Special article

Perioperative and Periprocedural Management of Antithrombotic Therapy: Consensus Document of SEC, SEDAR, SEACV, SECTCV, AEC, SECPRE, SEPD, SEGO, SEHH, SETH, SEMERGEN, SEMFYC, SEMG, SEMICYUC, SEMI, SEMES, SEPAR, SENEC, SEPA, SERVEI, SECTO and AEU

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ABSTRACT

During the last few years, the number of patients receiving anticoagulant and antiplatelet therapy has increased worldwide. Since this is a chronic treatment, patients receiving it can be expected to need some kind of surgery or intervention during their lifetime that may require treatment discontinuation. The decision to withdraw antithrombotic therapy depends on the patient’s thrombotic risk versus hemorrhagic risk. Assessment of both factors will show the precise management of anticoagulant and antiplatelet therapy in these scenarios. The aim of this consensus document, coordinated by the Cardiovascular Thrombosis Working Group of the Spanish Society of Cardiology, and endorsed by most of the Spanish scientific societies of clinical specialties that may play a role in the patient-health care process during the perioperative or periprocedural period, is to recommend some simple and practical guidelines with a view to homogenizing daily clinical practice.© 2018 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

INTRODUCTION

The number of patients on anticoagulant therapy has risen significantly in recent years. In Spain alone, over 800,000 patients are estimated to be taking anticoagulants, mainly for atrial fibrillation (AF).1 Use of antiplatelet drugs is also rising because these drugs are prescribed for the secondary prevention of atherosclerotic disease and because there has been a rise in the number of percutaneous coronary interventions (PCIs) and stent implantations.2–6 As most patients on antithrombotic therapy have chronic disease, at some point in their lives they will more than likely need surgery or an invasive procedure that requires temporary interruption of their anticoagulant or antiplatelet therapy.7 Decisions regarding interruptions in antiplatelet therapy are particularly important, as premature withdrawal has been linked to a higher risk of cardiovascular events, including stent thrombosis.8 The decision to continue or discontinue therapy prior to a surgical intervention or invasive procedure should be taken following an evaluation of thrombotic and bleeding risk. In short, both anticoagulation and antiplatelet management strategies will be determined by the interaction between these 2 risk factors.9–17

Although numerous guidelines have been published on the perioperative management of antithrombotic therapy, their application to clinical practice is limited.7,9–17 Many of the publications address only some of the players involved in perioperative care (eg, surgeons or anesthesiologists), while others focus on specific areas of action (eg, endoscopic procedures) or have become obsolete following the appearance of new pharmacologic treatments. To address these shortcomings, a working group formed by members of the majority of Spanish scientific societies that represent professionals involved in perioperative or periprocedural care was created under the supervision of the Spanish Cardiology Society (Table 1). One of the outcomes of this group was the current consensus document, which is designed to provide a series of clear, practical recommendations on the management of antithrombotic drugs in patients undergoing

Abbreviations

AF: atrial fibrillation
DAPT: dual antiplatelet therapy
DES: drug-eluting stent
DOAC: direct oral anticoagulant
PCI: percutaneous coronary intervention
VKA: vitamin K antagonist
surgery or other procedures that require the temporary interruption of anticoagulant or antiplatelet therapy. The ultimate aim of these recommendations, which are endorsed by each of the participating societies, is to help standardize clinical practice.

**THROMBOEMBOLIC RISK**

**Anticoagulant Therapy**

Thromboembolic risk associated with the indication for anticoagulant therapy (a mechanical heart valve, AF, or venous thromboembolism) is classified as high when the annual risk of arterial or venous thromboembolism is greater than 10%, moderate when it is between 5% and 10%, and low when it is less than 5%. Recent recommendations that use CHADS₂ scores for stroke risk assessment were taken into account for patients with AF. The risk stratification for thromboembolism according to the indication for anticoagulant therapy is presented in Table 3.

**Antiplatelet Therapy**

The following aspects should be considered when defining thrombotic risk associated with atherosclerotic conditions that require antiplatelet therapy: time to intervention, disease

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**Table 1**

Scientific Societies That Participated in the Working Group and Endorse the Recommendations in This Consensus Document

<table>
<thead>
<tr>
<th>Scientific Societies That Participated in the Working Group and Endorse the Recommendations in This Consensus Document</th>
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**Table 2**

Stratification of Thromboembolic Risk in Patients on Anticoagulant Therapy

<table>
<thead>
<tr>
<th>Risk</th>
<th>Indication for anticoagulant therapy</th>
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<tbody>
<tr>
<td>High</td>
<td>CHADS₂-VASc score 7-9 Stroke/TIA in last 3 mo, Rheumatic mitral valve disease</td>
</tr>
<tr>
<td></td>
<td>Recent VTE (in last 3 mo) Severe thrombophilia (homozygous factor V Leiden, prothrombin 20210,</td>
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<td></td>
<td>protein C, protein S, or antithrombin deficiency, multiple defects, antiphospholipid syndrome)</td>
</tr>
<tr>
<td>Moderate</td>
<td>CHADS₂-VASc 5-6 Stroke/TIA &gt; 3 mo ago, VTE in last 3-12 mo Nonsevere thrombophilia (heterozygous</td>
</tr>
<tr>
<td></td>
<td>factor V Leiden or prothrombin 20210 A mutation) VTE + active cancer</td>
</tr>
<tr>
<td>Low</td>
<td>CHADS₂-VASc 1-4 No history of stroke/TIA, VTE &gt; 12 mo previously</td>
</tr>
</tbody>
</table>

*AF, atrial fibrillation; DM, diabetes mellitus; HF, heart failure; TIA, transient ischemic attack; VTE, venous thromboembolism.

1 CHADS₂-VASc: 1 point for heart failure, hypertension, diabetes mellitus, female sex, age 65–74 y, and vascular disease (peripheral artery disease, ischemic heart disease, or complicated aortic plaque) and 2 points for age ≥ 75 y and a history of stroke, TIA, or peripheral embolism.
Table 3
Stratification of Thrombotic Risk in Patients on Antiplatelet Therapy

<table>
<thead>
<tr>
<th>Risk</th>
<th>Time on treatment (mo)</th>
<th>Reason for antiplatelet therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute coronary syndrome</td>
<td>Stable coronary disease</td>
</tr>
<tr>
<td>High</td>
<td>&lt; 3</td>
<td>Medical treatment</td>
</tr>
<tr>
<td></td>
<td>&lt; 6</td>
<td>PCI + BMS/DES/DEB or CABG</td>
</tr>
<tr>
<td></td>
<td>&lt; 12</td>
<td>PCI + BMS/DES/DEB or CABG</td>
</tr>
<tr>
<td>Moderate</td>
<td>3-6</td>
<td>Medical treatment</td>
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<td></td>
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<tr>
<td>Low</td>
<td>&gt; 6</td>
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</tr>
<tr>
<td></td>
<td>&gt; 12</td>
<td>PCI + BMS/DES/DEB or CABG</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; CABG, coronary artery bypass grafting; CRF, chronic renal failure; DES, drug-eluting balloon; DM, diabetes mellitus; HF, heart failure; LVEF, left ventricle ejection fraction; TIA, transient ischemic attack.

a Particularly high risk of thrombosis during the first month.
b Associated risk factors: history of stroke/TIA, DM, CRF, complex procedure (long, multiple, or overlapping stents, bifurcation or left main stents, or stents in single vessels, vessels < 2.5 mm or saphenous vein grafts).

presentation (acute vs stable), the patient’s clinical characteristics, and the treatment received (PCI and stent type, surgery, or medical treatment only). It is important to emphasize that these risks have not been evaluated in clinical trials and that the recommendations presented are based on observational and retrospective studies and consensus documents by other groups. Based on a combination of the above factors, risk of thrombosis in patients taking antiplatelet agents is classified as high, moderate, or low, as shown in Table 3.13,20

Time from the ischemic event to the intervention is the most important determinant of events related to the interruption of dual antiplatelet therapy (DAPT) prior to surgery or an invasive procedure. Recent findings indicate that patients who undergo emergency surgery or surgery within 6 months of stent placement have an increased risk of thrombosis. The recommendations of the Cardiovascular Thrombosis Working Group of the Spanish Cardiology Society on the optimal duration of DAPT in patients with atherothrombotic disease are summarized in Figure 1.23,24

Stent type is another important factor when evaluating thrombotic risk. PCI with a first-generation drug-eluting stent (DES) vs a bare metal stent is associated with a higher incidence of late and very late stent thrombosis. Second-generation DESs, however, offer greater safety as they incorporate improved design features and polymer coatings. They have even been associated with a lower incidence of thrombosis than metal stents. In addition, the emergence of new platforms and PCIs with drug-eluting balloons is driving the search for devices that offer increased safety without compromising effectiveness. Although experience with bioabsorbable vascular scaffolds is still limited, several studies have reported a higher incidence of long-term stent thrombosis with their use. The recommendation in such cases is to maintain DAPT for at least 12 months. Finally, patients who have undergone coronary artery bypass grafting or noninvasive medical treatment have a much lower risk of complications, as the risk of stent thrombosis, which is frequently catastrophic, is eliminated.

Another important consideration is acute vs stable disease. Patients with acute coronary syndrome have a greater risk of thrombosis than those with stable coronary artery disease. Comorbidity should also be evaluated. Conditions such as diabetes mellitus, chronic kidney disease, severe left ventricular dysfunction, and a history of stroke and/or transient ischemic attack have
Figure 1. Recommendations on the optimal duration of dual antiplatelet therapy for patients with atherothrombotic disease. A, aspirin; BMS, bare metal stent; BVS, bioabsorbable vascular scaffold; C, clopidogrel; CABG, coronary artery bypass grafting; DEB, drug-eluting balloon; DES, drug-eluting stent; P, prasugrel; PCI, percutaneous coronary intervention; T, ticagrelor. Adapted with permission from Gómez-Polo et al.23.
traditionally been associated with an increased risk of thrombosis.26
Patients who have undergone a complex PCI (placement of long, multiple, or overlapping stents, bifurcation or left main stents, or stents in vessels < 2.5 mm or saphenous vein grafts) should also be
taken into consideration to have an increased risk of thrombosis.28

Surgical intervention in patients with a recent history of stroke is a risk factor for new events, particularly in the 30 days following
the stroke and after discontinuation of antplatelet therapy.29 Stent
thrombosis associated with peripheral artery disease has mainly
been described in the first month. The risk is greatest in patients
with DESs or stents used to treat chronic occlusions. The recent
guidelines on the diagnosis and treatment of peripheral arterial
diseases recommend DAPT for at least 1 month in patients who
have undergone stenting for lower-extremity peripheral artery
disease, regardless of stent type.24

BLEEDING RISK

Bleeding risk, like thrombotic risk, is stratified into 3 levels
according to the characteristics of the procedure the patient is to
undergo.7,10,13,16 Procedures with a low bleeding risk are those in
which adequate hemostasis can be achieved and in which bleeding
would not jeopardize the patient’s life, affect the outcome of
surgery, or require transfusion. Procedures with a moderate
bleeding risk, in turn, are those in which it may be difficult to
secure hemostasis or in which bleeding would increase the
likelihood of the need for a transfusion or a repeat operation.
Finally, procedures with a high bleeding risk are those in which
perioperative bleeding could place the patient’s life at risk or
compromise the outcome of surgery. The stratification of risk for
nonsurgical procedures (interventional cardiology, endoscopies,
bronchoscopies, dental procedures, or vascular and interventional
radiology) is less clear, as it is often not possible to achieve
adequate primary hemostasis or compression in such cases. We
therefore recommend considering percentages of risk and
classifying procedures with a risk of less than 1% as low-risk
procedures and others as moderate-to-high-risk procedures.
Another useful factor for assessing risk is the potential severity
of bleeding, which will vary according to location or the likelihood
of achieving adequate hemostasis. We have summarized the most
common surgeries and procedures identified by each of the
scientific societies according to risk of bleeding in Table 1 of the
supplementary material.5,9,10,13,16,30

Although bleeding risk is mainly influenced by type of
procedure, it can be increased by factors inherent to the patient
and/or the environment.30 In general, these factors are already
covered in risk assessment systems for common diseases, such as
AF and acute coronary syndrome, and include age > 65 years,
kidney/liver failure, and concomitant pharmacological treatment
that can alter hemostasis (eg, combination of antplatelet and
anticoagulant therapy).31–33 Other factors are a history of
spontaneous bleeding in the 3 months before the intervention
or in previous interventions, thrombocytopenia and/or thrombo-
pathy, and variations in the international normalized ratio in
patients being treated with a vitamin K antagonist (VKA).34

RECOMMENDATIONS FOR STOPPING AND RESTARTING
ANTICOAGULANT THERAPY

We have established a series of simple recommendations to
guide perioperative/periprocedural anticoagulation strategies
according to the risk of thromboembolism and bleeding. These
recommendations are summarized in the algorithm shown in
Figure 2.9,16,30,34

Is It Necessary to Stop Anticoagulant Therapy?

In general, anticoagulant therapy should be stopped before the
vast majority of surgical and other invasive procedures. There are,
however, cases in which maintaining treatment carries a very low
risk of bleeding that may be acceptable to the operator.35 The
BRUISE CONTROL trial36 showed that maintaining VKA therapy
(INR < 3) in patients with a high risk of thromboembolism who
required pacemaker or defibrillator surgery was associated with a
lower risk of bleeding than bridging therapy with low-molecular-
weight heparin (LMWH).37 The recent results of the BRUISE
CONTROL-2 trial showed no differences in the incidence of ischemic
and/or bleeding events between patients who stopped and
who continued taking direct oral anticoagulants (DOACs).38
In the COMPARE trial of patients with pulmonary vein catheter
ablation, those who discontinued anticoagulant therapy with an
oral VKA (INR 2–3) had a lower risk of bleeding and thromboem-
bolism events than those who switched to LMWH.39 Although recent
evidence suggests that certain procedures are safe when DOAC
therapy is not withdrawn, more studies are needed to allow a
definitive recommendation.39 In conclusion, this working group
recommends considering not stopping anticoagulant therapy for
low-risk procedures with a risk of very minor or clinically
insignificant bleeding deemed acceptable by the operator
(Table 1 of the supplementary material).

When Should Anticoagulant Therapy Be Stopped?

The moment at which anticoagulant therapy should be stopped
is largely determined by the drug’s elimination route. VKAs are
metabolized mainly through the liver and only minimally through
the kidneys. With the exception of patients with a liver disease that
alters drug behavior (and in whom anticoagulants are generally
contraindicated), we recommend stopping acenocoumarol 3 days
before an intervention and warfarin 5 days before (Figure 2).9,16
This recommendation, however, is only applicable to patients with
INR values within the therapeutic range (INR 2–3) 7 days before
the intervention. In patients with supratherapeutic INR values or
scheduled for a procedure with a high risk of bleeding, the moment
for withdrawing anticoagulant therapy will depend on the exact
figure and on the target figure for the operation or procedure.
In patients with subtherapeutic INR values, VKAs can be discontinued
1 day later (2 days before the procedure for acenocoumarol and
4 days for warfarin). INR values should always be checked before
the procedure. In general, the target should be an INR < 1.5.
As DOACs have predictable pharmacokinetics and depend on renal
function, the decision on when to withdraw them will depend on
the creatinine clearance rate and the risk of bleeding associated
with the scheduled procedure.34,40,41

Is Bridging Therapy Necessary?

In general, there is a low risk of thromboembolism when oral
anticoagulant therapy is discontinued without bridging therapy
with heparin.42 In addition, recent data suggest that heparin
bridging is associated with an increased risk of bleeding but does
not confer any benefits in terms of the incidence of thromboem-
bolistic events.43 In the BRIDGE trial, which analyzed bridging
anticoagulation in 1884 patients with AF,44 no significant
differences were observed for rate of thromboembolic events,
but patients in the bridging therapy group experienced more
bleeding episodes than those in the placebo group. The main
limitation of the trial was that it included patients with a low risk
of thromboembolism (exclusion of patients with mechanical heart
valves, a history of stroke in the previous 3 months, and a mean
**Figure 2.** Recommendations for interrupting and reintroducing oral anticoagulants according to type of intervention and the risk of thromboembolism and bleeding. CrCl, creatinine clearance (mL/min); INR, international normalized ratio; LMWH, low-molecular-weight heparin; OAC, oral anticoagulant; UFH, unfractionated heparin; VKA, vitamin K antagonist. *Low-risk procedures with an acceptable risk of very minor or clinically insignificant bleeding for the operator (Table 1 of the supplementary material).* aClassification of thromboembolic risk (Table 2). bClassification of bleeding risk (Table 1 of the supplementary material).

CHADS2 score of 2.3) and a low risk of bleeding (only 11% of the procedures carried a moderate to high risk). A similar trial is currently underway to assess patients with a high risk of thromboembolism (PERIOP-2, NCT00432796).

Based on the available evidence, we recommend only using heparin bridging for patients with a high thromboembolic risk (Table 2). In patients being treated with a VKA, it is sufficient to start LMWH (or unfractionated heparin in patients with kidney failure and creatinine clearance < 30 mL/min) when the INR is less than 2 or, where this value is not available, when 2 to 3 doses of the drug have been omitted. We do not recommend DOACs as bridging therapy (although some protocols still contemplate their use after the omission of 2 to 3 doses of the VKA). The last dose of LMWH should be administered 12 hours before the operation or procedure in the case of prophylactic doses and 24 hours in the case of therapeutic doses. Unfractionated heparin should be administered 4 to 6 hours in advance.

**Restarting Anticoagulant Therapy: When and How?**

Achieving adequate hemostasis during the procedure and absence of postprocedural bleeding are the 2 most important factors to consider when restarting a patient on anticoagulant therapy. The moment at which the drug is to be reintroduced should therefore be decided in conjunction with the surgical/ intervention team. As a general rule, and under the previous proviso, we recommend resuming anticoagulant therapy 24 hours after the procedure. As the anticoagulant effect of VKAs starts to set in at 24 to 72 hours, we recommend using heparin bridging
therapy in patients with a high thromboembolic risk. This is not necessary with DOACs. Reintroduction of oral anticoagulant therapy should be postponed for 48 to 72 hours only in patients with a high risk of postoperative bleeding (Figure 2). If it is not possible to restart oral anticoagulant therapy, we recommend evaluating the option of parenteral anticoagulation, preferably with balanced doses of LMWH to cover the risk of thrombosis and minimize that of bleeding.

**RECOMMENDATIONS FOR STOPPING AND RESTARTING ANTIPLATELET THERAPY**

Decisions regarding antplatelet strategies during the perioperative/periprocedural period depend not only on the balance between thrombotic and bleeding risks but also on the type of antplatelet therapy and the corresponding indication. It is important to note that antplatelet therapy is currently not recommended for primary prevention. A simple algorithm based on a series of questions designed to facilitate decisions on antplatelet strategies is presented in Figure 3.

**Single Versus Dual Antiplatelet Therapy**

Aspirin should be maintained in patients on single antiplatelet therapy, as it has been found to reduce ischemic risk without significantly increasing bleeding risk. Withdrawal for 3 days should only be considered for procedures with a very high risk of bleeding (eg, neurosurgical procedures). Unless contraindicated, a low dose (100 mg/d) should be administered and maintained, although detection of higher doses (eg, 300 mg) before the procedure does not justify deferral. In patients on P2Y12 inhibitor monotherapy, we recommend withdrawing the drug 3 to 7 days before the procedure (3-5 days for ticagrelor, 5 days for clopidogrel, and 7 days for prasugrel) and replacing it with aspirin 100 mg where possible.

In patients receiving DAPT and scheduled for an elective procedure, the first step should be to consider postponing the procedure if the patient has a moderate-to-high risk of thrombosis. Where possible, the procedure should be deferred until the risk is low. In other cases, we recommend the following:

- Maintain aspirin for all procedures unless contraindicated (eg, neurosurgery).

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Figure 3. Recommendations for stopping and restarting antiplatelet therapy according to type of intervention and thrombotic and bleeding risk. DAPT, dual antiplatelet therapy. Classification of thrombotic risk (Table 3). Classification of hemorrhagic risk (Table 1 of the supplementary material). If necessary, withdraw aspirin 3 days before the intervention.
In patients with a moderate risk of thrombosis (and with the exception of procedures with a low bleeding risk), discontinue the P2Y₁₂ inhibitor 3 to 7 days before the procedure as follows: 3 to 5 days for ticagrelor, 5 days for clopidogrel, and 7 days for prasugrel. For emergency procedures that can be deferred for 72 hours (eg, hip fracture surgery), evaluate the indication for surgery 3 days after withdrawing ticagrelor or clopidogrel and 5 days after withdrawing prasugrel.

The strategy in patients with a high thrombotic risk will depend on the bleeding risk associated with the procedure. If this is low, we recommend not stopping DAPT. Cases of moderate-to-severe risk are more controversial and we therefore recommend evaluating patients on a case-by-case basis within a multidisciplinary team. In general, it is important not to stop DAPT in the 30 days after the index event for which it was prescribed.

Is Bridging Therapy Necessary?

Unlike the case of anticoagulation, there are few publications and little clinical experience with the use of bridging therapy in patients on antiplatelet therapy. It is a common mistake to consider heparin in this setting, as heparin can increase platelet reactivity and have the opposite effect to that desired. If bridging therapy is necessary, we recommend using an antiplatelet rather than an anticoagulant, as heparin can be harmful. Of note among the intravenous antiplatelet agents studied to date are the glycoprotein IIb/IIIa inhibitors, ticagrelor and epifibatide, and the P2Y₁₂ adenosine diphosphate receptor inhibitor, canegrelor.

The perioperative use of intravenous ticagrelor and epifibatide, 2 fast-acting glycoprotein IIb/IIIa inhibitors, has been evaluated in small series of patients with a high thrombotic risk (mainly patients treated with PCI and DES placement), and the results have been controversial. Canegrelor, an intravenous reversible P2Y₁₂ inhibitor, has been evaluated in a phase II trial of patients on DAPT who underwent coronary artery bypass grafting surgery. Compared with placebo, the drug was associated with a similar incidence of thrombotic events and a slightly higher number of minor bleeding episodes. The trial, however, was designed to study platelet reactivity and not thrombotic or bleeding events, and therefore the findings should be interpreted with caution. Furthermore, the perioperative use of canegrelor has not yet been approved. For the moment, the drug is only indicated for PCI.

Accordingly, and considering the little evidence available for bridging therapy in patients on antiplatelet therapy, we recommend restricting its use to patients with a high thrombotic risk (essentially patients receiving DAPT for an event that occurred in the previous 30 days) who are scheduled for an unpostponable operation or procedure with a moderate to severe risk of bleeding. The risk-benefit relationship in such cases should be analyzed on a case-by-case basis by a multidisciplinary team. If it is decided that bridging therapy is indicated, the patient should be started on a glycoprotein IIb/IIIa inhibitor 72 hours after withdrawal of the P2Y₁₂ inhibitor. The recommended doses are 0.1 μg/kg/min for ticagrelor and 2 μg/kg/min for epifibatide and these should be maintained for up to 4 to 6 hours before the procedure. A loading dose is not required.

Restarting Antiplatelet Therapy: When and How?

The 2 most important considerations when restarting a patient on antiplatelet therapy are having achieved adequate hemostasis during the procedure and absence of postprocedural bleeding. The moment at which the drug is to be reintroduced should thus be decided in conjunction with the surgical/intervention team. As a general rule, and under this proviso, we recommend resuming antiplatelet therapy 24 hours after the procedure. If the patient has a high risk of thrombosis and is receiving DAPT, consider restarting the P2Y₁₂ inhibitor with a loading dose of 300 to 600 mg for clopidogrel, 60 mg for prasugrel, and 180 mg for ticagrelor. Restarting of oral anticoagulant therapy should only be delayed (for 48 to 72 hours) in patients with a high risk of postoperative bleeding (Figure 3).

ANTICOAGULATION AND EMERGENCY SURGERY

Patients in need of emergency surgery or an emergency invasive procedure do not have the luxury of time associated with an elective procedure. In such cases, it is important to determine the following aspects as quickly as possible (Figure 4):

- The coagulation status of the patient via laboratory tests (INR for patients on VKA therapy). Quantitative tests offer greater precision in the case of DOACs, but as these are often not available, routine qualitative tests, such as activated partial thromboplastin time for dabigatran and prothrombin time for rivaroxaban and probably also edoxaban, can be useful. In most cases, a normal result (understood as a value < 1.2) would strongly rule out significant anticoagulant activity, indicating that the intervention can proceed as planned. The hemostasis laboratory should be familiar with the sensitivity of the different coagulation tests to these drugs.

- A patient on VKA therapy with an INR < 1.5 can undergo surgery without delay. If the value is higher, the decision will depend on the urgency of the situation. If the procedure can be deferred for 8 to 12 hours, the patient should be administered 10 mg of intravenous vitamin K. When emergency surgery is required, the most widely accepted option is to administer prothrombin complex concentrate adjusted to the patient’s weight (25–50 IU/kg depending on the current and target INR).

- In the case of DOACs, if the hemostasis assay shows anticoagulant activity (or if adherence to treatment with apixaban or edoxaban is adequate), the patient’s clinical situation (bleeding, hemodynamic stability, presence of a life-threatening situation, or risk of sequelae) should be evaluated to determine the maximum time for which surgery can be deferred. Ideally, it should be delayed for at least 24 hours from the last intake of DOAC (ie, for at least 2 elimination half-lives of the drug in patients with normal renal function). In other cases, the option of using a reversal agent should be evaluated in accordance with the type of procedure, the time since the last drug intake, and the patient’s renal function. As a general rule, neuraxial anesthesia should be avoided in these patients.

Reversal agents act as antidotes by inhibiting the effects of anticoagulants. Patients on VKA therapy should be administered intravenous vitamin K (5–10 mg depending on INR). However, as vitamin K does not take effect for 6 to 8 hours, this strategy will be of little use in patients who require emergency surgery or have active bleeding. In such cases, the option of administering a hemostatic agent should be evaluated. Idarucizumab is a humanized monoclonal antibody fragment that completely and selectively inhibits the anticoagulant activity of dabigatran in a question of minutes. It has been shown to be very effective in clinical practice studies. It is administered by rapid intravenous infusion (two 2.5-g vials administered 15 minutes apart) and does not require complex coagulation assays. Idarucizumab is indicated for patients under the anticoagulant effect of dabigatran who have major acute bleeding or bleeding in a critical organ and/or who require emergency surgery or an emergency invasive procedure with a high risk of bleeding in the next 8 hours. New reversal agents currently under development are the specific factor Xa.
inhibitor andexanet alfa (intravenous bolus dose of 400-800 mg administered over 15-30 minutes followed by an infusion dose of 480-960 mg administered over 2 hours) and ciraparantag, a reversal agent with a broader spectrum of action.

Procoagulant agents are products that provide procoagulant factors and other substances to the coagulation cascade and contribute to the generation of thrombin and hence the achievement of effective hemostasis. They are not reversal agents. A human plasma-derived prothrombin complex concentrate containing factors II, VII, IX, and X is the hesthetic agent of choice, although, depending on the dose, the need for repeat use, and the underlying disease, there may be a risk of thrombotic complications. Unlike the case with VKAs, there is little experience with the use of prothrombin complex concentrates in patients taking DOACs.

Fresh frozen plasma is a second-choice hesthetic agent and is only effective (at a dose of 15–30 mL/kg) in patients receiving VKA therapy. It should only be used when no other hesthetic agents are available. Finally, there is little experience with other hesthetic agents, such as FEIBA, an activated prothrombin complex concentrate that is indicated exclusively for use in patients with hemophilia with inhibitors, or activated recombinant factor VII, which has no established indication in this field and in addition carries a high risk of thromboembolic complications.

**ANTIPLATELET THERAPY AND EMERGENCY SURGERY**

Generally speaking, treatment with an antiplatelet agent before an emergency operation or procedure is of little consequence, even in elderly patients scheduled for neurosurgery. It is widely agreed that, following an evaluation of the risk of bleeding versus the need for the procedure, deferral of surgery because of antiplatelet therapy is not justified (even in patients on DAPT). Some clinical guidelines suggest considering platelet function tests in selected cases as detection of normalization would shorten the antiplatelet withdrawal time. The use of these tests, however, is limited as they are not usually available in emergency laboratories.

From both a practical perspective and to guide the choice of anesthesia, it is useful to take note of the antiplatelet the patient is taking. Neuraxial anesthesia, for example, is acceptable in patients being treated with aspirin, but is not recommended in patients undergoing active treatment with a P2Y₁₂ inhibitor. It is also important to emphasize that the most useful and proven strategies for treating a major bleeding episode that is not caused by another coagulation disorder or simultaneous anticoagulant therapy are achievement of surgical hemostasis and intraoperative platelet transfusion. Prophylactic platelet transfusion is not indicated, and, to be effective, would need to be performed at least 6 to 12 hours between drug intake and transfusion. There is much less consensus on the role of hesthetic agents in patients on antiplatelet therapy. Desmopressin has been found to be useful in different heart surgery studies, although results vary considerably from one study to the next. There is thus insufficient evidence to justify the systematic use of hesthetic agents and less still the administration of hesthetic agents such as prothrombin complex concentrate, FEIBA, and activated factor VII that generate
thrombin and therefore act at a different level of the coagulation cascade to antplatelets and carry a high prothrombotic risk. This is a particularly important consideration in patients with stable ischemic disease.3,30

CONCLUSIONS

Variations in antithrombotic management strategies during the perioperative or periprocedural period are a common problem in everyday clinical practice. The aim of this consensus document, which draws on the opinions of experts across Spanish scientific societies involved in perioperative care, is to synthesize the most important findings on how to manage anticoagulant and antiplatelet drugs and present our recommendations in a simple, practical, and easy-to-apply format. It is essential to create local multidisciplinary working groups to evaluate the available evidence and recommendations, such as those provided in this document, so that they can be adapted to local needs and resources and help to standardize care.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at https://doi.org/10.1016/j.rec.2018.01.029.

REFERENCES


