Standard Review Article

OPEN

# Thromboprophylaxis an update of current practice

## Can we reach a consensus?

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**Abstract**

Diagnosis, prophylaxis, and management of venous thromboembolism (VTE) in patients with fractures remain a highly controversial topic with little consensus in clinical practice or the literature. The following manuscript represents a summary of evidence presented at the 2017 OTA Annual Meeting Symposium; "Thromboprophylaxis an Update of Current Practice: Can We Reach A Consensus?" The need for prophylaxis in pelvic and acetabular fracture patients; the existing body of evidence related to VTE, pulmonary embolism (PE), and prophylaxis for patients with fractures about the knee; current evidence in Edinburgh Scotland, regarding VTE prophylaxis in patients with isolated ankle fractures and the risk of VTE in patients with a hip fracture are topics that are addressed. The reader will benefit from the wisdom of this compilation of global contributions on thromboprophylaxis.

**Keywords:** deep venous thrombosis prophylaxis, thromboprophylaxis, venous thromboembolism, pulmonary embolism, fracture

### 1. Thromboprophylaxis after pelvic/acetabulum fractures

Although thromboprophylaxis is generally recommended after pelvis and acetabulum trauma, practitioners must remember that no evidence demonstrates prophylaxis reduces mortality or secondary outcome of pulmonary embolus.[1] Furthermore, the typically utilized pharmacologic agents do not carry specific indications for pelvis and acetabulum trauma.

A recent review of survival after pelvic fracture at a single ACS Level I trauma center makes no mention of VTE prophylaxis as contributing to improved survival rates.[2] The authors instead attribute other interventions like use of pelvic binders, selective angiography, and exploratory laparotomy to improving the survivability of pelvic ring disruption.

Several authors conclude that sequential duplex screening for VTE is not necessary as a matter of course. Moed et al[3] found that PE risk was not diminished with sequential screening protocols in pelvic and acetabular fracture patients. In a review of almost 1000 patients, Borer et al[4] found no difference in PE prevalence with or without screening.

Some question if the increasingly sensitive screening and diagnostic tests available currently may find small emboli of questionable clinical relevance, leading to overdiagnosis of PE.[5] These authors caution that the risks of anticoagulation are not minor.

Still, pelvis and acetabulum fractures represent relatively high-risk injuries for development of VTE. A risk assessment model based on review of 38,000 patients identified a number of higher risk factors including admission to ICU and injury location of thorax, abdomen, and lower extremity.[2] Another review identifies spinal cord injury, pelvic fracture, lower extremity fracture, increased injury severity, and ventilator support as significant risk factors for VTE.[6]

No evidence-based recommendations specific to pelvis and acetabulum fracture patients yet exist. Early use of low molecular weight heparin (LMWH) appears to decrease VTE and PE according to some experts.[7,8]

The OTA Evidence Based Quality Value and Safety Committee surveyed practitioners and experts to generate a consensus set of assumptions and recommendations.[9] According to this work, spinal cord injury and increasing age represent primary risk factors, and pelvic and lower extremity long bone fractures add to increased risk. The consensus recommendations for pelvis and acetabulum patients favor LMWH begun within 24 hours provided no ongoing blood loss. Typically, LMWH doses are held 12 hours before through 12 hours after surgery. The consensus supports a 4-week duration of prophylaxis. Routine asymptomatic screening gains no support. It should be noted that bleeding is a potential complication with chemical VTE prophylaxis. The frequency and severity of such complications are highly varied depending upon the agent utilized, the injury pattern, and the host.

### 2. Thromboprophylaxis after fractures around the knee

Thromboembolic complications are a well-recognized risk after lower limb trauma in general. Although more common injuries such as hip fractures have reasonable evidence base to guide current practice, for less common fractures the evidence is rather

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*The authors have no conflicts of interest to disclose.*

*Source of funding: Nil.*

*Institutional Review Board approval was not required.*

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*OTA (2019) e027*

*Received: 20 October 2018 / Accepted: 17 December 2018*

*Published online 22 November 2019*

*http://dx.doi.org/10.1097/OI9.0000000000000027*

sparse, and this applies to fractures around the knee. The relevant fractures in relation to the knee are distal femoral fractures and tibial plateau fractures. However, these fractures are relatively uncommon compared to more common lower limb injuries such as hip and ankle fractures. The relative incidence in relation to hip fractures is about 5%: so for every 1000 hip fractures treated surgically each year there will only be 50 distal femur and 50 tibial plateau fractures requiring fixation, on average, in the same time period.

It is perhaps not surprising, therefore, that the data regarding incidence and management of thromboembolic complications related to fractures around the knee is less detailed and guided by literature that may not specifically be concerned with these fractures. However, thromboembolic complications remain a major concern in distal femoral and proximal tibial fractures because most of these injuries require surgical treatment and fatal pulmonary embolism remains the third most common cause of death in trauma patients after the first 24 hours.[10]

### 2.1. Incidence and prevalence

Estimates for the incidence of deep venous thrombosis and pulmonary embolism vary widely in smaller studies but larger cohort studies have given a more accurate estimate of the scale of the problem. Paffrath et al[11] analyzed 7937 trauma patient datasets from the Trauma Registry of the German Society for Trauma Surgery and screened them for all clinically relevant VTE episodes. There were 146 VTE during the acute hospitalization period, an incidence of 1.8%. Of the 146 cases, 72 (49%) patients had developed a VTE, 54 (37%) patients had a PE alone, and 20 (14%) patients had a combined VTE and PE. This gives an overall incidence for deep venous thrombosis and pulmonary embolism of 1.16% and 0.93%, respectively.

In another series of 18,151 orthopaedic trauma and elective patients, Gudipati et al[12] reported a pulmonary embolism occurred in 85 (0.47%) of which 13 (15%) were fatal. There were 7503 trauma cases and 61 PEs in this group, an incidence of 0.81%. There were no fatal PEs after distal femur fractures but 1 death due to PE occurred after tibial plateau fractures, an incidence of 1.2%. The median time to the occurrence of the pulmonary embolism was 23 days. Interestingly, a concomitant VTE was found in only 33% of patients with a pulmonary embolism. This has been a feature of several other studies where concomitant VTE and PE have been found in only 15% to 30% of patients.[13–16]

Data on the specific incidence of deep venous thrombosis after fractures around the knee are limited. Abelseth et al[17] reported on use of venography carried out 9 days after operative fixation of lower limb fractures in 102 patients. The incidence of occult VTE was 28%. The incidence of VTE was higher in fractures around the knee with an incidence of 40% and 43% for femoral shaft and plateau fractures, respectively. Godzik et al[10] analyzed data from the National Trauma Data Bank which contains prospectively collected data from patients with traumatic injury who were treated in 770 trauma centers in the United States and Puerto Rico. A total of 199,952 patients with pelvic and lower extremity fracture were identified. Of these patients, 918 (0.46%) had a pulmonary embolism and 117 (12%) of them died during hospitalization. They did not specifically report on pulmonary embolism after periarticular knee fractures but reported an overall rate of PE of 0.46% and 0.44%, respectively, which would suggest the rates of thromboembolism are similar for fractures on either side of the knee.

**Table 1**

**Risk factors for thromboembolism.**

| | |
|---|---|
| Intrinsic patient factors | Increasing age |
| | Previous history of thromboembolism |
| | Family history in first-degree relatives |
| | Thrombophilia (e.g., Factor V Leiden) |
| Associated medical problems | Obesity |
| | Immobility |
| | Smoking |
| | Active malignancy |
| | Cardiac disease |
| | Medication (e.g., hormonal therapy/oral contraceptive) |
| Specific fractures | Spinal fractures |
| | Pelvic/acetabular fractures |
| | Hip fractures |

### 2.2. Risk factors

The risk factors for thromboembolic complications may be specific to the injury or more general patient risk factors (Table 1). Certain fractures including spinal injury and pelvic and acetabular fractures are associated with increased risks, and the same applies to multiple trauma patients. More complex surgical procedures and increased length of hospital stay with impaired mobility will also increase the risk. Some patients have prothrombotic conditions (e.g., antiphospholipid syndrome; factor V Leiden in heterozygous patients) and these will usually merit consideration of extended prophylaxis regimens. Patients with a previous history of thromboembolic disease or with first-degree relatives with a history of the same should also be considered high risk. Patients who have an active malignancy will also be more susceptible to venous thromboembolic events. Finally, morbid obesity and smoking will also contribute to increased risk. Lower limb trauma patients should be screened to assess risk of thromboembolic complications in order to guide selection of the most appropriate thromboprophylaxis.

### 2.3. Plateau fractures

Numerous studies regarding results of plateau fractures have been published in the literature but many publications do not give the rate of thromboembolic complications. Chan and Keating[18] studied the outcome of internal fixation versus external fixation for bicondylar plateau fractures. They had 35 cases treated by external fixation and 24 cases treated by internal fixation. There were no thromboembolic complications in the external fixation group and there were 2 VTEs in the internal fixation group, a rate of 8%. Elsworth et al[19] compared early versus delayed fixation for plateau fractures reporting on 29 cases treated with early fixation and 20 in the delayed group. They reported only 1 VTE in the early group and none in the delayed group. In a meta-analysis of external fixation versus internal fixation for plateau fractures, Metcalfe et al[20] identified 7 comparative studies. Only 3 reported deep venous thrombosis rates. The overall rate of VTE was 3.8% and there was no relationship to treatment type.

A Cochrane review published in 2015 by McNamara et al[21] reviewed surgical methods for fixation of tibial plateau fractures. Six trials involving 429 participants were identified, including studies comparing fine wire fixators versus internal fixation; locked plating versus standard plating; minimally invasive fixation versus open reduction and plating; and finally the use of bone grafting versus calcium phosphate cements. Venous

thrombosis rates were only reported for the comparison of locked plating versus standard plates and the rate was not significantly different.

### 2.4. Distal femoral fractures

Most studies reporting on the outcome of distal femoral fractures do not even mention the rate of thromboembolic complications. In a recent meta-analysis of the literature Griffin et al[22] identified 7 comparative studies with 444 cases. Only 1 study by Butt et al[3] quoted a figure for VTE. This was a comparative trial of nonoperative versus operative fixation published in 1996. There were 42 cases with 4 VTEs, a rate of 9.5%. In a more recent publication comparing open reduction to distal femoral replacement, Hart et al[23] reported on 38 cases with only 1 VTE in the replacement group, an overall incidence of 2.6% for the series. More recent publications do not quote rates of thromboembolic complications, and even in a well-established trauma textbook the chapter on distal femoral fractures does not mention the complication. The true incidence of thromboembolism in these fractures is therefore impossible to estimate with any accuracy.

The literature is therefore not particularly illuminating regarding the exact rates of VTE and PE that can be expected after fractures around the knee. Based on the published literature, it does appear that periarticular knee fractures probably have a rate of symptomatic VTE of less than 5% and the rate of pulmonary embolism, although perhaps underreported is probably less than 1%.

### 2.5. Thromboprophylaxis

Thromboprophylaxis may be either mechanical or chemical. The most popular mechanical methods are use of graduated compression stockings or pneumatic compression devices, often in sequence with pneumatic compression devices being used when the patient is recumbent in the early postoperative period and replacing this method with compression stockings when the patient becomes mobile. The most commonly used method of chemical prophylaxis in modern practice is with LMWH. Many other options are available with newer agents such as fondaparinux, rivoroxaban and similar agents increasing in use and there is accumulating evidence from randomized trials that they are as effective as LMWH in prevention of VTE.[24] These newer agents have the advantage of being administered orally and are therefore more convenient than self-injection of LMWH by outpatients who require extended prophylaxis after discharge. They also have the advantage over older agents such as warfarin of not requiring regular monitoring of the international normalized ratio (INR).

There are no clinical trials which specifically address the thromboprophylaxis after fractures of the distal femur or proximal tibia. However, there are a number of studies that have evaluated methods of prophylaxis after lower limb injuries in general. These were reviewed by Barrera et al[25] in a Cochrane collaboration publication in 2013. They identified a total of 16 randomized studies which included 3005 patients with major trauma. They concluded that using prophylaxis reduced the rate of symptomatic VTE in comparison with no prophylaxis. For recognized methods of VTE prophylaxis, chemical prophylaxis appeared to be superior to mechanical prophylaxis. There was not convincing evidence that LMWH was superior to unfractionated heparin in prevention of PE but it was more effective in the prevention of VTE. There was also evidence that a combination of mechanical and chemical prophylaxis was superior to either method used in isolation. This review concluded that although there was evidence to suggest the rate of symptomatic VTE was reduced, there was no convincing evidence that the incidence of PE was reduced nor was there a decline in mortality. One possible explanation for this latter finding is that mortality and PE are fortunately rare events even with no thromboprophylaxis, and therefore it is not easy to demonstrate significant reductions in incidence even if a given method of prophylaxis is effective in reducing PE. Sagi et al[26] noted this in a review of the literature and concluded that: "it would require a prospective RCT of several hundred thousand patients to show a statistical decrease in fatal embolus of one treatment over another." Considering the relatively uncommon occurrence of fractures around the knee, it is safe to assume large randomized trials that specifically address the issue of the effectiveness of thromoboprophylaxis in these injuries are unlikely to be feasible.

More recent reviews have not added anything substantial to knowledge in this area, mainly because of a dearth of relevant studies. In a National Institute for Health and Clinical Excellence (NICE) report[27] published in 2018 on thromboprophylaxis, the authors reviewed the literature on knee arthroplasty and nonarthroplasty knee surgery and noted that although other types of nonarthroplasty knee surgery were searched for, including osteotomy, fracture surgery, and peri-articular trauma, no suitable studies involving these populations were identified for inclusion. It was necessary therefore to extrapolate from available evidence in the knee arthroplasty surgery literature to make a recommendation for patients undergoing surgery for fractures around the knee. The recommendation in this report for this type of surgery was that surgeons should consider VTE prophylaxis for people undergoing major nonarthroplasty knee surgery (e.g., osteotomy or fracture surgery) whose risk of VTE outweighs their risk of bleeding.

Fixation of the majority of distal femoral fractures and tibial plateau fractures are probably not dissimilar in terms of the magnitude of the surgery to primary knee arthroplasty, although the population demographics will differ. Based on knee arthroplasty surgery, there is evidence to support the following regimen of thrombophylaxis options:

- Aspirin for 14 days; or
- LMWH for 14 days; or
- Rivaroxaban

Any of the above regimens should be combined with foot pumps in the perioperative period and compression stockings when patients commence mobilization.

For the purposes of the current review, the author reviewed a consecutive series of 225 patients who underwent internal fixation of tibial plateau fractures. All patients had prophylaxis with LMWH. There was no routine screening for postoperative VTE which was diagnosed on the basis of clinical signs and Doppler ultrasound imaging. A total of 4 (1.7%) patients were symptomatic and had a VTE confirmed on imaging. There was 1 additional patient who had a nonfatal pulmonary embolism confirmed on a CTPA, an incidence of 0.4%. This could be considered an acceptably low rate of thromboembolic complications following fixation of a significant peri-articular knee fracture, using an accepted modern prophylaxis regimen.

The actual optimum duration of thromboprophylaxis remains a matter of debate and there is not good evidence to support any particular time period. It is the authors' policy to maintain thromboprophylaxis in all patients during the in-patient stay. All

patients should be risk assessed for thromboembolic complications and it would seem wise to use an extended period of thromboprophylaxis in those considered at higher risk in line with risk factors noted above (Table 1). For patients who are maintained on outpatient prophylaxis, it is generally recommended to continue until patients commence weight-bearing, usually at 6 weeks postoperatively, depending on the complexity of the fracture, among other considerations.

### 2.6. Conclusions

There is a lack of published evidence to give specific guidance for selection of the optimum thromboprophylaxis after surgery for fractures around the knee. Older studies suggest the incidence of deep venous thrombosis is high and there is evidence from the general literature that modern methods of prophylaxis reduce the rate of VTE. A combination of mechanical prophylaxis and chemical prophylaxis seems to be most effective in reducing VTE rates. Although convincing evidence of reduction in PE rates is lacking, this probably reflects the relative rarity of this complication. Better evidence to support current practice is needed with larger studies of periarticular fractures around the knee.

## 3. Thromboprophylaxis: foot/ankle fracture

Unlike the situation pertaining to more proximal lower limb fractures, there is now good evidence that thromboprophylaxis is not justified in the management of most foot and ankle injuries. Despite this, the issue remains the focus of some concern, both in routine clinical practice, and at meetings and conferences. This concern is driven by several factors: First, there are rare, catastrophic, fatal VTE events that occur after seemingly innocuous foot and ankle injuries, which are nonetheless well publicized in the journals,[28] and in the media. This contributes to the second driver: the fear of litigation. Third, there remains some confusion and uncertainty in the literature despite good quality recent research. The influential Cochrane collaboration contributed to this uncertainty by reporting very recently that LMWH prophylaxis is effective in reducing VTEs in patients with lower extremity immobilization.[29] However, like many meta-analyses, the quality of evidence from which it draws is low, and on closer inspection, surprisingly heterogeneous. Five RCTs are included in the Cochrane analysis[29] and are from high-quality journals, with large numbers of patients. However, they reached varying conclusions as to whether thromboprophylaxis was effective, possibly because they included heterogeneous groups of patients. Most importantly, however, they all used venography as their primary outcome measure. This, the fourth and possibly most important driver of controversy, is one of the main sources of confusion in the field of VTE research: There is a spectrum of event severity from the surprisingly common sonographically or venographically detected but asymptomatic VTE (up to 40% lower limb injuries), to rare clinically evident VTEs (2%), to the extremely rare fatal pulmonary embolism (0.001%). Of course, the clinical importance of venographically detected VTE is questionable; it seems likely that many or indeed most such events cause no clinical harm and would have resolved spontaneously, undetected, had the patient not been enrolled in a trial. Thus, trials with such surrogate end-points are probably of little direct clinical relevance. Whereas the bulk of the established literature on thromboprophylaxis relies on surrogate outcome measurements, more recent trials have instead focussed on "clinically important VTE" (CIVTE), and these important trials are discussed in greater detail below. The fifth and final driver of controversy is variability in clinical practice: some European centers use thromboprophylaxis routinely in 80% of low-risk cases,[30] while this is uncommon in the United Kingdom and North America.

We have recently reviewed our own data in Edinburgh in order to study the local incidence of CIVTEs and relate them to other postsurgical risks and bleeding risks. We reviewed a consecutive series of 1283 patients with ankle fractures presenting over 2 years. One-third was operatively managed and virtually all were allowed full weight-bearing in an orthosis boot postoperatively. Thromboprophylaxis was used during any in-patient stay only, and discontinued at the time of discharge. We used national statistics to determine whether any patient had suffered a CIVTE at any point between 1981 and 2014: there were 22 events, giving an incidence of 1.7% over the 34-year period. Of these, 6 occurred postoperatively within 90 days of the fracture: an incidence of 0.4%. However, more than half occurred before the ankle fracture, and overall more than two-thirds of events occurred at a time point remote from injury. We concluded that patients have a baseline risk of known and unknown predispositions to thrombosis, and that ankle fractures are just 1 possible precipitant of a CIVTE, with other, unrelated triggers being twice as likely to prompt a VTE as having an ankle fracture.

There are 2 randomized controlled trials that assess the impact of thromboprophylaxis on CITEV: The first was published in 2015 by a group from Toronto[31] who screened 1926 patients with isolated lower extremity fractures. Of these, 1611 were excluded; in half the cases this was because the patients declined to self-administer the injections. This left 265 patients with isolated lower limb fractures. Patients were randomized to either dalteparin 5000 IU daily for 2 weeks, or a placebo injection. Interim analysis demonstrated 2 CIVTEs in the intervention group and 3 in the placebo group, offset by a slightly higher rate of minor bleeding in the heparin group. The overall rate of CIVTE, at 2%, was considerably lower than allowed for by the initial power calculations, and faced with the inability to complete recruitment to the trial, the steering committee opted to halt the study early.

Earlier this year, a group from the Netherlands published a larger study of 1435 injuries of the lower limb treated in cast.[32] Of these, 479 were ankle fractures and 94 were tendo Achilles disruptions. The study group received 2500 iu dalteparin while they were in cast (a duration of 3–7 wks), the control group received a placebo. In the final analysis, there were 10 CIVTEs (1.4%) in the intervention group and 13 (1.8%) in the placebo group, and this was not statistically significantly different. The conclusions that can be drawn from these 2 RCTs are that for the majority of cases, the incidence of CIVTE is low, and prophylaxis is ineffective in reducing these events. In offering thromboprophylaxis to these patients, there is a cost–benefit ratio which is unlikely to be favorable. Given that the possible prophylactic interventions also have their own intrinsic risk (such as hemorrhage and heparin-induced thrombocytopaenia), the risk–benefit ratio is also unlikely to be favorable.

While thromboprophylaxis has been shown to be without efficacy for the generality of isolated lower extremity injuries, there are likely to be patients at elevated risk of VTE for whom the risks of thromboprophylaxis might be justified. While these groups have not been studied in this context, it seems reasonable to adopt a precautionary principle. The most important step is risk assessment, and high-risk groups probably include patients

with a personal or first-degree family history of a prothrombotic condition, a history of malignancy, morbid obesity, or currently taking prothrombotic drugs such as unopposed oestrogens. A group from the Netherlands[33] have proposed a predictive score for use after lower limb surgery, and prospective trial confirmation regarding this score is awaited.

In summary, despite emotive case reports, medicolegal concerns, and research based on surrogate end points of improbable relevance, it is clear that thromboprophylaxis after foot and ankle injuries is without efficacy in most patients. Defining high-risk groups who may be exceptions to this rule, and introducing coherent, evidence-based guidelines into international orthopaedic practice, will be the next challenges.

## 4. Thromboprophylaxis for hip fracture surgery: risk of VTE in patients with a hip fracture

Thromboembolic events (i.e., deep venous thrombosis and pulmonary embolism) are the fourth most common major adverse events in patients undergoing surgical management for hip fracture (following mortality, sepsis, and myocardial infarction).[34]

The American College of Chest Physicians (ACCP) puts hip fracture surgery in the highest risk category for VTE. Without thromboprophylaxis, deep venous thrombosis occurs at a rate of approximately 50%, and fatal pulmonary embolism occurs at a rate of 1.4% to 7.5%.[35] With thromboprophylaxis, the rate of symptomatic VTE can be reduced to 1% to 2%.[36]

Clearly all patients with a hip fracture are at significant risk of VTE, and prophylaxis is indicated in this group of patients to minimize this risk.

### 4.1. Role of early surgical management

Patients with a hip fracture have a high prevalence of VTE preoperatively, approximately 10%.[37] Delayed surgical management is a significant risk factor for VTE. Even with use of preoperative chemoprophylaxis, a delay in surgical intervention more than 48 hours post injury has been shown to increase the prevalence of preoperative VTE to 62%.[38]

### 4.2. Clinical practice guidelines

Clinical practice guidelines (CPGs) have been developed by several national and international groups, with recommendations based on robust statistical review of the extensive evidence base for this clinical problem. Guidelines in most common usage are those developed by the ACCP,[36] the American Academy of Orthopaedic Surgeons (AAOS),[39] the NICE,[40] and the Scottish Intercollegiate Guidelines Network (SIGN).[41] While the recommendations of each organization have many similarities, differences in the methodology that was followed in the development of each organization's guidelines have resulted in some differences. For example, the AAOS guideline does not recognize VTE (symptomatic or asymptomatic) as a surrogate marker for the complications associated with VTE, and the AAOS guideline puts a greater emphasis on the risk of complications resulting from surgical wound bleeding than does the ACCP guideline.[42]

### 4.3. Summary of VTE prophylaxis recommendations

**4.3.1. Acetylsalicylic acid (aspirin).** There is considerable evidence that aspirin is an effective, inexpensive, and safe pharmacologic agent for VTE prophylaxis in patients with a hip fracture.[43] However, since other pharmacologic agents are more effective than aspirin alone as an agent treatment for VTE,[44] the role of aspirin for VTE prophylaxis is controversial. For example, although the current ACCP CPG supports use of aspirin for VTE prophylaxis, the guideline indicates a preference for LMWH over aspirin. CPGs (such as the SIGN guidelines) recommend that if aspirin is used as the pharmacologic agent, it should be used as part of a multimodal approach that includes use of an intermittent pneumatic compression device (IPCD) from the time of patient admission to hospital until the patient no longer has significantly reduced mobility following surgical management.

Recommendations for dosing and length of administration of aspirin have been inconsistent, but recent evidence suggests that a low dose of aspirin (81 mg BID) is not inferior to a higher dose of aspirin (325 mg BID) taken for 4 weeks following surgery.

**4.3.2. IPCDs.** While all CPGs recognize that IPCDs are effective as a prophylaxis for VTE associated with hip fractures, it is recommended that IPCDs be used routinely and in combination with pharmacologic therapy. Use of IPCDs should be implemented immediately after patient presentation to hospital, their use should be closely monitored to ensure the device is properly applied and in-use for as much of the day as possible, and they should remain in use until the patient is discharged from hospital.

**4.3.3. Warfarin.** Warfarin is a recommended as a prophylaxis for VTE in hip fracture surgery by the most recent ACCP guideline. A disadvantage for use of warfarin is the need for monitoring until a stable target INR of 2.5 is achieved, with ongoing monitoring at intervals no longer than every 4 weeks. Warfarin should be continued until 28 to 35 days postsurgery.

Since it may take 2 to 3 days to achieve a stable therapeutic INR after administration of warfarin has started, heparin or a LMWH should be started at the same time until the target INR has been reached. Routine use of warfarin for VTE prophylaxis is not recommended by the NICE and SIGN guidelines due to the many issues associated with its use: its slow onset of action and long half-life (which also precludes preoperative administration) and its interactions with food and other medications.

**4.3.4. LMWH.** Use of LMWH is supported by all CPGs, and many studies favor LMWH over all other pharmacologic agents for VTE prophylaxis. All CPGs recommend LMWH administration begin immediately following patient admission to hospital, stopping 12 hours prior to surgery, and restarting 6 to 12 hours postsurgery. LMWH should be continued until 28 to 35 days postsurgery.

**4.3.5. Fondaparinux.** Use of fondaparinux is supported by all CPGs. However, due to its long half-life and slow onset of action, it is not recommended for use preoperatively. Administration should begin 6 to 8 hours postoperatively, and should be continued until 28 to 35 days postsurgery.

### 4.4. Summary

VTE is a common complication in patients with a hip fracture. Several CPGs have been developed to guide clinical practice for reduction of the risk of VTE. In addition to early surgical management, current standards of care dictate use of pharmacologic prophylaxis for VTE in all patients with hip fracture.

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