

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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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be continued perioperatively in the majority of surgical operations, whereas dual antiplatelet therapy should not be withdrawn for surgery in the case of low bleeding risk.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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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 consequences¹⁻⁶. On the other hand, antiplatelet therapy can significantly raise intraoperative haemorrhagic risk in surgical or endoscopic procedures⁷.

Editorial, see page 17

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 surgery⁸⁻¹⁸. 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 strategy¹³. 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 creation¹⁹. 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 document¹⁹. 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 implanted²², 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 prognosis²³.

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 years²². 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 thrombosis²². On the other hand, bleeding risk might be 3.4 times higher during dual antiplatelet therapy compared to aspirin alone²⁵.

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

Aspirin can significantly reduce the risk of cardio-cerebrovascular events in secondary prevention²⁶. Abrupt discontinuation of aspirin therapy can be associated with a “rebound” effect²⁷ 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 stenting³⁴.

The increase of MACE might, in part, be due to the perioperative discontinuation of antiplatelet therapy³⁵⁻³⁷. In Schouten's series, the MACE rate was 2.6% in the overall population, which increased to 13.3% in patients undergoing early surgery³⁷. 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 implantation⁴⁰, even though data are not consistent⁴¹. In a recent study by Wijeysondera and colleagues⁴², 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 disease⁴³⁻⁴⁶, 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 therapy⁴⁹. 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 therapy⁴⁹. 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 treatment⁴⁵, but the precise risk of spinal or epidural haematoma with dual antiplatelet therapy is unknown⁴⁶.

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 P2Y₁₂ 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 alone⁵¹. 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 therapy²⁹. 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 patients³⁵. 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 study³⁷ 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 consistent⁵⁸. 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 complications⁶²⁻⁶⁴. 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 reintervention⁶⁷. In patients with femoral fracture, perioperative clopidogrel therapy does not seem to be associated with a significant increase in mortality and morbidity⁶⁸.

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 P2Y₁₂ 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 trial⁷⁴, 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 groups⁷⁴.

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 published⁸⁻¹⁸. 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 effect⁷⁵.

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 therapy⁹. 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 surgery⁸³, 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 >12 months after PCI with DES	>1 month <6 months after PCI with BMS >6 <12 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)	<1 month after PCI with BMS <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)
<p>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</p>		

Of note, second-generation DES have been developed with an improved design that may help to overcome the current limitations of the first-generation DES⁸¹. Improved stent designs with thinner struts and more biocompatible polymers may enhance endothelial coverage and functional recovery⁸¹⁻⁸³. 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 necessary⁷⁹⁻⁸³.

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 surgery⁸⁸. 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 comorbidities¹²⁸⁻¹³⁰. 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	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	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, duodenocephalopansectomy 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 eptifibatide¹³²⁻¹³⁴. 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). P2Y₁₂ 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 P2Y₁₂ 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 eptifibatid 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 period²⁹. 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.

		Thrombotic risk			
		Low risk	Intermediate risk	High risk	
Haemorrhagic 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.

		Thrombotic risk			
		Low risk	Intermediate risk	High risk	
Haemorrhagic 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 P2Y₁₂ 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 necessary¹³⁵.

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.

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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

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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

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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 / laparotomy 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	- Resectoscopic 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> – 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	<ul style="list-style-type: none"> – 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	<ul style="list-style-type: none"> – 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	<ul style="list-style-type: none"> – 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