

DVT PROPHYLAXIS - 1

Goals

Illuminate the need for Greater Prophylaxis in High Risk Patients

Educate regarding New Agents

Present Evidence for Current Therapy

Risk Stratify:

Table 3. Risk Factors:

- advanced age, malignancy, previous venous thromboembolism, obesity, heart failure, paralysis, or the presence of an inhibitor deficiency state (i.e Factor V Leiden).

[Return to article](#)

Table 3. Risk Factors for VTE

Surgery
Trauma (major or lower extremity)
Immobility, paresis
Malignancy
Cancer therapy (hormonal, chemotherapy, or radiotherapy)
Previous VTE
Increasing age
Pregnancy and the postpartum period
Estrogen-containing oral contraception or hormone replacement therapy
Selective estrogen receptor modulators
Acute medical illness
Heart or respiratory failure
Inflammatory bowel disease
Nephrotic syndrome
Myeloproliferative disorders
Paroxysmal nocturnal hemoglobinuria
Obesity
Smoking
Varicose veins
Central venous catheterization
Inherited or acquired thrombophilia

Table 5. Levels of Thromboembolism Risk in Surgical Patients Without Prophylaxis

- The high risk associated with orthopedic, inflation of a thigh, intimal injury may result from positioning of the extremity, and compression of the femoral vein may occur due to flexion and adduction of the hip during surgery on this joint.

[Return to article](#)

Table 5. Levels of Thromboembolism Risk in Surgical Patients Without Prophylaxis*

Level of Risk	DVT, %		PE, %		Successful Prevention Strategies
	Calf	Proximal	Clinical	Fatal	
Low risk Minor surgery in patients < 40 yr with no additional risk factors	2	0.4	0.2	< 0.01	No specific prophylaxis; early and "aggressive" mobilization
Moderate risk Minor surgery in patients with additional risk factors Surgery in patients aged 40–60 yr with no additional risk factors	10–20	2–4	1–2	0.1–0.4	LDUH (q12h), LMWH (\leq 3,400 U daily), GCS, or IPC
High risk Surgery in patients > 60 yr, or age 40–60 with additional risk factors (prior VTE, cancer, molecular hypercoagulability)	20–40	4–8	2–4	0.4–1.0	LDUH (q8h), LMWH (> 3,400 U daily), or IPC
Highest risk Surgery in patients with multiple risk factors (age > 40 yr, cancer, prior VTE) Hip or knee arthroplasty, HFS Major trauma; SCI	40–80	10–20	4–10	0.2–5	LMWH (> 3,400 U daily), fondaparinux, oral VKAs (INR, 2–3), or IPC/GCS + LDUH/LMWH

Primary Prophylaxis: Options

1. Low dose heparin

- Lancet 1975 16 patients in the control group and 2 in the heparin group were found at necropsy to have died due to acute massive pulmonary embolism (P smaller than 0-005). The frequency of isotopic D.V.T. was reduced from 24-6% in the control group 7-7% in the heparin group (P smaller 0-005). In 30 patients D.V.T. was detected at necropsy; 24 in the control and 6 in the heparin group (P smaller 0-005). 32 patients in the control group and 11 in the heparin group developed clinically diagnosed D.V.T. which was confirmed by venography (P smaller than 0-005)

2. Adjusted dose unfractionated heparin – difficult, not used

3. Low molecular weight heparin –

- Lower incidence of thrombocytopenia than with unfractionated heparin (NEJM 1995) 9 of 332 patients (2.7 percent) receiving unfractionated heparin compared to none of 333 receiving low molecular weight heparin.
- BJS 1991 - Positive FUTs (UH = 4.2 per cent, Logiparin 2500 units daily = 7.9 per cent, Logiparin 3500 units daily = 3.7 per cent) and positive angiograms (UH = 3.0 per cent, Logiparin 2500 units daily = 5.6 per cent, Logiparin 3500 units daily = 2.3 per cent) were significantly more common in the Logiparin 2500 units daily group than in the UH and Logiparin 3500 units daily groups. The rates of major complications (severe haemorrhage, death, pulmonary embolism, reintervention) were similar in the three groups.
- Lancet 1992 - For all surgical studies the relative risk (LMWH versus standard heparin) for deep vein thrombosis was 0.74 (95% CI 0.65-0.86), for pulmonary embolism 0.43 (95% CI 0.26-0.72), and for major bleeding 0.98 (95% CI 0.69-1.40). When the analysis for the general surgery studies was limited to those of strong methodology, assessed by eight criteria defined in advance, the benefit/risk ratio was less favourable--relative risk for deep vein thrombosis 0.91 (95% CI 0.68-1.23), for major bleeding 1.32 (95% CI 0.69-2.56).
- Lancet 1993 - Severe bleeding was less frequent in the LMWH group (1.0% vs 1.9%; p = 0.02), as was wound haematoma (1.4% vs 2.7%; p = 0.007). No significant differences were found in the efficacy of the two agents. Perioperative death rates were 3.3% in the LMWH group and 2.5% in the SH group; pulmonary emboli were detected in 0.7% and 0.7%; and deep-vein thrombosis was diagnosed in 0.6% of patients in each group.
- Arch Int Med 2001 - LMWH started immediately before or early after surgery in patients undergoing total hip replacement resulted in significantly lower rates of both total and proximal DVT when compared with warfarin.

4. Oral anticoagulants (International Normalized Ratio [INR] of 2.0 to 3.0) -

- There have been four randomized clinical trials comparing LMWH with oral anticoagulants in patients undergoing total knee replacement. When the data are pooled the total DVT rates with oral anticoagulants were 45.2 versus 33.2 percent with LMWH

5. Intermittent pneumatic compression (IPC) -

- Pneumatic compression also reduces plasminogen activator inhibitor-1 (PAI-1) levels via an unknown mechanism and consequently increases endogenous fibrinolytic activity

6. Compression Stockings -

- They reduce the incidence of postoperative venous thrombosis only in low risk general surgical patients and in selected moderate risk patients (eg, neurosurgical). It is unclear whether the use of graduated compression stockings in combination with other forms of prophylaxis results in any further risk reduction

7. ASA – Not recommended

8. New Agents

A. Fondaparinux (Arixtra): The synthetic heparin pentasaccharide fondaparinux (Arixtra, Org31540/SR90107A) catalyzes factor Xa inactivation by AT III without inhibiting thrombin. Approved for hip fracture, hip replacement, or knee replacement. \$44 per day.

- The efficacy of fondaparinux has been demonstrated in patients undergoing major orthopedic surgery in whom there was an overall 50 to 60 percent reduction in risk of venous thromboembolic disease when compared to low molecular weight heparin. In a separate study, use of fondaparinux for one month, rather than one week, reduced the incidence of documented VTE from 35 to 1.4 percent.

B. Ximelagatran (Exanta): Antithrombin Agent. Better than Lovenox when used preop, not as good when used post op. higher bleeding rates.

- Thromb Haemos 2003 - The main safety endpoint was bleeding. Venous thromboembolism occurred in 355/1146 (31.0%) and 306/1122 (27.3%) patients in the ximelagatran and enoxaparin group, respectively, a difference in risk of 3.7% in favour of enoxaparin (p = 0.053). Bleeding was comparable between the two groups.
- At bilateral venography, deep vein thrombosis was found in 20.5% (16/78) of patients who had received s.c. melagatran and oral ximelagatran and in 18.5% (5/27) of patients in the dalteparin group.
- The frequency of VTE was significantly lower with the highest dose of melagatran/ximelagatran than with dalteparin (15.1% vs 28.2%, p<0.0001). There were no reoperations due to bleeding and no critical organ bleeding. Excessive surgical bleeding was uncommon but more frequent in the highest dose group.

C. Hirudin: Antithrombin agent. Not approved in US for DVT prophylaxis, only HIT. Better for DVT prophylaxis and prevention, but high bleeding risk in studies for coronary disease.

- After an 8 to 12 day study period, venography was performed. The recombinant hirudin group had a significantly lower rate of lower extremity deep venous thrombosis (18.4 versus 25.5 percent) and proximal deep venous thrombosis (4.5 versus 7.5 percent). The superior results with hirudin could be due to a more efficient mode of action of this agent or to the timing of the first dose (within 30 minutes or two hours before surgery). No difference in bleeding complications between the two treatment groups was observed.

Highest Risk – Practical – Hip Fracture, Total Hip, Total Knee, Cancer patients, Acute Spinal Cord injury, Multiple Trauma

Major trauma

- NEJM 1996 - Sixty patients given heparin (44 percent) and 40 patients given enoxaparin (31 percent) had deep-vein thrombosis (P=0.014). The rates of proximal-vein thrombosis were 15 percent and 6 percent, respectively (P=0.012). Only six patients (1.7 percent) had major bleeding (one in the heparin group and five in the enoxaparin group, P=0.12).

Cancer Patients

- In a survey of clinical trials of thromboprophylaxis in surgical patients with cancer, the average incidence of DVT in untreated patients was 29 percent, placing them in the "high risk" category.
- ENOXACAN I - The frequency was 18.2 per cent in the heparin group and 14.7 per cent in the enoxaparin group (95 per cent confidence interval of the difference -9.2-2.3 per cent).
- ENOXACAN II - The rates of venous thromboembolism at the end of the double-blind phase were 12.0 percent in the placebo group and 4.8 percent in the enoxaparin group (P=0.02). This difference persisted at three months (13.8 percent vs. 5.5 percent, P=0.01).

Sean Fitzsimmons, M.D.
December 16, 2004