Guidelines

Venous thromboembolism prevention in surgery and obstetrics: clinical practice guidelines

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Summary

Background and objective: To produce up-to-date clinical practice guidelines on the prevention of venous thromboembolism in surgery and obstetrics. Methods: A Steering Committee defined the scope of the topic, the questions to be answered, and the assessment criteria. Eight multidisciplinary working groups (total of 70 experts) performed a critical appraisal of the literature in the following disciplines: pharmacology of antithrombotic agents, orthopaedics; general surgery (gastrointestinal (GI) and varicose vein surgery); urology; gynaecology and obstetrics; thoracic, cardiac and vascular surgery; surgery of the head, neck and spine; and surgery of burns patients. The resultant reports and guidelines were submitted for comment and completion of the Appraisal of Guidelines Research & Evaluation questionnaire to a total of 150 peer reviewers, before producing definite guidelines. Results: The report answers the following questions for each type of surgery: (i) What is the venous thromboembolism incidence according to clinical and/or paraclinical criteria in the absence of prophylaxis? (with stratification of venous thromboembolism risk into low, moderate and high categories); (ii) What is the efficacy and safety of the prophylactic measures used? (iii) When should prophylaxis be introduced and how long should it last? (iv) Does ambulatory surgery affect efficacy and safety of prophylaxis? Conclusions: Apart from answering the above questions, the guidelines provide a summary table for each discipline. This table stratifies types of surgery into the three risk categories, specifies the recommended prophylaxis for venous thromboembolism (pharmacological and/or mechanical) and grades each recommendation. In addition, whenever appropriate, the recommended prophylaxis is adjusted to low- and high-risk patients.

Keywords: VENOUS THROMBOSIS, prevention; PULMONARY EMBOLISM; SURGERY, orthopaedics, trauma, urology, obstetrics, ambulatory, thoracic, vascular, cardiac, head and neck, spinal, neurosurgery, burns; CRITICAL CARE; HEPARIN; HEPARIN LOW-MOLECULAR-WEIGHT; INTERMITTENT PNEUMATIC COMPRESSION DEVICES; THROMBOEMBOLISM CLOTHING, compression stockings.
Introduction

These good practice guidelines were requested in 2002 by the Committee for Good Practice Standards of the French Society for Anaesthesiology and Intensive Care (SFAR) for several reasons:

1. an earlier, outdated report of the French National Health Insurance had noted that postoperative use of antithrombotics did not comply with French Drug Marketing Authorization requirements (AMM);
2. the National Agency for Healthcare Products Safety (AFSSAPS) did not have available any French guidelines for surgery and anaesthesia, and used those of the American College of Chest Physicians;
3. there were no recent guidelines; the last French consensus conference had taken place in 1991;
4. there was a vast amount of published literature;
5. new preventive measures had been developed;
6. surrogate criteria were considered weak and were being replaced by clinical criteria;
7. there were new products about to be marketed or already marketed.

For all these reasons, SFAR decided to develop the present guidelines.

Assessment method

Steering Committee

A Steering Committee was formed, comprising members of SFAR, a medical doctor representing the French National Agency of Accreditation and Evaluation in Healthcare (ANAES) (now part of the Haute Autorité de Santé) and members of surgical and other societies (see list in Appendix).

Working groups

The Steering Committee set up 8 working groups in mechanical prophylaxis and pharmacological agents, orthopaedics (including trauma to the limbs); general surgery (GI surgery and varicose vein surgery); urology; gynaecology and obstetrics; thoracic, cardiac and vascular surgery; surgery of the head and neck (including trauma to the head and spine); surgery and intensive care of burns patients. These groups were multidisciplinary. They included anaesthesiologists, surgeons, intensivists, haematologists and rehabilitation specialists, and their members came from different regions from all over France. A total of 70 experts were contacted.

Each group was run by a chairman whose job was to explain the work method to members, hand out the questions and coordinate the work. Members either met or exchanged information by E-mail or by telephone conference calls. Members of all 8 groups met in March 2004 to present and discuss their guidelines before sending them out for peer review.

Questions

The Steering Committee defined the scope of the topic, set the questions and established assessment criteria.

1. Question 1: Which prophylactic measures (physical, mechanical, pharmacological) are available to prevent venous thromboembolism (VTE) in surgical patients and in obstetrics, and how are they monitored?
2. Question 2:

   2.1 In the absence of prophylaxis, what is the incidence of clinical TE (deep vein thrombosis, pulmonary embolism (PE)) and of paraclinical events (information on thrombosis obtained by venography, ultrasound or labelled fibrinogen uptake)? Stratify surgical (including technical) risk into three risk categories (low, moderate or high).
   2.2 What is the efficacy and safety of the prevention measures in each risk category? (mechanical or physical methods used alone, heparins, vitamin K antagonists (VKAs), other antithrombotics, drugs combined with mechanical methods).
   2.3 When should these prophylactic measures be introduced and for how long should they be prescribed?
   2.4 Does ambulatory surgery affect the efficacy and safety of these measures?
   2.5 Does the type of anaesthesia affect the efficacy and safety of these measures?

Each working group had to answer Question 2. Question 2.4 was not applicable to all fields. Question 2.5 was not addressed because of lack of data for most surgical procedures.

The following were beyond the scope of these guidelines: description of patient-related risk factors, prevention in children, intensive care (guidelines issued in 2001 by the French-language Society for Intensive Care) and interactions between neuraxial anaesthesia and anticoagulants because SFAR is currently developing guidelines on operating theatres (expected in 2006).

Assessment criteria

The clinical criteria for efficacy were PE (fatal, non-fatal) and deep vein thrombosis (proximal, distal). The paraclinical criteria were those obtained by venography, ultrasound and labelled fibrinogen uptake. The
clinical safety criteria were blood loss, haematoma and transfusion requirements. The biological safety criterion was thrombocytopenia.

Critical review of the literature and evidence levels
The literature search was performed by a professional in database queries using the specific key words provided by study groups. Working group members carried out the literature review. Each selected study was analysed using the principles of critical appraisal to judge the quality of the study design and to allocate an evidence level. The guideline grading scheme is given in Table 1.

Peer review and validation
A balanced multidisciplinary group of over 150 peer reviewers was formed. It included both general practitioners and specialists (orthopaedic surgeons, general and GI surgeons, urologists, neurosurgeons, cardiothoracic and vascular surgeons, ENT surgeons, gynaecologists and obstetricians, anaesthesiologists and intensive care specialists, pharmacologists, haematologists, specialists in internal medicine, angiologists and specialists in rehabilitation). Peer reviewers sent a letter giving their opinion on the report and completed the AGREE questionnaire (Appraisal of Guidelines Research & Evaluation). Whenever possible, they provided appropriate references in support of their criticisms. All comments were handed to the group chairmen who met to discuss their relevance and inclusion in the guidelines.

Before implementation, the assessment method was approved by an expert in guideline methodology (Professor Valeron, Saint Antoine Hospital, Paris). The guidelines were produced in partnership with ANAES. The Agency provided methodological support, carried out the literature searches, and requested information on conflicts of interest. The production of the guidelines was financed jointly by SFAR and ANAES. The guidelines were presented and discussed at the SFAR topical meeting on 23 September 2004.

Accounting for patient-related risk
ANAES’ initial intention was to produce guidelines on VTE disease diagnosis and patient-related risk factors for thrombosis but had to suspend the work owing to organizational constraints. In view of this situation, SFAR decided to adopt the risk factors that are well described in the literature (Box 1).

Once the guidelines had been produced, SFAR drew up reference tables to help clinicians account for patient-related risk. Whenever appropriate and possible, prevention measures were given for patients with and without personal risk factors. These tables are numbered from A1 to A8 in the present document. The Steering Committee considered these tables a pragmatic summary of the recommendations even though the grades given were often low because patient-related risks are not taken into account in the literature.

Table 1. Grading of recommendations.

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level 1</strong></td>
<td></td>
</tr>
<tr>
<td>High-power randomized controlled trials</td>
<td>A: Established scientific evidence</td>
</tr>
<tr>
<td>Meta-analyses of randomized controlled trials</td>
<td></td>
</tr>
<tr>
<td><strong>Level 2</strong></td>
<td></td>
</tr>
<tr>
<td>Low-power randomized controlled trials</td>
<td>B: Presumption of scientific foundation</td>
</tr>
<tr>
<td>Properly conducted non-randomized controlled trials</td>
<td></td>
</tr>
<tr>
<td>Properly conducted uncontrolled prospective trials (e.g. cohort studies)</td>
<td></td>
</tr>
<tr>
<td><strong>Level 3</strong></td>
<td></td>
</tr>
<tr>
<td>Case-control studies</td>
<td>C: Low level of evidence</td>
</tr>
<tr>
<td><strong>Level 4</strong></td>
<td></td>
</tr>
<tr>
<td>Controlled studies with bias</td>
<td></td>
</tr>
<tr>
<td>Retrospective studies and case series</td>
<td></td>
</tr>
<tr>
<td>Observational epidemiological studies (transversal, longitudinal)</td>
<td></td>
</tr>
<tr>
<td><strong>No published evidence</strong></td>
<td>D: Agreement among professionals</td>
</tr>
</tbody>
</table>

Box 1. Patient-related risk factors for thrombosis.

- Immobilization, bed rest, limb paralysis
- Cancer and cancer treatment (hormones, chemotherapy, radiotherapy)
- History of VTE
- Age over 40 yr
- Oestrogen-containing contraception or hormone replacement therapy
- Selective oestrogen response modifiers (SERM)
- Acute disease
- Heart insufficiency, lung insufficiency
- Inflammatory bowel disease
- Nephrotic syndrome
- Myeloproliferative syndrome
- Paroxysmal nocturnal haemoglobinuria
- Obesity (BMI > 30)
- Smoking
- Varicose veins
- Central venous catheter
- Idiopathic or acquired thrombophilia
An important point to note with regard to patient risk factors is that many cardiovascular diseases call for both anticoagulant and antiplatelet treatment. Antiplatelet treatment must often be maintained in surgical patients. VTE prevention must take this into account, particularly because of the increased risk of bleeding.

Some key messages of these guidelines
To help the reader follow these guidelines, we provide a few introductory key messages:

1. These guidelines focus on symptomatic clinical VTE events rather than on the risk of asymptomatic events (e.g. thrombosis detected by venography). The risk of bleeding was analysed in each case and weighed against any benefit with respect to asymptomatic thrombosis.

2. The value of mechanical prophylaxis (elastic compression stockings (ECS), intermittent pneumatic compression (IPC)) is stressed. It should be combined with pharmacological prophylaxis whenever possible.

3. The dogma of preoperative low-molecular-weight-heparin (LMWH) injection was questioned, especially by the orthopaedics working group. Prophylaxis can be introduced before or after surgery.

4. The ‘moderate-risk’ LMWH dose no longer applies in orthopaedics; only the ‘high-risk’ dose is applicable. However, the ‘moderate-risk’ dose still applies in GI, urological, gynaecological, and burns surgery. In other contexts, the literature does not permit the choice of an optimal dose. In these instances, only the pharmacological class (i.e. LMWH) is mentioned.

5. In orthopaedics, no antithrombotic agent is preferred to any other with the exception of fondaparinux which is used for long-term prophylaxis in hip fracture patients. In all other situations, the use of either LMWH, fondaparinux or ximelagatran depends on the patient and on the surgical procedure.

6. Some risk levels have been reassessed (mostly decreased). Thus, lower extremity surgery (patient with a plaster cast for a fracture) has been downgraded from the high to moderate risk category. Arthroscopy and varicose vein surgery are considered to be low risk.

7. Long-term (4–6 weeks) prophylaxis is recommended in total hip replacement and femoral neck fracture patients. Prophylaxis need not be continued as a matter of routine 14 days after total knee replacement. Long-term prophylaxis is recommended in patients undergoing surgery for cancer of the abdomen or pelvis.

Which prophylactic measures (physical, mechanical, medicinal) are available and how are they monitored?

1. Physical or mechanical prevention

The origin of the formation of a venous thrombosis is multifactorial. Virchow’s triad still describes the causal factors: venous stasis, blood hypercoagulability and damage to the vessel wall. Physical and mechanical methods aim to counter venous stasis by replacing the ‘pump’ function of the calf and foot in order to speed up blood flow to the lower limbs. During bed rest or immobilization of a limb, there is a decrease in blood flow and onset of venous stasis, which is especially marked if upstream venous stasis is present and/or if return blood flow is hindered by compression (pregnant uterus, solid tumour, bone fracture …).

The mechanical methods currently available are elastic compression (ECS, socks or wraps), IPC devices and foot compression. Like passive and active mobilization used by physiotherapists, elevation of the legs, and early ambulation, they are used for the early rehabilitation of patients after surgery.

Whenever possible, mechanical methods are offered in conjunction with antithrombosis, as their effects differ and combining them is beneficial. They are particularly useful when anticoagulants are contraindicated or when the benefit/risk ratio precludes the use of antithrombosis, for instance because of a risk of bleeding.

2. Prevention by drugs

The aim of antithrombosis is to prevent the formation of a venous thrombus and/or restrict its extension by acting on the mechanisms of physiological haemostasis. However, there is a risk of bleeding. Their use therefore depends on assessing, for each individual patient, the antithrombotic benefit vs. the risk of bleeding. Drugs developed for this indication are given in Table 2 and classified according to mechanism of action. Most of the anticoagulants developed for the prevention of deep vein thrombosis act on thrombin (factor IIa) either directly (by blocking the active site either reversibly or irreversibly) or indirectly by reducing thrombin formation by inhibiting the activation of the factors involved in the coagulation cascade. New mechanisms of action are currently being explored, such as interaction with the tissue factor and/or activated factor VII and amplification of natural antithrombotic mechanisms. Prophylactic drug doses used in surgery are given in Table 3.

3. Clinical and biological monitoring

All treatments generally require monitoring of efficacy (especially if the therapeutic margin is
and possibly monitoring of the onset of the main side-effects. Reference drugs for VTE are unfractionated heparin (UFH), LMWHs and VKAs. The risk of bleeding is not to be ignored. Surveillance is mostly clinical. Mandatory monitoring tests are given in Table 4.

Table 2. Antithrombotics used in VTE prophylaxis.

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indirect inhibitors of thrombin (IIa) and/or of factor Xa</td>
<td>Via antithrombin (AT)</td>
</tr>
<tr>
<td></td>
<td>UFH</td>
</tr>
<tr>
<td></td>
<td>LMWH</td>
</tr>
<tr>
<td></td>
<td>Danaparoid sodium</td>
</tr>
<tr>
<td></td>
<td>Fondaparinux (anti-Xa only)</td>
</tr>
<tr>
<td></td>
<td>Via heparin cofactor (HC-II)</td>
</tr>
<tr>
<td></td>
<td>Dermapan sulphate (anti IIa only)</td>
</tr>
<tr>
<td>Direct inhibitors of thrombin (IIa)</td>
<td>Recombinant hirudin</td>
</tr>
<tr>
<td></td>
<td>(lepirudin, desirudin)</td>
</tr>
<tr>
<td></td>
<td>Hirudin derivatives</td>
</tr>
<tr>
<td></td>
<td>(bivalirudin)</td>
</tr>
<tr>
<td></td>
<td>Non-covalent inhibitors: small molecules acting as competitive inhibitors (argatroban, melagatran/ximelagatran)</td>
</tr>
<tr>
<td>Inhibitors of the tissue factor/factor VII complex</td>
<td>Complex TF/F VIIa: NAPc2</td>
</tr>
<tr>
<td>Action on coagulation factor synthesis</td>
<td>VKA</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>Aspirin</td>
</tr>
</tbody>
</table>

Table 3. Calcium heparin and LMWH doses used in surgery (according to French drug marketing authorizations).

<table>
<thead>
<tr>
<th>Moderate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium heparin s.c. injection bid</td>
<td>s.c. injection tid</td>
</tr>
<tr>
<td>0.2 mL (5000 IU)</td>
<td>0.2 mL (5000 IU)</td>
</tr>
<tr>
<td>LMWH s.c. injection once daily</td>
<td>Orthopaedics: 0.3–0.4 mL</td>
</tr>
<tr>
<td>0.3 mL (2800 IU)</td>
<td>(1860–3700 IU) depending on pre-op weight and until day 3; then 0.3–0.6 mL (2800–5600 IU) depending on pre-op weight from day 4</td>
</tr>
<tr>
<td>Enoxaparin 20 mg (2000 IU)</td>
<td>40 mg (4000 IU)</td>
</tr>
<tr>
<td>Dalteparin 2500 IU</td>
<td>5000 IU</td>
</tr>
<tr>
<td>Tinzaparin 2500 IU</td>
<td>3500 IU (cancer)</td>
</tr>
<tr>
<td></td>
<td>4500 IU (orthopaedics)</td>
</tr>
</tbody>
</table>

Orthopaedics and trauma

Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis? Stratify risk

Types of surgery can be stratified into three risk categories (high, moderate, low) by estimating the post-surgery VTE risk in the absence of prophylaxis (asymptomatic DVT) as detected by venography, labelled fibrinogen uptake, or Doppler ultrasound; symptomatic DVT and/or PE). However, the incidence of VTE may be overestimated because most of the underlying epidemiological data is out of date and does not take into account the considerable progress made in surgical and anaesthesia techniques. It is also necessary to know the incidence of VTE after short-term prophylaxis (7–14 days) in patients undergoing major orthopaedics surgery in order to decide whether prophylaxis should be continued and/or whether new strategies further reducing VTE risk, but without increasing risk of bleeding, should be developed.

1. VTE risk after major orthopaedic surgery (hip or knee replacement, hip fracture)
   - In the absence of prophylaxis, the risk of early postoperative (14 days) VTE is high after total hip or knee replacement and hip fracture surgery. The estimated risk of asymptomatic VTE is 50% and of clinical VTE is 5–15%.
   - After short-term prophylaxis (7–14 days), the risk of postoperative VTE remains high for 4–6 weeks after total hip replacement and hip fracture surgery. The risk of symptomatic VTE 4–6 weeks after short-term prophylaxis for total knee replacement is more moderate.
Table 5. Risk categories for VTE after trauma surgery and ambulatory surgery.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Risk category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple trauma</td>
<td>Not known with accuracy as estimated in highly heterogeneous populations</td>
</tr>
<tr>
<td>Trauma of lower extremities (fracture or ligament lesion of tibia–peroneal muscle, ankle, foot)</td>
<td>Moderate (higher for fractures than soft tissue lesions)</td>
</tr>
<tr>
<td>Knee ligament reconstruction (anterior cruciate ligament)</td>
<td>Low</td>
</tr>
<tr>
<td>Knee arthroscopy</td>
<td>Low</td>
</tr>
<tr>
<td>Isolated fractures of femoral diaphysis</td>
<td>No reliable data available</td>
</tr>
</tbody>
</table>

Table 6. Risk of VTE in orthopaedic and trauma surgery.

<table>
<thead>
<tr>
<th></th>
<th>Mean estimated risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip replacement, knee replacement, and hip fracture</td>
<td></td>
</tr>
<tr>
<td>Total DVT*</td>
<td>~50</td>
</tr>
<tr>
<td>Proximal DVT*</td>
<td>&gt;15</td>
</tr>
<tr>
<td>PE and/or clinical VTE</td>
<td>&gt;5</td>
</tr>
<tr>
<td>Multiple trauma</td>
<td></td>
</tr>
<tr>
<td>Total DVT*</td>
<td>~15–60</td>
</tr>
<tr>
<td>PE and/or clinical VTE</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Fracture or lesion of the ligament (tibia–peroneal muscle, ankle and foot)</td>
<td></td>
</tr>
<tr>
<td>Total DVT*</td>
<td>~15</td>
</tr>
<tr>
<td>Proximal DVT*</td>
<td>&lt;5</td>
</tr>
<tr>
<td>PE and/or clinical VTE</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Knee ligament reconstruction (anterior cruciate ligament)</td>
<td></td>
</tr>
<tr>
<td>Total DVP</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Clinical PE</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Ambulatory surgery (knee arthroscopy)</td>
<td></td>
</tr>
<tr>
<td>Total DVT*</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>

*Detected by venography and/or ultrasound.
DVT: deep vein thrombosis; PE: pulmonary embolism.

2. Risk of VTE after trauma surgery and ambulatory surgery

VTE risk has been stratified for different types of surgery in Table 5.

Mean estimated risks of VTE in orthopaedic and trauma surgery patients are given in Table 6.

Question 2.2: Efficacy and safety of prevention measures

1. Major orthopaedic surgery (total hip or knee replacement, hip fracture)
   - After major orthopaedic surgery, VTE risk is high and warrants routine prescription of preventive measures (evidence level 1).
   - UFH, LMWHs and VKAs reduce the risk of VTE by about 50% irrespective of type of surgery. The efficacy of fixed-dose UFH seems to be increased if the dose is adjusted to activated partial thromboplastin time (aPTT) (evidence level 2).
   - Aspirin reduces the risk of symptomatic postoperative VTE after hip replacement and hip fracture surgery but its intrinsic effect is difficult to assess as patients also receive other prophylactic agents, in particular heparin (evidence level 2).
   - LMWHs are more effective than UFH in hip or knee replacement and hip fracture patients (level 1). The risk of bleeding is lower with LMWHs than UFH in knee replacement surgery (level 1). LMWHs are more effective than VKAs in hip or knee replacement and in hip fracture patients, and do not have an impact on bleeding risk (level 1). However, this is not true in countries such as France where there are no specialist centres for monitoring VKA treatment. In these countries, VKAs are associated with an increased risk of bleeding compared to LMWHs (level 1).
   - Fondaparinux is more effective than LMWHs in the prophylaxis of asymptomatic DVT (distal and proximal) but has an increased risk of major bleeding (level 1). The risk of thrombocytopenia however seems to be lower (level 2).
   - Melagatran/ximelagatran are no less effective and no less safe than LMWHs after hip or knee replacement surgery (level 1). When injected more than 4 h postoperatively, it could reduce the number of patients requiring transfusion as compared to LMWHs treated patients (level 2). It does not induce thrombocytopenia.
   - Danaparoid (level 2) and desirudin (level 1) reduce the risk of VTE in hip replacement patients. Desidurin is more effective than a LMWH in the prophylaxis of asymptomatic VTE after hip replacement surgery only.
   - Mechanical methods, in particular IPC, reduce the risk of postoperative VTE (level 1).

2. Trauma surgery
   - Multiple trauma: LMWHs reduce the risk of VTE; the risk of bleeding compared to that of UFH is acceptable (level 1). IPC also reduces VTE risk without increasing the risk of bleeding (level 2).
   - Trauma of the lower extremities: LMWHs reduce the risk of asymptomatic VTE without increasing the risk of major bleeding after a plaster cast for a fracture or after a ligament lesion of the lower extremities (tibia–peroneal muscle, ankle, foot) (level 1).

3. Arthroscopy (knee ligament reconstruction) and ambulatory surgery
LMWHs effectively reduce the risk of VTE without significantly increasing the risk of major bleeding after arthroplasty (level 1).

Guidelines derived from the above observations and by professional agreement are given in Box 2.

Question 2.3: When to start prescribing and for how long?

1. Introduction of prophylaxis
   - LMWHs: The risk of VTE and bleeding apparently does not depend on whether LMWHs are given either 12 h before or 12 h after surgery. However, administration from 2 h before surgery to 4 h after surgery seems to be associated with an increased risk of bleeding (level 2).
   - Fondaparinux (hip or knee replacement, hip fracture): A first injection increases the risk of bleeding when given earlier than 6 h after surgery but does not increase risk nor affect efficacy when given 6–8 h after surgery (level 2).
   - Melagatran/ximelagatran is as effective and as safe as LMWHs when administered between 4 and 12 h after total hip or knee replacement (level 1).

2. Duration of prophylaxis
   - Long-term prophylaxis with LMWHs until postoperative day 42 reduces the risk of VTE after hip replacement surgery without increasing the risk of severe bleeding (level 1).
   - Long-term prophylaxis with LMWHs until postoperative day 30–42 does not seem to reduce the risk of VTE after knee replacement surgery (level 2).
   - Long-term administration of fondaparinux and melagatran/ximelagatran has not been studied in hip or knee replacement surgery.
   - For hip fracture, prophylaxis with fondaparinux until postoperative day 35 reduces the VTE risk after hip fracture without increasing the risk of major bleeding (level 1).
   - Long-term administration of LMWHs and melagatran/ximelagatran has not been studied in hip fracture patients. However, some LMWHs have been approved in France for long-term prophylaxis in this indication.

Guidelines on the introduction and duration of prophylaxis derived from the above observations and obtained by agreement among professionals are given in Boxes 3 and 4.

Question 2.4: Ambulatory surgery

Available efficacy and safety data for prophylactic measures in the ambulatory setting concern knee arthroscopy only. The studies are rather dated and do not distinguish between diagnostic and therapeutic arthroscopy that may require hospital admission. The VTE risk after arthroscopy is low (level 1). LMWHs reduce risk after arthroscopy without increasing the risk of severe bleeding (level 2). This has been noted after short-term prophylaxis (level 2).
In view of the low risk of VTE, routine prophylaxis is not justified after arthroscopy (Grade B). Prescription beyond day 14 should be envisaged in patients with an additional risk factor for VTE (Grade B).

For hip fracture, the prescription of fondaparinux until postoperative day 35 is justified (Grade A).

For other orthopaedic and trauma surgery, in view of the moderate or low risk, routine long-term prophylaxis beyond postoperative day 14 is not recommended (Grade C). The indication for long-term prophylaxis will depend on the presence of additional VTE risk factors (Grade C).

In the absence of prophylaxis, the risk of distal venous thrombosis, as detected by paraclinical examinations, is 20–40%; the risk of proximal venous thrombosis is 3–8%. The incidence of PE is 1.5–4% (0.4–1% for fatal PE). The overall TE risk, confirmed by paraclinical examinations, is 30% for cancer surgery; it is 35% for colorectal surgery and 45% for pelvic surgery. Fatal PE occurs in 3% of patients undergoing colorectal surgery. One in four cases is fatal. There are no data for VTE risk for bariatric surgery (digestive surgery for obesity) in the absence of prophylaxis. The clinical VTE incidence is >2% in the presence of prophylaxis suggesting that the risk is high in its absence.

2. Non-major abdominal surgery (abdominal wall surgery, appendix, non-inflammatory bladder, proctology)

The VTE risk is low but not known with precision for each of these types of surgery. The clinical incidence is 0.1–0.6%. The risk is no higher for minimal access surgery for symptomatic bladder stones.

3. Surgery for varicose veins

The risk of VTE complications seems low: 0.2% for DVT, 0.11% for PE and 0.02% for fatal PE. VTE risk has been stratified for different types of surgery in Table 7.

Question 2.2: Efficacy and safety of prevention measures

1. Low risk situations

Pharmacological prophylaxis is not justified for low-risk surgical procedures (when patient-related risk is excluded) (Grade B). However, ECS
might be indicated; they lack adverse effects and, in general, have proven efficacy in patients undergoing abdominal surgery (Grade A).

2. Moderate risk situations

No specific studies address these situations. Prophylaxis with moderate-dose UFH (5000 IU bid) or with LMWHs may be offered (Grade D).

3. High risk situations

- Unfractionated heparin: UFH (5000 IU s.c. bid or 5000 IU s.c. tid) reduces the risk of both paraclinical venous thrombosis and PE by 60% (level 1). The risk of bleeding is twice that of placebo but the incidence remains low (about 3%).
- LMWHs reduce the incidence of paraclinical (venography) and clinical events by 72% compared to a placebo (level 1). The incidence of bleeding is doubled but remains low (about 2.8%) (level 1). Because of the reduced risk of paraclinical and clinical DVT and of bleeding, LMWHs are preferred to UFH (level 1). For reasons of efficacy, safety and ease of use, LMWHs are recommended as first-line prophylaxis in the absence of renal impairment (Grade A). A LMWH dose for a high risk situation is recommended for major abdominal surgery (Grade A).
- Danaparoid sodium seems to reduce the risk of paraclinical DVT but the statistical power of the studies is low (level 2). It is an alternative only when UFH and LMWHs are contraindicated (Grade B).
- Aspirin is effective in preventing VTE when compared to a placebo (level 2), but the studies are dated and do not have the same design quality as studies with heparin. Aspirin cannot therefore be currently recommended in this indication (Grade B).
- VKAs are not recommended in this indication (Grade B).
- Fondaparinux: In a GI trial, fondaparinux was not superior to other products.
- Melagatran/ximelagatran: There are no studies for GI surgery.
- ECS reduce the incidence of paraclinical VTE by 66% in general surgery when compared to ‘no ECS’ (level 1). When combined with UFH, they reduce incidence by 72% compared to UFH alone (level 2). ECS are recommended when anticoagulants are contraindicated (Grade A) and when combined with drug prophylaxis (Grade B). The efficacy of IPC alone or in conjunction with drug prophylaxis has not been proven in this indication (level 3).

**Question 2.3: When to start prescribing and for how long?**

1. Introduction of prophylaxis

Most studies have used preoperative injection. The value of starting prophylaxis after surgery has not been investigated. There is no evidence for preferring one schedule to the other.
2. Duration of prophylaxis
Duration in most available studies is 7–10 days for GI surgery. Longer-term prophylaxis has been studied and is recommended for major abdominal cancer surgery. In this case, extending prophylaxis to 1 month has reduced paraclinical thrombosis by 50% without increasing the risk of bleeding (level 1). Prolonged prophylaxis is therefore recommended for major abdominal cancer surgery (Grade A).

Question 2.4: Ambulatory care
The impact of ambulatory surgery and short hospital stays has not been assessed in GI surgery.

Recommendations for VTE prophylaxis in GI and varicose vein surgery are summarized in Table A2.

Urology

Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis? Stratify risk
There has been little assessment in the literature of the measures taken to prevent VTE risk in urology. Most reports rely on epidemiological data for VTE and on a few dated randomized trials.

1. Surgery of the upper urinary tract
The estimated risk of clinical VTE is 1–5% for open surgery of the upper urinary tract. Cases of fatal PE have been reported. Endoscopic surgery of the upper urinary tract has a low risk of postoperative venous thrombosis.

2. Surgery of the lower urinary tract
In the absence of prophylaxis, the risk of proximal venous thrombosis after open surgery is 10–30% and that of PE is 1–10% (fatal PE 5%). When Doppler ultrasound or labelled fibrinogen uptake are used to detect venous thrombosis, the incidence is 28–51%.

After endoscopic surgery of the lower urinary tract, the frequency of symptomatic phlebitis is 0.1–0.75% and that of clinical PE is 0.1–0.84%. The frequency of asymptomatic venous thrombosis is 4–29% and the risk of subclinical PE is 0–6%.

3. Kidney transplantation
In the absence of prophylaxis, the risk of clinical proximal venous thrombosis is about 5%.

4. Lymph node dissection (lumbar or pelvic)
The VTE risk is about 5%.

5. Laparoscopy
The spontaneous risk of VTE after laparoscopic urological surgery cannot be determined from published data.

VTE risk has been stratified for different types of urological surgery in Table 8.

Question 2.2: Efficacy and safety of prevention measures
– Open urological procedures: The need for VTE prevention and its efficacy have been established in several studies and in one meta-analysis (level 1). Anticoagulant use, sometimes combined with mechanical methods, reduces VTE risk (level 1). Prophylaxis with UFH reduces VTE risk after open pelvic surgery (cystectomy and prostatectomy) (level 1) and after nephrectomy (level 2).
– Kidney transplantation: Prophylaxis seems justified (level 4).
– Endoscopic surgery of the upper or lower urinary tract: The efficacy of anticoagulants and mechanical methods in reducing the risk of postoperative VTE has not been proven (level 2).
– Endoscopic resection of the prostate: Anticoagulant prophylaxis does not increase the risk of bleeding (level 2).
– Other types of urological surgery: Anticoagulant prophylaxis does not seem to increase the risk of bleeding (level 4).

Table A2. Summary of recommendations for VTE prophylaxis in GI and varicose vein surgery.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Type of surgery</th>
<th>Patient-related risk</th>
<th>Recommendations</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Varicose veins</td>
<td>−</td>
<td>ECS</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Non-major abdominal surgery (appendix, non-inflammatory bladder, proctology, wall surgery)</td>
<td>+</td>
<td>Moderate-dose LMWH or ECS</td>
<td>D</td>
</tr>
<tr>
<td>Moderate</td>
<td>Extensive and/or bloody dissection</td>
<td>−</td>
<td>Moderate-dose LMWH or ECS</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Abnormally long operative time</td>
<td>+</td>
<td>High-dose LMWH</td>
<td>D</td>
</tr>
<tr>
<td>High</td>
<td>Major abdominal surgery (liver, pancreas, colon, inflammatory or malignant disease of GI tract)</td>
<td></td>
<td>High-dose LMWH combined with ECS</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Bariatric surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ECS: elastic compression stockings.
Recommendations derived from the above observations and by agreement among professionals are given in Box 5.

**Question 2.3: When to start prescribing and for how long?**

When the first injection should be given has not been addressed in urology studies. In most studies, the injection was given before surgery. However, it may be delayed in the event of local and regional anaesthesia, and should then occur 6–12 h after surgery (level 4). In most studies, prophylaxis was continued until patients were discharged from hospital (7–10 days). The superiority of high-dose LMWHs given for 4–6 weeks compared to short-term prophylaxis was demonstrated in a study in patients undergoing surgery for abdominal and pelvic cancer, that included a small number of patients undergoing surgery for urological cancer.

There is no evidence for recommending initiating prophylaxis either before or after surgery. In the case of regional anaesthesia, prophylaxis may be introduced after surgery (Grade B). The recommended duration is 7–10 days (Grade B) except for cancer surgery (4–6 weeks) (Grade B). However, the data underlying these recommendations need to be confirmed.

**Question 2.4: Ambulatory surgery**

Urological surgical procedures performed in an ambulatory setting have a low risk of VTE. There is no need to modify the prophylaxis schedule for ambulatory surgery (Grade D).

Recommendations for VTE prophylaxis in urological surgery are summarized in Table A3.

### Table 8. Risk categories for symptomatic VTE after urological surgery.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Risk category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous kidney surgery</td>
<td>Low</td>
</tr>
<tr>
<td>Surgery of the adrenals</td>
<td>Low</td>
</tr>
<tr>
<td>Ureteroscopy, ureter surgery</td>
<td>Low</td>
</tr>
<tr>
<td>Endoscopic bladder and prostate surgery</td>
<td>Low</td>
</tr>
<tr>
<td>Perineal incontinence surgery</td>
<td>Low</td>
</tr>
<tr>
<td>Surgery of the testes, urethra</td>
<td>Low</td>
</tr>
<tr>
<td>Open kidney surgery (nephrectomy, ureteropelvic junction obstruction; surgery for stones)</td>
<td>High</td>
</tr>
<tr>
<td>Open lower urinary tract surgery (prostate, bladder, cure for incontinence)</td>
<td>High</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>High</td>
</tr>
<tr>
<td>Lymph node dissection (pelvis; abdomen)</td>
<td>High</td>
</tr>
</tbody>
</table>

**Gynaecological surgery**

**Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis?**

**Stratify risk**

The postoperative risk of VTE in the absence of prophylaxis has not been assessed in any depth. VTE risk has been stratified for different types of gynaecological procedures in Table 9. The use of a laparoscopic procedure does not modify antithrombotic prophylaxis. Patient-related risk factors need to be considered in addition to surgical risk factors but no studies have shown how important they may be, nor how they may increase surgical risk.

**Question 2.2: Efficacy and safety of prevention measures**

1. **Mechanical methods only (early mobilization, ECS)**

   Mechanical methods are useful to reduce the risk of postoperative VTE in gynaecological surgery. The number needed to treat (NNT) ranges from 5 for IPC (≥5 days) to 23 for ECS. ECS thus have a prophylactic effect but this effect is limited. Mechanical methods should be preferred when there is a risk of bleeding and anticoagulants are contraindicated (Grade A). They have disadvantages with regard to ease of use rather than contraindications and are an effective adjuvant to pharmacological prophylaxis (Grade D).

2. **Heparins**

   UFH reduces the risk of DVT (NNT = 11) (level 1) but it is associated with a significant increase in the number of haematomas at the injection site. UFH and LMWHs are no different in terms of efficacy or side-effects (bleeding, transfusion).

**Box 5. Guidelines for prophylaxis in urological surgery.**

- Prophylaxis is recommended in patients undergoing open pelvic surgery (Grade A), nephrectomy (Grade B) or a kidney transplant (Grade D).
- Prophylaxis is not recommended in patients undergoing endourological surgery of the lower urinary tract in the absence of additional risk factors (Grade B).
- Prophylaxis is not recommended in patients undergoing endourological surgery of the upper urinary tract in the absence of additional risk factors (Grade D).
- No recommendations can be made for urological surgery by laparoscopy on the basis of published studies.
Because of their ease of use, heparins are considered to be the standard reference treatment in gynaecological surgery (Grade A).

3. VKAs

VKAs have shown significant efficacy in surgery for both malignant and non-malignant disease (NNT = 6) (level 1). There is no evidence for a significant difference between VKAs and UFH in terms of efficacy and postoperative bleeding risk (level 1).

4. Other anticoagulants

Other antithrombotic agents (hirudin, danaparoid, fondaparinux, melagatran/ximelagatran) have not been assessed in gynaecological surgery.

5. Aspirin

The efficacy of aspirin alone vs. either placebo, UFH or LMWHs has not been assessed.

6. Combinations

Drugs combined with mechanical methods have not been assessed.

**Question 2.3: When to start prescribing and for how long?**

1. Introduction of prophylaxis

ECS should be fitted preoperatively and maintained during and after surgery until the patient is ambulatory (Grade D). If IPC is the chosen compression method, it should be maintained for the first 5 days after surgery (Grade B).

In available studies, anticoagulants are usually given 12 to 2 h before surgery (level 1). No study has compared the efficacy of starting heparins (UFH or LMWHs) before and after surgery. A platelet count should be performed before initiating anticoagulant treatment. A routine heparin assay (anti-Xa activity or aPTT) is not recommended for LMWH prophylaxis (Grade D).

2. Duration of prophylaxis

Prophylaxis usually lasts for 7–14 days for surgery with a moderate risk (Grade D) and for 4 weeks if the risk is high (Grade A).

**Question 2.4: Ambulatory surgery**

No anticoagulant prophylactic measure other than early mobilization is recommended for the vast majority of patients undergoing gynaecological surgery in the ambulatory setting (Grade D). However, when a risk of thrombosis has been found, ECS and/or heparin should be prescribed (Grade D).

Recommendations for VTE prophylaxis in gynaecological surgery are summarized in Table A4.
Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis?

Stratify risk

1. Natural incidence of VTE
   - *During pregnancy and postpartum.* The incidence of VTE is difficult to assess in obstetrics, and the numbers given below should be considered with caution. In France, there are 5–10 maternal deaths/year (i.e. 6–12/1 000 000 births) due to PE; care is suboptimal in one-third of cases. The overall incidence of VTE seems to have fallen over recent decades. It is 1/1000 according to recent studies. DVT tends to occur prepartum and PE postpartum. It is uncertain whether VTE occurs most often during the third trimester of pregnancy. Several studies suggest occurrence at any time during pregnancy, and other studies reveal a higher incidence at the start of pregnancy. DVT is 6–7 times more common in the left than right limb.
   - *Caesarean section* increases the risk of VTE by a factor of 2–5. However, an elective Caesarean section is a procedure with a low risk of VTE.

2. Risk factors and categories
   - *Pregnancy itself* is a risk factor so that the VTE risk in obstetrics patients is 5 times higher than in the general population.
   - *Individual factors before pregnancy:* Many clinical or biological risk factors have been identified by methods of variable validity. Their exacerbating role may be minor (age, smoking, obesity, non-O blood group), marked (history of heart disease) or poorly known (history of superficial phlebitis). A personal history of VTE increases the risk of recurrence; the estimated incidence of clinical events is 0–20%. A family history of VTE would similarly increase the risk. The wide incidence range could be due to at least two related factors: (i) whether a risk factor during a previous VTE episode was temporary or not. The risk of recurrence is considered to be lower if the risk factor was temporary rather than permanent, (ii) the presence of biological thrombophilic defects. The relationship between thrombophilia (idiopathic or acquired) and pregnancy has been the subject of a recent French consensus conference. The prevalence of VTE and relative risk due to heritable risk factors is summarized in Table 10. The homozygote mutation methylenetetrahydrofolate reductase (MTHFR) is not related to a significant risk of VTE during pregnancy, in particular in the case of folic acid supplementation. Among acquired deficiencies, the antiphospholipid antibody syndrome is the most common (prevalence about 0.5–1/1 000). The relative risk of maternal VTE is high, probably close to that for antithrombin deficiency, and warrants similar prophylaxis.
   - *Pregnancy-related factors:* These factors are parity, multiple pregnancies, strict bed rest, pre-eclampsia, postpartum suppression of lactation, post-caesarean thrombocytosis, haemorrhage/anaemia and transfusion. Opinion on their importance varies, suggesting that the risk associated with each of these factors is low.

Case series have shown no evidence for a relationship between onset of obstetrical VTE and the plasma level of D-dimers or of thrombin–antithrombin complexes. VTE risk in obstetrics has been stratified in Table 11.
Question 2.2: Efficacy and safety of prevention measures

1. Mechanical methods
   - ECS: They can be used alone in low-risk patients and combined with other measures in high-risk patients (Grade D).
   - Temporary vena cava filters: They have been proposed for DVT during pregnancy when anticoagulants are contraindicated or for recent extensive thrombosis at high risk of embolism during the peripartum (Grade D).

2. UFH and LMWHs
   Few studies have compared UFH and LMWH; they suggest similar efficacy (level 2). UFH does not cross the placental barrier and can therefore be used throughout pregnancy (level 2). LMWHs that have been studied (dalteparin and enoxaparin) do not cross the placental barrier during the second and third trimesters and do not increase the risk of malformations or neonatal haemorrhage (level 2). UFHs and LMWHs do not alter the course of pregnancy. The higher incidence of premature births seems to be related to the patient receiving prophylaxis (level 2). Maternal haemorrhage is more common in treated than untreated patients (level 2). UFH seems to cause maternal haemorrhage more often than a LMWH (level 3). Similarly, the risk of osteoporosis due to prolonged prophylaxis is more common and severe with UFH than with a LMWH in comparative trials (level 2). During pregnancy, the incidence of heparin-induced thrombocytopenia seems to be higher with UFH (level 2). This risk is less than 1% with LMWHs (level 4).

Table 10. Prevalence and risk of DVT in patients with a biological thrombophilic risk factor.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Prevalence in the general population (%)</th>
<th>Prevalence in patients with previous VTE (%)</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin deficiency</td>
<td>0.01–0.02</td>
<td>1–3</td>
<td>25–80</td>
</tr>
<tr>
<td>Protein C deficiency (heterozygote)</td>
<td>0.2–0.5</td>
<td>3–22</td>
<td>3–10</td>
</tr>
<tr>
<td>Protein S deficiency (heterozygote)</td>
<td>0.14–0.8*</td>
<td>5–8</td>
<td>7</td>
</tr>
<tr>
<td>Factor V Leiden (heterozygote)</td>
<td>2–9</td>
<td>30–60</td>
<td>3–8</td>
</tr>
<tr>
<td>Prothrombin gene mutation 20210A (heterozygote)**</td>
<td>2–3</td>
<td>4–6</td>
<td>1.2–4</td>
</tr>
</tbody>
</table>

*Difficult to establish because of different assay methods.
**Few data for homozygote status.

Table 11. Risk categories for maternal VTE during pregnancy, the postpartum and after Caesarean section (adapted from the French Thrombophilia and Pregnancy consensus conference, 2003).

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Patient population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major risk</td>
<td>History of multiple VTE episodes Patients receiving long-term anticoagulants before pregnancy for a previous thrombophilia-related VTE episode</td>
</tr>
<tr>
<td>High risk</td>
<td>History of VTE, with no detected risk factor History of VTE, with one of the following biological risk factors: AT deficiency*, APLS* Isolated homozygote 20210A mutation or F V Leiden Combined heterozygote abnormalities* (especially 20210A mutation + homozygote Leiden) History of VTE during a previous pregnancy or during oestrogen treatment</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>History of VTE with temporary trigger factor during a previous episode History of VTE with biological risk factor (other than those cited above) Presence of a biological risk factor that was asymptomatic and detected in the context of familial VTE, in particular if AT deficiency*, APLS* Isolated homozygote 20210A mutation or F. V. Leiden Combined heterozygote abnormalities* (especially 20210A mutation + homozygote Leiden) Emergency Caesarean section Caesarean section with major pelvic surgery Presence of ≥3 low-risk factors</td>
</tr>
<tr>
<td>Low risk</td>
<td>No risk factor Or presence of &lt;3 of the following factors: Age &gt; 35 yr, obesity (BMI &gt; 30 or weight &gt; 80 kg), varices, hypertension Obstetrical factors: Caesarean section, multiparity &gt; 4, pre-eclampsia, prolonged bed rest, postpartum haemorrhage, etc. Underlying thrombogenic disease (nephrotic syndrome, episodes of chronic inflammatory bowel disease, intercurrent systemic infection, etc.)</td>
</tr>
</tbody>
</table>

* For asymptomatic AT deficiency or APLS (antiphospholipid syndrome), risk was assessed on a case-by-case basis according to the importance of family history. BMI: body mass index.
LMWH dose should be adapted to patient weight and/or anti-Xa activity (Grade D).

3. VKAs
VKAs cross the placental barrier and cause typical embryopathy when given between 6 and 12 weeks of amenorrhea (level 2). There is an increased risk of foetal haemorrhage when VKAs are used later during pregnancy (level 2). There are no studies documenting their use in obstetrics. The risk of maternal haemorrhage is also increased (level 2).

4. Fondaparinux and ximelagatran
Warfarin is not transferred into maternal milk and can be used postpartum (level 2). According to an experimental study, fondaparinux does not cross the placental barrier (level 4).

Question 2.3: When to start prescribing and for how long?
Indications and treatment durations are given in Table A5 for different clinical situations and risk categories (Grade D). All these recommendations are based on a low level of evidence (level 4).

Thoracic surgery

Question 2.1: What is the VTE incidence in the absence of prophylaxis?
The incidence of VTE diagnosed by labelled fibrinogen uptake after lobectomy and pneumonectomy ranges from 9% to 18%. The incidence after diagnosis by Ultrasonography is 4%. The incidence of symptomatic PE after thoracotomy ranges from 3% to 5% and that of lethal PE from 0.2% to 1%. This suggests a high risk of VTE complications.
The incidence of PE after thoracic surgery by thorascopy, assessed in a single study, was 1.3%. That after mediastinoscopy, also reported in a single study, was 2%.

Question 2.2: Efficacy and safety of prevention measures
1. Mechanical methods
A retrospective study found a decrease in PE after thoracic surgery in patients with IPC (0%) compared to those without prophylaxis (2%) (Grade D).

2. Heparins (UFH, LMWH) and VKAs
Antithrombotics are recommended after resection by thoracotomy or thorascopy (Grade C). A prophylactic dose of a LMWH should be administered by the subcutaneous route, or alternatively UFH should be given by continuous infusion or subcutaneously (Grade D). According to a single study, VKA would also be effective but its use has not been considered in clinical practice (Grade D).

No recommendations can be made for mediastinoscopies.
The safety of antithrombotic treatments has not been evaluated in thoracic surgery.

Table A5. Summary of recommendations for VTE prophylaxis in obstetrics.

<table>
<thead>
<tr>
<th>Risk</th>
<th>During pregnancy</th>
<th>Postpartum and after Caesarean section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>No anticoagulants</td>
<td>No routine anticoagulants during postpartum. ECS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-dose LMWH (enoxaparin 4000 IU/day or dalteparin 5000 IU/day) for 6–8 weeks. Reduced dose and duration for lower risk (e.g. emergency Caesarean without additional risk factor (enoxaparin 20 mg or dalteparin 2500 IU/day 7–14 days). ECS</td>
</tr>
<tr>
<td>Moderate</td>
<td>No anticoagulants routinely ECS</td>
<td>High-dose LMWH (enoxaparin 4000 IU/day or dalteparin 5000 IU/day) for 6–8 weeks after delivery. ECS</td>
</tr>
<tr>
<td>High</td>
<td>High preventive dose LMWH (enoxaparin 4000 IU/day or dalteparin 5000 IU/day) or intermediate curative dose LMWH (enoxaparin 4000 IU bid or dalteparin 5000 IU bid) during 3rd trimester or throughout pregnancy* ECS</td>
<td>VKAs for at least 3 months ECS</td>
</tr>
<tr>
<td>Major</td>
<td>Curative treatment with UFH during the 1st trimester, then with a LMWH (adjusted to weight or to anti-Xa) during the 2nd and 3rd trimesters ECS</td>
<td></td>
</tr>
</tbody>
</table>

*In the case of asymptomatic antiphospholipid syndrome, low-dose aspirin is often recommended.
ECS: elastic compression stockings.

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Question 2.3: When to start prescribing and for how long?
Antithrombotic prophylaxis should usually be started between hours 4 and 12 after surgery (Grade D). There is no consensus on the duration of prophylaxis.

Question 2.4: Ambulatory surgery
Not applicable.

Vascular surgery

Question 2.1: What is the incidence VTE in the absence of prophylaxis?
After surgery of the aorta, the incidence of VTE, as diagnosed by labelled fibrinogen uptake, ranges from 20% to 27% and that of DVT from 4% (ultrasound) to 18% (venography). The laparoscopic route does not modify the incidence of DVT. This suggests a high risk of VTE. The incidence after peripheral vascular surgery ranges from 1.8% (ultrasound) to 28% (venography). The VTE incidence after thoracic aorta surgery or carotid surgery is not known.

Question 2.2: Efficacy and safety of prevention measures
1. Mechanical methods
   A randomized controlled trial with several methodological flaws did not establish the efficacy of IPC combined with UFH.
2. Heparins (UFH, LMWHs)
   Antithrombotics should be prescribed after aortic or peripheral vascular surgery (Grade D). Because the efficacy of LMWHs and UFH is similar, either drug can be prescribed in this indication (Grade B and Grade D).
3. VKAs
   The efficacy of warfarin, administered from day 1, in preventing DVTs has not been established (Grade B). VKAs should not be prescribed in this indication (Grade D).
   The safety of antithrombotic drugs has not been assessed in vascular surgery.

Question 2.3: When to start prescribing and for how long?
There are no published data on which to base recommendations for choice of dose or for the introduction and duration of prophylaxis (Grade D).

Question 2.4: Ambulatory surgery
Not applicable.

Cardiac surgery

Question 2.1: What is the incidence of VTE in the absence of prophylaxis?
1. Coronary artery grafting
   The reported incidence of DVT (ultrasound) after coronary artery grafting bypass surgery is 22%. The incidence of proximal DVT is 3%. The incidence of PE, suspected clinically and confirmed by paraclinically, ranges from 0.6% to 9.5%. This suggests a high risk of VTE complications. The incidence of DVT or PE in the absence of prophylaxis in patients undergoing coronary artery beating-heart-bypass surgery is not known.

2. Valve surgery
   The incidence of VTE complications in the absence of prophylaxis cannot be assessed after valve surgery because effective anticoagulant treatment is indicated in most cases.

Question 2.2: Efficacy and safety of prevention measures
There are few studies. Most are uncontrolled and do not enable any conclusions to be drawn.

1. Coronary artery grafting (with or without extracorporeal circulation)
   Antithrombotic drugs are recommended (Grade D).
   – UFH or LMWH: A prophylactic dose of a LMWH should be administered by the subcutaneous route, or alternatively UFH should be given by continuous infusion or by the subcutaneous route (target aPTT = 1.1–1.5 times control value) (Grade D). The efficacy of VKAs has not been assessed in this type of surgery.
   – IPC alone is ineffective (Grade B) but it could reduce the incidence of VTE complications when combined with UFH (Grade B).

Antiplatelet drugs, which are in virtually routine use during the perioperative period, do not appear to affect the incidence of VTE.
   The safety of these prevention strategies have not been assessed.

2. Valve replacement surgery
   Antithrombotic treatment for the prevention of valve thrombosis is recommended and seems to be effective in preventing DVT and PE. Incidence is reduced to a very low level (0–0.5%). Mechanical methods alone or combined with pharmacological prophylaxis have not been assessed. Antithrombotic treatment does not seem to affect unduly the risk of bleeding immediately after surgery.
Question 2.3: When to start prescribing and for how long?

1. Bypass surgery
   Antithrombotic prophylaxis should usually begin 6–12 h after surgery (Grade D). The duration of prophylaxis has not been the subject of a consensus.

2. Valve surgery
   Antithrombotic prophylaxis depends on the age of the patient, the type and position of the valve, underlying heart disease and any heart rhythm disorder.

Question 2.4: Ambulatory surgery
Not applicable.
Recommendations for VTE prophylaxis in thoracic, cardiac and vascular surgery are summarized in Table A6.

Head and neck surgery, spine and spinal trauma surgery

Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis?

Stratify risk

1. Neurosurgery
   The risk of DVT is high for intracranial neurosurgery. DVT occurrence is 20–35% (venography) with a frequency of 2.3–6% for symptomatic DVT in the absence of prophylaxis. Specific risk factors are a motor deficit, a malignant tumour or a meningioma, a large tumour, age over 60 yr, chemotherapy, and surgery lasting for more than 4 h. The risk of DVT in patients with an isolated head trauma is less well known but is also high (about 5%).

2. Spine and spinal trauma surgery
   The VTE risk in spine surgery in the absence of trauma depends on the type of surgery. For ‘minor’ surgery (herniated disk, laminectomy performed at one or two levels), the clinical risk of VTE is less than 1%. In ‘major’ surgery of the spine (osteosynthesis, extended laminectomy), the clinical risk of VTE ranges from 0.3% to 2.2%. The incidence of DVT (venography) is 15%. The risk is higher for surgery of the lumbar than cervical spine.

   Spinal cord injury is an important risk factor for VTE. The risk of DVT diagnosed by venography is 81% and that of symptomatic DVT is 12–25%. In studies published before 1990, the risk of PE in para- or tetraplegic patients was about 4.6%. The extent of the motor deficit (paraplegia or tetraplegia vs. a partial deficit) is an important risk factor for DVT. On the other hand, the level of the lesion seems to have little effect on risk.

3. ENT and maxillofacial surgery
   The risk of thrombosis is low for ENT or maxillofacial surgery. The incidence of clinical VTE is about 0.5%. The risk is mostly patient-related.

Risk levels and categories for different types of head, neck and spine surgery are given in Tables 12 and 13.

Question 2.2: Efficacy and safety of prevention measures

1. Neurosurgery
   The value of prophylaxis with mechanical methods or LMWHs in preventing VTE has been demonstrated in neurosurgery (Grade A). Mechanical methods reduce the risk of thrombosis by about 50% but are inadequate when used alone. Prophylaxis with heparin also reduces the risk of thrombosis by at least 50% (NNT = 6–8). There is no significant difference in the efficacy of UFH and LMWHs. The incidence of postoperative intracranial haemorrhage is 1–2%.

   Postoperative heparin prophylaxis does not seem to increase the risk of bleeding significantly (Grade C).

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2. Spine and spinal trauma surgery

There is no study available to recommend a particular type of prophylaxis for spine surgery. In minor surgery, routine prophylaxis seems unnecessary in the absence of an additional risk factor. In major surgery, especially of the lumbar spine, prophylaxis is recommended.

- Because of their safety, mechanical methods can be recommended for use on their own in the absence of a patient-related risk. In the case of an additional, patient- or surgery-related risk factor, prophylaxis with a LMWH is recommended (Grade D).

- In patients with spinal cord injury, the DVT incidence (paraclinical tests) after fixed-dose UFH is 31–53% and the incidence of clinical VTE is 14–26%. Mechanical methods or fixed-dose UFH should not be used alone (Grade B). Fixed-dose UFH or LMWH should be combined with mechanical methods (Grade C). A heparin dose with aPTT target of 1.5 times the control value is effective but is associated with a high risk of bleeding (Grade B). A LMWH is more effective than fixed-dose UFH in preventing VTE (Grade B).

3. ENT and maxillofacial surgery

- Drug prophylaxis is not recommended for ENT and maxillofacial surgery in the absence of a risk factor. Prophylaxis should be adapted to patient-related risk factors.

- For major cancer surgery, prophylaxis is justified because of the duration of surgery and the context. LMWH prophylaxis introduced postoperatively is recommended (Grade D).

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in patients with a motor deficit in the absence of an additional risk factor (Grade C).

Question 2.4: Ambulatory surgery
Not applicable to neurosurgery or spinal trauma. There are no studies for ENT and maxillofacial surgery.

Recommendations for VTE prophylaxis in head, neck and spine surgery are summarized in Table A7.

Burns surgery and intensive care

Question 2.1: What is the incidence of clinical and paraclinical VTE in the absence of prophylaxis? Stratify risk
The incidence of VTE in burns patients has been studied only in low-power retrospective studies. It is 0.9–3% for clinical DVT and 0.4–1.2% for PE (level 4). A single prospective study reports the incidence of DVT (6%) as detected by routine screening using echo-Doppler.

Venography and ultrasound are hard to perform in the case of burns. The level of D-dimers is spontaneously high and a single normal value has negative predictive value (Grade C).

Question 2.2: Efficacy and safety of prevention measures
There are no published data on which to base a prevention strategy. In daily practice, specialist teams recommend routine LMWHs in patients with a moderate risk of VTE. Lesions extending over more than 50% of the total body surface area, an intense biological inflammatory response syndrome and prolonged femoral perfusion are associated with a high VTE risk. About half the teams prescribe LMWHs; the other half prescribe continuous i.v. heparin at a prophylactic dose, because of uncertain bioavailability after s.c. injection in patients with diffuse oedema and with maybe with few suitable injection sites (Grade D). Recourse to simple mechanical methods such as elastic compression wraps is routine if the topography of the lesions allows them (Grade D).

Question 2.3: When to start prescribing and for how long?
Pharmacological prophylaxis is initiated as soon as initial biological haemostasis abnormalities (decrease in prothrombin rate, thrombocytopenia, spontaneously prolonged aPTT) have been corrected. It is continued

Table A7. Summary of recommendations for VTE prophylaxis in head, neck and spine surgery.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Type of surgery</th>
<th>Patient-related risk</th>
<th>Recommendations</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>ENT</td>
<td>−</td>
<td>None or ECS</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Herniated disk</td>
<td>+</td>
<td>LMWH</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Laminectomy (1 or 2 levels)</td>
<td>−</td>
<td>UFH ± ECS</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Extensive laminectomy</td>
<td>−</td>
<td>LMWH ± ECS</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Spine osteosynthesis</td>
<td>+</td>
<td>IPC</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>LMWH</td>
<td>D</td>
</tr>
<tr>
<td>Moderate</td>
<td>Intracranial neurosurgery</td>
<td>−</td>
<td>LMWH/UFH + ECS or IPC</td>
<td>A/B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IPC</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Spinal cord injury</td>
<td>+</td>
<td>LMWH or UFH + ECS or IPC</td>
<td>B</td>
</tr>
</tbody>
</table>

ECS: elastic compression stockings; IPC: intermittent pneumatic compression.

Table A8. Summary of recommendations for VTE prophylaxis in burns surgery and intensive care.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Type of surgery</th>
<th>Patient-related risk</th>
<th>Recommendations</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Burns &lt;20% TBSA and lower limbs unscathed</td>
<td>−</td>
<td>None or ECS</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>Moderate-dose LMWH ± ECS</td>
<td>D</td>
</tr>
<tr>
<td>Moderate</td>
<td>Burns 20–50% TBSA</td>
<td>−</td>
<td>Moderate-dose LMWH</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Burns of lower limbs</td>
<td></td>
<td>High-dose LMWH</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Grafts from lower limbs</td>
<td>+</td>
<td>High-dose LMWH</td>
<td>D</td>
</tr>
<tr>
<td>High</td>
<td>Burns &gt;50% TBSA</td>
<td>−</td>
<td>High-dose LMWH</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Biological hypercoagulability</td>
<td></td>
<td>Or UFH i.v.</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Femoral infusion</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TBSA: total body surface area; ECS: elastic compression stockings.
for as long as biological signs of inflammation persist and until the patient has regained autonomy; in the case of the more severe burns patients, this is at the end of their stay in a rehabilitation centre (Grade D).

Question 2.4: Ambulatory surgery
Not applicable.

Recommendations for VTE prophylaxis in burns surgery and intensive care are summarized in Table A8.

Acknowledgement
These recommendations have been presented in part during the meeting of the French Society of Anaesthesiology and Intensive Care (SFAR), Paris, September 2004.
Appendix

Participating scientific societies
Société française de chirurgie orthopédique et traumatologique, Association française de chirurgie, Association française d'urologie, Société de chirurgie vasculaire de langue française, Collège national des gynécologues obstétriciens, Groupe d'étude sur l'hémostase et la thrombose, Société de réanimation de langue française, Société française d'étude et de traitement des brûlures, Société française de médecine vasculaire, Société française de médecine physique et de réadaptation.

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