

GUIDELINES

European guidelines on perioperative venous thromboembolism prophylaxis

Chronic treatments with antiplatelet agents

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Antiplatelet agents (APA) are considered first-line therapy in preventing cardiovascular thrombotic events, but they are of limited value in the prophylaxis of venous thromboembolism (VTE) during the perioperative period. Consequently, many patients should receive both an APA and an anticoagulant. This combination can increase the bleeding risk and it is necessary to make some recommendations to minimise that risk. In patients receiving APA chronically, if the risk of VTE outweighs the risk of bleeding, we suggest pharmacological prophylaxis (grade 2C). In patients treated with dual antiplatelet therapy undergoing a procedure associated with a high risk of VTE, resuming both APA shortly after the procedure must be prioritised over pharmacological VTE prevention (grade 2C). If the risk of bleeding from a combination

of an APA and an anticoagulant outweighs the risk of VTE, we suggest mechanical thromboprophylaxis over anticoagulant prophylaxis, without discontinuing the APA (grade 2C). Patients in whom neuraxial anaesthesia is planned, a higher rate of complications could occur if pharmacological thromboprophylaxis is administered concurrently and postoperative thromboprophylaxis initiation should be suggested (grade 2C). After surgery, the first dose of aspirin should be given once haemostasis is guaranteed (grade 2B). In the case of clopidogrel, give the drug without a loading dose between 24 and 48 h after surgery (grade 2C).

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The article is part of the European guidelines on perioperative venous thromboembolism prophylaxis. For details concerning background, methods and members of the ESA VTE Guidelines Task Force, please refer to:

Samama CM, Afshari A, for the ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. *Eur J Anaesthesiol* 2018; 35:73–76.

A synopsis of all recommendations can be found in the following accompanying article:

Afshari A, Ageno W, Ahmed A, *et al.*, for the ESA VTE Guidelines Task Force. European Guidelines on perioperative venous thromboembolism prophylaxis. Executive summary. *Eur J Anaesthesiol* 2018; 35:77–83.

Introduction

Other than in orthopaedic surgery, where aspirin is considered as a pharmacological means to prevent postoperative venous thromboembolism (VTE), antiplatelet agents (APA; such as acetylsalicylic acid, clopidogrel, prasugrel, ticagrelor) are not adequate to prevent VTE in the majority of patients undergoing surgery. However, an increasing number of patients are treated with APA to prevent cardiovascular thromboembolic events (e.g. stroke, myocardial infarction). In these patients, two questions must be considered.

Suitability and efficacy of antiplatelet agents to prevent venous thromboembolism after surgery

The first question is dealt with mainly in another chapter of these guidelines (aspirin and VTE prophylaxis¹) although some additional observations are pertinent.

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As the mechanism of action of acetylsalicylic acid (aspirin) is the inhibition of the enzyme cyclo-oxygenase, resulting in a reduction in the synthesis of thromboxane A₂ for platelet lifespan,² the main indication for this drug is not related to perioperative VTE prevention. The 2008 American College of Chest Physicians' (ACCP) guidelines on prevention of VTE recommended against the use of aspirin alone as thromboprophylaxis for any patient group, with an evidence ranking of 1A.³ The rationale at that time was that more effective methods of thromboprophylaxis were readily available.

The role of aspirin was reevaluated in the most recent iteration of the ACCP guidelines and although it cannot be considered the first choice for thromboprophylaxis, some indications remain.

The 2012 version of the ACCP guidelines recommends the use of aspirin rather than no antithrombotic prophylaxis in major orthopaedic surgery (total knee replacement, total hip replacement, hip fracture surgery; grade 1B).⁴ In these patients, if thromboprophylaxis with low molecular weight heparins (LMWH) is contraindicated, aspirin and mechanical prophylaxis devices (intermittent pneumatic compression; better than compression stockings), could be enough as VTE prevention, provided that they are a part of a multimodal approach.⁵

In patients receiving aspirin chronically scheduled to undergo nonorthopaedic surgery and not at high risk of major bleeding but at a high risk of VTE, and in whom thromboprophylaxis with LMWH or unfractionated heparin is contraindicated, the use of aspirin as the only drug for VTE prevention may be an option, at the same level of recommendation as the use of fondaparinux or mechanical prophylaxis, over no prophylaxis (grade 2C).⁶

Other guidelines do not recommend aspirin as the sole pharmacological agent for VTE prophylaxis in any type of surgical patient, as other available agents are more effective.^{7,8}

How to manage bleeding risks in patients needing both antiplatelet agents and pharmacological venous thromboembolism prevention with anticoagulants

In most surgical settings, aspirin therapy should be maintained perioperatively⁹ because its continuation is not associated with significant bleeding events or with increased mortality,¹⁰ although the initiation of its administration close to surgery is not indicated because of a possible increase in the bleeding risk.¹¹

In some patients with a high risk of bleeding, if aspirin withdrawal is considered, the current recommended time interval is 3 days.¹² Clopidogrel, ticagrelor and prasugrel should be interrupted 5, 5 and 7 days, respectively, before surgery.¹² Nevertheless, assessment of the 'arterial thrombotic risk' is recommended on an individual basis to know whether the indication for the administration of the APA by itself outweighs the bleeding risk associated

with the surgical procedure. In this case, the main decision is not to withdraw the APA, and to adjust the VTE prophylaxis from this premise.

The concomitant administration of any anticoagulant (at prophylactic or therapeutic doses) with an APA or a nonsteroidal anti-inflammatory drug increases the bleeding risk.¹³ Therefore, such associations should be carefully balanced against the potential benefit in each clinical situation.

In patients treated with APA at high risk of cardiovascular events (recent myocardial infarction, recent coronary stent implantation), in which APA should be maintained before surgery and must be resumed early after it, mechanical VTE prevention must be considered to decrease bleeding risk. Pharmacological VTE prevention with anticoagulants (LMWH, fondaparinux, novel oral anticoagulants) should be delayed until the postoperative bleeding risk is sufficiently low.

The administration of aspirin at low dose as the unique antithrombotic does not increase the risk of spinal haematoma and spinal or epidural puncture can be undertaken safely. When the patient receives an antithrombotic drug for VTE prophylaxis, a postoperative start may be advantageous, especially in patients also receiving aspirin, because preoperative administration should be considered as an option and not as a requirement.¹⁴

Recommendations

1. In patients receiving APA chronically, we recommend thromboprophylaxis in cases of moderate/high VTE risk, whilst assessing the risk of perioperative bleeding (grade 1B).
2. In patients receiving APA chronically, if the risk of VTE outweighs the risk of bleeding, we suggest pharmacological (anticoagulant) prophylaxis (LMWH, direct oral anticoagulants, fondaparinux depending on the indication) (grade 2C).
3. In patients treated with dual antiplatelet therapy (recent coronary stent implantation) undergoing a procedure associated with a high risk of VTE, we suggest resuming APA shortly after the procedure, prioritising over pharmacological VTE prevention (grade 2C).
4. If an anticoagulant is associated with an APA, we suggest the administration of the lowest approved dose (grade 2C).
5. If the risk of bleeding of a combination of an APA and an anticoagulant outweighs the risk of VTE, we suggest considering intermittent pneumatic compression over anticoagulant prophylaxis, without discontinuing the APA (grade 2C).
6. Patients in whom neuraxial anaesthesia is planned, although the administration of aspirin alone does not increase the incidence of spinal haematoma, a higher

rate of complications could appear if pharmacological thromboprophylaxis is administered concurrently. In these cases, postoperative thromboprophylaxis initiation should be suggested (grade 2C).

7. After surgery, the first dose of aspirin should be given as soon as possible, once haemostasis is considered adequate (in general, the day after surgery; grade 2B). In the case of clopidogrel, the main recommendation is to give the drug without any loading dose between 24 and 48 h after surgery (grade 2C).
8. Monitoring for clinical signs of bleeding or unexplained anaemia is recommended during concomitant administration of an anticoagulant for thromboprophylaxis (LMWH, unfractionated heparin, fondaparinux, warfarin or any other) and an APA throughout the postoperative period (grade 1C).
9. Nonsteroidal anti-inflammatory drugs should be avoided in patients treated with APA (grade 2C).

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