New clinical practice guidelines for venous thromboembolism prevention: orthopedic surgery as a paradigm

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SUMMARY

To produce up-to-date clinical practice guidelines on the prevention of venous thromboembolism (VTE) in orthopedic surgery. A Steering Committee defined the scope of the topic, the questions to be answered, and the assessment criteria. A multidisciplinary working group performed a critical appraisal of the literature. The resultant reports and guidelines were submitted for comment and completion of the AGREE questionnaire to peer reviewers, before producing definite guidelines. The report answers the following questions: (i) What is the VTE incidence according to clinical and/or paraclinical criteria in the absence of prophylaxis? (with stratification of VTE 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? Apart from answering the above questions, the guidelines provide a summary table. This table stratifies types of surgery into the three risk categories, specifies the recommended prophylaxis for VTE (pharmacological and/or mechanical) and grades each recommendation. In addition, whenever appropriate, the recommended prophylaxis is adjusted to low- and high-risk patients.

Recommendations issued by the French Society of Anaesthesiology and Intensive Care (SFAR) in 2005. Orthopedic section extracted from the short text. These recommendations were presented in part during the congress of the French Society of Anesthesiology and Intensive Care (SFAR), Paris, September 2004. They were prepared with the financial and logistical help from the Department of Recommendations and Guidelines, Haute Autorité en Santé, Saint Denis, France.

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INTRODUCTION

These up-to-date clinical practice guidelines on the prevention of venous thromboembolism (VTE) in orthopedic surgery are extracted from a larger body of recommendations: the French Clinical Practice Guidelines on VTE prevention in surgery and obstetrics.[1,2] A strong methodology has been applied (Table 1). A Steering Committee defined the scope of the topic, the questions to be answered, and the assessment criteria. Ten multidisciplinary working groups (a total of 70 experts) performed a critical appraisal of the literature in the following disciplines: pharmacology of antithrombotic agents, orthopedics; general surgery (gastrointestinal and varicose vein surgery); urology; gynecology 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 AGREE questionnaire to a total of 150 reviewers before producing definite guidelines. The report answers the following questions for each type of surgery: (i) What is the VTE incidence according to clinical and/or paraclinical criteria in the absence of prophylaxis? (with stratification of VTE 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?

We have extracted the orthopedic section for this *TATM* issue because it is the most comprehensive and educative one.[2] It may be considered as a paradigm for other surgical settings.

SOME KEY MESSAGES OF THESE GUIDELINES

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

- 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 analyzed in each case and weighed against any benefit with respect to asymptomatic thrombosis.
- The value of mechanical prophylaxis [elastic compression stockings (ECS), intermittent pneumatic compression (IPC)] is stressed. It should be combined with pharmacological prophylaxis whenever possible.
- The dogma of preoperative low-molecular-weight heparin (LMWH) injection was questioned, especially by the orthopedics working group. Prophylaxis can be introduced before or after surgery.

Table 1. Grading of recommendations

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

Table 2. Risk categories for venous thromboembolism after trauma surgery and ambulatory surgery

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

- The 'moderate-risk' LMWH dose no longer applies in orthopedics; only the 'high-risk' dose is applicable.
- 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.
- 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 the moderate-risk category. Arthroscopy is considered to be low risk.
- 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.

QUESTION 1: WHAT IS THE INCIDENCE OF CLINICAL AND PARACLINICAL VTE IN THE ABSENCE OF PROPHYLAXIS? STRATIFY THE RISK

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

VTE risk after major orthopedic 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 that 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.

Risk of VTE after trauma surgery and ambulatory surgery

VTE risk is stratified for different types of surgery in Table 2.

Mean estimated risks of VTE in orthopedic and trauma surgery patients are given in Table 3.

Table 3. Risk of VTE in orthopedic and trauma surgery

	Mean estimated risk (%)
Hip replacement, knee replacement and hip fracture	
Total DVT*	~50
Proximal DVT*	>15
PE and/or clinical VTE	>5
Multiple trauma	
Total DVT*	15–60
PE and/or clinical VTE	<5
Fraction or lesion of the ligament (tibia/peroneal muscle, ankle and foot)	
Total DVT*	~15
Proximal DVT*	<5
PE and/or clinical VTE	<1
Knee ligament reconstruction (anterior cruciate ligament)	
Total DVT*	<5
Clinical PE	<1
Ambulatory surgery (knee arthroscopy)	
Total DVT*	<10

*Detected by venography and/or ultrasound. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

QUESTION 2: EFFICACY AND SAFETY OF PREVENTION MEASURES

Major orthopedic surgery (total hip or knee replacement, hip fracture)

After major orthopedic surgery, VTE risk is high and warrants routine prescription of preventive measures (evidence level 1).

Unfractionated heparin (UFH), LMWHs and vitamin K antagonists (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 (evidence level 1). The risk of bleeding is lower with LMWHs than with UFH in knee replacement surgery (evidence 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 the bleeding risk (evidence level 1). However, this is not true in countries such as France where there are no specialist centers for monitoring VKA treatment. In these countries, VKAs are associated with an increased risk of bleeding compared with LMWHs (evidence 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 (evidence level 1). The risk of thrombocytopenia, however, seems to be lower (evidence level 2).

Danaparoid (evidence level 2) and desirudin (evidence level 1) reduce the risk of VTE in hip replacement patients. Desirudin is more effective than an LMWH in the prophylaxis of asymptomatic VTE after hip replacement surgery only.

Mechanical methods, in particular IPC, reduce the risk of postoperative VTE (evidence level 1).

Trauma surgery

Multiple trauma

LMWHs reduce the risk of VTE; the risk of bleeding compared to that of UFH is acceptable (evidence level 1). IPC reduces the VTE risk without increasing the risk of bleeding (evidence 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) (evidence level 1).

Arthroscopy (knee ligament reconstruction) and ambulatory surgery

LMWHs effectively reduce the risk of VTE without significantly increasing the risk of major bleeding after arthroplasty (evidence level 1).

Guidelines derived from the above observations and from professional agreement are given in Box 1.

Box 1. Guidelines for VTE prophylaxis in orthopedic surgery patients

Major orthopedic surgery

- LMWHs are the standard preventive treatment after hip replacement, knee replacement and hip fracture surgery (grade A). UFH (even aPTT-adjusted) and VKAs should not be used as first-line prophylaxis after major orthopedic surgery of the lower limbs (grade A). Aspirin should not be considered as a prophylactic measure for VTE (grade B).
- The two first-line prophylactic agents for hip and knee replacement surgery are LMWHs and fondaparinux (grade A).
- Because danaparoid and desirudin are less easy to use and because danaparoid development is less well advanced, they should be considered as second-line prophylactic measures (grade A).
- Mechanical methods should not be prescribed alone as first-line treatment in the absence of comparisons providing level 1 evidence (grade A), but they are a preferred choice when antithrombotics are contraindicated because of the risk of bleeding (grade A). Properly fitted elastic compression stockings are an effective adjuvant therapy to pharmacological prophylaxis because they have no interactions (grade B).

Trauma surgery

- Multiple trauma: LMWHs are the reference prophylactic treatment (grade A). In the case of a marked risk of bleeding, mechanical methods, in particular intermittent pneumatic compression (if applicable), are a first-line prophylactic measure (grade B).
- Trauma of lower extremities: In view of the moderate VTE risk, and the length of immobilization and consequently of prophylaxis (on average 45 days), LMWH administration should be adapted to patient-related risk factors (grade D). LMWHs could be prescribed more routinely for fractures (grade B).

Knee arthroscopy

- In view of the low risk associated with this type of surgery, LMWH prescription should not be routine but should be considered only if the patient has one or more additional risk factors (grade B).

QUESTION 3: WHEN TO START PRESCRIBING AND FOR HOW LONG?

Introduction of prophylaxis

LMWHs

The risk of VTE and bleeding apparently does not depend on whether LMWHs are given either 12 hours before or 12 hours after surgery. However, administration from 2 hours before surgery to 4 hours after surgery seems to be associated with an increased risk of bleeding (evidence level 2).

Fondaparinux (hip or knee replacement, hip fracture)

A first injection increases the risk of bleeding when given earlier than 6 hours after surgery but does not increase risk nor affect efficacy when given 6–8 hours after surgery (evidence level 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 (evidence level 1).

Long-term prophylaxis with LMWHs until postoperative days 30–42 does not seem to reduce the risk of VTE after knee replacement surgery (evidence level 2).

Long-term administration of fondaparinux 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 (evidence level 1).

Long-term administration of LMWHs 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 2 and 3.

QUESTION 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 (evidence level 1). LMWHs reduce risk after arthroscopy without increasing the risk of severe bleeding (evidence level 2). This has been noted after short-term prophylaxis (evidence level 2).

In view of the low risk of VTE, routine prophylaxis is not justified after arthroscopy (grade B). Administration of LMWHs is justified if there are additional VTE risk factors (grade B). Prophylaxis for longer than 10 days is not warranted (grade B). Other antithrombotic agents have not been tested in this indication.

Recommendations for VTE prophylaxis in orthopedic and trauma surgery are summarized in Table 4.

Box 2. Guidelines for when to start prophylaxis in orthopedic surgery

- LMWHs (hip replacement, knee replacement and hip fracture surgery): In view of the frequent use of local and regional anesthesia, postoperative administration of LMWHs seems to be the preferred option. Perioperative administration should be avoided (grade B). In the case of hip fracture and deferred surgery, preoperative administration is warranted; the last LMWH injection should be more than 12 hours (ideally 24 hours) before surgery (grade C).
- Fondaparinux (hip replacement, knee replacement and hip fracture surgery): The first injection of fondaparinux should be given at least 6 hours after surgery. The second injection should be given at least 12 hours after the first injection (grade B). In the case of moderate renal impairment and/or a body weight under 50 kg and/or age above 75 years, the first injection should preferably not be given until 8 hours after surgery (grade C).
- UFH, danaparoid, desirudin and VKA (hip replacement, knee replacement and hip fracture surgery): With the exception of desirudin which should be prescribed immediately before surgery, other antithrombotics should be prescribed after surgery (grade B).
- Other orthopedic and trauma surgery: If there is a moderate risk of VTE and/or a high risk of bleeding, LMWHs should not be administered before surgery (grade A).

Box 3. Guidelines for how long to prescribe prophylaxis in orthopedic surgery

- LMWH should be prescribed until postoperative day 42 for total hip replacement (grade A).
- After knee replacement, routine prescription of LMWHs beyond postoperative day 14 is not recommended (grade B). Prescription beyond day 14 should be considered 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 orthopedic 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).

Table 4. Summary of recommendations for VTE prophylaxis in orthopedic and trauma surgery

Risk	Type of surgery	Patient-related risk	Recommendations	Grade
Low	Knee arthroscopy	–	No prophylaxis	A
	Traumatic ligament lesion (without fracture of lower extremity)	+	High-dose LMWH	D
	Trauma to knee without fracture			
Moderate	Fracture of lower extremity (tibia/peroneal muscle, ankle, foot)		High-dose LMWH (especially if patient-related risk)	B
	Fracture of femoral diaphysis		High-dose LMWH	D
High	Hip or knee replacement		High-dose LMWH Fondaparinux	A
	Hip fracture		Fondaparinux High-dose LMWH	A C
	Severe multiple trauma without risk of bleeding		High-dose LMWH	A
	Severe multiple trauma with risk of bleeding		IPC	B

IPC, intermittent pneumatic compression; LMWH, low-molecular-weight heparin; VTE, venous thromboembolism.

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APPENDIX 1

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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