DVT Prophylaxis in Hospitalised Patients – Current Concepts

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Introduction

- 51% of 15 million medical patients discharged from hospital in the US estimated to be at risk for VTE(DVT and/or PE)
- Pulmonary embolism (PE)commonest preventable cause of hospital death
- Accounts for about 150,000 to 200,000 deaths/year in the United States
- Prevention of VTE is the number one strategy to improve patient safety in hospitals according to the Agency for Health Care Research and Quality
- In the absence of appropriate prophylaxis, the incidence of venous thromboembolic disease (ie,PE and DVT)in hospital patients is 10 to 80%

Am J Hematol 2007; 82:777

Obstet Gynecol 2006; 107:666

- Various randomized trials showed that appropriate thromboprophylaxis has a desirable benefit-to-risk ratio and is cost effective
- Evidence-based guidelines for effective and safe prophylactic measures are now available for most high risk patients for the prevention of VTE
- But appropriate thromboprophylaxis is not being offered to numbers of patients, particularly those hospitalized with medical conditions
- Fear of bleeding with prophylactic anticoagulation is compounded by lack of prospectively validated models for bleeding risk in medical patients

J Clin Oncol 2007; 25:5490

J Thromb Haemost 2011; 9:1340

ENDORSE STUDY

- Multinational cross-sectional study in 68,183 pts.at 358 hosp.in 32 countries
- To assess prevalence of VTE(DVT+PE) risk in acute hospital care setting, and to determine proportion of at-risk patients who receive effective prophylaxis
- Of the surgical patients at risk, 58.5% received ACCP-recommended VTE prophylaxis, compared with 39.5% at-risk medical patients
- India,from 10 hospitals,53.6% of hospitalised patients(61.3% surgical and 44.7% medical) were at risk for VTE
- But only 16.3% surgical and 19.1% medical at risk patients received ACCP-recommended thromboprophylaxis
- So there is a low rate of appropriate prophylaxis all over the world

Lancet 2008 Feb 2;371(9610):387-94
Indian J Med Res 136,July 2012,pp 60-67

Risk Factors For DVT

Pregnancy:

- Highest incidence seen in the post partum period, particularly in those undergoing caesarean delivery
- Risk of VTE in low risk pregnant women after 20 weeks is quite low (<1/3000) and approaches the background risk in nonpregnant women
- Anticoagulation of pregnant women placed at bed rest and routine antenatal prophylaxis for the pregnant medical patient is not recommended routinely
- But, presence of single or multiple thrombophilic defects (eg, marked obesity, prior episode of VTE) markedly increases risk of VTE

Risk Factors For DVT..

Hospitalization :

- There is a high risk of developing DVT while hospitalized
- Incidence of DVT increased with age and,except women <40 years of age, it was higher in hospitalized men than in women
- Half of community-based cases occurred in patients who developed DVT while residing in a nursing home or within 90 days of hospital discharge
- 60% DVT occurred in hospitalized/recently discharged/nursing home pts
- Autopsies demonstrate that death from unexpected PE remains common and the majority of these occur in hospitalized medical patients esp ICU

DVT risk assessment

- No **formal**, prospectively-validated risk for anticoagulation in medical pts.
- Classified as being at low, moderate, or high risk
- Conditions predisposing for DVT include

  - congestive failure,
  -acute exacerbations of chronic pulmonary disease,
  - stroke with lower limb paralysis, sepsis,
  - inflammatory bowel disease
  - thrombophilia
  -prolonged immobility
  -age >60 years
  -presence of cancer
  - previous VTE
  -admission to an intensive care unit

BMJ 2010; 340:c95
Chest 2011; 140:706

Risk Scores

- Two empirically generated risk models, based upon a number of the above-noted risk factors have been proposed:
- 1) The **Padua Prediction Score**
- 2) The **IMPROVE risk score**
- These prediction scores require confirmation from independent,prospective studies before they are used,but the following conclusions can be reached:
- VTE prophylaxis is reasonable for medical patients older than age 40 who have limited mobility for ≥3 days,& have at least one thrombotic risk factor
- All patients admitted to intensive care units are considered high risk for VTE, even after routine prophylactic anticoagulation

N Engl J Med 2007; 356:1438

Crit Care 2010; 14:R41

The **Padua Prediction Score** was used to determine DVT risk in 1180 consecutive medical patients

- Patients were followed for up to 90 days following admission to assess the occurrence of symptomatic DVT,pc of subjects developing VTE were:
- “Low risk” patients (711): 0.3 percent
- “High risk” patients receiving adequate in-hospital thromboprophylaxis (186): 2.2 percent
- “High risk” patients not receiving adequate in-hospital thromboprophylaxis (283): 11.0 percent

J Thromb Haemost 2010; 8:2450

- The **IMPROVE risk score** was used to determine DVT risk in 15,156 medical patients taken from the observational International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) study
- The observed rate of DVT within 92 days of admission was 0.4 to 0.5 percent if none of these risk factors was present, and was in the range of 8 to 11 percent in those with the highest risk scores.

Chest 2011; 140:706

PREVENTION OF DVT

Two approaches to the prevention of fatal DVT:

- Primary prophylaxis — using drugs or physical methods for preventing DVT
- Secondary prevention — early detection and treatment of subclinical cases by screening with objective tests sensitive for the presence of DVT
- No single screening method (eg, contrast venography, ultrasonography, MRI venography) has universal acceptance for secondary prevention
- Primary is preferred-cost effective than treatment of complications
- Secondary prevention-primary prophylaxis is contraindicated or ineffective

J Thromb Haemost 2007; 5:1431

Primary prophylaxis

The characteristics of an ideal primary prophylactic method include ease of administration, effectiveness, safety (particularly with respect to bleeding), and cost-effectiveness or at least cost-neutrality when compared with current standards

- The prophylactic measures currently available hospitalized medical pts.:
  - -low dose unfractionated heparin
  - -low molecular weight (LMW) heparins,fondaparinux
  - -intermittent pneumatic compression (IPC) and/or graduated compression stockings (GCS)
  - - oral factor Xa or factor IIa (thrombin) inhibitors

Chest 2008; 133:381S

Values and preferences

- Values and preferences concept was introduced in 2004 ACCP Guidelines
- In pulmonary embolism (PE),greater value placed on prevention of death from recurrent PE than from relatively low risk of bleeding from anticoagulation
- In orthopedic surgery,greater value placed on avoidance of bleeding from anticoagulation over lower risk of death from PE if DVT prophylaxis is not used
- **Definition of major bleeding** —Classification approved by the International Society for Thrombosis and Hemostasis

  -Fatal bleeding, and/or

  -Symptomatic bleeding in a critical area or organ, and/or

  -Bleeding causing a fall in hemoglobin of ≥2 g/dL or leading to transfusion of two or more units of whole blood or red cells

J Thromb Haemost 2005; 3:692

Bleeding risk assessment

No prospectively validated models ,difficult to assess risks-benefits of prophy.anticoag.

- Retrospective data from IMPROVE for risk factors at time of admission include:

  -Cumulative incidence of major & non-major in-hospital bleeding within 14 days of admission(3.2 percent)

  - Active gastroduodenal ulcer (OR 4.15; 95% CI 2.21-7.77)

  -Bleeding within the 3 months prior to admission (OR 3.64; 95% CI 2.21-5.99)

  -Platelet count <50,000/microL (OR 3.37; 95% CI 1.84-6.18) were the strongest independent risk factors for bleeding at the time of admission.

  -Increased age,

  -Hepatic and/or renal failure

  -Intensive care unit stay

  -Presence of a central venous catheter

  -Rheumatic disease

  -Cancer

  -Male sex.

Chest 2011; 139:69

- Each of the above risk factors, with appropriate weighting, was entered into a risk model (IMPROVE Bleeding risk model) with scores ranging from 0 to 15
- As examples, those with risk scores of 1, 4, 7, 10, and 15 had observed rates of clinically important bleeding of 0.5, 1.6, 4.1, 9.7, and 14.0 percent, respectively
- If this model is validated in other patient populations, it may assist clinicians in determining whether to offer prophylactic anticoagulation to a patient at risk for VTE

DVT prevention in medical patients

- In hospitalized & immobilized medical pts., unfractionated heparin (UFH), low molecular weight heparin (LMW heparin) & fondaparinux have all shown superiority over placebo in preventing DVT
- In a meta-analysis of 36 randomized trials comparing ability of various pharmacological agents to prevent DVT,following observations are made :
- Compared with placebo, UFH associated with a reduced risk of DVT (RR 0.33; 95% CI 0.26-0.42) and PE (RR 0.64; 95% CI 0.50-0.82), as was LMW heparin (RR 0.56; 95% CI 0.45-0.70 & RR 0.37; 95% CI 0.21-0.64, resp.)
- UFH in a dose of 5000 U TDS (RR 0.27; 95% CI 0.20-0.36) more effective in preventing DVT than UFH in a dose of 5000 U BID (RR 0.52; 95% CI 0.28-0.96)

Arch Intern Med 2007; 167:1476

- Directly compared with UFH, LMW heparin was associated with a significantly lower risk of DVT (RR 0.68; 95% CI 0.52-0.88) and injection site hematoma (RR 0.47; 95% C, 0.36-0.62)
- But no difference was seen between the two agents in the risk of bleeding or thrombocytopenia
- Both UFH and LMW heparin reduced venous thromboembolic risk in hospitalized medical patients, but neither agent altered mortality
- When directly compared, LMW heparin was more effective in preventing DVT than was UFH

J Thromb Haemost 2011; 9:464

- In patients suffering ischemic stroke with leg paralysis, LMW heparin was either superior or non-inferior to UFH in the prevention of VTE
- A meta-analysis of 3 studies indicated that use of LMW heparin, when compared with UFH, was associated with a significantly greater risk reduction for any DVT (OR 0.54; 95% CI 0.41-0.70), with no significant increase in clinically relevant bleeding
- A decision analytic model compared the prophylactic use of LMW heparin in critically ill patients to weekly compression ultrasound screening for DVT, and concluded that such prophylactic anticoagulation provided better value in terms of costs and health care gains

Lancet 2007; 369:1347
Am J Respir Crit Care Med 2011

Extended duration prophylaxis

- Extended prophylactic anticoagulation (eg, 4 wks)significantly reduce DVT compared with standard regimen (eg, 1 week) in high-risk surgical pts.
- Two studies assessed efficacy and safety of extended duration prophylactic anticoagulation in acutely ill medical patients
- Randomly assigned to enoxaparin(40 mg/day sc) or placebo for 28 days after receiving enoxaparin for an initial 10 days (the EXCLAIM Study)
- Results included :
- Extended-duration enoxaparin reduced incidence of DVT compared with placebo (2.5 vs 4.0%),but increased major bleeding events (0.8 vs 0.3%)
- Sub-group analysis--extended-duration enoxaparin benefits restricted to women, subjects >75 yrs of age, and those with recently reduced mobility (ie, bed rest or sedentary without bathroom privileges)

Ann Intern Med 2010; 153:8

Extended duration prophylaxis ..

- In ANCIANOS study, a prospective, observational, multicenter cohort study of effectiveness and safety of extended use of LMW heparin bemiparin
- 507 non-surgical elderly medical patients (mean age 82 years) bedridden for at least four days due to acute medical illness,benefits are seen
- Patients considered to be at moderate or high risk for DVT were treated with 2500 or 3500 IU/day, respectively, for a mean of 33 days
- Results included :
- The incidence of DVT was 0.6 percent; no cases of PE were seen
- There were two major (0.4 percent) and eight minor (1.6 percent) bleeding events. No deaths were attributable to the study medication

Clin Drug Investig 2010; 30:337

PHARMACOLOGIC AGENTS FOR DVT PREVENTION

- **Heparins** —
- In a meta-analysis of trials determining the effectiveness and safety of UFH or LMWH vs either placebo or no treatment for the prevention of DVT in general medical patients, the following observations were made :
- Reduction in DVT by 60 %(RR 0.40; 95% CI 0.31-0.53) and PE by 42% (RR 0.58; 95% CI 0.43-0.80) with heparins vs placebo/no treatment
- Heparins resulted in increase in hemorrhage--major (RR 2.18; 95% CI 1.28-3.72) and minor (RR 1.74; 95% CI 1.26-2.41) vs placebo or no treatment

Cochrane Database Syst Rev 2009; :CD003747

Low dose unfractionated heparin

- In a meta-analysis of 12 RCTs of UFH given BID or TID for prevention of DVT in medical patients, the following findings noted :
- No difference in the overall rate of DVT between BID (5.4/1000 patient-days) and TID (3.5/1000 patient-days) UFH heparin dosing
- TID heparin showed a trend toward a decrease in PE (BID 1.5/1000 patient-days, TID 0.5/100 patient-days) and in proximal DVT plus PE (BID 2.3/1000 patient-days, TID 0.9/1000 patient-days).
- Major bleeding was significantly greater with TID than with BID UFH dosing (BID 0.35/1000 patient-days, TID 0.96/1000 patient-days)

Chest 2007; 131:507

- But, a second meta-analysis of 16 studies found no difference between BID and TID UFH dosing in the RR for DVT, PE, death, or major bleeding
- Low dose UFH advantage--relatively inexpensive,low side effect profile, easily administered, and anticoagulant monitoring is not required
- But,platelet be monitored regularly in all patients receiving low dose UFH to detect the development of heparin-induced thrombocytopenia

Chest 2011; 140:374

- **Low molecular weight heparin** —
- A number of low molecular weight heparin (LMWH) preparations are available.
- These drugs have the advantage that they can be given subcutaneously once or twice daily at a constant dose without laboratory monitoring
- In addition, there is a lower incidence of heparin-induced thrombocytopenia than with UFH

Unfractionated vs LMW heparin

- In two meta-analyses of RCTs comparing UFH versus LMW heparin for prevention of DVT in medical pts., no difference seen in efficacy
- But, earlier meta-analysis found 72 % risk reduction in major bleeding when LMWH compared with UFH (RR 0.28; 95% CI 0.10-0.78), although the 95 percent confidence limits for these comparisons were quite wide
- So in hospitalized medical pts. & pts. with ischemic stroke and leg paralysis, LMW heparin is considered the prophylactic agent of choice for preventing DVT in high risk medical patients

Chest 2011; 140:374

Chest 2008; 133:149

Fondaparinux

- Fondaparinux is synthetic,highly sulfated pentasaccharide,with a sequence derived from the minimal antithrombin (AT) binding region of heparin
- Using end point of asymptomatic/symptomatic DVT & non-fatal/fatal PE , fondaparinux compared with placebo for 6-14 days in 644 medical pts.
- DVT detected in 5.6% of pts. treated with fondaparinux vs 10.5% of pts. with placebo, for a relative risk reduction of 47% (95% Cl 7.7-69)
- Fondaparinux in recommended doses has shown less efficacy than enoxaparin 30 mg BD, the enoxaparin regimen used in North America
- Fondaparinux in recommended doses appears to have the same efficacy as enoxaparin 40 mg once daily, the enoxaparin regimen favored in Europe

BMJ 2006; 332:325

Aspirin

- Aspirin, with/without other antiplatelets (eg, clopidogrel),effective in reducing major **arterial** thrombotic events in pts at risk/atherosclerotic ds
- Little evidence that aspirin and/or clopidogrel has a significant effect on the prevention of **venous** thromboembolic events in medical patients
- A meta-analysis and literature review indicated that aspirin reduced the incidence of DVT by 20% compared with placebo or no treatment
- However, other studies have shown either no significant benefit or inferiority when compared with other modalities such as LMW heparin
- So, the ACCP Guidelines recommend against the use of aspirin alone as thromboprophylaxis against DVT for any medical or surgical patient group

Br J Haematol 2009;146: 142

Warfarin

- Warfarin(VKA) is not an appropriate agent for immediate and short-term prevention of VTE in medical patients for the two following reasons:
- The use of warfarin can be associated with a transient hypercoagulable state in first 36 hours after administration, due to a warfarin-induced rapid decline in protein C levels.
- The ultimate anticoagulant effect of warfarin is delayed, and does not occur until 36 to 72 hours after drug administration.

MECHANICAL METHODS OF THROMBOPROPHYLAXIS

- Mechanical methods for the prevention of VTE are primarily indicated in patients at high risk of bleeding
- They are also used in patients because of the presence of a bleeding lesion such as peptic ulcer or intracranial hemorrhage.
- When used in all of these circumstances, it is recommended that consideration be given to the use of a pharmacologic agent such as LMW heparin as soon as the bleeding risk becomes acceptably low or when the bleeding lesion or bleeding risk has been reversed

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Intermittent pneumatic compression (IPC)

- IPC prevents DVT by enhancing blood flow in deep veins of legs, thereby preventing venous stasis
- It reduces plasminogen activator inhibitor-1 (PAI-1), thereby increasing endogenous fibrinolytic activity
- It is free of important side effects and offers an alternative for VTE prevention in patients with a high risk of bleeding should anticoagulants be employed
- It is contraindicated in patients with evidence of leg ischemia due to peripheral vascular disease
- Concern that patients at bed rest or immobilized ≥72 hours without any prophylaxis may be at risk of dislodging recently formed DVT following the use of IPC.

Intermittent pneumatic compression (IPC)..

- The ACCP guidelines and a 2010 literature review, the uses of IPC, graduated compression stockings (GCS), and the venous foot pump (VFP) were analysed
- The best evidence for efficacy was with IPC devices
- But attention must be paid to optimal patient compliance as well as insuring proper fit and duration of compression
- IPC started as soon as possible & continued with few interruptions until discharge
- While a meta-analysis showed that IPC is effective in preventing DVT, combination of IPC with a pharmacologic agent was superior in reducing incidence of DVT

Cochrane Database Syst Rev 2008; :CD005258

Graduated compression stockings

- Less convincing evidence regarding the efficacy of graduated compression stockings (GCS) and venous foot pump (VFP) in randomized clinical trials
- In a meta-analysis, GCS was found to be ineffective in the prevention of DVT in patients with ischemic stroke
- Though use of GCS is recommended,alone or with IPC , there is little evidence supporting the efficacy of GCS
- Even for thigh-length GCS, one randomized trial was associated with no benefit and a fourfold increase in skin ulcers and necrosis

Lancet 2009; 373:1958

Venous foot pump

- Few data providing convincing evidence for efficacy of VFP devices.
- Accordingly, where mechanical prophylaxis is recommended, the choice should be IPC, with or without the additional use of GCS, rather than GCS or VFP devices alone

Renal impairment

- Careful attention should be paid to renal function throughout the use of most anticoagulants
- Patients receiving LMW heparin,fondaparinux, or any antithrombotic agents primarily cleared by the kidneys, elderly patients, and those with diabetes mellitus or at high risk of bleeding require special attention
- This may require a decrease in the usual dose of the drug or use of an alternative form of thromboprophylaxis

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Medical center policies

- Every hospital should develop a formal active strategy for the prevention of VTE
- This should be in the form of a written institution-wide thromboprophylaxis policy endorsed by department heads and medical advisory boards
- Strategies should be developed to increase compliance with thromboprophylaxis recommendations, including the use of computerized order sets and prompts, pre-printed orders, and periodic audit, including follow-up with feedback

Thromb Haemost 2010; 103:312

Assignment of risk group

- No prospectively validated risk assessment model for medical patients
- Common conditions predisposing for DVT include congestive failure, acute exacerbations of chronic pulmonary disease, stroke with paralysis, sepsis, inflammatory bowel disease, a high degree of immobility, age >75 years, and the presence of cancer or a previous episode of DVT
- DVT prophylaxis is considered reasonable for medical patients older than age 40 who have limited mobility for ≥3 days, and have at least one thrombotic risk factor as listed above
- All patients admitted to intensive care units are considered high risk for DVT and will require some form of thromboprophylaxis

Specific recommendations

- For hospitalized medical patients without obvious risk factors, anticoagulation be not employed (**Grade 2C**)
- Options for this low risk group include early ambulation with or without mechanical methods of thromboprophylaxis
- For most patients who are hospitalized with an acute medical illness, have at least one risk factor for VTE, and do not have an increased risk of bleeding, use of prophylactic anticoagulation over mechanical methods (**Grade 1A**) advocated

- Available choices for acutely ill medical patients include LMW heparin, low dose unfractionated heparin, or fondaparinux at doses recommended by the manufacturer
- LMW heparin or UFH recommended over fondaparinux for intensive care patients at moderate risk for VTE, and LMW heparin over UFH or fondaparinux in critical care patients at higher risk for DVT

- DVT prophylaxis is continued until the patient is discharged from hospital
- For patients with risk factors for DVT for whom there is a contraindication to anticoagulant thromboprophylaxis, optimal use of mechanical methods of thromboprophylaxis recommended(Grade 1A)
- Consideration should be given to the use of a pharmacologic agent (eg, LMWH) as soon as the bleeding risk becomes acceptably low or when the bleeding lesion or bleeding risk has been reversed

Obesity

- **Anticoagulants** —
- The volume of distribution of heparin in obese patients differs from non-obese patients as adipose tissue has lower blood volume than lean tissue
- Total body weight (TBW) to calculate the initial bolus dose and infusion rate to achieve a therapeutic PTT measurements after 6 hrs recommended
- Variable absorption of LMWH by SC injection in severe obesity is a concern and anti-Xa monitoring, is better for monitoring LMWH
- Enoxaparin 40 mg every 12 hours SC provides effective prophylaxis against venous thromboembolism in bariatric surgery patients up to a BMI 50 kg/m2 and 60 mg every 12 hours for a BMI exceeding 50 kg/m2

J Arthroplasty 2010; 25:19
Ann Surg Oncol 2008; 15:3567

Pregnancy

- **Antepartum indications**
- Antithrombin deficiency, a single prior episode of DVT plus a higher risk thrombophilia (persistent antiphospholipid antibodies, compound heterozygosity for prothrombin and factor V Leiden mutations, homozygosity for prothrombin mutation, and homozygosity for factor V Leiden mutation), or multiple prior episodes of DVT, we suggest antepartum pharmacologic thromboprophylaxis (Grade 2B**)**
- For pregnant women with a single prior episode of DVT related to pregnancy or estrogen, a single prior episode of idiopathic DVT, or a single prior episode of DVT plus thrombophilia not considered higher risk, thromboprophylaxis determined on a case-by-case basis

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- **Postpartum indications**
- Those with thrombophilia or have had one or more prior episodes of DVT,pharmacologic thromboprophylaxis recommended(Grade 2B)
- Caesarean Section ,and risk factors for DVT other than pregnancy and CS, pharmacologic thromboprophylaxis while they are hospitalized (Grade 2B)
- When multiple risk factors exist, it is preferable to use both pharmacologic thromboprophylaxis and mechanical thromboprophylaxis

- **Regimen**
- Antepartum--LMWH-, rather (UFH)-based regimen (Grade 2B)
- Postpartum women willing to get s/c injections, LMWH-based regimen, rather than an UFH- or warfarin based regimen (Grade 2B)
- Postpartum women unwilling for s/c injections, warfarin-based regimen, rather than no pharmacologic thromboprophylaxis (Grade 2B)
- UFH-based regimen should be used instead of a LMWH-based regimen in severe renal insufficiency (creatinine clearance <30 mL/min)
- **Duration**
- Antepartum pharmacologic thromboprophylaxis continued until delivery,postpartum continued for four to six weeks (Grade 2C)

Deep vein thrombosis in stroke

- Overall prevalence of clinically evident DVT after acute stroke is 2 to 10 %
- With MRI proximal DVT it is 18% in 21 days,and fibrinogen scanning have detected occult DVT in 28 to 80 %
- Risk of death in untreated proximal DVT in pts. with stroke is about 15%
- The risk of DVT may be 75% in the paretic side and 7% on nonparetic side
- Presence of DVT on nonparetic side suggests its presence on paretic side
- Additional important risk factors for DVT include advanced age, high stroke severity, immobility, and atrial fibrillation

Circulation 2009; 119:e480
BMJ 2010; 340:c95

- Acute stroke with restricted mobility,DVT prophylaxis with early low-dose anticoagulant therapy with LMWH or UFH (Grade 1A) recommended
- Regimens include SC enoxaparin 40 mg OD/ SC heparin 5000 units BD/TDS
- For patients with C/I to anticoagulants, the less effective combination of intermittent pneumatic compression and aspirin can be used
- After acute stroke, graduated compression stockings (Grade 1A) not recommended for DVT prophylaxis
- Anticoagulants not be used for 24 hours after the thrombolytic therapy

Venous thromboembolism in acute ICH patients

- ICH often causes severe leg weakness and immobility, the risk of DVT is increased
- It may be more frequent in ICH patients than in those with acute ischemic stroke as a result of withholding subcutaneous heparin
- Without antithrombotic therapy or IPC, clinical DVT in the first week after stroke for acute ICH patients is estimated to be approximately 2-5%
- Few trials studied risks & benefits of restarting prophylactic heparin after an ICH,most are retrospective

BMJ 2010; 340:c95

Prevention of DVT in ICH

- One RCT & two guidelines/consensus statements support use of GCS &IPC
- At present,IPC should be considered the mainstay for prevention of venous thromboembolism in patients with acute ICH
- Out of several types of IPCs (eg, multichamber vs monochamber, pressure applied sequentially or uniformly, whole leg vs calf only), which one is optimal is unclear
- The value of graduated compression stockings has been challenged by negative results of a randomized trial that included patients with acute ICH
- Benefit vs risks of antithrombotic therapy for prevention of VTE remains uncertain
- American Heart Association/American Stroke Association Stroke Council guideline recommended, low-dose LMWH or UFH may be considered in patients at high risk (mostly bed bound), after documentation of cessation of bleeding

J Clin Oncol 2007; 25:5490

Catheter induced upper extremity venous thrombosis

- Commonest site of DVT for centrally placed catheters is internal jugular vein
- Pripherally Inserted Central Catheter(PICC)-brachial, axillary or subclavian veins
- Majority of DVT of upper extremity due to presence of IV catheters esp. PICC,less by anatomic abnormalities (eg, thoracic outlet syndrome)
- Risk factors include catheter-related factors (eg,size,tip malposition, size, infection), prothrombotic states (congenital/acquired), hormonal therapy, and infusion of irritatants(KCl,diazepam,vancomycin,oxacillin,chemotherapy agents, and hypo- or hypertonic solutions <250 />350 mosmol/kg)
- Prophy. anticoagulation not recommended for long-term central venous catheters
- Heparin-bonded catheters when available is used,if risk of thrombosis is high

J Thromb Haemost 2008; 6:1262
Chest 2010; 138:803
Ann Oncol 2009; 20:1459

Non orthopedic surgical patients

- Very low risk of DVT(0.5%),no pharmacological(Grade 1B) /mechanical(Grade 2C)prophylaxis—only early ambulation
- Low (1.5%) ,moderate (3%), high risk (6%) not at high major bleeding risk--varying combination of LMWH, low-dose UFH,IPC, elastic stockings
- High risk of DVT in abdom./pelvic cancer surgery,extended duration,postop., LMWH (4 wks) prefered over limited-duration prophylaxis(Grade1B)
- Mod. to high risk DVT,high bleeding risk,IPC prefered over no prophylaxis until bleeding risk diminish & pharmacologic prophylaxis initiated (Grade 2C)
- Inferior vena cava filter not be used for primary prevention (Grade 2C) & that surveillance with venous compression usg not be performed (Grade 2C)

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Patients Undergoing Major Orthopedic Surgery: Total Hip Arthroplasty (THA), Total Knee Arthroplasty (TKA), Hip Fracture Surgery (HFS)

- One/more in varying combination rather than no antithrombotic prophylaxis:
  - low-molecular-weight heparin (LMWH),
  -fondaparinux,
  -apixaban,
  -dabigatran,
  - rivaroxaban,
  - low-dose unfractionated heparin (LDUH),
  -adjusted-dose VKA,
  -aspirin (all Grade 1B) ,
  - an intermittent pneumatic compression device (IPCD) (Grade 1C)
- Asymptomatic pts,no ultrasound reqd.screening before discharge (Grade 1B)
- No prophy. in isolated lower-leg injury requiring leg immobilization (Grade 2C)

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Pharmacologic Properties of the New Oral Anticoagulants That Are Approved or in the Most Advanced Stages of Clinical Development

Property	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	Thrombin	Factor Xa	Factor Xa	Factor Xa
Molecular weight	628	436	460	548
Bioavailability, %	6	80	50	50
Dose frequency	od/bid	od/bid	bid	od
Tmax, h	2	3	3	1-2
Half-life, h	12-17	7-11	9-14	9-11
Protein binding, %	35	95	87	54
CYP metabolism, %	None	32	15	< 4
P-gp transport	Yes	Yes	Yes	Yes
Renal excretion, %	80	66	25	35
Extrarenal excretion, %	20	34	75	65

CYP = cytochrome P450; od = once daily; P-gp = p-glycoprotein efflux transporter; Tmax = time to maximum concentration.

Take home message

- Occurrence of VTE(DVT+PE) is high in hospitalised patients
- DVT prophylaxis in are underutilised in all patient groups worldwide
- LMWH despite its high cost is preferable over UFH in long term use
- Newer oral anticoagulants already proven useful in major orthopedic surgery
- If pharmacoprophylaxis is C/I,IPC is best choice amongst mechanical method