

Antithrombotic therapy

Topics

- Preexisting anticoagulation and timing of surgery
- Reversal of anticoagulation
- Perioperative thromboprophylaxis
- When should we be cautious?

Why should surgeons be interested in anticoagulation?

- Aging population: more anticoagulated patients requiring surgery
- Preexisting anticoagulation has an influence on:
 - Timing of surgery
 - Intraoperative and postoperative bleeding risk
 - Patient's risk of perioperative thromboembolic events

Antithrombotic agents

Antiplatelet drugs

- Acetylsalicylic acid (Aspirin®)
- Thienopyridines: clopidogrel (Plavix®) or ticlopidine (Ticlid®)

Anticoagulants

- Vitamin K antagonists (VKAs): coumarins (eg, Warfarin®, Marcumar®, Sintrom®)
- Unfractionated heparin (UFH)
- Low-molecular-weight heparins (LMWH) – eg, enoxaparin (Lovenox®)
- Synthetic Factor Xa inhibitor: fondaparinux (Arixtra®)

Medical indications

Antiplatelets are indicated in coronary artery, peripheral, and cerebrovascular disease. Furthermore, they are indicated after coronary artery stenting or bypass grafting.

Anticoagulants are indicated in atrial fibrillation (aFib), after mechanical heart valve (MHV) replacement, treatment of deep venous thrombosis (DVT), pulmonary embolism (PE), as well as perioperative thromboprophylaxis.

"New oral anticoagulants"

Rivaroxaban or Xarelto® (oral factor Xa-inhibitor) and Dabigatran or Pradaxa® (oral direct thrombin inhibitor)

- Approved for thromboprophylaxis after knee or hip replacement and for anticoagulation in atrial fibrillation
- Contraindicated in severe renal impairment
- Do not need anticoagulation monitoring
- No specific antidote
- More expensive, with no therapeutic advantages over Warfarin®, but better comfort

Timing of Surgery

Timing of Surgery

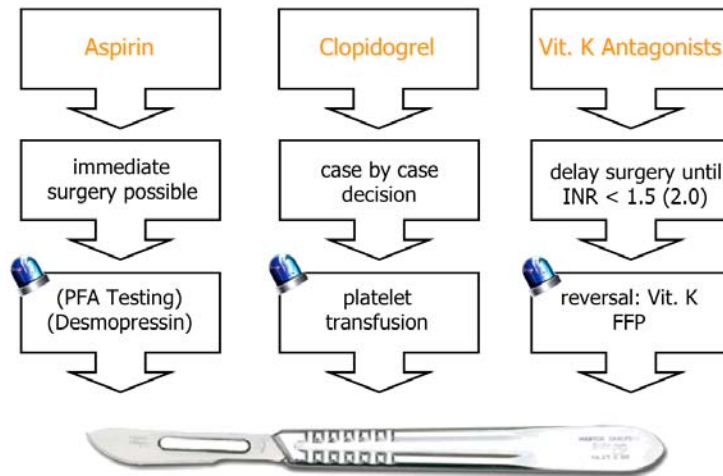


Fig 1 Timing of surgery for selected medications

Note: Prothrombin complex concentrates are now licensed for urgent reversal of warfarin and are preferable in a number of situations.

Timing of Surgery

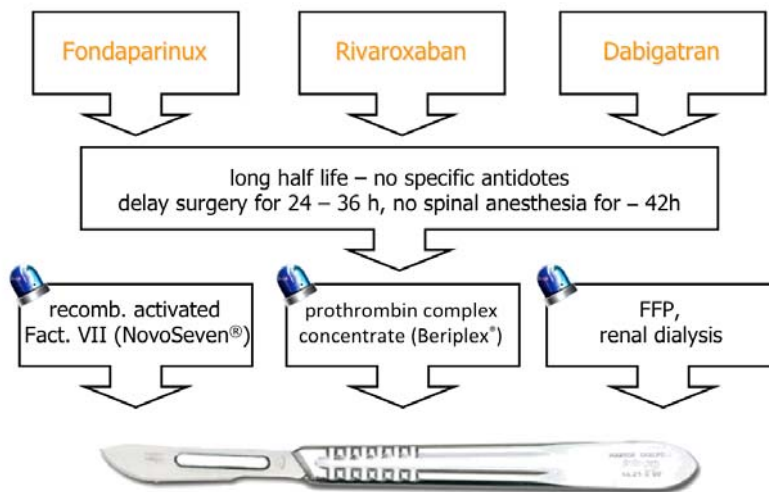


Fig 2 Timing of surgery for selected medications

Reversal of vitamin K antagonists

- Full elective surgery:
 - Stop VKAs 4–5 days before surgery to allow the international normalized ratio (INR) to fall to a subtherapeutic (1.5–2.0) or normal (1.0–1.5) level
- Semi-urgent surgery:
 - More rapid reversal over 1 or 2 days
 - Stop VKAs and give low dose vitamin K (1–3 mg) orally or intravenously
- Urgent surgery:
 - Reversal within < 1 day
 - Stop VKAs, give 2.5–5 mg vitamin K slowly and intravenously
 - check INR after 4 hours, give fresh frozen plasma (FFP) if necessary

- Consider prothrombin complex concentrate (in consultation with hematologist) for patient with acute major bleeding

Can we just stop anticoagulation therapy?

Basic questions:

- What is the clinical indication for anticoagulation?
- What is the individual risk for thromboembolism if anticoagulation is stopped or reduced?
- What are the clinical consequences of a thromboembolic event?
- What is the patient's risk for bleeding?

Bridging therapy:

- Means: covering the time of subtherapeutic INR after cessation of vitamin K antagonists by administering heparin in patients at risk for thromboembolic events
 - Mechanical heart valve replacement
 - Atrial fibrillation
 - Venous thromboembolism
- Weigh risk for thromboembolism against bleeding risk
- Consult a specialist (cardiologist) in unclear cases

Perioperative bridging therapy with a therapeutic-dose subcutaneous LMWH or intravenous UFH is recommended in patients with a mechanical heart valve, atrial fibrillation, or venous thromboembolism (VTE) at high or moderate risk for thromboembolism as estimated by the CHADS₂ score. Postoperatively, consider the bleeding risk and adequacy of hemostasis in the individual patient to determine the timing to resume anticoagulation therapy.

Regimens:

- Therapeutic dose LMWH, eg, enoxaparin 1 mg/kg subcutaneous twice daily up to 24 hours before surgery
- Therapeutic dose UFH: continuous intravenous infusion regulated to activated partial thromboplastin time (aPTT) up to 4 hours before surgery
- Low dose (prophylactic) LMWH, eg, enoxaparin 40 mg subcutaneous once daily up to 12 hours before surgery [1]

Special case: dual antiplatelet therapy after coronary stenting:

- Dual antiplatelet therapy consists of Aspirin® and Plavix® for 12 months after drug-eluting stents (DES) for at least 3 months after bare metal stents (BMS).
- Early discontinuation increases risk for stent thrombosis is about 90 folds.
- Mortality of stent thrombosis is 30–70%.
- Always consult the cardiologist: interdisciplinary decision.
- In emergency cases, keep Aspirin® and stop Plavix®.
- Do not carry out elective surgery in patients with drug-eluting stents within the first 12 months.

Perioperative thromboprophylaxis

- VTE is one of the leading causes of perioperative mortality in geriatric fracture patients.
- Fatal pulmonary embolism occurs in up to 7.5% of hip fracture patients within 3 months.

- High risk associated with orthopedic or trauma surgery includes venous stasis (immobilization), supine position on operating table, intimal injury, and release of tissue factors by fracture or surgery
- A routine aspect in the care of the geriatric fracture patient

Thromboprophylactic agents

The following agents are recommended:

- Low dose LMWH, eg, enoxaparin: 40 mg subcutaneous once or 30 mg subcutaneous twice daily
- Fondaparinux: 2.5 mg subcutaneous once daily
- New oral anticoagulants in elective knee and hip replacement
- Vitamin K antagonists dosed to a target value of INR 2.5
- low-dose UFH 5000 IU subcutaneous twice daily

Remark: Graduated compression stockings are not recommended any more for geriatric fracture patients who can be treated with anticoagulants.

Recommended reading:

- **Ortel TL.** Perioperative management of patients on chronic antithrombotic therapy. *Blood.* 2012 Dec 6;120(24):4699–4705.
- **Bauersachs RM, Gogarten W, Hach-Wunderle V, et al.** Perioperatives Management der Antikoagulation mit Rivaroxaban. *klinikaerzt,* 2012;41(9): 385–396.
- **Douketis JD, Spyropoulos AC, Spencer FA, et al.** Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e326S–350S.
- **Ganter MT, Hofer CK.** [Principles of perioperative coagulation management]. *Unfallchirurg.* 2012 Apr;115(4):353–362. German.
- **Falck-Ytter Y, Francis CW, Johanson NA, et al.** Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e278S–325S.
- **Keeling D, Baglin T, Tait Cet al.** Guidelines on oral anticoagulation with warfarin—fourth edition. *Br J Haematol.* 2011 Aug;154(3):311–324.
- **Douketis JD.** Perioperative management of patients who are receiving warfarin therapy: an evidence-based and practical approach. *Blood.* 2011 May 12;117(19):5044–5049.
- **Douketis JD.** Pharmacologic properties of the new oral anticoagulants: a clinician-oriented review with a focus on perioperative management. *Curr Pharm Des.* 2010;16(31):3436–3441.
- **Gogarten W, Vandermeulen E, Van Aken H, et al** Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol.* 2010 Dec;27(12):999–1015.
- **Gage BF, van Walraven C, Pearce L, et al.** Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation.* 2004 Oct 19;110(16): 2287–2292.

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