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REVIEW ARTICLE

Prevention of postoperative venous thromboembolism

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The publication of the 1991–1992 report of the National Confidential Enquiry into Perioperative Deaths (NCEPOD) [10] drew attention to prophylaxis against venous thromboembolism in surgical patients as an area of clinical practice that requires attention. The report found that pulmonary embolism is an important cause of mortality in postoperative surgical patients and was responsible for 7 % of all deaths. The role of prophylaxis against venous thromboembolism was not investigated in great detail but the findings suggested that it is not being given to all patients in whom it could be considered appropriate. In high-risk hip replacement patients, for example, 33 % did not receive any prophylaxis against venous thromboembolism.

The recommendations made in the NCEPOD report were that every hospital should have an agreed policy for prophylaxis against venous thromboembolism, all surgeons should be made aware of the problem and implementation of the policy should be audited regularly.

The aim of this review of the prevention of venous thromboembolism is to identify patients who benefit, discuss the merits of different methods, investigate areas of controversy and explore the role of anaesthetists.

Definition of terms and abbreviations

There are many terms and abbreviations used with reference to venous thromboembolism. More than one term has been applied to describe identical conditions, for example both mini-dose heparin [2] and low-dose heparin [46] refer to the use of low-dose unfractionated heparin for prophylaxis. There is also a confusing array of abbreviations, a small selection from one article includes "LDH", "HDHE", "FUT", "FPE", "PE" [12]. Definitions of terms and abbreviations to be found in this review are outlined here in order to avoid confusion.

Venous thromboembolism (VTE) is a broad term that refers to all aspects of thrombosis and embolism in the venous system. Deep venous thrombosis (DVT) refers to thrombosis within the deep limb veins. Pulmonary embolism (PE) is embolism to the pulmonary vasculature of any substance, but in the context of this review it is usually caused by blood clots unless otherwise stated. Fatal PE refers to pulmonary embolism that is the direct cause of death while non-fatal PE is pulmonary embolism that does not itself cause the death of the patient. Low-dose unfractionated heparin (LDUH) is the use of standard unfractionated heparin preparations in sub-therapeutic doses as prophylaxis against VTE, that is sodium heparin 5000 u. s.c. two or three times a day. Low-molecular-weight heparins (LMWH) are a group of products that are prepared by fractionating heparin to exclude the larger molecules with a weight greater than 10 000 Da. LMWH prophylaxis refers to the use of these products in sub-therapeutic doses to prevent VTE.

What cause venous thromboembolism in surgical patients?

Several perioperative factors may cause an increased incidence of VTE. General anaesthesia induces a reduction in blood flow to the lower limbs which is enhanced by surgical procedures such as cross-clamping of the aorta [38]. As a result, areas of the endothelium in the calf veins become hypoxic and release mediators that attract and activate platelets and leucocytes. The subsequent clot propagates, particularly in the presence of reduction in fibrinolytic activity [38]. General anaesthesia therefore gives rise to Virchow's triad (venous stasis, abnormal coagulation and intimal damage) [38] and predisposes to intravascular coagulation. In addition, surgery causes a reduction in fibrinolytic activity after operation which has been shown to be related to an increased incidence of DVT [39].

In addition to surgical and anaesthetic factors, several patient-related variables have been identified that further increase the incidence of VTE. The more important of these variables are listed in table 1.

How common is venous thromboembolism?

DEEP VENOUS THROMBOSIS (DVT)

DVT is a common postoperative complication but varies in incidence after different types of surgery and in association with the VTE risk factors

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Key words

Embolism, thromboembolism. Complications, thrombosis. Complications, haematoma. Complications, embolism. Blood, anticoagulants, heparin.

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Table 1 Risk factors for venous thromboembolism [38, 46]

Age	Major trauma or surgery
Obesity	Surgery to hip, pelvis and lower limb
Immobility	General anaesthesia
Previous venous thromboembolism	Pregnancy
Thrombotic tendency	Contraceptive pill
Malignancy	Heart failure
Paralysis of lower limb	Infection

Table 2 Classification of risk of venous thromboembolism [69] (DVT = deep venous thrombosis, PE = pulmonary embolism)

Risk group	Criteria	Risk of DVT	Risk of PE
Low risk	Minor surgery <30 min, no other risk factors. Major surgery <40 yr, no other risk factors.	<10 %	0.01 %
Medium risk	Major surgery >40 yr or other risk factors. Minor surgery, trauma or illness in patient with history of venous thrombosis.	10–40 %	0.1–1 %
High risk	Major orthopaedic surgery or fracture of pelvis hip or knee. Abdominal or pelvic surgery for cancer. Major surgery in patients with a history of venous thrombosis. Lower limb paralysis or amputation.	40–80 %	1–10 %

described above. DVT is particularly common after hip surgery. Meta-analysis of patients who had undergone elective hip replacement followed-up with venography, found that the incidence of DVT without prophylaxis was 50 % [58]. Patients may be stratified into groups on the basis of their individual risk factors, with the incidence of DVT varying from <10 to 80 % [69] (table 2).

DVT of the lower limb is also the most common precursor of PE and is responsible for more than 90 % of cases [38, 70]. Venous thrombosis in the upper limb and right atrium is less common but is still an important and underdiagnosed source of PE. It is more important in intensive care patients and in the presence of long-term central venous catheterization [7, 34].

PULMONARY EMBOLISM (PE)

PE is a relatively rare cause of death in the general population. Official figures for England and Wales for 1992 show it to be the cause of 0.2 % of all deaths [59], although this is probably an underestimate because of underdiagnosis [10, 36, 70]. PE occurs more commonly in postoperative patients. The NCEPOD study [10] found that in patients who underwent post mortem, 15 % died from PE. However, the proportion of deaths from PE varied markedly between different surgical procedures (see table 3).

Other studies of post-mortem findings have found that the incidence of PE varies between 9 and 21 % of deaths in hospital patients [70]. In a meta-analysis of a mixed surgical population, the incidence of PE among those patients not receiving VTE prophylaxis was found to be 3 % while that of fatal PE was 0.9 % [14]. When stratified on the basis of risk factors, the incidence of PE in hospital patients varied from 0.01 to 10 % (table 3) [69].

Table 3 Percentage of patients with pulmonary embolism (PE) at post mortem in the NCEPOD report [10], according to surgical procedure

Type of surgery	PE at post mortem (%)
Elective hip replacement	52
Prostatectomy	20
Amputation of lower limb	18
Colorectal resection	12
Craniotomy	4
Coronary artery bypass grafts	0

Methods of prophylaxis against venous thromboembolism

Comparison of the efficacy of different forms of prophylaxis against VTE in postoperative patients is difficult because of the number of subjects required to reach significant conclusions. Although DVT is relatively common (see above), more than 500 patients would be required to show a 50 % reduction in incidence in a randomized trial [14]. Reliable diagnosis requires that all patients have either venography or fibrinogen-uptake testing performed [57] which would be expensive and time consuming on such a large scale. PE is relatively rare (see above) and therefore a patient population of 5000 would be needed to demonstrate a 50 % reduction in mortality. A total of 100 000 patients would be needed in a study with enough power to demonstrate a significant decrease in overall mortality [14]. The diagnosis of PE also presents difficulties as the end-point for diagnosis in most trials is a clinical diagnosis confirmed by an objective test [12]. Very few individual studies of sufficient size have been performed that allow reliable conclusions to be reached regarding the effect of different agents on the incidence of PE, fatal PE and overall mortality. To overcome these problems it has been necessary to organize multicentre or multinational trials [4, 22, 35] or pool data from several trials together in the form of meta-analyses [1, 12, 14, 58]. The studies included in meta-analyses may involve different patient populations, different end-points and different levels of methodological strength, and there may also be "publication bias" if only published data are included [45, 77], There are therefore reservations about the conclusions of meta-analyses. However, at present, they are the only studies available that can provide information on the relative efficacy of different types of VTE prophylaxis.

LOW-DOSE UNFRACTIONATED HEPARIN (LDUH)

S.c. LDUH is the method of prophylaxis against VTE that has been most widely used and investigated in the United Kingdom [10, 32]. There is strong evidence that prophylaxis with LDUH is

effective in reducing the incidence of DVT after moderate- or high-risk operations. This was first established by the international multicentre trial of Kakkar and colleagues [35]. Three more recent meta-analyses have also demonstrated a reduction in the risk of DVT when LDUH was used compared with either placebo or no treatment [12, 14, 35]. The risk of developing a DVT is reduced by 64 % [14]. Orthopaedic, urological and general surgical patients all show a similar reduction in incidence [14]. The incidence of PE and fatal PE is also reduced [12, 14, 35] by about the same order as that demonstrated for DVT [14]. The effect of prophylaxis on overall mortality is not as well defined. The meta-analysis by Collins and colleagues [14] found that administration of LDUH resulted in a significant reduction in overall mortality. However, in a multinational study [35], overall mortality was not reduced significantly in patients receiving LDUH compared with controls.

Assuming that the rate of fatal embolism in patients not receiving VTE prophylaxis is 0.9 % [14], these studies imply that routine use of LDUH prophylaxis could prevent six deaths from PE in every 1000 patients undergoing major urological, orthopaedic and general surgery.

Problems with heparin

LDUH causes an increase in haemorrhagic complications after surgery [14, 35]. Wound haematomas are also more common [35], but mortality from major haemorrhage does not occur more frequently [14, 35].

There are many patients for whom LDUH is contraindicated. Conditions and procedures such as hypertension, aneurysms, history of peptic ulcer, oesophageal varices, thrombocytopenia, bleeding disorders, endocarditis, pleuritis, regional anaesthetic techniques, neurosurgery, eye surgery and hypersensitivity to heparin raise concerns about the use of heparin [38].

Thrombocytopenia may be caused by heparin and occurs in 0.3 % of patients given prophylactic porcine heparin [26]. Therefore, monitoring platelet count is required after more than 5 days of therapy with prophylactic heparin [9]. Other problems with long-term use include skin rashes, raised serum transaminase concentration and osteoporosis [26].

LOW-MOLECULAR-WEIGHT HEPARINS (LMWH)

LMWH and heparinoids have a mechanism of action different from that of unfractionated heparin. Heparins exert their anticoagulant effect by binding and activating antithrombin III. Heparin–antithrombin III inhibits activated IX, X, XI and XII and thrombin. Inhibition of thrombin requires that the heparin molecule binds to both antithrombin III and thrombin. LMWH and heparinoid molecules, which have a lower mean molecular weight than unfractionated heparin [29], are unable to bind both thrombin and antithrombin III simultaneously. Therefore, they cannot catalyse the inhibition of thrombin although they are able to catalyse the inhibition of activated IX, X, XI and XII by antithrombin III [26]. LMWH have less effect on platelet activity than LDUH and would be expected to inhibit haemostasis less and produce less bleeding [29]. LMWH also have a longer duration of action than unfractionated heparin and twice or even once daily regimens are effective in preventing VTE [33, 63].

LMWH compared with LDUH

Three meta-analyses [41, 57, 58] and a large European multicentre trial [43] have reached the conclusion that LMWH can further reduce the risk of DVT compared with LDUH. A meta-analysis published in 1992 [57] found significant differences in the incidence of PE between patients receiving LMWH and LDUH. There was a significant reduction in the incidence of PE (fatal and non-fatal) in patients who had undergone both orthopaedic and general surgical procedures. The relative risk of PE (fatal and non-fatal) in the LMWH prophylaxis group compared with the LDUH group was 0.43 (95 % confidence interval 0.26–0.72). No significant conclusions were made about the incidence of fatal PE and overall mortality.

Postoperative haemorrhage does not appear to be more common with LMWH than with LDUH nor has any decrease in clinically significant bleeding been demonstrated [28, 41, 57,].

Dose of LDUH and LMWH for prophylaxis for VTE

The recommended dose of unfractionated heparin is 5000 u. 8–12 hourly [46]. A meta-analysis in general surgical patients suggested that 8-hourly administration is more effective than 12-hourly, without increasing the risk of major haemorrhage or haematomas [12].

The dose for LMWH is not as well established. LMWH have greater bioavailability than unfractionated heparin and therefore lower doses (measured in anti-factor Xa units [42]) give rise to higher plasma concentration of anti-Xa activity [8]. Studies using dalteparin 5000 u. daily have shown an increased risk of bleeding [41] while 2500 u. daily appeared to be safe and effective [8].

There are three commercially available preparations of LMWH: dalteparin, enoxiparin and tinzparin. On a daily basis, LMWH are no more expensive than LDUH. A regimen of dalteparin 2500 u. daily (Fragmin, Kabi) costs £1.96 while a regimen of LDUH 5000 u. three times a day (Minihep, Leo) would cost £2.19 per day [56].

What overall conclusion can be reached regarding LDUH *vs* LMWH? Recent editorial and review articles [62, 63] have suggested that LMWH may become the treatment of choice for DVT prophylaxis. The authors stopped short of unreservedly recommending LMWH because a reduction in incidence of fatal PE and overall mortality is unproven so far [62, 73]. Despite this, LMWH have a number of advantages over other methods of prophylaxis. They have a once daily dosing regimen, are the most effective agents in the prevention of DVT [55] and there is no requirement for labora-

tory monitoring tests when LMWH are used in prophylactic doses. These advantages should establish LMWH as the preferred method of VTE prophylaxis.

Adjusted-dose heparin

This refers to the use of a variable dose of unfractionated heparin to keep the activated partial thromboplastin time 1–3 s above normal. This procedure may be more effective than LDUH in preventing DVT in high-risk patients, but is more difficult to manage, requiring laboratory investigations to monitor dose and effect [44, 76].

Dihydroergotamine combined with heparin

The addition of dihydroergotamine to heparin results in an increase in smooth muscle tone, reduced peripheral pooling and increased femoral blood flow velocity [21]. Any advantage over heparin alone has not been proved [58] and arterial spasm with consequent ischaemia is a side effect of dihydroergotamine.

Warfarin

The administration of warfarin leads to the production of inactive precursors of the vitamin K-dependent clotting factors, II, VII, IX and X, thus inhibiting the clotting cascade, decreasing clot propagation and promoting clot breakdown [38, 69]. Warfarin has been shown to be effective in prophylaxis against VTE [27, 58]. Recommended prothombin ratio (INR) is in the range 2–3. Bleeding problems can be minimized by starting therapy after operation [27]. Problems with this method of prophylaxis are that laboratory tests are needed to monitor the degree of anticoagulation and oral administration is required which can present difficulties in the immediate postoperative period. In addition, the effects on the clotting system last longer and are more difficult to reverse than those of heparin. For these reasons warfarin is not the preferred method of prophylaxis for surgical patients in the United Kingdom, although it is frequently used for VTE prophylaxis in the United States [69].

Dextrans

Dextrans reduce platelet aggregation, improve blood flow and facilitate clot breakdown by altering the structure of the clot and increasing fibrinolysis [21]. Both dextran 40 and 70 have been shown to reduce the incidence of DVT [21, 58], A large multicentre trial has demonstrated that dextran 70 is also able to reduce the mortality from PE [22]. Dextran 40 and 70 are associated with an increased risk of bleeding, allergic reactions and require i.v. access for administration [46].

Antiplatelet agents

The results of individual trials with antiplatelet agents have not shown a significant effect on the incidence of VTE. Meta-analysis of five trials [58] failed to show any benefit, although indobufen has been shown to prevent recurrent DVT in known sufferers [3]. Consequently, until recently it has been thought that antiplatelet agents do not have a role in the prophylaxis of VTE [10]. However, a recent overview of 53 studies involving 8400 patients [1] concluded that significant reductions in the incidences of DVT in addition to non-fatal and fatal PE were produced by the use of antiplatelet agents. This benefit was observed separately in general surgery, traumatic orthopaedic surgery and elective orthopaedic surgery. There was a significant increase in complications caused by bleeding and in non-fatal but not fatal major bleeds [1]. The study [1] suffers, as do other meta-analyses, from the fact that the methods and drug regimens differed between the individual studies. Different drugs, doses and different combinations of drugs were all analysed together. Aspirin and dipyridimole, either alone or in combination, were the most common agents used in individual studies but studies involving other drugs were included in the overall analysis. When individual treatment regimens were analysed, not all (for instance aspirin alone) achieved significant reductions in the incidence of DVT (table 4). The antiplatelet trialists collaboration III [1] has opened up the possibility of a role for antiplatelet agents in VTE prophylaxis but further studies are required to confirm this.

Table 4 Indirect comparisons of proportional effects of different platelet regimen on deep venous thrombosis detected by systematic fibrinogen scans or venography, or both [1]. *95 % confidence intervals of odds ratio compared with untreated controls do not overlap one

Antiplatelet regimen	% Odds reduction (SD)
Aspirin	23 (10)
Aspirin + dipyridamole	56 (9)*
Hydroxychloroquine	62 (14)*
Ticlopidine	27 (19)
All antiplatelet agents	41 (6)*

Regional anaesthesia

There are several mechanisms that may contribute to a reduced tendency to form thromboses in the lower limb veins in association with regional anaesthesia. Peripheral vasodilatation and the reduction in viscosity resulting from fluid loading may play a role. Extradural anaesthesia reduces fibrinolysis and activation of clotting factors [5, 52]. Local anaesthetics themselves decrease platelet adhesion, aggregation and release [48].

There is evidence to show that spinal or extradural anaesthesia in the absence of other prophylactic measures is associated with a reduction in the incidence of VTE [48, 52, 64]. A relative risk reduction after hip surgery for DVT of 46–55 % has been demonstrated in one review [64]. However, only four relatively small studies (30–85 patients) were used to reach these conclusions. Modig and colleagues [53, 54] performed two studies that found a significant decrease in the incidence of PE (33 to 10 %; $P < 0.05$), as measured by perfusion lung scanning in patients undergoing hip replacement under extradural block compared with those having

general anaesthesia. Overall numbers were small (154 patients) however, and in the absence of larger studies this evidence can only be considered as suggestive but unproven [48].

In summary regional anaesthesia reduces the risk of DVT and may reduce the risk of PE. It is not known if there is any long-term benefit. Other questions that remain to be answered include whether or not the duration of the block has any influence and the effect of combining regional anaesthesia with other forms of VTE prophylaxis before, during or after operation [48].

Mechanical methods

In the NCEPOD report [10], mechanical methods of prophylaxis were the second most common form of prophylaxis after heparin and were used in 40 % of patients. Elastic compression stockings have been shown to reduce the incidence of DVT, although a reduction in the rate of PE has not been clearly demonstrated [12, 46]. The same is true of intermittent calf compression devices [12, 46]. Where these methods of prophylaxis have an advantage over anticoagulants is that they are not associated with an increased risk of haemorrhage after operation [13], although pneumatic intermittent calf compression devices have been shown to increase intraoperative bleeding in patients undergoing radical pelvic surgery [74].

A combination of a mechanical and anticoagulant method of VTE prophylaxis is a common practice. In a survey of general surgeons in Merseyside (United Kingdom), 20 % always used heparin in combination with compression stockings for prophylaxis [32]. There have been studies that have found benefit from using this combination of methods of prophylaxis [23]. However, a recent review [83] concluded that not enough methodologically sound studies have been published to be sure that there is any advantage to be gained by combining compression stockings with other methods of prophylaxis.

Antithrombotic agents

Defibrotide and hirudin are two new agents that may have some role to play in VTE prophylaxis. Hirudin is a potent cofactor-independent thrombin inhibitor which has little effect on platelets [6]. Defibrotide is a deoxyribonucleic acid derivative that increases fibrinolysis and has antithrombotic activity also. It probably acts by selectively increasing levels of prostaglandins I_2 and E_2 and increasing tissue plasminogen activator [61]. Early trials appear to show that defibrotide and hirudin are effective in preventing DVT but whether or not they have any advantages over established methods is still to be determined [6, 61].

Situations with particular implications for VTE prophylaxis

NEUROSURGERY

There is a high incidence of DVT in patients who have undergone neurosurgery (29–43 %), as would be expected in patients who have long procedures and are confined to bed for long periods after operation [31, 81]. The use of anticoagulants is of concern as haemorrhage after craniotomy or spinal surgery could result in serious complications. LDUH has been shown to reduce the incidence of DVT without increasing complications related to haemorrhage in craniotomy patients [2, 11, 20], although the number of patients in these studies was relatively small (100–150). Mechanical methods of prophylaxis have also been shown to be effective in reducing the incidence of DVT [79]. Recent review articles of VTE prophylaxis in neurosurgical patients still recommend that mechanical methods are used in preference to anticoagulants [38, 46]. If a DVT does develop it has been recommended that 5 days after surgery should elapse before anticoagulation is commenced [75].

TRAUMA

Patients with trauma may be immobilized, for long periods of time and have a hypercoagulable state induced by circulating procoagulants produced by tissue and endothelial injury [38]. The incidence of DVT varies from 4 % in young patients with minor trauma to 63 % in patients with multiple injuries and prolonged immobilization [40, 72]. The presence of DVT may be difficult to diagnose because of plaster casts, external fixators and swelling caused by injury. PE is one of the leading causes of late death in trauma patients [71].

Trauma patients therefore are a high-risk group for DVT and PE but there are concerns,about the possible effect on haemorrhage of administering anticoagulants. Most research on trauma patients and VTE has been done in patients with hip fractures and the conclusions are the same as for elective surgery, that is anticoagulants are effective and associated with an acceptable incidence of bleeding complications [17]. Mechanical methods are also effective and remain popular because of concerns about bleeding [38]. There is little information in patients with severe multiple trauma on the safety or efficacy of anticoagulants, and early mobilization and mechanical methods of prophylaxis are recommended in these patients [38].

THE CONTRACEPTIVE PILL

The combined contraceptive pill is recognized to be associated with an increase in thrombotic complications [46]. The risk of postoperative thromboembolism is doubled, and this has led to the suggestion that the pill should be stopped before operation [82]. The THRIFT consensus group [46] concluded that there was insufficient evidence to support, routinely, cessation of the combined pill before major surgery unless additional risk factors were present. They also felt that there was not enough evidence to support routine thromboembolic prophylaxis in oral contraceptive users without additional risk factors. Minor procedures in healthy women do not require any further prophylaxis than normal women. Progesterone only preparations do not predispose to VTE [19].

HORMONE REPLACEMENT THERAPY

Postmenopausal hormone replacement regimens contain much less oestrogen than the contraceptive preparations and there is no evidence of an increased risk of thromboembolism. No additional precautions need to be taken in these patients [46].

PREGNANCY

PE is the second most common cause of maternal deaths in the United Kingdom [66]. Pregnancy itself gives rise to a six-fold increase in the risk of thromboembolism and the puerperium is the time of highest risk. Obese older women (>35 years) with their third pregnancy or more are at particularly high risk and this is increased further by Caesarean section. These patients should be considered for VTE prophylaxis which may need to continue until 6 weeks after delivery [46].

CARDIOVASCULAR SURGERY

Patients undergoing bypass or valve surgery are usually fully anticoagulated in the preoperative period and it is interesting to note that in the NCEPOD study, none of the deaths in cases of coronary bypass grafts was caused by PE (table 3) [10]. However, in thoracic and peripheral vascular surgery, the incidence is thought to be about the same as in general surgery [46] and prophylaxis is recommended.

Spinal–extradural anaesthesia and anticoagulant prophylaxis

How common are spinal haematomas as a complication of spinal–extradural anaesthesia in normal patients? Seventeen cases of post extradural spinal haematomas were identified in a review of the English literature in 1990 [68]; 12 of these were associated with a bleeding disorder, although none was associated with DVT prophylaxis. One study revealed no cases of symptomatic spinal haematoma in 100 000 patients with normal anticoagulation who had undergone spinal–extradural anaesthesia (although two patients with abnormal coagulation did develop spinal haematomas) [68]. A second, single-institution series in 80 000 obstetric patients who had extradural blocks did not find any cases of spinal haematoma [67]. On the basis of this evidence, the incidence of spinal haematomas after spinal-extradural anaesthesia in normal patients would appear to be less than 1 in 100 000. Compared with normal patients, those with abnormal coagulation probably have a higher incidence of spinal haematomas after spinal–extradural anaesthesia.

Are haematomas more common in patients receiving anticoagulant VTE prophylaxis? There are three reports of spinal haematomas occurring in association with extradural anaesthesia and s.c. anticoagulant VTE prophylaxis. Two occurred after the use of LDUH [16, 50] and one after LMWH [78]. There are at least two published case series of patients who have received VTE prophylaxis and spinal–extradural anaesthesia. Of 950 patients receiving oral anticoagulants who had an extradural inserted, none developed a clinically significant spinal haematoma [58]. Meta-analysis of studies involving patients receiving a combination of LMWH prophylaxis and spinal–extradural anaesthesia did not identify any spinal haematomas in 9013 patients [5].

It would appear therefore that the incidence of clinically significant spinal haematomas in both normal patients and patients receiving anticoagulant VTE prophylaxis who undergo spinal–extradural anaesthesia is very low. An increase in the incidence in patients receiving anticoagulant VTE prophylaxis has not been established nor has it been excluded. However, when a spinal haematoma does occur it can lead to permanent paraplegia despite surgical intervention, although early intervention (<12 h) may allow recovery [58].

The benefits of regional anaesthesia are controversial but seem to be greatest in those patients most at risk of VTE. There is some evidence that after major abdominal and thoracic surgery, by combining an extradural block with general anaesthesia there is a reduction in postoperative pain scores, tracheal intubation time, intensive care stay and reduced respiratory and pulmonary complications [24, 30, 37]. After surgery for a fractured hip there is a well established reduction in early postoperative mortality associated with regional techniques, although long-term mortality is unaffected [49, 80]. Therefore, spinal–extradural anaesthesia may confer benefits in terms of postoperative morbidity and mortality. These advantages should be weighed against the possible but unproven concerns about performing spinal–extradural procedures in patients receiving VTE prophylaxis.

The uncertainty surrounding this issue is reflected in the finding that 38% of Danish anaesthetic departments thought LDUH prophylaxis was a contraindication to extradural block and 62% did not [85]. There is also a subtle difference in opinion in the current literature on the advisability of performing spinal–extradural blocks in patients receiving anticoagulant VTE prophylaxis. There are some authors who feel that the combination is safe to use with certain conditions attached [6, 51, 78]. Others feel that until more information is available, spinal–extradural procedures are unsafe in these circumstances and should not be used unless there are strong indications [18, 60].

If spinal–extradural techniques are to be performed in patients receiving anticoagulant VTE prophylaxis, there are measures that can be taken to reduce the risk of spinal haematoma. A spinal–extradural block itself confers perioperative protection against VTE and so anticoagulant prophylaxis can be started either after operation or at least after insertion of the block [84]. If patients are already receiving prophylaxis, regional anaesthesia should not be given within 4–6 h of a dose of LDUH [84]. This is based on the observation that therapeutic changes to coagulation may occur for up to 4 h after a dose of 5000 u. of unfractionated heparin s.c. [15]. With regard to LMWH, 12 h is presently

Table 5 Summary of safety precautions when using spinal–extradural blocks in the presence of anticoagulants (LDUH = low-dose unfractionated heparin, LMWH = low-molecular-weight heparins)

Prophylactic status	Safety measures
LDUH	Site block before 1st dose or 4–6 h after last dose
LMWH	Site block before 1st dose or 12 h after last dose
Aspirin	Site block before 1st dose or 7–10 days after last dose
Preoperative therapeutic anticoagulation/coagulopathy	Block contraindicated
Itraoperative anticoagulation	Start 1 h after insertion of block
Postoperative anticoagulation	Stop 1–2 h before removal of extradural catheter

regarded as the safe dose–block interval before spinal–extradural anaesthesia [18, 63]. Although aspirin is not currently used for VTE prophylaxis, it may be in the future and many patients present who are receiving aspirin for other reasons. Ideally aspirin therapy should be stopped 7–10 days before operation. A bleeding time of less than 10 min has been accepted as a confirmatory test in patients who have been receiving aspirin [47], but the validity of this has been questioned because of concerns of variability of results and the need to standardize the normal range [25, 84]. After the procedure, patients should be monitored carefully for neurological sequelae and, if they do occur, facilities must be available for investigation and urgent laminectomy should it be required [54]. Patients given therapeutic anticoagulation regimens or with a coagulopathy should not have spinal–extradural anaesthesia until the coagulation profile is normal [84]. Bleeding during catheter insertion is considered by some to contraindicate subsequent anticoagulation [65] but there is no evidence to support this [84]. These guidelines are summarized in table 5.

What role should the anaesthetist play in prophylaxis against VTE?

Prevention of VTE is an area of clinical practice that has been delegated traditionally to the surgical team, and most publications on the subject direct their advice to surgeons [10, 38]. However, the anaesthetist does have a considerable interest in this aspect of patient care. Anaesthesia contributes to the risk of VTE, the method of prophylaxis may affect the anaesthetic technique (particularly if regional anaesthesia is being considered) and in areas where anaesthetists have responsibility for the long-term care of the patient, for example intensive care, they are directly responsible for implementing prophylaxis. Anaesthetists are able to co-ordinate VTE prophylaxis in the same way that they co-ordinate the management of postoperative fluids and pain. In the perioperative period the surgeon and anaesthetist can review the plan for prophylaxis (if it exists) and amend it if necessary to allow for anaesthetic requirements and ensure that prophylaxis is carried over into the postoperative period.

Table 6 Recommendations for prophylaxis against venous thromboembolism based on criteria for risk stratification (see table 2)

Risk status	Prophylaxis	Recommendation
Low risk	Early mobilization	± Compression stockings
Moderate or high risk	If no contraindication to anticoagulants one of the following:	If coagulation is contraindicated or in addition:
	LMWH/heparinoid, e.g. Kabi 2165 2500 s.c. daily	Regional anaesthesia
		Compression stockings
	LDUH:	
	Heparin sulphate 5000 u. s.c. 3 times daily	Intermittent calf compression
	Oral warfarin, adjusted dose heparin or dextran 70, as described in text	

General recommendations for VTE prophylaxis

All surgical patients should be assessed on admission as to their risk in terms of VTE (table 2) and there should be a plan for prophylaxis against VTE from admission until discharge [46]. A simple procedure is needed to guide clinicians through the complicated questions of who to give what form of prophylaxis. Table 6 summarizes an approach to VTE prophylaxis modified from the THRIFT study [46] in the light of the information reviewed in this article.

Conclusions

VTE is still a significant cause of postoperative morbidity and mortality. No method of prophylaxis can completely eliminate this complication of anaesthesia and surgery. Many methods of prophylaxis have been proved to prevent DVT and some to prevent fatal and non-fatal PE.

For ease of administration and side effects, LMWH are the most promising agents for prophylaxis, although clear benefits in terms of mortality have not been established over other methods. Further investigation is required into the efficacy of antiplatelet and antithrombotic agents arid these may gain a larger role in prophylaxis against VTE in the future.

There is disagreement in the literature about the advisability of performing spinal–extradural techniques on patients receiving anticoagulant VTE prophylaxis. Some authors feel that very strong indications should exist if spinal–extradural blocks are to be performed on patients given anticoagulant prophylaxis, while others feel that blocks under these circumstances are essentially safe if appropriate care is maintained. Before such a procedure, appropriate time intervals need to be observed between the last dose of the anticoagulant prophylactic regimen and the block, and patients need careful intra- and postoperative observation. If a spinal haematoma is suspected and confirmed, surgical evacuation must be performed as soon as possible.

The use of prophylaxis in postoperative patients is not as common as it should be. Recommendations of local policies and auditing of the implementation and

outcome of those policies, as suggested by the NCEPOD report [10], would allow a systematic approach to a complex and challenging problem. Venous thromboembolism prophylaxis should form part of the routine surgical and anaesthetic pre-operative assessment.

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