

GUIDELINES

European Guidelines on perioperative venous thromboembolism prophylaxis

Executive summary

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Introduction

The current Executive Summary includes all the recommendations from the 12 chapters of the European guidelines on perioperative venous thromboembolism (VTE) prophylaxis.^{1–12} The objective is to allow the reader to examine the guidelines rapidly and globally.

The rationale of each chapter and relevant references can be found in each separate article.

Surgery in the obese patient Bariatric surgery

- Laparoscopic bariatric procedures for obese patients have a lower risk of VTE than open procedures.¹
- We suggest using only anti coagulants or intermittent pneumatic compression (IPC) for obese patients with a low risk of VTE during and after bariatric procedures (Grade 2C).
- We recommend using anti coagulants and IPC together for obese patients with a high risk of VTE (age >55 years, BMI > 55 kg.m⁻², history of VTE, venous disease, sleep apnoea, hypercoagulability and pulmonary hypertension) during and after bariatric procedures (Grade 1C).
- We recommend the use of low molecular weight heparin (LMWH) over low-dose unfractionated heparin (LDUH) (Grade 1C).
- We suggest a dose of LMWH (3000 to 4000 anti-Xa IU every 12 h subcutaneously) depending on BMI as acceptable for obese patients with a lower risk of VTE (Grade 2B).
- We suggest the use of a higher dose of LMWH (4000 to 6000 anti-Xa IU every 12 h subcutaneously) as acceptable for obese patients with a higher risk of VTE (Grade 2B).

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- We recommend extended prophylaxis for patients with a high risk of VTE during the post-discharge period for 10 to 15 days (Grade 1C).

Non-bariatric surgery

- We suggest that in surgery with an indication for VTE prophylaxis, a higher prophylactic dose of LMWH (3000 to 4000 anti-Xa IU every 12 h subcutaneously) should be considered for obese patients with a BMI more than 40 kg m⁻² undergoing non-bariatric surgery (Grade 2C).
- For additional and general recommendations, we refer to the section on 'VTE prophylaxis of obese patients in bariatric surgery'.¹

Surgery during pregnancy and the immediate post-partum period

Non-obstetric surgery during pregnancy

- We recommend thromboprophylaxis following surgery during pregnancy or the post-partum period, when they imply, as a consequence, bed-rest, until full mobility is recovered (Grade 1C).²
- We suggest that thromboprophylaxis should be used in cases of perioperative infection during pregnancy or the postpartum period (Grade 2C).

Caesarean section

- Thromboprophylaxis is recommended after caesarean section in all cases, except elective caesarean section in low-risk patients (Grade 1C), but there is no clear consensus on the definition of this population.
- The duration of thromboprophylaxis following caesarean section should be at least 6 weeks for high-risk patients, and at least 7 days for other patients requiring anticoagulation (Grade 1C).

Surgery in the elderly

- Age over 70 years is a risk factor for postoperative VTE (Grade B).³
- In elderly patients, we suggest identification of comorbidities increasing the risk for VTE (e.g. congestive heart failure, pulmonary circulation disorders, renal failure, lymphoma, metastatic cancer, obesity, arthritis, post-menopausal oestrogen therapy), and correction if present (e.g. anaemia, coagulopathy) (Grade 2C).
- We suggest against bilateral knee replacement in elderly and frail patients (Grade 2C).
- We suggest timing and dosing of pharmacological VTE prophylaxis as in the non-aged population (Grade 2C).
- In elderly patients with renal failure, low-dose unfractionated heparin (UFH) may be used or weight-adjusted dosing of LMWH (Grade 2C).
- In the elderly, we recommend careful prescription of postoperative VTE prophylaxis and early postoperative mobilisation (Grade 1C).

- We recommend multi-faceted interventions for VTE prophylaxis in elderly and frail patients, including pneumatic compression devices, LMWH [and/or direct oral anticoagulants (DOACs) after knee or hip replacement] (Grade 1C).

Day surgery and fast-track surgery

- We recommend that all patients undergoing an ambulatory/fast-track protocol should be assessed for the VTE risk of the procedure and for any personal/additional VTE risk (Grade 1B).⁴
- For patients undergoing a low-risk procedure, without additional risk according to the Caprini score, we recommend general measures of thromboprophylaxis (including early ambulation and optimal hydration) over other specific measures (mechanical or pharmacological) (Grade 1B).
- For patients undergoing a low-risk procedure with additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation and optimal hydration) (Grade 1B). We suggest assessing pharmacological prophylaxis with LMWH over other drugs (Grade 2B). We suggest the use of specific mechanical measures (IPC devices) in patients with an increased bleeding risk (Grade 2C).
- For patients undergoing a high-risk procedure without additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation, and optimal hydration) (Grade 1B). We suggest the administration of pharmacological prophylaxis with LMWH over other drugs (Grade 2B). We suggest assessing specific mechanical measures (IPC) in patients with an increased bleeding risk (Grade 2C).
- For patients undergoing a high-risk procedure with additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation and optimal hydration) and pharmacological prophylaxis with LMWH over other drugs (Grade 1B), or specific mechanical measures (IPC) in patients with an increased bleeding risk (Grade 2C).
- We suggest the use of aspirin for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (high-risk orthopaedic procedures) in patients without high VTE risk (Grade 2C).
- We suggest the use of aspirin for VTE prevention after low-risk orthopaedic procedures in patients with high VTE risk, or other high-risk orthopaedic procedures (e.g. knee arthroscopy) in patients without high VTE risk (Grade 2C).
- We recommend no pharmacological VTE prevention after low-risk orthopaedic procedures in patients without high VTE risk (Grade 1C).
- For pharmacological prophylaxis, we recommend a minimum of 7 days' duration of treatment over protocols lasting 3 days or single-dose protocols (Grade 1B), although in selected cases of fast-track surgery, thromboprophylaxis only during

hospitalisation could be an option (Grade 2C). We recommend extending the duration of thromboprophylaxis for up to 4 weeks in specific cases of high-risk procedures, according to general rules (Grade 2B).

- When the choice of thromboprophylaxis is a LMWH, the first dose could be administered before surgery (about 12 h before the beginning of the procedure) or after surgery (optimal time from 6 to 8 h after the end of the procedure) (Grade 2C). In case of planned neuraxial anaesthesia for the procedure, postoperative administration seems to be the preferred option (Grade 2C).

Intensive care

- In critically ill patients, we recommend against the routine use of compression duplex ultrasound screening of deep vein thrombosis (DVT) (Grade 1B).⁵
- We recommend an institution-wide protocol for the prevention of VTE that includes the use of mechanical thromboprophylaxis, that is IPC (Grade 1B).
- For critically ill patients, we recommend using thromboprophylaxis with LMWH or LDUH (Grade 1B), and we recommend LMWH over LDUH (Grade 1B).
- For VTE prophylaxis in critically ill patients with severe renal insufficiency, we suggest the use of LDUH (Grade 2C), dalteparin (Grade 2B) or reduced doses of enoxaparin (Grade 2C). Monitoring of anti-Xa activity may be considered when LMWH is used in these patients (Grade 2C).
- The use of pharmacological prophylaxis in patients with severe liver dysfunction should be carefully balanced against the risk of bleeding. If a treatment is administered, the use of LDUH or LMWH is suggested (Grade 2C).
- We suggest no prophylaxis or the use of IPC in patients with a platelet count less than $50 \times 10^9 \text{ l}^{-1}$ and a high-risk of bleeding (Grade 2C).
- For critically ill patients, we recommend against the routine use of inferior vena cava (IVC) filters for the primary prevention of VTE (Grade 1C). We suggest the use of IVC filters in patients who can neither receive pharmacological prophylaxis nor IPC (Grade 2C).
- In critically ill patients with suspected or confirmed diagnosis of heparin-induced thrombocytopenia (HIT), all forms of heparin must be discontinued (Grade 1B). In these patients, immediate anticoagulation with a non-heparin anticoagulant rather than discontinuation of heparin alone is recommended unless there is a strong contra-indication to anticoagulation (Grade 1C). The selection of non-heparin anticoagulants should be based on patient characteristics: argatroban is the first choice in case of renal insufficiency, and bivalirudin in patients undergoing or after cardiac surgery (Grade 2C). The use of fondaparinux can also be considered in these patients (Grade 2C).

Cardiovascular and thoracic surgery

Cardiac and vascular surgery

- In the absence of risk factors, we suggest considering the risk of VTE as moderate in patients undergoing coronary artery bypass graft and bioprosthetic aortic valve implantation surgery (Grade 2C). If the risk of bleeding is to be considered high, we suggest the use of mechanical prophylaxis using IPC (Grade 2C).⁶
- The presence of one or more risk factors (age above 70 years, transfusion of more than four units of red blood cell concentrates/fresh frozen plasma/cryoprecipitate/fibrinogen concentrate, mechanical ventilation more than 24 h, postoperative complication (e.g. acute kidney injury, infection/sepsis, neurological complication) should place the cardiac population at high risk for VTE. In this context, we suggest the use of pharmacologic prophylaxis as soon as satisfactory haemostasis has been achieved, in addition to IPC (Grade 2C).
- Patients undergoing other valve surgery and those with atrial fibrillation should be considered a specific entity at high risk of VTE, as they will mostly require postoperative therapeutic medical 'bridging' prior to long-term anticoagulation.
- Patients undergoing peripheral vascular surgery are considered to have a low risk of VTE and a low risk of bleeding. Stringent medical prophylaxis appears to reduce the event rate significantly. In this population, we suggest medical therapy (Grade 2C).
- In patients undergoing abdominal aortic aneurysm repair, particularly when an open surgical approach is used, the risk for VTE is higher, with a high bleeding risk. These patients should be considered as having a moderate risk. Patients with additional risk factors, including BMI at least 30 kg m^{-2} , preoperative dyspnoea, chronic steroid usage, ruptured aneurysm, open surgery, operative duration at least 5 h, transfusion of at least 5 U, postoperative mechanical ventilation more than 48 h, postoperative complication (acute kidney injury, infection/sepsis) and re-operation, should be considered as moderate to high risk. In this context, we suggest the use of pharmacological prophylaxis as soon as satisfactory haemostasis is achieved (Grade 2C).
- We suggest that low-dose aspirin could be used to decrease the incidence of VTE in cardiac and vascular patients, but should not be considered as the sole agent in high-risk patients. (Grade 2C).
- UFH is associated with the highest risk of developing the prothrombotic condition of HIT. Therefore, in an attempt to minimise the risk of HIT, we suggest that UFH should be used as briefly as possible and replaced by LMWH as soon as the bleeding risk decreases (Grade 2C).
- In patients with severely impaired renal function (Cockcroft and Gault clearance $<30 \text{ ml min}^{-1}$) and a high risk of haemorrhagic complications, we suggest

close monitoring of the administration of therapeutic UFH and LMWH and adaptation of the dosage (Grade 2C).

Thoracic surgery

- Based on the current literature, patients undergoing thoracic surgery in the absence of cancer could be considered at low risk of VTE. However, as the vast majority of patients undergoing thoracic surgery have a diagnosis of primary or metastatic cancer, they should be considered at high risk for VTE with an equally high bleeding risk.
- In the absence of evidence regarding patients undergoing minimally invasive procedures, the same risk stratification should be applied as described above.
- In low-risk patients, we suggest the use of mechanical prophylaxis using IPC (Grade 2C). In high-risk patients, we suggest the use of pharmacological prophylaxis in addition to IPC (Grade 2B).

Neurosurgery

Patients undergoing craniotomy

- We recommend that if IPC is used, it should be applied before the surgical procedure or on admission, used continuously (except when the patient is actually walking) and monitored frequently to optimise compliance (Grade 1C).⁷
- If LMWH or LDUH are used, we suggest delayed initiation until at least 24 h after surgery. (Grade 2C).
- In craniotomy patients at particularly high risk of VTE (additional risk factors including malignancy, motor impairment, prolonged operative time), we suggest considering the initiation of mechanical thromboprophylaxis with IPC preoperatively with addition of LMWH or LDUH postoperatively when the risk of bleeding is presumed to be decreased (Grade 2C).
- We suggest that thromboprophylaxis should be continued until discharge (Grade 2C).

Patients with non-traumatic intra cranial haemorrhage

- We suggest thromboprophylaxis with IPC (Grade 2C).
- We recommend the application of IPC on admission, used continuously (except when the patient is actually walking) and monitored frequently to optimise compliance (Grade 1C).
- For patients who have had non-traumatic intracranial haemorrhage, we suggest giving consideration to commencement of LMWH or LDUH when the risk of bleeding is presumed to be low (Grade 2C).
- We suggest continuing thromboprophylaxis until full mobilisation of the patient (Grade 2C).

Spinal surgery

- For patients with no additional risk factors, we suggest no active thromboprophylaxis intervention apart from early mobilisation (Grade 2C).

- For patients undergoing spinal surgery with additional risk factors (limited mobility, active cancer, complex surgical procedure), we recommend starting mechanical thromboprophylaxis with IPC preoperatively (Grade 1C), and we suggest the addition of LMWH postoperatively when the risk of bleeding is presumed to be decreased (Grade 2C).
- If LMWH is used, we recommend delayed initiation at least until 24 h after surgery and only when haemostasis occurs (Grade 1C).
- We suggest continued thromboprophylaxis until discharge in high-risk patients (Grade 2C).
- In patients with spinal cord injury or significant motor impairment, we suggest extending the thromboprophylaxis into the rehabilitation phase of hospital care (Grade 2C).

Chronic treatments with anti-platelet agents

- In patients receiving anti-platelet agents (APA) chronically, we recommend thromboprophylaxis in case of moderate/high VTE risk, whilst assessing the risk of perioperative bleeding (Grade 1B).⁸
- In patients receiving APA chronically, if the risk of VTE outweighs the risk of bleeding, we suggest pharmacological (anticoagulant) prophylaxis (LMWH, DOAC, fondaparinux, depending on the indication) (Grade 2C).
- In patients treated with dual anti-platelet therapy (recent coronary stent implantation) undergoing a procedure associated with a high risk of VTE, we suggest resuming both APA shortly after the procedure, prioritising over pharmacological VTE prevention (Grade 2C).
- If an anti-coagulant is associated with an APA, we suggest the administration of the lowest approved dose (Grade 2C).
- If the risk of bleeding of a combination of an APA and an anticoagulant outweighs the risk of VTE, we suggest considering IPC over anticoagulant prophylaxis, without discontinuing the APA (Grade 2C).
- 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 patients, postoperative thromboprophylaxis initiation should be suggested (Grade 2C).
- 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).
- Monitoring for clinical signs of bleeding or unexplained anaemia is recommended during concomitant administration of an anticoagulant for

thromboprophylaxis (LMWH, UFH, fondaparinux, warfarin or any other) and an APA throughout the postoperative period (Grade 1C).

- Non-steroidal anti-inflammatory drugs should be avoided in patients treated with APA (Grade 2C).

Patients with pre-existing coagulation disorders and after severe perioperative bleeding

- In patients with inherited bleeding disorders undergoing surgery, we recommend assessment of individual risk for VTE, taking into account the nature of the surgery and anaesthetic, type and severity of haemophilia, age, BMI, history of thrombosis and the presence of malignancy and other high-risk comorbidities. VTE risk should be balanced against the increased bleeding risk associated with anticoagulant use in patients with haemophilia (Grade 1C).⁹
- For the perioperative management of patients with inherited bleeding disorders, we suggest liaison with haematologists to guide treatment (Grade 2C).
- We suggest that if factor replacement therapy is required for perioperative haemostasis, excess use should be avoided and factor levels monitored carefully (Grade 2C).
- In patients with inherited bleeding disorders undergoing major surgery, we suggest mechanical thromboprophylaxis, (Grade 2C), especially in factor VII deficiency (Grade 1C).
- In patients with inherited bleeding disorders undergoing major surgery, we recommend against routine postoperative use of pharmacological thromboprophylaxis, especially for patients with haemophilia A or B (Grade 1B).
- If the balance of risks favours pharmacological thromboprophylaxis, we suggest that LMWH should be administered as for patients without haemophilia undergoing the same surgery, and factor VIII/IX levels should be maintained at 0.6 to 1.0 IU ml⁻¹ (Grade 2C).
- In haemophilia patients with inhibitors, we suggest against the use of pharmacological thromboprophylaxis (Grade 2C).
- We recommend that patients with haemophilia who require perioperative factor concentrate are monitored with daily factor levels for the first 3 to 5 days to guide treatment and to avoid wide fluctuations in factor levels (Grade 1C).
- We recommend that, for major surgery, factor levels of 0.8 to 1.0 IU ml⁻¹ should be aimed for and not be allowed to fall below 0.5 IU ml⁻¹ or rise above 1.5 IU ml⁻¹ in the postoperative period (Grade 1B).
- In general, we recommend against routine thrombophilia screening for patients with haemophilia undergoing surgery (Grade 1C).
- We recommend that patients treated with factor concentrate in the perioperative and postoperative period should have both factor VIII and von Willebrand factor levels monitored to avoid an excessive rise in factor levels and accumulation of factor VIII. We recommend checking levels every 12 h for the first 24 h after major surgery, and daily thereafter (Grade 1B).
- We recommend that the use of factor concentrate with the highest ratio between vWF:RCo and factor VIII:C should be considered to minimise the risk of factor VIII accumulation (Grade 1C).
- We recommend that use of factor XI concentrate is kept to a minimum to avoid increasing the thrombotic risk (Grade 1C).
- We recommend that all patients receiving factor XI concentrate have mechanical thromboprophylactic measures (Grade 1C) and suggest that they are considered for pharmacological thromboprophylaxis (Grade 2C).
- We suggest that tranexamic acid alone is useful for patients with mild factor XI deficiency but should not be given as haemostatic prophylaxis to patients receiving factor XI concentrate (Grade 2C).
- In patients with factor VII deficiency, we suggest that they are considered for pharmacological thromboprophylaxis, if they have associated risk factors (Grade 2C).
- We suggest that for major surgery, fibrinogen levels should be closely monitored aiming to maintain levels 1 to 1.5 g l⁻¹ for 10 to 14 days postoperatively (Grade 2C).
- Perioperative management may require simultaneous use of fibrinogen concentrate and LMWH, depending on the clinical phenotype (Grade 2C).
- Glomerular filtration rate should be assessed before any direct oral anticoagulant (DOAC) is initiated and again, at least once yearly or more frequently as needed, such as postoperatively before the resumption of therapeutic DOAC administration, when it is suspected that renal function could decline or deteriorate (Grade 1C).
- The use of the Cockcroft–Gault method to evaluate renal function of patients with DOAC is suggested (Grade 2C).
- We suggest that anti-Xa levels may be measured in cases of severe bleeding in patients with renal impairment receiving LMWH (Grade 1C).
- Clinical exclusion of signs of postoperative bleeding is more relevant for postponing the commencement of VTE prophylaxis rather than relying on any specific laboratory tests (Grade 2C).
- We suggest against the systematic use of standard laboratory tests to exclude persistence of acquired perioperative coagulopathy before VTE prophylaxis (Grade 2C).
- Reduced dosages of LMWHs may be used relatively safely during transient severe (<50 × 10⁹ l⁻¹) thrombocytopenia (Grade 2C).
- Monitoring anti-Xa level may be used to adjust the doses of LMWH in patients with moderate or severe thrombocytopenia (Grade 2C).

- In cancer patients or patients with haematological disorders and mild thrombocytopenia (platelet count $>80 \times 10^9 l^{-1}$), pharmacological prophylaxis may be used; if the platelet count is below $80 \times 10^9 l^{-1}$, pharmacological prophylaxis may only be considered on a case-by-case basis and careful monitoring is recommended (Grade 2C).
- Patients with a high thrombotic risk (e.g. mechanical heart valves) may benefit from resuming warfarin therapy despite ongoing risk for recurrent gastrointestinal bleeding (Grade 2C).
- Patients with a HAS-BLED score lower than the CHADS₂ score may benefit from earlier resumption (Grade 2C).
- The delay between major gastrointestinal bleeding and warfarin resumption should be at least 7 days (Grade 2C).
- We suggest International Normalised Ratio at the time of bleeding may also be considered to resume anticoagulation (Grade 2C).
- We suggest resuming anticoagulant therapy 12 h after removal of drains in cases of cardiac tamponade (Grade C).
- When the risk of bleeding diminishes, pharmacological VTE prophylaxis may be initiated depending on thrombotic risk factors (Grade 2C).
- We recommend that, when the risk of postoperative bleeding is higher than the risk of a thromboembolic event, full dose anticoagulation may be resumed 48 or 72 h after the procedure (Grade 2B).
- For patients at high risk for thromboembolism and with a high bleeding risk after surgery, we consider that administering a reduced dose of DOAC on the evening after surgery and on the following day (first postoperative day) after surgery is good practice (Grade 2B).

Mechanical prophylaxis

- We recommend an institution-wide protocol for the prevention of VTE that integrates early ambulation, pharmacological thromboprophylaxis with anticoagulants and mechanical thromboprophylaxis (Grade IB).¹⁰
- We recommend against the routine use of graduated compression stockings (GCS) without pharmacological thromboprophylaxis to prevent VTE in patients at intermediate and high risk (Grade IB).
- In patients with contra-indications to pharmacological thromboprophylaxis, we recommend the use of mechanical prophylaxis with IPC or GCS (Grade IB) and suggest the use of IPC over GCS (Grade 2B).
- In patients with contra-indications for pharmacological thromboprophylaxis who are not at high risk for VTE, we suggest no prophylaxis over GCS alone (Grade 2C).
- In patients receiving pharmacological thromboprophylaxis who are not at very high risk for VTE, we recommend against the routine use of mechanical thromboprophylaxis with GCS or IPC (Grade IB).

- We suggest combined mechanical and pharmacological prophylaxis in selected patients at very high risk for VTE (grade 2B). We suggest the use of IPC rather than GCS in selected high-risk patients in addition to pharmacological thromboprophylaxis (Grade 2B).

Aspirin

- We recommend the use of aspirin as an option for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (Grade 1B).¹¹
- We suggest the use of aspirin for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (high-risk procedures) in patients without high VTE risk (Grade 2C).
- We suggest the use of aspirin for VTE prevention after low-risk orthopaedic procedures in patients with a high VTE risk or other high-risk orthopaedic procedures in patients without a high VTE risk (Grade 2C).
- We suggest the use of aspirin for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery in patients with an increased bleeding risk (Grade 2C).
- We suggest the use of aspirin for VTE prevention after total hip arthroplasty or total knee arthroplasty in a rapid recovery (fast-track) programme (Grade 2C).
- We recommend combining aspirin with IPC devices for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (Grade 1C).
- We recommend no pharmacological VTE prevention after low-risk orthopaedic procedure in patients without high VTE risk (e.g. knee arthroscopy) (Grade 1C).
- No recommendation can be made concerning dose and duration of aspirin treatment and patient selection.
- We do not recommend aspirin for thromboprophylaxis in general surgery (grade 1C). However, this type of prophylaxis could be interesting, especially in low-income countries (Grade 2C), and adequate large-scale trials with proper study designs should be carried out (Grade 1C).

Inferior vena cava filters

- There is currently no clear evidence on the efficacy and safety of IVC filters (IVCF) in patients with a contra-indication for pharmacological and mechanical thromboprophylaxis undergoing high-thrombotic-risk surgery or procedures (Grade B).¹²
- IVCF-associated complications often seem to outweigh a potential benefit (Grade B).
- We suggest considering temporary IVCF placement in patients at high VTE risk when pharmacological and mechanical thromboprophylaxis are fully contra-indicated (Grade 2C).
- We suggest considering temporary IVCF placement in patients with documented recent DVT, and with an absolute contra-indication for full anticoagulation and planned non-deferrable major surgery (Grade 2C).

- We suggest not systematically using IVCFs to prevent pulmonary embolism in the perioperative setting (Grade 2B).

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