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Prevention of Venous Thromboembolism in Surgical Patients

Giancarlo Agnelli, MD

Abstract—Venous thromboembolism (VTE) is a common complication of surgical procedures. The risk for VTE in surgical patients is determined by the combination of individual predisposing factors and the specific type of surgery. Prophylaxis with mechanical and pharmacological methods has been shown to be effective and safe in most types of surgery and should be routinely implemented. For patients undergoing general, gynecologic, vascular, and major urologic surgery, low-dose unfractionated heparin or low-molecular-weight heparin (LMWH) are the options of choice. For low-risk urologic surgery, early postoperative mobilization of patients is the only intervention warranted. For higher-risk patients, including those undergoing elective hip or knee replacement and surgery for hip fracture, vitamin K antagonists, LMWH, or fondaparinux are recommended. For patients undergoing neurosurgery, graduated elastic stockings are effective and safe and may be combined with LMWH to further reduce the risk of VTE. The role of prophylaxis is less defined in patients undergoing elective spine surgery, as well as laparoscopic and arthroscopic surgery. A number of issues related to prophylaxis of VTE after surgery deserve further clarification, including the role of screening for asymptomatic deep vein thrombosis, the best timing for initiation of pharmacological prophylaxis, and the optimal duration of prophylaxis in high-risk patients. (*Circulation*. 2004;110[suppl IV]:IV-4-IV-12.)

Key Words: venous thromboembolism ■ deep vein thrombosis ■ pulmonary embolism ■ heparin
■ low-molecular-weight heparin ■ vitamin K antagonists

Venous thromboembolism (VTE) is a common complication in patients undergoing surgery.¹ Pulmonary embolism (PE) is the most common cause of preventable death in patients hospitalized for surgical procedures. The risk for VTE in surgical patients is determined by the combination of individual predisposing factors and features of the specific type of surgery (Table 1).¹ More extended use of prophylaxis, early mobilization, and improved perioperative care have reduced the risk of VTE in surgical patients. However, many patients remain at high risk for VTE because of advanced age, more extensive operative procedures, and greater medical comorbidities.

Postoperative deep vein thrombosis (DVT) of the lower limbs is often asymptomatic; in many patients, fatal PE is the first clinical manifestation of postoperative VTE. Therefore, it is inappropriate to rely on early diagnosis and treatment of postoperative thromboembolism. In addition, routine screening for asymptomatic DVT of the lower limbs has a low sensitivity and is quite impractical. For these reasons, routine and systematic prophylaxis in patients at risk is the strategy of choice to reduce the burden of VTE after surgery. If used appropriately, such prophylaxis is cost effective because it reduces the incidence of symptomatic thromboembolic events, which require costly diagnostic procedures and prolonged anticoagulation therapy.¹

This review details the risk for VTE and the available effective methods of prophylaxis for each surgical category.

General Surgery

In patients undergoing general surgery without prophylaxis, the rates of DVT and fatal PE range from 15% to 30% and from 0.2% to 0.9%, respectively.^{1,2} The figures for DVT are derived chiefly from screening studies with radioactive fibrinogen carried out in the 1970s and 1980s. In patients undergoing general surgery, the current risk for VTE in the absence of prophylaxis is difficult to estimate. More rapid mobilization and improved perioperative care may have reduced the risk for these events; alternatively, the practice of more extensive procedures in patients with comorbidities and the use of preoperative cancer chemotherapy likely increases the risk. Indeed, in such high-risk patients, studies without prophylaxis are no longer performed. Risk factors for thrombosis in general surgery patients include cancer as the reason for surgery, duration of procedure, previous VTE, advanced age, and obesity.³

Routine use of thromboprophylaxis is recommended in surgical patients who are >40 years of age or undergoing major general procedures.¹ Compared with no prophylaxis, both subcutaneous, low-dose unfractionated heparin (LDUH) and low-molecular-weight heparin (LMWH) have been

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TABLE 1. Degree of Thromboembolism Risk in Surgical Patients Without Prophylaxis

Risk level	Calf DVT	Proximal DVT	Clinical PE	Fatal PE
Low risk Minor surgery in patients aged <40 y with no additional risk factors	2%	0.4%	0.2%	<0.01%
Moderate risk Minor surgery in patients with additional risk factors Surgery in patients aged 40–60 y with no additional risk factors	10%–20%	2%–4%	1%–2%	0.1%–0.4%
High risk Surgery in patients >60 y or with additional risk factors (eg, prior VTE, cancer)	20%–40%	4%–8%	2%–4%	0.4%–1.0%
Highest risk Surgery in patients with multiple risk factors (age >40 y, cancer, prior VTE) Hip or knee arthroplasty, hip fracture surgery	40%–80%	10%–20%	4%–10%	0.2%–5%

Adapted from Geerts WH, Heit JA, Clagett GP, et al. *Chest*. 2001;119(suppl 1):132S–175S.

shown to reduce the risk of VTE in these patients by at least 60%.^{2,4}

In most prophylaxis trials, LDUH was given at the dose of 5000 U starting 2 hours before surgery followed by 5000 U 2 or 3× daily until patients were ambulatory or discharged. The clinical value of LDUH in general surgery has been confirmed by a meta-analysis of randomized trials in which this prophylactic regimen was compared with no prophylaxis or placebo.⁴ The frequency of DVT was significantly reduced by unfractionated heparin (UFH) (from 22% to 9%), as was clinically overt PE (from 2.0% to 1.3%), fatal PE (from 0.8% to 0.3%), and all-cause mortality (from 4.2% to 3.2%). The use of LDUH was associated with an increase in bleeding events (from 3.8% to 5.9%). Another meta-analysis showed an association between LDUH and an increased rate of wound hematomas but not of major bleeding.⁵ Both meta-analyses showed that UFH given 3× daily is more effective and not less safe than the same agent given twice a day; this is particularly true in patients undergoing general surgery for cancer.^{4,5}

No single study showed a difference between LDUH and LMWH in the prevention of symptomatic VTE after general surgery. However, in several trials, LMWH was associated with significantly less venography-detected DVT than LDUH. At least 9 meta-analyses and systematic reviews have compared various LMWH regimens with UFH for the prevention of VTE in general surgery.¹ Taken together, these analyses indicate that these approaches have comparable efficacy and safety for the prevention of VTE. The ease of once-daily administration and the reduced risk of heparin-induced thrombocytopenia are clinical advantages of LMWH over LDUH.⁶ In patients undergoing surgery for cancer, prophylactic doses >3400 anti-Xa units of LMWH provide greater protection than lower doses.⁷

Graduated compression stockings effectively reduce the risk for VTE in patients undergoing general surgery and constitute the prophylactic measure of choice in patients with

a high risk of bleeding. A systematic review showed a 52% relative risk reduction with graduated compression stockings in comparison with no prophylaxis. Graduated compression stockings also have been shown to enhance the protection from VTE provided by LDUH by a further 75%, from 15% to 4%.⁸ Graduated compression stockings should be combined with pharmacological prophylaxis in high-risk patients whenever possible.

Gynecologic Surgery

In patients undergoing major gynecologic surgery, the rates of DVT, PE, and fatal PE are comparable to those seen after general surgical procedures.^{1,9} Surgery for cancer, advanced age, previous VTE, prior pelvic radiation therapy, and abdominal resection (in contrast to vaginal resection) appear to increase the thromboembolic risk after gynecologic surgery.¹⁰

In patients undergoing gynecologic surgery for benign disease without additional risk factors, LDUH given twice daily is effective in reducing DVT.¹ Mechanical prophylaxis with intermittent pneumatic compression also appears to be efficacious and should be considered for patients at high risk for bleeding.¹¹

Twice-daily LDUH offers less protection to patients having surgery for cancer than those with benign disease. LDUH given 3× daily or LMWH administered in daily doses of at least 4000 anti-Xa units appear to be more effective than twice-daily LDUH in these patients.^{11–14} There is no evidence that once-daily LMWH has superior efficacy than thrice-daily LDUH. Increased convenience is the major advantage of LMWH.¹

The risk of VTE after laparoscopic gynecologic surgery is unclear. Therefore, the decision to provide prophylaxis should be individualized, taking into consideration the patient's individual risk factors and comorbidities.

Urologic Surgery

Venous thromboembolism is a common complication of major urologic surgery.^{1,15} Between 1% and 5% of patients

TABLE 2. VTE Prevalence After Major Orthopedic Surgery in Absence of Prophylaxis

Procedure	DVT		PE	
	Total	Proximal	Total	Fatal
Hip arthroplasty	42%–57%	18%–36%	0.9%–28%	0.1%–2.0%
Knee arthroplasty	41%–85%	5%–22%	1.5%–10%	0.1%–1.7%
Hip fracture surgery	46%–60%	23%–30%	3%–11%	2.5%–7.5%

Adapted from Geerts WH, Heit JA, Clagett GP, et al. *Chest*. 2001;119(suppl 1):132S–175S.

undergoing such procedures experience clinically overt VTE. Pulmonary embolism remains the most common cause of postoperative death in these patients, and fatal PE has been estimated to occur in 1 of 500 patients.^{16,17}

Advanced age, malignancy, intraoperative lithotomy position, and pelvic surgery with or without lymph node dissection are established risk factors for VTE in patients undergoing urologic surgery.¹

LDUH and LMWH are efficacious in patients undergoing urologic surgery.^{1,18,19} In these patients, the use of intermittent pneumatic compression or graduated elastic stockings is likely to be effective as well. The combination of mechanical and pharmacological prophylaxis may be more effective than either modality alone.¹⁹

Most data concerning VTE in urologic surgery has been obtained from patients undergoing prostatectomy. The risk of VTE seems to be low in patients undergoing transurethral prostatectomy.^{17,18} Moreover, the use of perioperative LDUH or LMWH may increase the risk for bleeding.²⁰ Thus, early postoperative mobilization is probably the only intervention warranted in these and other low-risk urologic surgery patients. Routine prophylaxis with LDUH and LMWH is recommended for more extensive open procedures, including radical prostatectomy, cystectomy, or nephrectomy.

Vascular Surgery

Patients undergoing vascular surgery have a high risk for VTE. Potential risk factors in vascular surgery include advanced age, limb ischemia, long duration of surgery, and venous injury.²¹ The incidence of clinically overt VTE occurring during the hospital stay or requiring rehospitalization within 3 months after surgery is 2.5% to 2.9%.¹ The rates of DVT after aortoiliac or aortofemoral surgery are similar to those seen in other types of abdominal and pelvic procedures.²² In the absence of prophylaxis, the rate of DVT is \approx 21% when routine contrast venography is obtained^{23–25} and 15% when routine postoperative ultrasonography is performed.^{22,26} Patients undergoing major vascular procedures who have additional thromboembolic risk factors should receive antithrombotic prophylaxis with LDUH or LMWH. Although the optimal time to start prophylaxis with antithrombotic agents in patients undergoing vascular surgery remains unclear, some practitioners prefer to administer the first dose after surgery.

Orthopedic Surgery

Patients undergoing major orthopedic surgery, which includes elective hip and knee replacement and surgery for hip fracture, are at particularly high risk for VTE (Table 2).¹ Despite the use of prophylaxis, the rate of clinically overt VTE in these patients remains almost 3%.²⁷ Venous thromboembolism is the most common cause for readmission to the hospital after hip replacement.²⁸

Elective Hip Replacement

Elective hip replacement is a common surgical procedure, which is performed in 1 of 1000 people in the population each year.¹ In patients undergoing elective total hip replacement in absence of any prophylaxis, the incidence of venography-detected DVT ranges from 40% to 60% and that of clinically overt VTE between 2% and 5%.^{1,29} Approximately 50% of the venographically-detected DVT is proximal. Fatal PE occurs in \approx 1 of 500 patients undergoing elective hip replacement.^{30–32}

A number of anticoagulant-based regimens have been evaluated for the prophylaxis of VTE in patients undergoing total hip replacement (Table 3).¹ Although meta-analyses have shown that prophylaxis with LDUH⁴ and aspirin³³ are more effective than no prophylaxis in patients undergoing hip replacement, both these agents are less effective than the standard prophylactic regimens in use today. Three pharmacological antithrombotic regimens are currently recommended for the prophylaxis of VTE. These include LMWHs, the vitamin K antagonists, and the synthetic factor Xa inhibitor, fondaparinux. In addition, the oral direct thrombin inhibitor, ximelagatran, has been recently evaluated in this clinical setting.¹

A number of studies^{34–36} and meta-analyses^{7,37,38} have compared the efficacy of LMWH with that of UFH for prophylaxis of VTE after total hip replacement. Overall, LMWH is more efficacious than LDUH or adjusted-dose UFH with a relative risk reduction of \approx 50% and 25%, respectively.

Vitamin K antagonists should be administered in doses sufficient to prolong the international normalized ratio (INR) to a target of 2.5 (range 2.0 to 3.0). The initial dose of these agents should be administered either the evening before surgery or the day of surgery.

Five venography-based studies compared the efficacy and safety of LMWH and vitamin K antagonists for the prevention of VTE in patients undergoing total hip replacement.^{40–44} These studies showed that in comparison with vitamin K

TABLE 3. Prevention of DVT After Total Hip Replacement

Prophylaxis Regimen	No. of Trials	Combined Enrollment	Total DVT		Proximal DVT	
			Prevalence % (95%CI)	RRR %	Prevalence % (95%CI)	RRR %
Placebo/control	11	598	54.8(51–59)	—	26.6(23–31)	—
GCS	5	318	41.5(36–47)	24	26.4(22–32)	0
Aspirin	5	429	41.7(37–47)	24	11.4(8–16)	57
Low-dose heparin	11	1097	19.2(26–32)	47	18.5(16–21)	31
Warfarin	12	1793	22.3(20–24)	59	5.2(4–6)	81
IPC	7	423	20.3(17–24)	63	13.7(11–17)	49
Recombinant hirudin	3	1172	16.3(14–19)	70	4.1(3–5)	85
LMWH	31	8655	15.4(15–16)	72	4.9(4–5)	82

GCS indicates graduated compression stockings; IPC, intermittent pneumatic compression; RRR, relative risk reduction.

Adapted from Geerts WH, Heit JA, Clagett GP, et al. *Chest*. 2001;119(suppl 1):132S–175S.

antagonists, LMWH significantly reduced the rate of DVT from 20.7% to 13.7%. The rate of proximal DVT was reduced from 4.8% to 3.4%. Pooled rates of major bleeding were 3.3% in patients receiving vitamin K antagonists and 5.3% in patients receiving LMWH. A large open study compared the incidence of clinically overt VTE in patients receiving the LMWH enoxaparin, at a dose of 30 mg twice daily started postoperatively with adjusted-dose warfarin (target INR 2.0 to 3.0).⁴⁵ The rate of VTE was 0.3% in patients receiving LMWH compared with 1.1% in those receiving warfarin, a statistically significant reduction. However, major bleeding occurred in 0.6% of the enoxaparin patients compared with 0.3% of the warfarin group. In summary, LMWH is more effective than vitamin K antagonists in the prevention of VTE in patients undergoing elective hip replacement. A slight increase in surgical site bleeding and wound hematoma can be anticipated with LMWH.

Two venography-based studies have shown that fondaparinux is effective for prevention of VTE in patients undergoing total hip replacement.^{46,47} In a European study, fondaparinux given at the dose of 2.5 mg once daily starting 4 to 8 hours after surgery significantly reduced the incidence of DVT from 9% to 4% in comparison with enoxaparin given at a dose of 40 mg once daily starting 12 hours before surgery. The rate of proximal DVT also was significantly reduced by fondaparinux from 2% to 1%.⁴⁶ In a North American trial, the same fondaparinux regimen was compared with enoxaparin 30 mg twice daily started 12 to 24 hours after surgery.⁴⁷ In this study, the rate of overall VTE was reduced from 8% to 6% ($P=NS$) in the fondaparinux group. The rate of proximal DVT was 2% and 1% in fondaparinux and enoxaparin groups, respectively. In both studies, major bleeding occurred more often in the fondaparinux group, solely because of an increased bleeding index. This was calculated as the number of units of blood transfused summed with the change in hemoglobin values before and after the bleeding episode.

Recent trials have used the direct thrombin inhibitor, melagatran, and its oral prodrug, ximelagatran, in patients undergoing major orthopedic surgery.^{48,49} In the most recent of the European studies, patients undergoing elective hip or

knee replacement were randomly assigned to prophylaxis with subcutaneous melagatran at the dose of 2 mg immediately before surgery and 3 mg on the evening of surgery, followed by oral ximelagatran at the dose of 24 mg twice a day versus enoxaparin at the dose of 40 mg started on the evening before surgery.⁴⁸ The rate of overall and proximal DVT was significantly lower in the melagatran/ximelagatran group, although bleeding and transfusion rates were greater.

In a North American trial, oral ximelagatran 24 mg twice a day started the morning after surgery was compared with enoxaparin given at the dose of 30 mg twice a day started after surgery.⁴⁹ Venous thromboembolism was observed in 4.6% of the enoxaparin patients and 7.9% of the ximelagatran group, a statistically significant difference. Major bleeding was documented in less than 1% of patients in both groups.

Nonpharmacologic methods of prophylaxis, including graduated compression stockings and intermittent pneumatic compression, reduce the incidence of DVT by 20% to 70%. However, these methods seem to be less effective for prevention of proximal DVT than anticoagulant-based prophylaxis strategies in hip replacement patients.¹

Elective Total Knee Replacement

Without prophylaxis, the rate of venography-detected DVT in patients undergoing total knee replacement is ≈60%.¹ In these patients, ≈25% of venography-detected DVT is proximal.¹

Aspirin and LDUH, which are associated with small reductions in the risk for thrombosis, are not recommended in patients undergoing total knee replacement. As with elective hip replacement, pharmacological regimens currently recommended include vitamin K antagonists, LMWHs, and fondaparinux (Table 4).¹ In addition, ximelagatran, is also effective and safe in these patients. In venography-based studies, vitamin K antagonists reduce the risk for total and proximal DVT by 31% and 40%, respectively, compared with no prophylaxis.¹

Six randomized venography-based trials have directly compared LMWH with vitamin K antagonists in the prevention of VTE in patients undergoing total knee replacement.^{40–42,53–55}

TABLE 4. Prevention of DVT After Total Knee Replacement Surgery

Prophylaxis Regimen	No. of Trials	Combined Enrollment	Total DVT		Proximal DVT	
			Prevalence % (95%CI)	RRR %	Prevalence % (95%CI)	RRR %
Placebo/control	6	199	64.3(57–71)	—	15.3(10–23)	—
GCS	2	145	60.7(52–69)	6	16.6(11–24)	—
Aspirin	5	416	54.6(50–59)	15	8.9(6–12)	42
VFP	5	271	46.9(41–53)	27	3.0(1–6)	80
Warfarin	10	1501	44.2(42–47)	31	9.2(8–11)	40
Low dose heparin	2	236	43.2(37–50)	33	11.4(8–16)	26
LMWH	18	2776	33.5(32–35)	48	5.3(4–6)	65
IPC	4	110	28.2(20–38)	56	7.3(3–14)	52

GCS indicates graduated compression stockings; IPC, intermittent pneumatic compression; RRR, relative risk reduction; VFP, venous foot pump.

Adapted from Geerts WH, Heit JA, Clagett GP, et al. *Chest*. 2001;119(suppl 1):132S–175S.

After pooling, the observed rates of DVT were 48.2% in patients receiving vitamin K antagonists and 33.3% in patients receiving LMWH. The proximal DVT rates in the vitamin K antagonists and LMWH groups were 10.4% and 7.1%, respectively. Two meta-analyses confirmed the higher efficacy of LMWH compared with vitamin K antagonists without an increase in bleeding events.^{56,57} In summary, LMWH is more effective than vitamin K antagonists in preventing VTE in patients undergoing total knee replacement. LMWH may be associated with a small increase in wound hematomas, especially if started early after surgery.

Subcutaneous fondaparinux, at the dosage of 2.5 mg once daily started ≈6 hours after surgery, was compared with enoxaparin at the dosage of 30 mg twice daily started 12 to 24 hours after surgery.⁵⁸ Fondaparinux significantly reduced the rate of overall DVT from 27.8% to 12.5% and that of proximal DVT from 5.4% to 2.4%. Major bleeding occurred more often in the fondaparinux group, solely because of an increased bleeding index.

Oral ximelagatran at a dosage of 24 mg or 36 mg twice a day started the evening after surgery was compared with warfarin.⁵⁹ Ximelagatran at a dose of 36 mg significantly reduced the rate of overall DVT from 27.6% to 20.3%. The rate of DVT with 24 mg ximelagatran was similar to that seen in warfarin patients. The rates of proximal DVT, 2.7% with

36-mg ximelagatran and 4.1% with warfarin, were not significantly different. The rates of major and minor bleeding were low and did not differ significantly among the 3 groups.

Intermittent pneumatic compression devices provide effective prophylaxis in patients undergoing total knee replacement.^{60–62} The utility of intermittent pneumatic compression is limited by poor compliance, patient intolerance, and the inability to continue prophylaxis after hospital discharge. Graduated compression stockings provide modest protection in these patients.

Surgery for Hip Fracture

Patients undergoing surgery for hip fracture have a very high risk of VTE. In the absence of any prophylaxis, the rates of venography-assessed total and proximal DVT after hip fracture are ≈50% and 27%, respectively.¹ In the 3 months after surgery, the rate of fatal PE ranges from 1.4% to 7.5%. In comparison to elective hip and knee arthroplasty, fewer thromboprophylaxis trials have been conducted in patients undergoing surgery for hip fracture (Table 5).¹

In the Pulmonary Embolism Prevention Trial, 160 mg of enteric-coated aspirin administered before surgery and continued for 35 days was associated with a significant absolute risk reduction of 0.4% for DVT and fatal PE in comparison with placebo.⁶³ Aspirin did not reduce fatal and nonfatal

TABLE 5. Prevention of DVT After Hip Fracture Surgery

Prophylaxis Regimen	No. of Trials	Combined Enrollment	Total DVT		Proximal DVT	
			Prevalence % (95%CI)	RRR %	Prevalence % (95%CI)	RRR %
Placebo/control	8	364	50(45–56)	—	27(22–32)	—
GCS	1	23	39(20–61)	22	17(5–39)	35
Aspirin	3	204	39(32–46)	23	13(8–19)	53
Low-dose heparin	1	30	20(8–39)	60	17(6–35)	38
Warfarin	3	126	20(13–28)	61	9(4–19)	66
LMWH	5	887	18(15–21)	65	6(4–8)	78

GCS indicates graduated compression stocking; RRR, relative risk reduction.

Adapted from Geerts WH, Heit JA, Clagett GP, et al. *Chest*. 2001;119(suppl 1):132S–175S.

arterial events such as myocardial infarction, stroke, and all-cause mortality.

As with replacement surgery, the current pharmacological recommendations for prophylaxis of VTE are vitamin K antagonists, LMWHs, and fondaparinux.¹

The pooled results from the studies on vitamin K antagonists showed a reduction in relative risk of overall and proximal DVT of 61% and 66%, respectively, compared with no prophylaxis.^{64–66} Similarly, the pooled results from the studies on prophylaxis with LMWH showed a risk reduction of between 60% and 80% for both overall and proximal DVT.^{67–70} Unfortunately, no study has directly compared LMWH and vitamin K antagonists in the prevention of VTE after hip fracture.

Recently, fondaparinux has been compared with enoxaparin for the prevention of VTE in patients undergoing surgery for hip fracture.⁷¹ The incidence of venography-detected DVT was significantly reduced by fondaparinux from 19.1% to 8.3%. The rate of proximal DVT also was significantly reduced by fondaparinux, from 4.3% to 0.9%, while the incidence of major bleeding was 2.2% in both groups.

There is evidence that delaying surgery after hip fracture increases the risk of VTE. Therefore, if surgery is delayed more than 24 hours, prophylaxis with LMWH should be given during the preoperative period.⁷²

Mechanical prophylaxis with intermittent pneumatic compression appears to be effective in the prevention of VTE in patients undergoing surgery for hip fracture. Data on the benefit from graduated compression stockings are less convincing.

Elective Spine Surgery

Limited data are available on the incidence of VTE in patients undergoing elective spine surgery. In these patients, rates of clinically overt DVT (3.7%) and of PE (2.2%) have been reported.⁷³ The incidence of venography-detected DVT has been reported to be 18%.⁷⁴ Advanced age, cervical versus lumbar surgery, anterior surgical approach, surgery for malignancy, prolonged procedure, and reduced preoperative and postoperative mobility are risk factors for VTE in these patients.¹

In absence of additional risk factors, early and persistent mobilization is recommended in patients undergoing elective spinal surgery. In patients with additional risk factors, intermittent pneumatic compression may be useful.¹

The role of pharmacological prophylaxis is less defined in this population; postoperative LDUH and LMWH are the regimens of choice.¹ Patients with multiple risk factors benefit from the combination of pharmacological and mechanical prophylaxis.

Neurosurgery

The rate of clinically overt VTE is \approx 23% within 12 to 15 months after surgery for primary glioma.¹ Risk factors that increase the risk for VTE in these patients include intracranial surgery in comparison to spinal surgery, surgery for malignancy, duration of surgery, lower limb paralysis, and increased age.⁷⁵

Patients undergoing major neurosurgical procedures require routine prophylaxis for VTE.⁷⁶ The options for prophylaxis of VTE include perioperative use of intermittent pneumatic compression with or without graduated compression stockings, perioperative LDUH, or postoperative LMWH plus graduated compression stockings.¹

Physical methods of prophylaxis are commonly used in neurosurgery because of concerns about intracranial or spinal bleeding. Comparable rates of DVT have been found in patients receiving graduated compression stockings alone or in combination with intermittent pneumatic compression.⁷⁷ Both regimens were more effective than no prophylaxis.

In patients undergoing craniotomy, compared with no prophylaxis, LDUH was associated with a reduction of 82% in DVT, as diagnosed by fibrinogen scanning. The combination of LDUH and mechanical prophylaxis seems to be more effective than either method alone.¹

Two double-blind, randomized, venography-based studies compared graduated compression stockings alone or a combination of graduated elastic stockings and LMWH started postoperatively in neurosurgical patients.^{78,79} In the first trial, the rates of overall DVT and proximal DVT were 26% and 12% in patients given graduated compression stockings alone and 19% and 7%, respectively, in those given the stockings plus LMWH.⁷⁸ In the second study, the rates of overall and proximal DVT were 33% and 13% in the group wearing graduated compression stockings compared with 17% and 5%, respectively, in patients receiving the combined prophylaxis.⁷⁹ Therefore, prophylaxis with the combination of LMWH and graduated compression stockings is more efficacious than prophylaxis with the stockings alone. Pooled results from randomized trials in neurosurgery patients found that the rates of intracranial bleeding were 2.1% in the patients receiving postoperative LMWH and 1.1% in those who had mechanical or no prophylaxis.⁸⁰ Pending further safety data, preoperative or early postoperative LMWH should be used in craniotomy patients with caution.

Neurosurgical patients may require multimodality prophylaxis for VTE. One study found that there were no signs of DVT in 150 consecutive patients who received enoxaparin 40 mg once a day or UFH 5000 U twice a day, both in combination with graduated compression stockings, intermittent pneumatic compression, and predischARGE surveillance with venous ultrasonography of the legs. Overall, the rate of ultrasonography-detected DVT was similar in the enoxaparin and UFH patients, averaging 9.3%.⁸¹

Unresolved Issues

A number of issues related to the prevention of VTE in surgical patients need to be further defined.

Patients on long-term oral anticoagulation undergoing surgery require the interruption of treatment and the administration of UFH or LMWH. The optimal procedure for prophylaxis in these patients remains unclear. Temporary self-administration of LMWH at home is the less expensive approach for surgery requiring an interruption of treatment with vitamin K antagonists.⁸²

The benefit of prophylaxis for VTE after laparoscopic and arthroscopic surgery is unclear. In the majority of patients,

routine prophylaxis other than early mobilization is not required. Pharmacological prophylaxis with LDUH or LMWH should be used in patients with additional risk factors for VTE or in those undergoing prolonged or complicated surgical procedures. The optimal duration of pharmacological prophylaxis after laparoscopic and arthroscopic surgery also is unclear.

The clinical value of routine screening for VTE after high-risk surgery, chiefly orthopedic procedures, has been a matter of debate for many years. The diagnostic value of these noninvasive procedures is limited by their low sensitivity for asymptomatic DVT. There is no evidence that routine screening for VTE before discharge could help decide whether extended prophylaxis is needed after hospital discharge.

The optimal start of pharmacological prophylaxis for VTE in surgical patients is another unresolved issue. In patients having spinal surgery or an epidural catheter placed for neuraxial anesthesia or analgesia, prophylaxis with anti-thrombotic agents should be initiated postoperatively. In general, perioperative prophylaxis (that administered between 2 hours before and 4 hours after surgery) is more effective than the other regimens; however, it is associated with an increased risk of bleeding. Thus, perioperative prophylaxis should be given to patients at high risk for DVT and low risk of bleeding.

The results of several studies support extended prophylaxis after discharge in high-risk surgical patients.¹ Prophylaxis should be extended for 4 weeks in patients undergoing elective hip replacement and surgery for cancer. The optimal duration of antithrombotic prophylaxis for VTE in other types of surgery needs to be evaluated in prospective studies.

Conclusion

In the majority of patients undergoing surgery, the risk for VTE has been adequately evaluated and the benefit of thromboprophylaxis established. When pharmacological prophylaxis is used properly, the risk of bleeding complications is low. Prophylaxis with mechanical methods is preferred in patients at high risk of bleeding complications. Prophylaxis against VTE is cost effective for many surgical patients and should be implemented in all clinical settings where its effectiveness and safety has been established.

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