
- PCI
- stent
- surgery

Abstract

Optimal perioperative antiplatelet therapy in patients with coronary stents undergoing surgery still remains poorly defined and a matter of debate among cardiologists, surgeons and anaesthesiologists. Surgery represents one of the most common reasons for premature antiplatelet therapy discontinuation, which is associated with a significant increase in mortality and major adverse cardiac events, in particular stent thrombosis. Clinical practice guidelines provide little support with regard to managing antiplatelet therapy in the perioperative phase in the case of patients with non-deferrable surgical interventions and/or high haemorrhagic risk. Moreover, a standard definition of ischaemic and haemorrhagic risk has never been determined. Finally, recommendations shared by cardiologists, surgeons and anaesthesiologists are lacking. The present consensus document provides practical recommendations on the perioperative management of antiplatelet therapy in patients with coronary stents undergoing surgery. Cardiologists, surgeons and anaesthesiologists have contributed equally to its creation. On the basis of clinical and angiographic data, the individual thrombotic risk has been defined. All surgical interventions have been classified according to their inherent haemorrhagic risk. A consensus on the optimal antiplatelet regimen in the perioperative phase has been reached on the basis of the ischaemic and haemorrhagic risk. Aspirin should be continued perioperatively in the majority of surgical operations, whereas dual antiplatelet therapy should not be withdrawn for surgery in the case of low bleeding risk. In selected patients at high risk for both bleeding and ischaemic events, when oral antiplatelet therapy withdrawal is required, perioperative treatment with short-acting intravenous glycoprotein IIb/IIIa inhibitors (tirofiban or eptifibatide) should be taken into consideration.

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SUBMITTED 15/08/2013 - REVISION RECEIVED ON 08/10/2013 - ACCEPTED ON 02/12/2013

DOI: 10.4244/EIJV10I1A8

Introduction

The number of patients with coronary stents undergoing surgery is increasing significantly. Premature discontinuation of antiplatelet therapy, especially if it occurs within the first months after stent implantation, is associated with a higher risk of stent thrombosis, a feared complication that might have dramatic clinical consequences[1-6]. On the other hand, antiplatelet therapy can significantly raise intraoperative haemorrhagic risk in surgical or endoscopic procedures[7].

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Perioperative management of antiplatelet therapy is often arbitrary and may be controversial for cardiologists, surgeons and anaesthesiologists. In recent years, international cardiological, anaesthesiological and haematological societies have proposed guidelines and joint position papers on the management of antiplatelet therapy in patients undergoing non-cardiac surgery[8-18]. However, some limitations of these recommendations are evident. Elective surgical procedures should be postponed until completion of the mandatory dual antiplatelet regimen, aspirin therapy should be stopped only if haemostasis is difficult to control during surgery, and a multidisciplinary approach is required (e.g., cardiologist, anaesthesiologist, haematologist, and surgeon) to determine the patient's risk and to choose the best strategy[13]. However, little support is provided with regard to managing antiplatelet therapy in the perioperative phase in case of semi-elective or urgent surgical or endoscopic procedures, the definition of perioperative bleeding risk is not provided, and the suggested multidisciplinary approach on an individual basis does not allow for a standard approach. Moreover, guidelines shared with cardiologists, surgeons and anaesthesiologists are lacking, although the surgeon's point of view is crucial. The management of the risk ratio between bleeding and thrombosis requires an exact knowledge of risk stratification defined for each condition, coupled with offering the minimal surgical impact. The purpose of this manuscript is to provide practical recommendations for a tailored and standardised antiplatelet treatment management, even in difficult or unusual scenarios, that are specific to each type of surgery (cardiac and non-cardiac), which has been elaborated from a previously reported consensus document from the Italian Society of Interventional Cardiology (GISE) and the Italian Association of Hospital Cardiologists (ANMCO)[19].

THE GISE-ANMCO CONSENSUS DOCUMENT

To overcome the aforementioned limitations of existing guidelines, the Italian Society of Interventional Cardiology (GISE) and the Italian Association of Hospital Cardiologists (ANMCO) promoted the creation of a consensus document with regard to the optimal antiplatelet regimen in patients with coronary stents undergoing surgical and endoscopic procedures. The Writing Committee was composed of clinical and interventional cardiologists, surgeons and anaesthesiologists, who met seven times in Milan and contributed equally to its creation[19]. Most of the members of the Writing Committee were delegates of the most important national societies of cardiologists, surgeons and anaesthesiologists. Cardiologists defined the thrombotic risk on the basis of procedural features, such as stent type, time from percutaneous coronary interventions (PCI) to surgery, and clinical features, such as acute coronary syndrome at the time of PCI, previous stent thrombosis, concomitant diabetes, renal impairment, and low cardiac ejection fraction. Surgeons classified all interventions according to the haemorrhagic risk as low, medium, and high. Finally, on the basis of both ischaemic and thrombotic risk, an agreement with regard to the most appropriate antiplatelet therapy in the perioperative phase was reached for each procedure.

The manuscript provides practical recommendations that are specific to each type of surgery. The methodology is aimed at allowing for a tailored and standardised management even in difficult or unusual scenarios.

This document is an elaboration from the previous Italian consensus document[19]. As distinct from the Italian published version, the present manuscript also received the endorsement of the Italian Society of Anaesthesiology. Anaesthesiologists contributed significantly to the paper, thus providing a multidisciplinary approach with the additional advantage of recommendations coming from different perspectives. Of note, due to lack of evidence from clinical trials, the present consensus document derives mostly from experts' opinion, which represents the main limitation. It has now been officially endorsed by 16 cardiology, anaesthesiology and surgery societies. A free English application for I-phone and I-pad can be downloaded at the site https://itunes.apple.com/us/app/stent-surgery/id551350096?mt=8.

"STENT AND SURGERY": THE DIMENSION OF THE PROBLEM

The number of PCI is increasing worldwide[20,21]. Every year more than one million PCI are performed in the USA and Europe[20,21]. In more than 85% of cases a coronary stent is implanted[22], and prolonged antiplatelet therapy is mandatory after stent implantation. The most common causes of discontinuation are surgery and bleeding events which are often associated with a poor prognosis[23].

The management of antiplatelet drugs in the perioperative period is relevant, both from an epidemiologic and a clinical point of view. It has been estimated that 4-8% of patients undergo surgery within the first year after coronary stent implantation and 23% within five years[22]. The withdrawal and sometimes also the maintenance of antiplatelet therapy may have dramatic consequences[7,24]. Surgery can lead to inflammatory, hypercoagulable and hypoxic states which are associated with plaque instability and perioperative arterial thrombosis[22]. On the other hand, bleeding risk might be 3.4 times higher during dual antiplatelet therapy compared to aspirin alone[25].

ASSESSMENT OF THE PERIOPERATIVE ISCHAEMIC RISK (THE CARDIOLOGIST'S POINT OF VIEW)

Aspirin can significantly reduce the risk of cardio-cerebrovascular events in secondary prevention[26]. Abrupt discontinuation of aspirin therapy can be associated with a "rebound" effect[27] and surgical interventions increase coagulation *per se*[28]. Previous studies demonstrated that perioperative discontinuation of aspirin therapy is

associated with a significant increase in major adverse cardiac events (MACE)[27,29]. Also, in coronary artery bypass grafting (CABG), maintenance of aspirin in the perioperative phase is associated with a significant reduction of mortality[30,31].

Data on the effect of the association of aspirin and clopidogrel are lacking and derive mostly from *post hoc* analyses of randomised trials and from registries[32,33].

The incidence of perioperative MACE is high, especially if surgery is performed early after coronary stenting[34].

The increase of MACE might, in part, be due to the perioperative discontinuation of antiplatelet therapy[35-37]. In Schouten's series, the MACE rate was 2.6% in the overall population, which increased to 13.3% in patients undergoing early surgery[37]. However, the protective effect of perioperative antiplatelet therapy did not emerge in other studies[38,39]. These (apparently) discordant data might be explained by a bias in patient selection: antiplatelet therapy maintenance might identify a population at high risk for MACE, which seems likely to be the result of complex unidentified interactions between clinical and surgical risk factors. Previous studies demonstrated that the risk of perioperative MACE is higher within the first months after stent implantation[40], even though data are not consistent[41]. In a recent study by Wijeysundera and colleagues[42], the overall rate of 30-day events was 2.1%. It demonstrated that elective non-cardiac surgery could be performed reasonably safely in carefully selected patients when at least six months have elapsed since DES implantation and from 46 to 180 days after BMS implantation.

INTRA-OPERATIVE MANAGEMENT (THE ANAESTHESIOLOGIST'S POINT OF VIEW)

In the modern anaesthesia scenario, anaesthesiologists are facing a double challenge: the choice of the best and safest anaesthesiological technique for the patient, and how to manage haemostasis in the perioperative period.

Contrary to common belief, at present there is no evidence about a real superiority of a single anaesthesia technique in patients with coronary artery disease[43-46], neither regarding inhalation vs. intravenous general anaesthesia nor general vs. loco-regional or blended techniques. Nevertheless, there is a certain agreement towards preferring blended or loco-regional anaesthesia whenever possible due to its intrinsic better control of perioperative pain and ability to lower sympathetic stimulation[47,48]. However, loco-regional anaesthesia might have an intrinsic and unavoidable risk when performed in patients on antiplatelet therapy[49]. The field of loco-regional anaesthesia is greatly affected by antiplatelet therapy, especially in terms of neuraxial techniques, due to the increased risk of catastrophic neurological events in the presence of abnormal bleeding status. Nowadays, it is well known that a safe neuraxial technique can be safely performed in patients on aspirin therapy[49]. By contrast, dual antiplatelet therapy with aspirin and clopidogrel during the week preceding a surgical intervention is an accepted contraindication to any form of regional anaesthesia[18,43,47,49]. Spinal haematoma has been described during clopidogrel treatment[45], but the precise risk of spinal or epidural haematoma with dual antiplatelet therapy is unknown[46].

Therefore, the latest recommendations of the American Society of Local Anaesthesia to stop clopidogrel seven days prior to surgery are based on clinical judgement and on isolated reports of epidural haematomas after spinal analgesia, combined spinal-epidural analgesia or both, rather than on results provided by clinical trials[18,45,49,50]. Afterwards, a loco-regional anaesthesia can be performed using the neuraxial technique in patients on aspirin therapy, whereas dual antiplatelet therapy represents a contraindication. If $P2Y_{12}$ inhibitors cannot be discontinued, a general anaesthesia is advisable.

THE PERIOPERATIVE HAEMORRHAGIC RISK: THE SURGEON'S POINT OF VIEW

It is well known that antiplatelet therapy confers an increased risk of bleeding[26,32]. Conversely, the association between antiplatelet agents and perioperative bleeding risk has not been adequately addressed. The vast majority of the available data derives from registries or observational studies, which do not have sufficient statistical power.

A meta-analysis on the effects of low-dose aspirin on perioperative bleeding complications demonstrated that aspirin increased the frequency of bleeding complications by approximately 50%[7]. However, the definition used in the included studies was extremely heterogenous and often did not use a standard definition. Moreover, when surgeons were blinded regarding aspirin application, they could not differentiate patients on aspirin from patients off aspirin from bleeding behaviour alone[51]. The authors concluded that, with the possible exception of intracranial neurosurgery and transurethral prostatectomy, where bleeding-related fatalities after aspirin ingestion were reported[7,24,52], low-dose aspirin increases bleeding only quantitatively. Additionally, only a few studies analysed in the meta-analysis were randomised, and therefore low-dose aspirin might be considered simply a risk indicator for increased comorbidity with an increased bleeding risk *per se*[53]. Only one double-blind randomised trial has investigated the perioperative bleeding risk in patients undergoing non-cardiac surgery while on 75 mg aspirin therapy[29]. No significant increase of bleeding events was identified in those patients taking aspirin as compared with those who were not on antiplatelet therapy. In Albaladejo's series, major and minor haemorrhagic complications were observed in 9.5% of patients[35]. Most bleedings were at the surgical site (85.2%) and were associated with repeat surgery in 18.5% of patients. The death rate in patients with bleeding complications was 12.0% (95% CI: 6.6 to 19.7). Another study[37] demonstrated a very low rate of excessive blood loss during surgery (1%), whereas blood transfusion was required in 24% of patients who continued vs. 20% of those who discontinued antiplatelet therapy.

Data on the role of clopidogrel on perioperative bleeding risk are lacking. An increased haemorrhagic risk emerged in patients undergoing CABG while on clopidogrel therapy, which was reduced by stopping the drug at least five days prior to intervention[33,54-57]. However, published data are not consistent[58]. On the basis of these data, the latest guidelines on non-ST-elevation myocardial infarction of the European Society of Cardiology recommend the perioperative

maintenance of clopidogrel in high-risk patients undergoing coronary artery bypass grafting (CABG) if coronary anatomy is complex, with special attention to reducing bleeding[59,60]. The bleeding risk in patients undergoing non-cardiac surgery while on antiplatelet therapy has been poorly investigated. The few available studies indicate an increased haemorrhagic risk[39,61]. Prostate biopsy and ureteroscopy can be performed in patients on aspirin therapy without a significant increase of major bleeding complications[62-64]. On the other hand, in case of transurethral prostatectomy aspirin seems to be associated with an increased risk of late bleeding events and a need for reintervention[65,66]. In case of abdominal surgery, therapy with clopidogrel significantly increases the post-intervention bleeding risk, but it does not seem to be associated with an increase of mortality due to haemorrhage or need for reintervention[67]. In patients with femoral fracture, perioperative clopidogrel therapy does not seem to be associated with a significant increase in mortality and morbidity[68].

NEW ORAL ANTIPLATELET AGENTS

Prasugrel is a novel thienopyridine with a more rapid onset of action and a higher antiplatelet effect, as compared to clopidogrel, but it has been associated with an increased bleeding risk[69,70]. In the TRITON-TIMI 38 trial, in the subgroup of patients undergoing CABG within seven days after withdrawal of thienopyridines, the number of CABG-related bleeding events was fourfold higher in patients treated with prasugrel as compared to those treated with clopidogrel. Nevertheless, the risk of mortality was reduced[70,71]. Ticagrelor is a novel non-thienopyridine antiplatelet agent that inhibits the $P2Y_{12}$ receptor, through a reversible binding mechanism of action. Like prasugrel, it is characterised by a more rapid onset of action, higher antiplatelet activity and clinical efficacy, as compared to clopidogrel. Ticagrelor does not increase overall bleeding events, but is associated with a significant increase of non-CABG-related bleeding[72,73]. As in the TRITON-TIMI 38 trial[74], in the PLATO trial patients undergoing CABG within seven days after discontinuation of antiplatelet therapy showed a significant decrease of overall and cardiovascular mortality in the ticagrelor group. Apparently, this protective effect was not due to a different haemorrhagic risk, which was similar in both groups[74].

In patients undergoing surgery in whom discontinuation of antiplatelet therapy is required, prasugrel and ticagrelor should be stopped seven and five days before intervention, respectively.

GUIDELINES: WHAT THEY SAY (AND DO NOT SAY)

Several guidelines and expert recommendations on the perioperative management of antiplatelet therapy have been published[8-18]. Of note, they derive mostly from expert opinion rather than from randomised studies. A multidisciplinary approach with cardiologists, anaesthesiologists and surgeons is recommended on an individual basis. The assessment of the ischaemic and haemorrhagic risk should be provided for each patient, in order to tailor the optimal perioperative antiplatelet regimen. If perioperative antiplatelet therapy discontinuation is required, bridge therapy with unfractionated or low molecular weight heparin is generally not recommended, as it might be associated with increased bleeding risk, without conferring an anti-ischaemic protective effect[75].

Of note, the existing guidelines on perioperative antiplatelet therapy have the following limitations, which negatively affect their applicability in daily clinical practice: I) are not shared with cardiologists, surgeons and anaesthesiologists; II) do not provide a standard classification of surgical interventions, according to the haemorrhagic risk; III) do not provide a standard classification of the patient's thrombotic risk; IV) do not provide general, practical advice on the optimal perioperative regimen on the basis of the surgical intervention and the ischaemic risk but rather recommend a risk/benefit evaluation on an individual basis; V) provide little support with regard to managing antiplatelet therapy in the perioperative phase in case of non-deferrable and/or high haemorrhagic risk interventions; VI) do not provide practical advice on the timing and modalities of antiplatelet therapy discontinuation and resumption.

DEVELOPMENT OF THE THROMBOTIC VERSUS BLEEDING RISK ALGORITHM

DEFINITION OF THROMBOTIC RISK

The genesis of stent thrombosis is multifactorial and is influenced by patient characteristics, coronary lesions, procedural features, coagulation cascade, and antiplatelet therapy[9]. Therefore, the difficulty of appropriate risk stratification for stent thrombosis becomes evident.

In the present document, thrombotic risk is defined on the basis of four factors **(Table 1)**: I) type of implanted stent (BMS vs. DES)[76-82], II) time from PCI to surgery[83], III) angiographic features of coronary lesions[9,84-86], IV) clinical characteristics[4,6,38,39,87].

Table 1. Thrombotic risk definition.

Low risk	Intermediate risk	High risk
>6 months after PCI with BMS	>1 month <6 months after PCI with BMS	<1 month after PCI with BMS
>12 months after PCI with DES	>6 <12 months after PCI with DES	<6 months after PCI with DES
	>12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel)	<12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel)

PCI in ACS, previous stent thrombosis, LVEF <35%, chronic renal failure and diabetes mellitus increase the thrombotic risk. Use of second-generation DES might reduce the thrombotic risk. Patients submitted to CABG or with ACS medically treated are considered at high risk in the first month, at intermediate risk between the 1st and 6th month, and at low risk after 6 months. Patients treated with POBA are considered at high risk within the first 2 weeks, at intermediate risk between 2 and 4 weeks, and at low risk after 4 weeks[1,2,4,6,12,38,39,76-86]. ACS: acute coronary syndrome; BMS: bare metal stent; CABG: coronary artery bypass graft; DES; drug-eluting stent; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty

Of note, second-generation DES have been developed with an improved design that may help to overcome the current limitations of the first-generation DES[81]. Improved stent designs with thinner struts and more biocompatible polymers may enhance endothelial coverage and functional recovery[81-83]. Due to their safer profile, as demonstrated by previous studies, second-generation DES may confer a lower thrombotic risk as compared to first-generation DES, thus allowing an earlier discontinuation (beyond six months) of dual antiplatelet therapy, when necessary[79-83].

A large retrospective study from Hawn et al has recently challenged the concept that the timing of surgery from PCI and antiplatelet discontinuation are potential triggers for cardiac events at the time of surgery[88]. MACE within 30 days were associated with emergency surgery and advanced cardiac disease but were not associated with stent type or timing of surgery beyond six months after stent implantation. Moreover, there was no significant relationship between perioperative antiplatelet cessation and 30-day MACE (odds ratio 0.86, 95% confidence interval 0.57-1.29). Although the authors concluded that the guideline emphasis on stent type and surgical timing for both DES and BMS should be re-evaluated, their findings should be judged with caution because they arise from an observational study with potential for residual confounding, where the surgical population was heterogeneous (e.g., the procedures ranged from minor outpatient to emergent in-patient operations) and clinical decision-making factors that influenced stent selection were largely unavailable or limited to administrative data. Moreover, the study was underpowered to detect a true association between perioperative antiplatelet cessation and 30-day MACE.

DEFINITION OF BLEEDING RISK

On the basis of the haemorrhagic risk, the main surgical interventions have been classified into three groups: high, medium, and low risk **(Table 2-Table 8, Online Table 1-Online Table 7)**. The definition was mostly derived both from previous published studies, whenever available, and from the experts' opinion[9,11,13,54-59,61-66,89-127]. **Table 2-Table 8** and **Online Table 1-Online Table 7** include general, practical recommendations, while they do not consider clinical characteristics on an individual basis. Of note, the overall risk derives from the interaction between procedural and individual features. The present document focuses mostly on perioperative bleeding risk related to surgical procedures rather than to a patient's haemorrhagic profile. Each table on surgical bleeding risk is given to provide the reader with a standard frame that might be adapted depending on individual patients' characteristics. Once the surgical haemorrhagic risk has been defined, it is advisable to evaluate carefully each patient's risk on an individual basis, which might be taken into account by using *ad hoc* bleeding risk scores. Several practical bleeding risk scores are available and are mostly based on sex, renal function, and comorbidities[128-130]. Therefore, when applying these recommendations to daily clinical practice, each single case should be carefully evaluated in terms of ischaemic and bleeding risk.

Resumption of antiplatelet drugs after surgery may be deferred in case of clinically relevant bleeding complications. It could be recommended that high-risk patients be referred to centres where the most minimally invasive therapies such as pure laparoscopic, robotic-assisted procedures and new-generation lasers are available.

BRIDGE THERAPY

Even if controlled clinical studies are lacking, guidelines and expert reviews recommend the use of short half-life GPI in the perioperative phase in patients at high thrombotic and bleeding risk[13,14,17,18]. "Bridge" therapy with iv GPI is reserved to patients at high risk of stent thrombosis for whom the perioperative discontinuation of antiplatelet drugs is required because of an unacceptably high

Table 2. Cardiac surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	–	–	–	–
	Intermediate risk	– Minithoracotomy – TAVI (apical approach) – OPCAB – CABG – Valve replacement	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors [b]
	High risk	– Reintervention – Endocarditis – CABG in PCI failure – Aortic dissections	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors [b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References[30,31,33,55-60,74,79-87,89]. ASA: aspirin; CABG: coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass; PCI: percutaneous coronary intervention or coronary angioplasty; TAVI: transcatheter aortic valve implantation

Table 3. General surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	Hernioplasty, plastic surgery of incisional hernias, cholecystectomy, appendectomy and colectomy, gastric resection, intestinal resection, breast surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	Haemorrhoidectomy, splenectomy, gastrectomy, obesity surgery, rectal resection, thyroidectomy	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GPIIb/IIIa inhibitors [b]
	High risk	Hepatic resection, duodenocefalopancreasectomy	ASA: Discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GPIIb/IIIa inhibitors [b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [66, 101]. ASA: aspirin

Table 4. Vascular surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	Carotid endarterectomy, bypass or endarterectomy of lower extremity, EVAR, TEVAR, limb amputations	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: not contraindicated. Consider PTA or stenting ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone at least 30 days after PCI Consider PTA or stenting ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	Open abdominal aorta surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone or consider EVAR Urgency/ emergency ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone or consider EVAR Urgency/ emergency ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	High risk	Open thoracic and thoracoabdominal surgery	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone or consider TEVAR Urgency/emergency ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone or consider TEVAR Urgency/ emergency ASA: continue $P2Y_{12}$ receptor inhibitors: continue

[a] 7 days prior for prasugrel; References [90-100]. ASA: aspirin; EVAR: endovascular repair for aortic aneurysm; PCI: percutaneous coronary intervention or coronary angioplasty; PTA: percutaneous transluminal angioplasty; TEVAR: thoracic endovascular aortic/aneurysm repair

bleeding risk[1,2]. Savonitto et al[22,131] carried out a prospective study on 60 patients with DES considered at high risk for stent thrombosis, and candidates for major surgery. All patients received GPI therapy with tirofiban in the perioperative phase. No cardiac ischaemic event was observed. The rates of bleeding and transfusion were low, in relation to the types of surgery, and no bleeding complications requiring new surgery were observed. Similar studies on more limited patient populations have been performed with eptifibatide[132-134]. Based on the results of these studies, in highly selected patients, a bridge therapy with iv tirofiban or eptifibatide can reasonably be recommended. GPI infusion, at the dose reported in the summary of product characteristics (decreased by 50% in patients with renal failure and increased pre-/post-surgery bleeding risk) should start three days prior to surgical intervention, whereas clopidogrel and ticagrelor should be discontinued five days prior to surgery (seven days with prasugrel). GPI infusion should be stopped at least four hours prior to surgery (eight hours in patients with creatinine clearance <30 ml/min). $P2Y_{12}$ inhibitors should be resumed within 24-48 hours after the intervention, with a loading dose (300 mg for clopidogrel, 60 mg for prasugrel and 180 mg for ticagrelor). In selected cases (especially in abdominal surgery, if gastrointestinal function has not yet recovered), infusion with tirofiban or eptifibatide can be restarted (with loading dose) a few hours after the end of the intervention, after a careful evaluation of the bleeding risk. After complete intestinal recanalisation, therapy with $P2Y_{12}$ inhibitors can be resumed with a loading dose, and, after two hours,

Table 5. Orthopaedic surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Hand surgery – Shoulder and knee arthroscopy – Minor spine surgery I	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Prosthetic shoulder surgery – Major spine surgery – Knee surgery (anterior cruciate ligament, osteotomies) – Foot surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors [b]
	High risk	– Major prosthetic surgery (hip or knee) – Major traumatology (pelvis, long bones) – Fractures of the proximal femur in the elderly	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a, c] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors [b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient; [c] in case of femur fracture may be appropriate to proceed immediately to surgery, despite dual antiplatelet therapy, without waiting for the 5-day suspension. References [68, 123-125]. ASA: aspirin.

Table 6. Urology surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	Flexible cystoscopy, Ureteral catheterisation, Ureteroscopy	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: not contraindicated ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: not contraindicated ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	Prostate biopsy, Orchiectomy, Circumcision	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b] Bridge therapy with GP IIb/IIIa inhibitors [b]
	High risk	Radical and partial nephrectomy, Percutaneous nephrostomy, Percutaneous lithotripsy, Cystectomy and radical prostatectomy, TURP, TURBT, Penectomy, Partial orchiectomy	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue, if possible $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b] Bridge therapy with GP IIb/IIIa inhibitors [b] if ASA is discontinued	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before [a] - Resume within 24-72 hours, with a loading dose [b] Bridge therapy with GP IIb/IIIa inhibitors [b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [62-66, 125-127]. ASA: aspirin; TURP: transurethral resection of prostate; TURBT: transurethral resection of bladder tumour

the infusion of tirofiban or eptifibatide can be stopped. Of note, GPI are potent antiplatelet agents and might be associated with an increased risk of bleeding during their infusion. Afterwards, they might be contraindicated in patients with an active, clinically relevant bleeding (i.e., macrohaematuria). This therapy should be prescribed by cardiologists and administered in a cardiology ward. GPI administration is currently off-label as a "bridge therapy" in the perioperative period[29]. The perioperative maintenance of aspirin therapy, which might be administered iv, is strongly recommended in the vast majority of interventions. As ischaemic complications occur most frequently soon after surgery, a close clinical and electrocardiographic monitoring of the patient is strongly recommended.

Table 7. Thoracic surgery.

Haemorrhagic risk		Thrombotic risk: Low risk	Thrombotic risk: Intermediate risk	Thrombotic risk: High risk
Low risk	Wedge resection Diagnostic videothoracoscopy Chest wall resection	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
Intermediate risk	– Lobectomy – Pneumonectomy – Mediastinoscopy – Sternotomy – Mediastinal mass excision	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
High risk	– Oesophagectomy – Pleuropneumonectomy – Decortication of lung	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]	Elective surgery: postpone Non-deferrable surgery: ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [8-10,12-15,90]. ASA: aspirin

Table 8. Digestive endoscopy.

Haemorrhagic risk		Thrombotic risk: Low risk	Thrombotic risk: Intermediate risk	Thrombotic risk: High risk
Low risk	– EGD or colonoscopy +/– biopsy – Echoendoscopy without biopsy – Polypectomy/polyps <1 cm – ERCP, stent, dilated papilla without sphincterotomy	ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: not contraindicated ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone ASA: continue $P2Y_{12}$ receptor inhibitors: continue
Intermediate risk	– Endoscopy + fine needle aspiration biopsy (FNA) for solid lesions – Stenosis dilatation (oesophageal, colorectal) – Gastroenteric stents – Argon plasma coagulation treatment – Polypectomy/polyps >1 cm – PEG (percutaneous endoscopic gastrostomy) – Binding/variceal sclerosis – Binding/haemorrhoids sclerosis	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
High risk	– Dilatation in achalasia – Mucosectomy/submucosal resection – Echography with FNA biopsy of pancreatic cystic lesions – Ampullectomy of the ampulla of Vater	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b] Bridge therapy with GP IIb/IIIa inhibitors[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [111-126]. ASA: aspirin; EGD: oesophago-gastro-duodenoscopy; ERCP: endoscopic retrograde cholangiopancreatography

Antithrombotic therapy with unfractionated or low molecular weight heparin is not recommended, unless administered as prophylaxis for venous thromboembolism.

Cangrelor is a new potent antiplatelet agent that inhibits the $P2Y_{12}$ receptor competitively. On the basis of the BRIDGE trial results, it might be used in future as a "bridge" therapy in patients undergoing surgery, in whom the perioperative discontinuation of oral antiplatelet drugs is necessary[135].

Limitations

The present consensus document derives mostly from experts' opinions rather than from the results of randomised trials, which

represents its main limitation. Moreover, many procedures require a more urgent management according to the severity of the clinical presentation, and often the distinction between "deferrable" and "un-deferrable" surgery is not a clear issue and can be misleading both for the surgeon and for the cardiologist. Finally, the haemorrhagic risk is determined not only by the type of surgical intervention, but also by the patient's clinical characteristics, which have not been considered in the bleeding risk assessment.

Acknowledgement

This manuscript and supplementary data have been adapted with permission from Rossini et al[19].

Conflict of interest statement

R. Rossini received payment as an individual for consulting fees or honoraria from Eli Lilly and Co., and Daiichi Sankyo, Inc and Astra Zeneca. L.O. Visconti received payment as an individual for consulting fees or honoraria from Eli Lilly, and Daiichi Sankyo, Astra Zeneca, Menarini, Bayer, Pfizer, BMS and Boehringer. D. Angiolillo reports receiving payment as an individual for: a) consulting fees or honoraria from Bristol Myers Squibb, Sanofi-Aventis, Eli Lilly, Daiichi Sankyo, The Medicines Company, AstraZeneca, Merck, Evolva, Abbott Vascular and PLx Pharma; b) participation in review activities from Johnson & Johnson, St. Jude, and Sunovion. He also reports receiving institutional payments for grants from Bristol Myers Squibb, Sanofi-Aventis, Glaxo Smith Kline, Otsuka, Eli Lilly, Daiichi Sankyo, The Medicines Company, AstraZeneca, Evolva; and having other financial relationships with the James and Esther King Biomedical Research Program. D. Capodanno reports receiving honoraria for lectures/consulting from Eli Lilly and Co., The Medicines Company, and AstraZeneca. G. Guagliumi reports receiving consulting fees from Boston Scientific, St. Jude Medical and AstraZeneca and receiving grant support from St. Jude Medical, Medtronic Vascular, Boston Scientific and Abbott Vascular. M. Lettino reports speaker's fees and being an advisory board member for AZ, Bayer, Boehringer, Daiichi Sankyo, Eli Lilly, The Medicines Company, BMS, MSD, Pfizer. G. Musumeci reports receiving honoraria for lectures from Eli Lilly and Co., Daiichi Sankyo, AstraZeneca, St. Jude Medical and Abbott Vascular. L. Francetti reports receiving payment as an individual for consulting from Valeas spa. S. Savonitto reports receiving research grants from Eli Lilly, Novartis, and Iroko. B. Castiglioni reports receiving payment as an individual for speaker fees from CID. G. Staurenghi reports receiving payment as an individual for consulting fees or honoraria from Heidelberg Engineering, OD-OS, Optos, Ocular Instruments, Quentel Medical, Carl Zeiss Meditec, Alcon, Allergan, Bayer, Boheringer, Genentech, GSK, QLT, Novartis and Roche. All the other authors have no conflicts of interest to report.

References

The references can be found in the online version of the paper.

Online data supplement

Appendix. Acknowledgements.
Online Table 1. Maxillofacial surgery.
Online Table 2. Plastic surgery.
Online Table 3. Gynaecology.
Online Table 4. Neurosurgery.
Online Table 5. Interventional pulmonology.
Online Table 6. Dentistry.
Online Table 7. Ophthalmology.

Online data supplement

References

1. Kolh P, Wijns W, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirlet C, Pomar JL, Reifart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, Sousa Uva M, Taggart D. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI). Guidelines on myocardial revascularization. *Eur Heart J.* 2010;31:2501-55.

2. Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC 2009 appropriateness criteria for coronary revascularization: a report by the American College of Cardiology Foundation Appropriateness Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and the American Society of Nuclear Cardiology endorsed by the American Society of Echocardiography, the Heart Failure Society of America, and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol.* 2009;53:530-53.

3. McFadden EP, Stabile E, Regar E, Cheneau E, Ong ATL, … Kinnaird T, Suddath WO, Weissman NJ, Torguson R, Kent KM, Pichard AD, Satler LF, Waksman R, Serruys PW. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. *Lancet.* 2004;364:1519-21.

4. Iakovou I, Schmidt T, Bonizzoni E, Ge L, Sangiorgi GM, Stankovic G, Airoldi F, Chieffo A, Montorfano M, Carlino M, Michev I, Corvaja N, Briguori C, Gerckens U, Grube E, Colombo A. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA.* 2005;293:2126-30.

5. Spertus JA, Kettelkamp R, Vance C, Decker C, Jones PG, Rumsfeld JS, Messenger JC, Khanal S, Peterson ED, Bach RG, Krumholz HM, Cohen DJ. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. *Circulation*. 2006;113:2803-9.

6. van Werkum JW, Heestermans AA, Zomer AC, Kelder JC, Suttorp MJ, Rensing BJ, Koolen JJ, Brueren BR, Dambrink JH, Hautvast RW, Verheugt FW, ten Berg JM. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. *J Am Coll Cardiol.* 2009;53:1399-409.

7. Burger W, Chemnitius JM, Kneissl GD, Rücker G. Low-dose aspirin for secondary cardiovascular prevention, cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. *J Intern Med.* 2005;257:399-414.

8. Brilakis ES, Banerjee S, Berger PB. Perioperative management of patients with coronary stents. *J Am Coll Cardiol.* 2007;49:2145-50.

9. Riddell JW, Chiche L, Plaud B, Hamon M. Coronary stents and noncardiac surgery. *Circulation*. 2007;116:e378-e382.

10. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 2002 guidelines on perioperative cardiovascular evaluation for noncardiac surgery) developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *J Am Coll Cardiol.* 2007;50:e159-241.

11. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, Hart JC, Herrmann HC, Hillis LD, Hutter AM Jr, Lytle BW, Marlow RA, Nugent WC, Orszulak TA, Antman EM, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation*. 2004;110:1168-76.

12. Grines CL, Bonow RO, Casey DE Jr, Gardner TJ, Lockhart PB, Moliterno DJ, O'Gara P, Whitlow P. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *J Am Coll Cardiol.* 2007;49:734-9.

13. Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G, Gorenek B, Hennerici MG, Iung B, Kelm M, Kjeldsen KP, Kristensen SD, Lopez-Sendon J, Pelosi P, Philippe F, Pierard L, Ponikowski P, Schmid JP, Sellevold OF, Sicari R, Van den Berghe G, Vermassen F; Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery, European Society of Cardiology (ESC). Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. *Eur Heart J.* 2009;30:2769-812.

14. Cardiac Society of Australia and New Zealand. Guidelines for the management of antiplatelet therapy in patients with coronary stents undergoing non-cardiac surgery. *Heart Lung Circ.* 2010;19:2-10.

15. Douketis JD, Berger PB, Dunn AS, Jaffer AK, Spyropoulos AC, Becker RC, Ansell J. The perioperative management of antithrombotic

therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest.* 2008;133:299S-339S.

16. Samama CM, Bastien O, Forestier F, Denninger MH, Isetta C, Juliard JM, Lasne D, Leys D, Mismetti P; French Society of Anesthesiology and Intensive Care. Antiplatelet agents in the perioperative period: expert recommendations of the French Society of Anesthesiology and Intensive Care (SFAR) 2001 - summary statement. *Can J Anaesth.* 2002;49:S26-35.

17. Korte W, Cattaneo M, Chassot PG, Eichinger S, von Heymann C, Hofmann N, Rickli H, Spannagl M, Ziegler B, Verheugt F, Huber K. Peri-operative management of antiplatelet therapy in patients with coronary artery disease: joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the Working Group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (ÖGARI) and the Working Group on Thrombosis of the European Society for Cardiology (ESC). *Thromb Haemost.* 2011;105:743-9.

18. Chassot PG, Delabays A, Spahn DR. Perioperative antiplatelet therapy: the case for continuing therapy in patients at risk of myocardial infarction. *Br J Anaesth.* 2007;99:316-28.

19. Rossini R, Bramucci E, Castiglioni B, De Servi S, Lettieri C, Lettino M, Musumeci G, Visconti LO, Piccaluga E, Savonitto S, Trabattoni D, Buffoli F, Angiolillo DJ, Bovenzi F, Cremonesi A, Scherillo M, Guagliumi G; Società Italiana di Cardiologia 259 Invasiva (GISE); Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO). Coronary stenting and surgery: peri-operative management of antiplatelet therapy in patients undergoing surgery after coronary stent implantation. *G Ital Cardiol (Rome).* 2012;13:528-51.

20. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18-e209.

21. Moschovitis A, Cook S, Meier B. Percutaneous coronary interventions in Europe in 2006. *EuroIntervention.* 2010;6:189-94.

22. Savonitto S, Caracciolo M, Cattaneo M, De Servi S. Management of patients with recently implanted coronary stents on dual antiplatelet therapy who need to undergo major surgery. *J Thromb Haemost.* 2011;9:2133-42.

23. Rossini R, Capodanno D, Lettieri C, Musumeci G, Nijaradze T, Romano M, Lortkipanidze N, Cicorella N, Biondi Zoccai G, Sirbu V, Izzo A, Guagliumi G, Valsecchi O, Gavazzi A, Angiolillo DJ. Prevalence, predictors, and long-term prognosis of premature discontinuation of oral antiplatelet therapy after drug eluting stent implantation. *Am J Cardiol.* 2011;107:186-94.

24. Thurston AV, Briant SL. Aspirin and post-prostatectomy haemorrhage. *Br J Urol*. 1993;71:574-6.

25. Payne DA, Hayes PD, Jones CI, Belham P, Naylor AR, Goodall AH. Combined therapy with clopidogrel and aspirin significantly increases the bleeding time through a synergistic antiplatelet action. *J Vasc Surg*. 2002;35:1204-9.

26. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *Br Med J.* 2002;324:71-86.

27. Biondi-Zoccai GG, Lotrionte M, Agostoni P, Abbate A, Fusaro M, Burzotta F, Testa L, Sheiban I, Sangiorgi G. A systematic review and meta-analysis on the hazards of discontinuing or not adhering to aspirin among 50,279 patients at risk for coronary artery disease. *Eur Heart J.* 2006;27:2667-74.

28. Priebe HJ. Triggers of perioperative myocardial ischaemia and infarction. *Br J Anaesth.* 2004;93:9-20.

29. Oscarsson A, Gupta A, Fredrikson M, Järhult J, Nyström M, Pettersson E, Darvish B, Krook H, Swahn E, Eintrei C. To continue or discontinue aspirin in the perioperative period: a randomized, controlled clinical trial. *Br J Anaesth.* 2010;104:305-12.

30. Mangano DT; Multicenter Study of Perioperative Ischemia Research Group. Aspirin and mortality from coronary bypass surgery. *N Engl J Med.* 2002;347:1309-17.

31. Topol EJ. Aspirin for bypass surgery: from taboo to new standard of care. *N Engl J Med.* 2002;347:1359-60.

32. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK; Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494-502.

33. Firanescu CE, Martens EJ, Schonberger JP, Soliman Hamad MA, van Straten AH. Postoperative blood loss in patients undergoing coronary artery bypass surgery after preoperative treatment with clopidogrel. A prospective randomised controlled study. *Eur J Cardiothorac Surg.* 2009;36:856-62.

34. Berger PB, Kleiman NS, Pencina MJ, Hsieh WH, Steinhubl SR, Jeremias A, Sonel A, Browne K, Barseness G, Cohen DJ; EVENT Investigators. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. *JACC Cardiovasc Interv.* 2010;3:920-7.

35. Albaladejo P, Marret E, Samama CM, Collet JP, Abhay K, Loutrel O, Charbonneau H, Jaber S, Thoret S, Bosson JL, Piriou V. Non-cardiac surgery in patients with coronary stents: the RECO study. *Heart.* 2011;97:1566-72.

36. Artang R, Dieter RS. Analysis of 36 reported cases of late thrombosis in drug eluting stents placed in coronary arteries. *Am J Cardiol.* 2007;99:1039-43.

37. Schouten O, van Domburg RT, Bax JJ, de Jaegere PJ, Dunkelgrun M, Feringa HH, Hoeks SE, Poldermans D. Noncardiac surgery after coronary stenting: early surgery and interruption of

antiplatelet therapy are associated with an increase in major adverse cardiac events. *J Am Coll Cardiol.* 2007;49:122-4.

38. Anwaruddin S, Askari AT, Saudye H, Batizy L, Houghtaling PL, Alamoudi M, Militello M, Muhammad K, Kapadia S, Ellis SG. Characterization of post-operative risk associated with prior drug-eluting stent use. *JACC Cardiovasc Interv.* 2009;2:542-9.

39. van Kuijk JP, Flu WJ, Schouten O, Hoeks SE, Schenkeveld L, de Jaegere PP, Bax JJ, van Domburg RT, Serruys PW, Poldermans D. Timing of noncardiac surgery after coronary artery stenting with bare metal or drug-eluting stents. *Am J Cardiol.* 2009;104:1229-34.

40. Cruden NL, Harding SA, Flapan AD, Graham C, Wild SH, Slack R, Pell JP, Newby DE; Scottish Coronary Revascularisation Register Steering Committee. Previous coronary stent implantation and cardiac events in patients undergoing noncardiac surgery. *Circ Cardiovasc Interv.* 2010;3:236-42.

41. Rabbitts JA, Nuttall GA, Brown MJ, Hanson AC, Oliver WC, Holmes DR, Rihal CS. Cardiac risk of noncardiac surgery after percutaneous coronary intervention with drug-eluting stents. *Anesthesiology.* 2008;109:596-604.

42. Wijeysundera DN, Wijeysundera HC, Yun L, Wasowicz M, Beattie WS, Velianou JL, Ko DT. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. *Circulation*. 2012;126:1355-62.

43. Fox J. Spinal and epidural anesthesia and anticoagulation. *Int Anesthesiol Clin.* 2001;39:51-61.

44. Horlocker TT, Wedel DJ, Benson H. Regional anesthesia in anticoagulated patients: defining the risks. *Reg Anesth Pain Med.* 2003;28:172-98.

45. Tam NL, Pac-Soo C, Pretorius PM. Epidural haematoma after a combined spinal-epidural anaesthetic in a patient treated with clopidogrel and dalteparin. *Br J Anaesth.* 2006;96:262-5.

46. Tyagi A, Bhattacharya A. Central neuraxial blocks and anticoagulation: a review of current trends. *Eur J Anaesthesiol.* 2002;19:317-29.

47. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, Sage D, Futter M, Saville G, Clark T, MacMahon S. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ.* 2000;321:1493.

48. Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia. Their role in postoperative outcome. *Anesthesiology.* 1995;82:1474-506.

49. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, Brown DL, Heit JA, Mulroy MF, Rosenquist RW, Tryba M, Yuan CS. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med.* 2010;35:64-101.

50. Litz RJ, Gottschlich B, Stehr SN. Spinal epidural hematoma after spinal anesthesia in a patient treated with clopidogrel and enoxaparin. *Anesthesiology.* 2004;101:1467-70.

51. Lindblad B, Persson NH, Takolander R, Bergqvist D. Does low dose acetylsalicylic acid prevent stroke after carotid surgery? A double-blind, placebo-controlled randomized trial. *Stroke.* 1993;24:1125-8.

52. Palmer JD, Sparrow OC, Iannotti F. Postoperative hematoma: a 5-year survey and identification of avoidable risk factors. *Neurosurgery.* 1994;35:1061-4.

53. Hui CK, Lai KC, Yuen MF, Wong WM, Lam SK, Lai CL. Does withholding aspirin for one week reduce the risk of post-sphincterotomy bleeding? *Aliment Pharmacol Ther.* 2002;16:929-36.

54. Fox KA, Mehta SR, Peters R, Zhao F, Lakkis N, Gersh BJ, Yusuf S. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) Trial. *Circulation*. 2004;110:1202-8.

55. Berger JS, Frye CB, Harshaw Q, Edwards FH, Steinhubl SR, Becker RC. Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: a multicenter analysis. *J Am Coll Cardiol.* 2008;52:1693-701.

56. Kapetanakis EI, Medlam DA, Boyce SW, Haile E, Hill PC, Dullum MK, Bafi AS, Petro KR, Corso PJ. Clopidogrel administration prior to coronary artery bypass grafting surgery: the cardiologist's panacea or the surgeon's headache? *Eur Heart J.* 2005;26:576-83.

57. Mehta RH, Roe MT, Mulgund J, Ohman EM, Cannon CP, Gibler WB, Pollack CV Jr, Smith SC Jr, Ferguson TB, Peterson ED. Acute clopidogrel use and outcomes in patients with non-ST-segment elevation acute coronary syndromes undergoing coronary artery bypass surgery. *J Am Coll Cardiol.* 2006;48:281-6.

58. Ebrahimi R, Dyke C, Mehran R, Manoukian SV, Feit F, Cox DA, Gersh BJ, Ohman EM, White HD, Moses JW, Ware JH, Lincoff AM, Stone GW. Outcomes following pre-operative clopidogrel administration in patients with acute coronary syndromes undergoing coronary artery bypass surgery: the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial. *J Am Coll Cardiol.* 2009;53:1965-72.

59. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, Wijns W, Zahger D; ESC Committee for Practice Guidelines. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2011;32:2999-3054.

60. Fitchett D, Eikelboom J, Fremes S, Mazer D, Singh S, Bittira B, Brister S, Graham J, Gupta M, Karkouti K, Lee A, Love M, McArthur R, Peterson M, Verma S, Yau T. Dual antiplatelet therapy in patients requiring urgent coronary artery bypass grafting surgery: a position statement of the Canadian Cardiovascular Society. *Can J Cardiol.* 2009;25:683-9.

61. Wilson SH, Fasseas P, Orford JL, Lennon RJ, Horlocker T, Charnoff NE, Melby S, Berger PB. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol.* 2003;42:234-40.

62. Giannarini G, Mogorovich A, Valent F, Morelli G, De Maria M, Manassero F, Barbone F, Selli C. Continuing or

discontinuing low-dose aspirin before transrectal prostate biopsy: results of a prospective randomized trial. *Urology.* 2007;70:501-5.

63. Maan Z, Cutting CW, Patel U, Kerry S, Pietrzak P, Perry MJ, Kirby RS. Morbidity of transrectal ultrasonography guided prostate biopsies in patients after the continued use of low-dose aspirin. *BJU Int.* 2003;91:798-800.

64. Halliwell OT, Yadegafar G, Lane C, Dewbury KC. Transrectal ultrasound-guided biopsy of the prostate: aspirin increases the incidence of minor bleeding complications. *Clin Radiol.* 2008;63:557-61.

65. Turna B, Stein RJ, Smaldone MC, Santos BR, Kefer JC, Jackman SV, Averch TD, Desai MM. Safety and efficacy of flexible ureterorenoscopy and holmium: YAG lithotripsy for intrarenal stones in anticoagulated cases. *J Urol.* 2008;179:1415-9.

66. Eberli D, Chassot PG, Sulser T, Samama CM, Mantz J, Delabays A, Spahn DR. Urological surgery and antiplatelet drugs after cardiac and cerebrovascular accidents. *J Urol.* 2010;183:2128-36.

67. Chernoguz A, Telem DA, Chu E, Ozao-Choy J, Tammaro Y, Divino CM. Cessation of clopidogrel before major abdominal procedures. *Arch Surg.* 2011;146:334-9.

68. Leonidou A, Cam NB, Chambers IR. Femoral neck fractures in patients on Clopidogrel. The effect of delaying surgery and the introduction of the new SIGN guidelines. *Surgeon.* 2011;9:318-21.

69. Wiviott SD, Trenk D, Frelinger AL, O'Donoghue M, Neumann FJ, Michelson AD, Angiolillo DJ, Hod H, Montalescot G, Miller DL, Jakubowski JA, Cairns R, Murphy SA, McCabe CH, Antman EM, Braunwald E; PRINCIPLE-TIMI 44 Investigators. Prasugrel compared with high loading and maintenance-dose clopidogrel in patients with planned percutaneous coronary intervention: the Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44 trial. *Circulation*. 2007;116:2923-32.

70. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM; TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2007;357:2001-15.

71. Prasugrel (LY640315; CS-747) as an anti-thrombotic therapy in patients with acute coronary syndromes (ACS). NDA 22-307, Effient™ (prasugrel). Presentation to the Cardiovascular and Renal Drugs Advisory Committee. February 3, 2009. Available at http://www.fda.gov/ohrms/dockets/AC/09/slides/2009-4412s1-02-sponsor.pdf [accessed March 29, 2012].

72. Gurbel PA, Bliden KP, Butler K, Tantry US, Gesheff T, Wei C, Teng R, Antonino MJ, Patil SB, Karunakaran A, Kereiakes DJ, Parris C, Purdy D, Wilson V, Ledley GS, Storey RF. Randomized double-blind assessment of the ONSET and OFFSET of the antiplatelet effects of ticagrelor versus clopidogrel in patients with stable coronary artery disease: the ONSET/OFFSET study. *Circulation*. 2009;120:2577-85.

73. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA; PLATO Investigators, Freij A, Thorsén M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2009;361:1045-57.

74. Held C, Asenblad N, Bassand JP, Becker RC, Cannon CP, Claeys MJ, Harrington RA, Horrow J, Husted S, James SK, Mahaffey KW, Nicolau JC, Scirica BM, Storey RF, Vintila M, Ycas J, Wallentin L. Ticagrelor versus clopidogrel in patients with acute coronary syndromes undergoing coronary artery bypass surgery: results from the PLATO (Platelet Inhibition and Patient Outcomes) trial. *J Am Coll Cardiol.* 2011;57:672-84.

75. McDonald SB, Renna M, Spitznagel EL, Avidan M, Hogue CW Jr, Moon MR, Barzilai B, Saleem R, McDonald JM, Despotis GJ. Preoperative use of enoxaparin increases the risk of postoperative bleeding and re-exploration in cardiac surgery patients. *J Cardiothorac Vasc Anesth.* 2005;19:4-10.

76. Windecker S, Meier B. Late coronary stent thrombosis. *Circulation*. 2007;116:1952-65.

77. Tsimikas S. Drug-eluting stents and late adverse clinical outcomes: lessons learned, lessons awaited. *J Am Coll Cardiol.* 2006;47:2112-5.

78. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, Kutys R, Skorija K, Gold HK, Virmani R. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol.* 2006;48:193-202.

79. Krucoff MW, Rutledge DR, Gruberg L, Jonnavithula L, Katopodis JN, Lombardi W, Mao VW, Sharma SK, Simonton CA, Tamboli HP, Wang J, Wilburn O, Zhao W, Sudhir K, Hermiller JB. A new era of prospective real-world safety evaluation primary report of XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System condition-of-approval post-market study). *JACC Cardiovasc Interv.* 2011;4:1298-309.

80. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F, Kimura T, Briguori C, Sabatè M, Kim HS, De Waha A, Kedhi E, Smits PC, Kaiser C, Sardella G, Marullo A, Kirtane AJ, Leon MB, Stone GW. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet.* 2012;379:1393-402.

81. Sarno G, Lagerqvist B, Fröbert O, Nilsson J, Olivecrona G, Omerovic E, Saleh N, Venetzanos D, James S. Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J.* 2012;33:606-13.

82. Kedhi E, Stone GW, Kereiakes DJ, Serruys PW, Parise H, Fahy M, Simonton CA, Sudhir K, Sood P, Smits PC. Stent thrombosis: insights on outcomes, predictors and impact of dual antiplatelet therapy interruption from the SPIRIT II, SPIRIT III, SPIRIT IV and COMPARE trials. *EuroIntervention.* 2012;8:599-606.

83. Gwon HC, Hahn JY, Park KW, Song YB, Chae IH, Lim DS, Han KR, Choi JH, Choi SH, Kang HJ, Koo BK, Ahn T, Yoon JH, Jeong MH, Hong TJ, Chung WY, Choi YJ, Hur SH, Kwon HM, Jeon DW, Kim BO, Park SH, Lee NH, Jeon HK, Jang Y, Kim HS. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus

Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. *Circulation*. 2012;125:505-13.

84. Valgimigli M, Borghesi M, Tebaldi M, Vranckx P, Parrinello G, Ferrari R; PROlonging Dual antiplatelet treatment after Grading stent-induced Intimal hyperplasia studY Investigators. Should duration of dual antiplatelet therapy depend on the type and/or potency of implanted stent? A pre-specified analysis from the PROlonging Dual antiplatelet treatment after Grading stent-induced Intimal hyperplasia studY (PRODIGY). *Eur Heart J.* 2013;34:909-19.

85. Heestermans AA, van Werkum JW, Zwart B, van der Heyden JA, Kelder JC, Breet NJ, van't Hof AW, Dambrink JH, Koolen JJ, Brueren BR, Zijlstra F, ten Berg JM. Acute and subacute stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: incidence, predictors and clinical outcome. *J Thromb Haemost.* 2010;8:2385-93.

86. Kuchulakanti PK, Chu WW, Torguson R, Ohlmann P, Rha SW, Clavijo LC, Kim SW, Bui A, Gevorkian N, Xue Z, Smith K, Fournadjieva J, Suddath WO, Satler LF, Pichard AD, Kent KM, Waksman R. Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus- and paclitaxel-eluting stents. *Circulation*. 2006;113:1108-13.

87. Farb A, Boam AB. Stent thrombosis redux - the FDA perspective. *N Engl J Med.* 2007;356:984-7.

88. Hawn MT, Graham LA, Richman JS, Itani KM, Henderson WG, Maddox TM. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. *JAMA.* 2013;310:1462-72.

89. Dunning J, Versteegh M, Fabbri A, Pavie A, Kolh P, Lockowandt U, Nashef SA; EACTS Audit and Guidelines Committee. Guideline on antiplatelet and anticoagulation management in cardiac surgery. *Eur J Cardiothorac Surg.* 2008;34:73-92.

90. Cerfolio RJ, Minnich DJ, Bryant AS. General thoracic surgery is safe in patients taking clopidogrel (Plavix). *J Thorac Cardiovasc Surg.* 2010;140:970-6.

91. Liapis CD, Bell PR, Mikhailidis D, Sivenius J, Nicolaides A, Fernandes e Fernandes J, Biasi G, Norgren L; ESVS Guidelines Collaborators. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. *Eur J Vasc Endovasc Surg.* 2009;37:1-19.

92. Moll FL, Powell JT, Fraedrich G, Verzini F, Haulon S, Waltham M, van Herwaarden JA, Holt PJ, van Keulen JW, Rantner B, Schlösser FJ, Setacci F, Ricco JB. European Society for Vascular Surgery. Management of abdominal aortic aneurysms clinical practice guidelines of the European Society for Vascular Surgery. *Eur J Vasc Endovasc Surg.* 2011;41:S1-S58.

93. Payne DA, Jones CI, Hayes PD, Thompson MM, London NJ, Bell PR, Goodall AH, Naylor AR. Beneficial effects of clopidogrel combined with aspirin in reducing cerebral emboli in patients undergoing carotid endarterectomy. *Circulation*. 2004;109:1476-81.

94. Rosenbaum A, Rizvi AZ, Alden PB, Tretinyak AS, Graber JN, Goldman JA, Sullivan TM. Outcomes related to antiplatelet or anticoagulation use in patients undergoing carotid endarterectomy. *Ann Vasc Surg.* 2011;25:25-31.

95. Neilipovitz DT, Bryson GL, Nichol G. The effect of perioperative aspirin therapy in peripheral vascular surgery: a decision analysis. *Anesth Analg.* 2001;93:573-80.

96. Stone DH, Goodney PP, Schanzer A, Nolan BW, Adams JE, Powell RJ, Walsh DB, Cronenwett JL; Vascular Study Group of New England. Clopidogrel is not associated with major bleeding complications during peripheral arterial surgery. *J Vasc Surg.* 2011;54:779-84.

97. Fleming MD, Stone WM, Scott P, Chapital AB, Fowl RJ, Money SR. Safety of carotid endarterectomy in patients concurrently on clopidogrel. *Ann Vasc Surg.* 2009;23:612-5.

98. Payne DA, Twigg MW, Hayes PD, Naylor AR. Antiplatelet agents and risk factors for bleeding postcarotid endarterectomy. *Ann Vasc Surg.* 2010;24:900-7.

99. Markus HS, Droste DW, Kaps M, Larrue V, Lees KR, Siebler M, Ringelstein EB. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using Doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. *Circulation*. 2005;111:2233-40.

100. Sharpe RY, Dennis MJ, Nasim A, McCarthy MJ, Sayers RD, London NJ, Naylor AR. Dual antiplatelet therapy prior to carotid endarterectomy reduces post-operative embolisation and thromboembolic events: post-operative transcranial Doppler monitoring is now unnecessary. *Eur J Vasc Endovasc Surg.* 2010;40:162-7.

101. Luckie M, Khattar RS, Fraser D. Noncardiac surgery and antiplatelet therapy following coronary artery stenting. *Heart.* 2009;95:1303-8.

102. O'Riordan JM, Margey RJ, Blake G, O'Connell PR. Antiplatelet agents in the perioperative period. *Arch Surg.* 2009;144:69-76.

103. Kotsovolis G, Komninos G, Kyrgidis A, Papadimitriou D. Preoperative withdrawal of antiplatelet treatment in lower limb vascular patients prior to surgical management under epidural or spinal anaesthesia: an evidence based approach and systematic review. *Int Angiol.* 2010;29:475-81.

104. Boustière C, Veitch A, Vanbiervliet G, Bulois P, Deprez P, Laquiere A, Laugier R, Lesur G, Mosler P, Nalet B, Napoleon B, Rembacken B, Ajzenberg N, Collet JP, Baron T, Dumonceau JM; European Society of Gastrointestinal Endoscopy. Endoscopy and antiplatelet agents. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy.* 2011;43:445-61.

105. Guerci Ph, Audibert G, Mertes PM. Management of chronic anticoagulant and antiplatelet treatment before scheduled neurosurgery. *Neurochirurgie.* 2009;55:H17-22.

106. Korinth MC. Low-dose aspirin before intracranial surgery - results of a survey among neurosurgeons in Germany. *Acta Neurochir.* 2006;148:1189-96.

107. Lehot JJ, Piriou V, Durand de Gevigney G, Coriat P. Patient at risk of endocoronary stent thrombosis during perioperative period: a frequent situation. *Ann Fr Anesth Reanim.* 2005;24:1247-9.

108. Di Roio C, Gaillac N, Pélissou I, Carillon R, Dailler F. Drug-eluting stent, intraventricular haemorrhage, ventricular drainage, favourable outcome. *Ann Fr Anesth Reanim.* 2007;26:91-2.

109. Mantz J, Samama CM. The national STRATAGEM study: the success needs everyone's contribution! *Ann Fr Anesth Reanim.* 2006;25:133-4.
110. Herth FJ, Becker HD, Ernst A. Aspirin does not increase bleeding complications after transbronchial biopsy. *Chest.* 2002;122:1461-4.
111. Chinsky K. Bleeding risk and bronchoscopy: in search of the evidence in evidence-based medicine. *Chest.* 2005;127:1875-7.
112. Johnson JR, Chin R, Conforti J. Bronchoscopic myths and legends: anti-platelet medications. *Clinical Pulmonary Medicine.* 2005;12:363-5.
113. Ernst A, Eberhardt R, Wahidi M, Becker HD, Herth FJ. Effect of routine clopidogrel use on bleeding complications after transbronchial biopsy in humans. *Chest.* 2006;129:734-7.
114. Pototski M, Amenábar JM. Dental management of patients receiving anticoagulation or antiplatelet treatment. *J Oral Sci.* 2007;49:253-8.
115. Elad S, Chackartchi T, Shapira L, Findler M. A critically severe gingival bleeding following non-surgical periodontal treatment in patients medicated with anti-platelet. *J Clin Periodontol.* 2008;35:342-5.
116. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G. Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. *Am J Cardiol.* 2011;108:964-7.
117. Krishnan B, Shenoy NA, Alexander M. Exodontia and antiplatelet therapy. *J Oral Maxillofac Surg.* 2008;66:2063-6.
118. Napenas JJ, Hong CH, Brennan MT, Furney SL, Fox PC, Lockhart PB. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual antiplatelet therapy. *J Am Dent Assoc.* 2009;140:690-5.
119. Kobayashi H. Evaluation of the need to discontinue antiplatelet and anticoagulant medications before cataract surgery. *J Cataract Refract Surg.* 2010;36:1115-9.
120. Barequet IS, Sachs D, Shenkman B, Priel A, Wasserzug Y, Budnik I, Moisseiev J, Salomon O. Risk assessment of simple phacoemulsification in patients on combined anticoagulant and antiplatelet therapy. *J Cataract Refract Surg.* 2011;37:1434-8.
121. Mason JO 3rd, Frederick PA, Neimkin MG, White MF Jr, Feist RM, Thomley ML, Albert MA Jr. Incidence of hemorrhagic complications after intravitreal bevacizumab (avastin) or ranibizumab (lucentis) injections on systemically anticoagulated patients. *Retina.* 2010;30:1386-9.
122. Kumar N, Jivan S, Thomas P, McLure H. Sub-Tenon's anesthesia with aspirin, warfarin, and clopidogrel. *J Cataract Refract Surg.* 2006;32:1022-5.
123. Joseph JJ, Pillai A, Bramley D. Clopidogrel in orthopaedic patients: a review of current practice in Scotland. *Thromb J.* 2007;5:6.
124. Collinge CA, Kelly KC, Little B, Weaver T, Schuster RD. The effects of clopidogrel (Plavix) and other oral anticoagulants on early hip fracture surgery. *J Orthop Trauma.* 2012;26:568-73.
125. Kariotis I, Philippou P, Volanis D, Serafetinides E, Delakas D. Safety of ultrasound-guided transrectal extended prostate biopsy in patients receiving low-dose aspirin. *Int Braz J Urol.* 2010;36:308-16.
126. Enver MK, Hoh I, Chinegwundoh FI. The management of aspirin in transurethral prostatectomy: current practice in the UK. *Ann R Coll Surg Engl.* 2006;88:280-3.
127. Carmignani L, Picozzi S, Stubinski R, Casellato S, Bozzini G, Lunelli L, Arena D. Endoscopic resection of bladder cancer in patients receiving double platelet antiaggregant therapy. *Surg Endosc.* 2011;25:2281-7.
128. Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK, Wang TY, Gibler WB, Ohman EM, Roe MT, Pollack CV Jr, Peterson ED, Alexander KP. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) Bleeding Score. *Circulation*. 2009;119:1873-82.
129. Mehran R, Pocock SJ, Nikolsky E, Clayton T, Dangas GD, Kirtane AJ, Parise H, Fahy M, Manoukian SV, Feit F, Ohman ME, Witzenbichler B, Guagliumi G, Lansky AJ, Stone GW. A risk score to predict bleeding in patients with acute coronary syndromes. *J Am Coll Cardiol.* 2010;55:2556-66.
130. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest.* 2010;138:1093-100.
131. Savonitto S, D'Urbano M, Caracciolo M, Barlocco F, Mariani G, Nichelatti M, Klugmann S, De Servi S. Urgent surgery in patients with a recently implanted coronary drug-eluting stent: a phase II study of "bridging" antiplatelet therapy with tirofiban during temporary withdrawal of clopidogrel. *Br J Anaesth.* 2010;104:285-91.
132. Wessler JD, Saldana F, Giugliano RP. Bridging therapy after recent stent implantation: case report and review of data. *Cardiovasc Revasc Med.* 2012;13:30-8.
133. Pickett AM, Taylor DA, Ackman ML. Prolonged infusion of eptifibatide as bridge therapy between bare-metal stent insertion and cardiovascular surgery: case report and review of the literature. *Pharmacotherapy.* 2010;30:127e-33e.
134. Bigalke B, Seizer P, Geisler T, Lindemann S, Gawaz M, May AE. Perioperative antiplatelet therapy in patients at risk for coronary stent thrombosis undergoing noncardiac surgery. *Clin Res Cardiol.* 2009;98:335-9.
135. Angiolillo DJ, Firstenberg MS, Price MJ, Tummala PE, Hutyra M, Welsby IJ, Voeltz MD, Chandna H, Ramaiah C, Brtko M, Cannon L, Dyke C, Liu T, Montalescot G, Manoukian SV, Prats J, Topol EJ; BRIDGE Investigators. Bridging antiplatelet therapy with cangrelor in patients undergoing cardiac surgery: a randomized controlled trial. *JAMA.* 2012;307:265-74.

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Appendix

Supplement to: Perioperative management of antiplatelet therapy in patients with coronary stents undergoing cardiac and non-cardiac surgery: a consensus document from Italian cardiological, surgical and anaesthesiological societies

Acknowledgements

Piersilvio Gerometta[1], Enrico Guffanti[2], Giada Beltramini[3], Luca Devalle[4], Sergiomaria Gaini[5], Stefano Corbella[6], Antonio Castelli[7], Emanuela Menozzi[7], Alessandro Locatelli[8], Lorenzo Mantovani[9], Nicolina Russo[10], Gennaro Savoia[11]

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Federazione Italiana delle Società scientifiche delle Malattie dell'Apparato Digerente (Marco Soncini, Giancarlo Spinzi, Maurizio Vecchi)
Associazione Ostetrici Ginecologi Ospedalieri Italiani Lombardia (Claudio Crescini, U.O. Ostetricia Ginecologia Ospedale di Treviglio (BG), Italy)
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Online Table 1. Maxillofacial surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	Closed reduction of zygomatic arch fracture, closed reduction of mandibular fracture; lipofilling; arthrocentesis and temporomandibular joint arthroscopy, skin cancer surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	Implantology and oral surgery, closed reduction of nasal bone fracture, open reduction of jaw fracture; parotidectomy, orthognathic surgery, facial reanimation paralysis in acute and chronic	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
	High risk	Radical and reconstructive cancer surgery of head and neck; open reduction of fracture orbito-zygomatic arch; sialoadenectomy submandibular	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [113-118]. ASA: aspirin

Online Table 2. Plastic surgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	Excision and suturing small epitheliomas and small benign skin lesions, scarring correction, treatment of soft tissue pathology of the hand (carpal tunnel, trigger finger, tendon and articular cysts, Dupuytren). Upper blepharoplasty, lower blepharoplasty, rhinoplasty, otoplasty, breast reconstruction after total removal (mastectomy) or part (quadrantectomy) for oncological reasons, positioning with artificial implants. Breast augmentation; lifting; flap microsurgical breast reconstruction, removal of tumours of considerable extent of face and neck soft tissues and plastic reconstruction using microsurgical flap	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	Treatment of breast abnormalities (asymmetry, tuberous breasts, tubular breasts, etc). Treatment of gynecomastia. Lower, upper limbs liposuction and abdomen of medium entity. Functional treatment of trauma (car accidents, surgery outcomes, etc.), loss of substance after demolishing of medium entity in the detail of the face, the region of peri-ocular (eyelid scars with functional alteration), upper and lower limbs peribuccal, by local flaps, skin graft, with or without use of artificial dermal substitute. Treat leg ulcers (ASA Class II - I). Correcting scars and depressions (lipofilling) of medium entity. Surgical treatment of burns (10% <X <15%). Facelift, breast reduction, abdominoplasty	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
	High risk	Functional treatment of trauma (car accidents, surgery outcomes, etc.), loss of substance after demolishing of substantial entity, especially of face and upper and lower limbs, abdomen, back, using microsurgical flaps or multi-tissue pedicled flaps of substantial entity. Lower limbs, upper abdomen serious liposuction. Surgical treatment of burns (>15%). Treat leg ulcers (ASA Class V - IV - III). Correcting scars and depressions (lipofilling) of significant entity. Post surgery – Bariatric surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References: [8-10, 12-15, 66]. ASA: aspirin; ASA class: American Society of Anesthesiology classification

Online Table 3. Gynaecology.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Diagnostic hysteroscopy with endometrial biopsy and polypectomy, rectoscopic hysteroscopy polypectomy, metroplasty, dilatation and curettage of uterus (D & C), – Cervical conisation with diathermy loop (LEEP), – Marsupialisation / Bartholins gland/cyst removal, laparoscopic removal / laparotomic annex for benign disease, laparoscopy / laparotomy for mild endometriosis, tubal sterilisation hysteroscopic/ laparoscopic, diagnostic laparoscopy or with minimal operation (simple adhesiolysis, endometriotic implants DTC)	ASA: continue $P2Y_{12}$ receptor inhibitors: continue - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Resettoscopic hysteroscopy /myomectomy, endometrial ablation – Laparoscopy / laparotomy for endometriosis (intermediate) – Simple abdominal hysterectomy for benign disease – Simple vaginal hysterectomy for benign disease / prolapse – Fascial vaginal reparative surgery (repair cystocele / rectocele) – Reparative vaginal prosthetic surgery – Radical Vulvar Surgery – Omentectomy	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
	High risk	– Laparotomy or laparoscopic hysterectomy for large uteri (>750 g) – Myomectomy laparotomic / laparoscopic – Laparoscopy / laparotomy for severe/deep endometriosis – Debulking surgery for ovarian cancer – Radical surgery for carcinoma of cervix and endometrium – Pelvic/ lombo-aortic lymphadenectomy – Pelvic evisceration	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. ASA: aspirin; DTC: diathermocoagulation

Online Table 4. Neurosurgery.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Spinal neurosurgery: disc herniation, laminectomy (≤2 spaces) without arthrodesis – Cranial neurosurgery: external ventricular derivation, intraventricular catheter placement for intracranial pressure monitoring, intraventricular reservoir placement	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Urgency: haemorrhage, cerebral oedema ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)[b]	Elective surgery: postpone Urgency: haemorrhage, cerebral oedema ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Spinal neurosurgery: laminectomy >2 spaces, spinal arthrodesis (any type) – Cranial neurosurgery: ventriculoperitoneal shunt, removal of extradural lesion	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Urgency: brain/spinal haematoma ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)[b]	Elective surgery: postpone Urgency: haematoma brain injury/ spinal ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)[b]
	High risk	– Spinal and cranial neurosurgery: removal of intradural lesions (intracerebral tumours, intraparenchymal haemorrhage)	ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)	Elective surgery: postpone Non-deferrable surgery: ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)[b] Urgency: intracerebral haematoma (platelet transfusion to be discussed)	Elective surgery: postpone Non-deferrable surgery: ASA: discontinue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Restart of antiplatelet therapy to be discussed (with a loading dose)[b] Urgency: intracerebral haematoma (platelet transfusion to be discussed)

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [105-108]. ASA: aspirin

Online Table 5. Interventional pulmonology.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Bronchoscopic inspection – Bronchoaspiration – Bronchoalveolar lavage	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective procedure: postpone Non-deferrable procedure: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective procedure: postpone Non-deferrable procedure: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Bronchial biopsy – Transbronchial needle aspiration	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective procedure: postpone Non-deferrable procedure: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective procedure: postpone Non-deferrable procedure: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
	High risk	– Lung and transbronchial biopsy – Rigid bronchoscopy – Medical thoracoscopy	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective procedure: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective procedure: postpone Non-deferrable procedure: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [110-114]. ASA: aspirin

Online Table 6. Dentistry.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Non-surgical periodontal therapy (including supragingival scaling); – Endodontic therapy; – Rubber dam positioning	ASA: continue $P2Y_{12}$ receptor inhibitors: continue	ASA: continue $P2Y_{12}$ receptor inhibitors: continue	ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Surgical periodontal therapy (resective surgery, regenerative surgery, mucogingival surgery) – Oral surgery in general (teeth extractions, pre-prosthetic reconstructive surgery), implant surgery	ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	High risk	–	–	–	–

References [113-118]. ASA: aspirin

Online Table 7. Ophthalmology.

			Thrombotic risk		
			Low risk	Intermediate risk	High risk
Haemorrhagic risk	Low risk	– Intravitreal injections – Cataract surgery – Peribulbar anaesthesia	Elective surgery: not contraindicated ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: continue
	Intermediate risk	– Vitrectomy – Trabeculectomy	ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose[b]	Elective surgery: postpone Non-deferrable surgery: ASA: continue $P2Y_{12}$ receptor inhibitors: - Discontinue 5 days before[a] - Resume within 24-72 hours, with a loading dose Bridge therapy with GP IIb/IIIa inhibitors[b]
	High risk	–	–	–	–

[a] 7 days prior for prasugrel; [b] collegial discussion of risk, even with family/patient. References [119-122]. ASA: aspirin