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European guidelines on perioperative venous thromboembolism prophylaxis

Day surgery and fast-track surgery

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In recent years, day surgery and fast-track surgery have experienced a continuous increase in volume. Many procedures are now performed on an outpatient protocol, including general, orthopaedic, oncological, reconstructive or vascular surgery. The management of these patients is safe, but the incidence of venous thromboembolism in this population remains unknown. Several risk factors can be identified and stratified derived from studies of inpatient surgical management (e.g. Caprini score). Recommendations for thromboprophylaxis should be tailored from the assessment of both personal and procedure-related risk factors, although with a lack of evidence for application in outpatient management. For patients undergoing a low-risk procedure without additional risk factors, we recommend only general measures of thromboprophylaxis (early ambulation, optimal hydration) (Grade 1B). For patients undergoing a low-risk procedure with additional risk factors, or a high-risk procedure without additional risk factors, we recommend general measures of thromboprophylaxis (Grade 1B) and we suggest the administration of pharmacological prophylaxis with low molecular weight heparins (Grade 2B). For patients undergoing a high-risk procedure with additional risk factors we recommend general measures of thromboprophylaxis (Grade 1B) and pharmacological prophylaxis with low molecular weight heparins over other drugs (Grade 1B), or suggest specific mechanical measures in case of increased bleeding risk (Grade 2C). Pharmacological prophylaxis should last a minimum of 7 days (Grade 1B), although in selected cases of fast-track surgery, thromboprophylaxis could be limited to hospitalisation only (Grade 2C) and in specific cases of high-risk procedures, thromboprophylaxis could be extended for up to 4 weeks (Grade 2B).

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

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

Introduction

Surgery has changed, thanks to surgeons, anaesthetists, major technological improvements, health insurances pressure, governments, and patients, of course. Ambulatory surgery, day surgery and fast-track procedures now represent the major part of surgical procedures in Europe. The global venous thromboembolism (VTE) risk is much more under control than before, and new questions are arising about the level of the surgical risk, the type of prophylaxis, the duration and the doses. Previous guidelines have not taken this evolution into account. No strong evidence-based studies are available yet, but there is a huge need for new guidelines, and new studies, built on new recommendations.

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Definitions

Before writing the recommendations for ambulatory surgery and for fast-track surgery, we found it important to define both concepts.

'Day surgery' (or ambulatory surgery) can be defined as 'a surgical procedure for which the patient is discharged on the same day as surgery or admitted and discharged within 24 h'.

'Fast-track' surgery can be defined as 'surgery after which patients are mobilised within hours post-operatively and fully mobilised no later than on the day after surgery, with discharge no later than the fifth day'.

Rationale

The true incidence of VTE, asymptomatic or symptomatic, in patients receiving thromboprophylaxis or not in ambulatory surgery or in fast-track surgery is not fully known, and existing data focused on VTE are scarce and limited to non-randomised studies. For instance, in a Danish survey which included 16 048 patients undergoing various types of day surgery (up to 18 736 procedures), the incidence of VTE was 0.04%, and 0.4% for haematomas or haemorrhage within 60 days of follow-up.[1] In a study aiming to identify independent predictors for venous thromboembolism after outpatient surgery, the 30-day overall incidence of VTE requiring therapy was 0.15%, and 1.18% among 'highest risk' patients.[2]

The recommendations for ambulatory surgery and fast-track surgery are mainly based on the review of the following literature:

The SysteMatische Datenerfassung im Ambulanten Bereich zur Risikoabschätzung Thromboembolischer Ereignisse bei chirurgischen Patienten—SysteMatic documentation within the Ambulatory setting to assess the Risk of Thromboembolic events in surgical patients study[3] examined enoxaparin prophylaxis in unselected patients undergoing day surgery and includes data from 11 794 patients. Patients received to 20 mg (63.6%) or 40 mg (36.4%) of enoxaparin for a mean of 12.4 ± 9.8 days. The choice of the dose was based on thrombotic risk stratification after risk assessment by the Haas' scorecard. Patients were usually young (meniscal resection was the most frequent intervention), 61.5% had no predisposing risk factor and 67.1% received no concomitant medication with the potential to increase the risk of bleeding. Forty-four patients (0.39%) had confirmed symptomatic deep vein thrombosis, whereas one patient had pulmonary embolism. Bleeding occurred in 3.47% of patients, with minor bleeding in 3.29% of the population. Thromboprophylaxis was instituted mainly on the day of surgery and often prior to surgery (75.7% of cases); only in 293 patients (2.6%) was the first dose given after surgery. Another point to highlight is the duration of the administration of enoxaparin: in most cases, the drug was given for between 7 and 13 days (64.3%), a 'short protocol' was employed in 14.1% and an extended strategy (>13 days) in 21.6%. There is no explanation for this difference in the duration of enoxaparin administration other than the thrombotic risk stratification of patients: longer duration for higher risk patients. Finally, mechanical methods were employed in most cases elastic stockings in 47.6% of patients and compression bandage in 24.7%); only in 33.9% of patients was no mechanical device or method employed. The authors concluded that the results showed a beneficial effect of thromboprophylaxis in this patient population, being more important as day surgery expands and includes more extensive procedures in older patients with more serious coexisting diseases. Additionally, the authors proposed thromboprophylaxis dosing according to the risk of thromboembolism in each patient.

In a large prospective observational cohort study published in 2012,[2] with data from 259 231 patients, the overall 30-day incidence of VTE was 0.15%. However, based on the stratification risk factors, the weighted risk index identified a 20-fold variation in 30-day VTE between low (0.06%) and highest risk (1.18%) patients. In this study, most patients were non-orthopaedic patients (only 9.1% of patients underwent 'musculoskeletal surgery'), whereas herniorrhaphy was the most frequent procedure (33%). The population included in this study increases the risk of bias in interpretation and reduces the external validity of their findings. Nevertheless, as the risk factors were developed specifically for ambulatory surgery, and despite the lack of validation in a prospective trial, one cannot entirely reject the stratification of ambulatory surgical patients. Other variables to be highlighted as independent predictors of VTE from a multivariable logistic regression model in day-case surgery are

- current pregnancy [adjusted odds ratio (OR) 7.80, $P = 0.044$],
- active cancer (OR 3.66, $P = 0.005$),
- age 41 to 59 years (OR 1.72, $P = 0.008$),
- age 60 years or more (OR 2.48, $P < 0.001$),
- body mass index 40 $kg\,m^{-2}$ or higher (OR 1.81, $P = 0.015$),
- operative time 120 min or more (OR 1.69, $P = 0.027$),
- arthroscopic surgery (OR 5.16, $P < 0.001$),
- sapheno-femoral junction surgery (OR 13.20, $P < 0.001$),
- venous surgery not involving the great saphenous vein (OR 15.61, $P < 0.001$).

A total of 254 patients were diagnosed with deep vein thrombosis (DVT)/pulmonary embolism (incidence of 0.15%). The most thrombogenic procedures were those involving 'arteries and veins' (0.85% of DVT/pulmonary embolism general incidence), followed by 'haemic and lymphatic system, mediastinum and diaphragm' (0.49%),

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'miscellaneous peritoneal procedures' (0.26%) and 'musculoskeletal procedures' (0.25%).

Based on all the risk factors (patient-related and procedure-related) and after the use of regression models, the authors proposed a score stratifying approach. The final score predicts the 30-days VTE rate, and can divide the patients based on low risk (<0.1%), moderate risk (0.1 to 0.3%), high risk (0.3 to 0.5%) and highest risk (up to 1.2%).

Despite its methodological limitations, this study could provide a basis for risk stratification in day-case surgery.

Another fast-track surgery study focused on major orthopaedic surgery (total hip arthroplasty and total knee arthroplasty) with a short protocol of thromboprophylaxis during hospitalisation.[4] The authors found that the incidences of venous thromboembolic events were pulmonary embolism 0.11%, any DVT 0.30% and any VTE 0.41%. The median length of stay (LOS) was 2 days (IQR 2 to 3).

When comparing the results of patients with LOS at least 5 days with patients with unsuccessful early discharge, the rate of thrombotic events was significantly higher in the second group (pulmonary embolism 1.89%, any DVT 0.75%, any VTE 2.62%). Increased LOS was often due to patient comorbidities (hypercholesterolaemia, hypertension) or the social situation (living alone or with others). The authors did not propose that thromboprophylaxis should be extended beyond hospitalisation in fast-track surgery, even among patients at high VTE risk.

However, the authors provided contradictory proposals compared with recommendations from most of the existing guidelines: the continuation of thromboprophylaxis in total hip replacement (THR) up to 28 to 35 days, and in total knee replacement for at least up to 14 days. They further propose that guidelines on thromboprophylaxis may need reconsideration in fast-track elective surgery.

A recent prospective observational study reviewed the effectiveness and safety of different durations of prophylaxis in hip replacement patients.[5] The study was not carried out in day case or fast-track surgery. The authors assessed all primary THR procedures performed in Denmark from 2010 through 2012 ($n = 16\,865$). They examined the risk of symptomatic VTE and major bleeding among patients prescribed short-term (1 to 6 days) and standard (7 to 27 days) thromboprophylaxis versus extended prophylaxis (≥28 days). Total VTE incidence was 1.1% in the short-duration group, 1.4% in the standard-duration group and 1.0% in the extended-duration group. The adjusted hazard ratio of short versus extended treatment was 0.83 (95% confidence interval [CI] 0.52 to 1.31), and 0.82 (95% CI 0.50 to 1.33) for standard versus extended strategy.

These results raise questions about the optimal duration of thromboprophylaxis in these patients, as comparisons of benefits and harms do not favour any of the three treatment durations.

Cancer has been described as one of the most important risk factors for VTE in various guidelines[6,7] and in most used scores (Caprini[8] or Rogers *et al*[9]). However, there is little evidence on the importance of cancer as a risk factor in ambulatory or fast-track surgery. We found a paper of oncological–gynaecological surgery[10] with 419 women undergoing a minimally invasive procedure with early discharge (within 1 day of surgery); 352 women (84%) did not receive VTE prophylaxis, whereas 67 (16%) received subcutaneous heparin (LMWH or UFH); the rate of VTE in the untreated group of patients was 0.57%, compared with none among those receiving thromboprophylaxis. However, among patients receiving prophylaxis, 57.8% had only one dose and 31.1% had two doses, whereas only five women (11.1% of patients in the group of thromboprophylaxis) received at least three doses of heparin.

Thus, this small cohort study indicates a low VTE rate among this selected group of cancer patients scheduled for fast track surgery.

In the updated National Institute of Health and Care Excellence (NICE) guideline from 2010,[6] no specific risk factor was associated with ambulatory surgery. The authors suggest the application of Caprini risk factors (Caprini score[8]), despite a lack of evidence for ambulatory surgery, for

- Active cancer or cancer treatment
- Age over 60 years
- Critical care admission
- Dehydration
- Known thrombophilia
- Obesity (BMI over 30 $kg\,m^{-2}$)
- One or more significant medical comorbidities (such as heart disease, metabolic, endocrine or respiratory pathologies, acute infectious diseases or inflammatory conditions)
- Personal history or a first degree relative with a history of VTE
- Use of hormone replacement therapy
- Use of oestrogen-containing contraceptive therapy
- Varicose veins with phlebitis
- Pregnancy and up to 6 weeks postpartum.

The authors recognise that their proposal is based on extrapolation of data from standard surgery, suggesting that assessment of 'global' risk of VTE in ambulatory surgery should be calculated not only from the personal risk but also the risk associated with various types of surgery.

Finally, in the ACCP guidelines,[7] no specific reference to ambulatory or fast-track surgery is to be found. Thus, one may again propose an extrapolation to ambulatory surgery

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mainly on the basis of the score stratification for general surgery (Rogers and Caprini scores), despite the absence of evidence. There are currently no recommendations for 'non-major' orthopaedic procedures in ambulatory or fast-track surgery.[11]

Venous thromboembolism risk factors

Global thrombotic risks are derived from the addition of procedure-related risk factors and patient risk factors. We acknowledge the lack of evidence for ambulatory or fast-track surgery, and recommendations are derived from extrapolated data obtained in non-ambulatory surgery, which could vary based on standard of care and logistics in each hospital.

Procedure-related risk factors

As previously discussed, there are currently no published studies solely for ambulatory or fast-track protocols and as a result we are unable to provide evidence-based proposals. Thus, a necessary stratification of the surgical procedures and extrapolation of recommendations from previously cited papers remains our only option.

From these general proposals, prophylaxis should be considered as for the closest comparable patient group:

- The majority of procedures can be classified as low VTE-risk (symptomatic VTE from 0.5 to 1.5% according to modified Caprini score).
- Some procedures can be classified as high risk of VTE (estimated risk about 3% to 6%).

Therefore, the first step for the global stratification should be to allocate each kind of procedure to the 'right box':

- Procedures of low VTE risk.
- Procedures of high VTE risk.

Patient risk factors

There is no fully validated score for ambulatory/fast-track surgery. Some observational studies have published an approach for specific risk factors, but one of them does not involve orthopaedic procedures[2] and the other one is not designed for the validation of them.[3] Although there is no evidence, the proposal is to include as personal risk factors for DVT those which derivate from the Caprini score and stratify them in two categories:

Minor risk factors:

- Age at least 60 years
- Obesity (BMI $\geq$40 kg m^{-2})
- Preoperative immobilisation at least 4 days
- Chronic venous insufficiency

Major risk factors:

- Active or in-treatment cancer
- Thrombophilia or personal history of DVT/pulmonary embolism
- Family history of DVT/pulmonary embolism
- Current pregnancy or puerperium
- Surgery lasting at least 120 min

Recommendations

From all these considerations, we can draw some proposals, derived from the last NICE[6] and ACCP[7] guidelines, and taking into account the research referred to above. All these recommendations have been specifically modified and applied to ambulatory/fast-track surgery (Table 1).

1. We recommend that all patients undergoing an ambulatory/fast-track protocol should be assessed for the VTE risk of the procedure and for any personal/additional VTE risk (Grade 1B).
2. For patients undergoing a low-risk procedure, without additional risk according to the Caprini score, we recommend general measures of thromboprophylaxis (including early ambulation and optimal hydration) over other specific measures (mechanical or pharmacological) (Grade 1B).
3. For patients undergoing a low-risk procedure with additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation and optimal hydration) (Grade 1B). We suggest assessing pharmacological prophylaxis with LMWH over other drugs (Grade 2B). We suggest the use of specific mechanical measures [intermittent pneumatic compression (IPC) devices] in patients with an increased bleeding risk (Grade 2C).
4. For patients undergoing a high-risk procedure without additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation and optimal hydration) (Grade 1B). We

Table 1 Compilation of recommendations for thromboprophylaxis in ambulatory or fast-track surgery derived from the procedure and patient risk factors

	Low VTE risk procedure	High VTE risk procedure
Low VTE risk patient	No specific VTE prophylaxis[a]	Choice: LMWH and/or IPC Alternative in OS: AAS and/or IPC
High VTE risk patient	Choice: LMWH and/or IPC[b] Alternative in OS: AAS and/or IPC	LMWH and/or IPC

AAS, aspirin; IPC, intermittent pneumatic compression; LMWH, low molecular weight heparin; OS, orthopaedic surgery; VTE, venous thromboembolism. [a]If these patients, for some reason (often complications), have to rest in bed for more than 2 days, begin LMWH during the in-hospital stay. [b]IPC could be used as an adjuvant to pharmacological thromboprophylaxis or as the first choice in case of a high risk of bleeding.

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suggest the administration of pharmacological prophylaxis with LMWH over other drugs (Grade 2B). We suggest assessing specific mechanical measures (IPC) in patients with an increased bleeding risk (Grade 2C).

5. For patients undergoing a high-risk procedure with additional risk factors, we recommend general measures of thromboprophylaxis (e.g. early ambulation and optimal hydration) and pharmacological prophylaxis with LMWH over other drugs (Grade 1B), or specific mechanical measures (IPC) in patients with an increased bleeding risk (Grade 2C).
6. We suggest the use of aspirin for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (high-risk orthopaedic procedures) in patients without a high VTE risk (Grade 2C).
7. We suggest the use of aspirin for VTE prevention after low-risk orthopaedic procedures in patients with high VTE risk, or other high-risk orthopaedic procedure in patients without a high VTE risk (Grade 2C).
8. We recommend no pharmacological VTE prevention after low-risk orthopaedic procedure (e.g. knee arthroscopy) in patients without a high VTE risk (Grade 1C).
9. For pharmacological prophylaxis, we recommend a minimum of 7 days' duration of treatment over protocols lasting 3 days or single-dose protocols (Grade 1B), although in selected cases of fast-track surgery, thromboprophylaxis only during hospitalisation could be an option (Grade 2C). We recommend extending the duration of thromboprophylaxis for up to 4 weeks in specific cases of high-risk procedures, according to general rules (Grade 2B).
10. When the choice of thromboprophylaxis is a LMWH, the first dose could be administrated before surgery (about 12 h before the beginning of the procedure) or after surgery (optimal time from 6 to 8 h after the end of the procedure) (Grade 2C). In case of planned neuraxial anaesthesia for the procedure, postoperative administration seems to be the preferred option (Grade 2C).

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References

1 Engbaek J, Bartholdy J, Hjortsø NC. Return hospital visits and morbidity within 60 days after day surgery: a retrospective study of 18,736 day surgical procedures. *Acta Anaesthesiol Scand* 2006; **50**:911–919.
2 Panucci CJ, Shanks A, Moote MJ, *et al.* Identifying patients at high risk for venous thromboembolism requiring treatment after outpatient surgery. *Ann Surg* 2012; **255**:1093–1099.
3 Haas S, Hohmann V, Bramlage P. Prevention of venous thromboembolism using enoxaparin in day surgery: results of the SMART non-interventional study. *Clin Appl Thromb Hemost* 2012; **18**:265–271.
4 Jorgensen CC, Jacobsen MK, Soeballe K, *et al.* Thromboprophylaxis only during hospitalization in fast-track hip and knee arthroplasty, a prospective cohort study. *BMJ Open* 2013; **3**:e003965.
5 Pedersen AB, Sorensen HT, Mehnert F, *et al.* Effectiveness and safety of different duration of thromboprophylaxis in 16,865 hip replacement patients – a real word prospective observational study. *Thromb Res* 2015; **135**:322–328.
6 National Institute for Health and Care Excellence. Venous thromboembolism: reducing the risks of venous thromboembolism (deep vein thrombosis and pulmonary embolism in patients admitted to hospital). London 2015. www.nice.org.uk/guidance/cg92. [Accessed 9 August 2017].
7 Gould MK, Garcia DA, Wren SM, *et al.* Prevention of VTE in nonorthopedic surgical patients. Antithrombotic therapy and prevention of thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141 (2 Suppl)**:e227S–e277S.
8 Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon* 2005; **51**:70–78.
9 Rogers SO, Kilaru RK, Hosokawa P, *et al.* Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the Patient Safety in Surgery Study. *J Am Coll Surg* 2007; **204**:1211–1221.
10 Bouchard-Fortier G, Geerts WH, Covens A, *et al.* Is venous thromboprophylaxis necessary in minimally invasive surgery for a gynecologic malignancy? *Gynecol Oncol* 2014; **134**:228–232.
11 Falck-Ytter Y, Francis CW, Johanson NA, *et al.* Prevention of VTE in orthopedic surgery patients. Antithrombotic therapy and prevention of thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141 (2 Suppl)**:e278S–e325S.

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