Falling in the Netherlands: prevention, care, and follow-up of fall-related injury
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Citation for published version (APA):

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Chapter 4

Prevention of Thrombosis in Traumatology


*Ned Tijdschr Geneeskd. 2007 27 januari; 151(4)*
Abstract

Background
Venous thromboembolism (VTE) is frequent in trauma patients and often runs an asymptomatic course. Prophylaxis in these patients, who often have an increased risk of bleeding, deserves extra attention.

Lower extremity injuries
After injuries to the lower extremities, low molecular weight heparin is advised during the period of immobilization.

Hip fractures
Following hip-fracture surgery, fondaparinux is indicated for 4 weeks.

Polytraumatized a neurotrauma patients
In polytrauma and neurotrauma patients, low molecular weight heparin has shown the best results.

Burns
VTE prophylaxis also seems to be indicated in burn patients.

Conclusion
This article is an ‘Evidence based’ tool for VTE prophylaxis in each trauma patient.
Introduction

The prevalence of Venous thromboembolisms (VTE) such as Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) is high among trauma patients and they often elapse asymptomatic. The prevalence varies between 6 and 60%.

A Californian study of the American National Trauma Data Bank (n = 730,000) has identified nine risk factors for VTE in trauma patients (see Table 1).

Table 1. Risk factors for VTE.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 40 years</td>
<td>2.29</td>
<td>2.07 – 2.55</td>
</tr>
<tr>
<td>Trauma capitis (AIS &gt;2)</td>
<td>2.59</td>
<td>2.31 – 2.90</td>
</tr>
<tr>
<td>Pelvic fracture</td>
<td>2.93</td>
<td>2.01 – 4.27</td>
</tr>
<tr>
<td>Lower extremity fracture (AIS &gt;2)</td>
<td>3.16</td>
<td>2.85 – 3.51</td>
</tr>
<tr>
<td>Spinal cord injury with paralysis</td>
<td>3.39</td>
<td>2.41 – 4.77</td>
</tr>
<tr>
<td>Shock at admission (systolic BP &lt;90 mmHg)</td>
<td>1.95</td>
<td>1.62 – 2.34</td>
</tr>
<tr>
<td>Mechanical ventilation &gt;3 days</td>
<td>10.62</td>
<td>9.32 – 12.11</td>
</tr>
<tr>
<td>Extensive Venous Injury</td>
<td>7.93</td>
<td>5.83 – 10.78</td>
</tr>
<tr>
<td>Large operation</td>
<td>4.32</td>
<td>3.91 – 4.77</td>
</tr>
</tbody>
</table>

Table legend: VTE = Venous Trombo-embolism; AIS: Abbreviated Injury Scale; systolic BP: Systolic Blood Pressure

Both symptomatic and asymptomatic DVT can cause significant morbidity and mortality such as the post-thrombotic syndrome and PE. The post-thrombotic syndrome is a collective term for chronic complaints of edema, spider naevi, varicose veins, and venous ulcers in the lower extremities. It develops in the years after DVT. Prophylaxis of thrombosis can be done with medication (anticoagulants), mechanically, or with a combination of the two. Intrinsic to giving anticoagulants is the increased risk of bleeding. However, the risk for bleeding seems to have decreased considerably in 24 hours after blunt trauma. Prevention of VTE is an important component of the treatment of trauma patients. A strategy for VTE prophylaxis must be considered in each immobilized patient. This article is designed as an Evidence Based tool for developing a strategy for VTE prophylaxis in each individual trauma patient.

Medicinal prophylaxis and gradual compression stockings
Medicinal prophylaxis is the most effective and will therefore be discussed
first. The ‘Golden Standard’ is formed by the Low Molecular Weight Heparins (LMWH). The effect is based on the inactivation of the activated factor Xa. A medicine on the rise is fondaparinux. This is a selective and synthetic inhibitor of the activated factor Xa. LMWH and fondaparinux are administered subcutaneously and act quick. Coumarin derivates (e.g. acenocoumarol) are another method of VTE prophylaxis. They block the recycling system of vitamin K in the liver. This causes a decrease in vitamin K dependent coagulation factors. The advantage is that the coumarin derivates can be administered orally. However, it often takes 8 to 10 days to reach an adequate and stable ‘International Normalized Ratio (INR)’. Furthermore, in many patients an adequate INR is not obtained. A simple and mechanical form of VTE prophylaxis is the gradual compression stocking. Other means are the foot pump and the leg pump (intermitting or sequential pneumatic compression). LMWH are significantly more effective than the foot pump. However, in daily practice the compliance of the pump is low. Reasons for this are the level of discomfort for the patient, strain in the nursing staff, and technical problems. All mechanical methods are more effective in combination with medicinal VTE prophylaxis. The use of a foot pump in the early phase after trauma followed by LMWH in a later stage is also effective. The effectiveness of Vena Cava filters has not been demonstrated unambiguously in studies.

**Indications**

In the following text the different categories of trauma patients are described with the methods for VTE prophylaxis that have the highest ‘Level of Evidence’ (see Table 2). Based on the ‘Level of Evidence’, we give an advice for VTE prophylaxis in each category of trauma patients. Children under 13 years have such a low prevalence of VTE that prophylaxis is not indicated. Children between 13 and 17 years require VTE prophylaxis if they have a significantly increased risk (e.g. a high ‘injury severity score or neurotrauma’).

**Injuries to the lower extremities**

Patients with a lower extremity fracture or Achilles tendon rupture with subsequent immobilization have a VTE risk of up to 40%. In a randomized controlled trial (RCT) with 253 patients, the patients who received prophylaxis with nadroparine had significantly less DVT compared with the patients that did not receive prophylaxis. In an RCT in 339 patients with conservatively treated lower leg injuries the patients that received no prophylaxis had significantly more DVT than the patients that received LMWH (4.3 vs. 0%).
Patients who receive operative treatment followed by a cast or brace also have an increased risk. In an RCT the prevalence of DVT was significantly – however in absolute terms moderately – lower after LMWH compared with no prophylaxis (9 vs. 10%). Based on this RCT the ‘Level of Evidence’ for VTE prophylaxis with LMWH in patients with lower extremity immobilization is two.

Advised: because of their relative immobility, hospitalized patients should receive VTE prophylaxis. In ambulant patients VTE prophylaxis is indicated when one or more large joints are immobilized. The same counts for patients with calcaneal fractures and stable pelvic ring fractures. In patients with conservative treatment with (plaster cast-) immobilization we advise to start with the administration of LMWH immediately after trauma. In operatively treated patients the LMWH can be administered until 10-24 hours before the operation. LMWH can be continued from 12-24 hours after the operation. Prophylaxis is continued during the period of immobilization. The self-administration of subcutaneous injections should not be a problem in ambulatory patients.

**Hip fractures**

Patients with a fracture of the proximal femur have a relatively high risk of developing VTE. This is partly because these patients generally have a higher age and consequently more co-morbidity than younger patients. The medicine with the best results in Orthopedic joint replacement surgery is fondaparinux. In a study of 1250 patients, the group that received fondaparinux had significantly less VTE than the group that received enoxaparine (LMWH) (8.3 vs. 19.1%). Another study with 656 patients revealed that the prevalence of VTE can be decreased to 1.4% if fondaparinux in continued between 25 to 31 days after the operation. The prevalence of VTE in the group of patients that received placebo in this study was 35%. The Level of Evidence for fondaparinux in patients with a hip fracture is 1. In a study where postoperative prophylaxis with vitamin K antagonists (n=65) was compared with placebo (n=63) were the vitamin K antagonists more effective. However, in a meta-analysis the vitamin K antagonists were less effective than LMWH after large Orthopedic operations. The Level of Evidence for vitamin K antagonists following hip fracture surgery is two.

Advised: fondaparinux is the medicine of choice for VTE prophylaxis in
patients with a hip fracture. The administration is started between 6-8 hours after the operation and continued for four weeks. If the operation is postponed LMWH can be given from admission until 10-24 hours before the operation.\textsuperscript{23} LMWH have a shorter half-life than fondaparinux. Therefore, they are more suitable for preoperative VTE prophylaxis.\textsuperscript{24} Patients that were using vitamin K antagonists before the fracture should stop this at least three days before the operation. In case the patient uses fenprocoumon (which has a longer half-life) this period is 5 to 7 days. Because these patients use the vitamin K antagonists for a reason, a longer stopping period is generally not desired. Postoperative continuation of the vitamin K antagonists (instead of fondaparinux) can be considered in these patients.

\textbf{Polytraumatized patients}

In polytraumatized patients the prevalence of VTE can be up to 60\%.\textsuperscript{25} There have been few randomized studies of VTE prophylaxis in this group of trauma patients. In a study in 265 patients with an Injury Severity Score of 8 or more, LMWH were more effective than unfractionated heparin (31 versus 44\%).\textsuperscript{26} In a study in 118 patients with blunt force trauma, LMWH proved to be a safe method of VTE prophylaxis. The prevalence of VTE in this study was 2\% (measured with Duplex).\textsuperscript{1} In a prospective cohort study for LMWH in pelvic-and acetabulum fractures the prevalence of VTE was significantly lower in patients who started within 24 hours after trauma (or shortly after they were hemodynamically stable) compared with patients who started later.\textsuperscript{27} In a retrospective study in 188 patients, those patients who got the LMWH within 48 hours after blunt splenic injury did not have more bleedings than patients who started after 48 hours.\textsuperscript{28} The ‘Level of Evidence’ for LMWH is 2.\textsuperscript{26-28} From a ‘Evidence’ point of view the gradual compression stockings are the best form of mechanical VTE prophylaxis.\textsuperscript{29} This is partly because the compliance of the pneumatic compression devices is low.\textsuperscript{8} The ‘Level of Evidence’ for the stockings is 2.\textsuperscript{29} The main problem in Vena Cava filters concerns the long-term risks. In a follow-up study of 30 patients with a Vena Cava filter, 47\% of the patients turns out to have DVT.\textsuperscript{30} In a study in 163 patients with removable filters, removal was attempted in only 23\% of the filters (which was successful in 84\% of these patients).\textsuperscript{11}

\textit{Advise:} we advise to use mechanical VTE prophylaxis in trauma patients with an absolute contra-indication for medicinal prophylaxis. Because the risk for bleeding is significantly reduced at 24 hours after trauma, LMWH could
be started at that time (after consulting a trauma surgeon). Prophylaxis is advised during the period of immobilization (at least during the period of hospitalization). In elective operations, LMWH can be administered until 19-24 hours before the operation and from 12-24 hours after the operation.

**Neurotrauma**
The prevalence of VTE in patients with neurotrauma is high. Probably because people fear for (intracranial) bleeding few articles describe the value of medicinal VTE prophylaxis in these patients. The safety of LMWH following traumatic intracranial bleeding has been assessed in a study in 150 patients who were administered LMWH 24 hours after trauma or craniotomy. The bleeding increased (according to the CT images) in 34 patients. In 28 of these patients this happened before the administration and in 6 patients after the administration of LMWH. Using Duplex, DVT was found in only 2% of these patients. They concluded that LMWH are safe in patients with neurotrauma. In another study in 344 patients with trauma capitis, LMWH was administered 25 hours after trauma (unless there were contra-indications). None of the patients was clinically suspected to have DVT. An increase of the intracranial bleeding was observed in 3%V of the patients. In an RCT with 120 patients with neurotrauma, the LMWH did not cause less DVT than pneumatic compression (5 and 7% respectively). The American College of Chest Physicians concluded in their Consensus Conference on Antithrombotic and Thrombolytic Therapy that the pooled rate of intracranial bleeding is 2.1% following LMWH and 1.1% following mechanical prophylaxis and no prophylaxis. In addition, the combination of gradual compression stockings and LMWH is more effective than the application of the stockings alone. The ‘Level of Evidence’ for LMWH and mechanical prophylaxis is two.

**Advise:** the pneumatic compression can be used in patients with neurotrauma during the operation. However, the exact value is unknown. LMWH can be of value and safe when started 24 hours after trauma or craniotomy. In case of contra indications for medicinal prophylaxis mechanical prophylaxis can be used. The prophylaxis is continued during the period of immobilization (at least during the period of hospitalization).
The prevalence of VTE in patients with burns can reach 23%. Factors that are related to an increased risk in these patients are a high age, large burnt body surface area, and obesity. In addition, immobility, surgical interventions and systemic hypercoagulopathy play an important role. A survey in 71 Burn Centers in the United States revealed that 76% routinely administered VTE prophylaxis. There are little studies with reliable screening methods or large numbers of patients. We did not find an RCT on the effect...
of VTE prophylaxis in burn patients. In a retrospective analysis of 4102 burn patients who were administered prophylactic heparin, 0.25% had DVT and 0.05 had PE. These were clinical diagnoses. The ‘Level of Evidence’ for VTE prophylaxis in burn patients is three.

Advise: there is no evidence for the effectiveness of VTE prophylaxis in burn patients. Based on the evidence in other trauma patients, VTE prophylaxis in these patients should be considered.
Discussion

The prevalence of VTE is a subject that has international interest. The morbidity and mortality that can be caused by (a)symptomatic thrombosis are widely recognized. The same counts for the need for VTE prophylaxis. The categories of trauma patients differ markedly in the number of well designed studies that are available. The category of patients with a hip fracture, where the prevalence of VTE is relatively high, has been studied most extensively. These are also the only patients in which fondaparinux has been tested. The effect of medicinal prophylaxis and the danger of bleeding in polytraumatized and neurotrauma patients has not been studied well. These are the patients where the highest risk of bleeding goes hand in hand with the highest risk of VTE. However, the risk of bleeding complications seems to be low. Little is known about the effectiveness and safety of VTE prophylaxis in burn patients. The advises are largely conform the guideline ‘Deep venous thrombosis and pulmonary embolism’ [1999] of the Dutch Institute for Healthcare Improvement (CBO).\(^{38}\) The advises are summarized in Figure 1.

Conclusion

VTE prophylaxis is indicated in most trauma patients. There is a trend towards a broader use in polytraumatized and neurotrauma patients.
References


