Venous Thromboembolic Disease (VTE): Guidelines for Management and Prevention

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OBJECTIVES

-On completion of the presentation, participants will be able to:

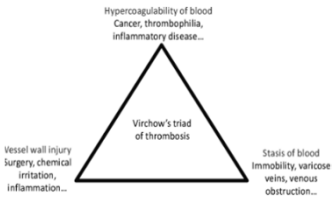
- Discuss the prevalence of venous thromboembolism in acute and critical care.
- Identify patients at risk for developing venous thromboembolism in acute and critical care.
- Summarize evidence based pharmacologic recommendations for prevention and treatment of venous thromboembolic disease (VDT).
- Adjust VDT pharmacologic dosing according to patient cohort to limit complications from chemoprophylaxis.

Venous Thromboembolic Disease (VTE)

- Deep vein thrombosis and pulmonary embolism, venous thromboembolism (VTE), affect an estimated 900,000 people per year (Hattab et. Al., 2017). VTE increases morbidity, mortality, and hospital length of stay
- Leading cause of preventable hospital death
- Readmission rates within 1 year for VTE 5.3%-14% (Spyropoulous, A., and Lin, J., 2007).

Pathophysiology VTE

- Virchow's Triad



Risk Factors VTE

- Major

Age > 60 years	Malignancy
Severe head injury (GCS <8)	Central venous access
Injury Severity Score (ISS) >/15	Morbid obesity (BMI >/40)
Spinal fractures/Spinal cord injury	History of VTE
Pelvic fractures	Immobilization >2 days
Long bone fractures	Laparotomy
Hip dislocation	Heparin-Induced Thrombocytopenia

(Obi, A., et. Al., 2015)

Risk Factors VTE

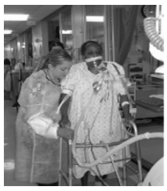
- Minor

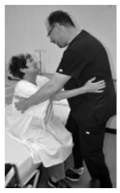
Age 40-60 years	Varicose veins
Coagulopathy	Inflammatory bowel disease
Oral Contraceptive Use/Hormone Replacement Therapy	Current leg edema
Immobilization </2 days	Minor surgery planned
Transfusion of 4U pRBCs in 1st 24 hours	Pregnancy

(Obi, A., et. Al., 2015)

Non-pharmacologic Prevention

- *Early mobility!! "Get em moving!!"*





Non-Pharmacologic Prevention

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Pharmacologic Prevention

- Low dose unfractionated heparin (LDUH)
- Low molecular weight heparin (LMWH) (enoxaparin/lovenox)
- Direct oral anticoagulants (DOACs; apixaban, rivaroxaban, edoxaban, dabigatran)
- Vitamin K antagonist (warfarin/coumadin)

Low Dose Unfractionated Heparin (LDUH)

- 5000 IU SQ TID usual dosing
- Heparin gtt – hospital standard dosing protocols based on indication

ACTION:

- **Binds w antithrombin to inactivate coagulation enzyme thrombin, (factor IIa); inhibits factor Xa, usually within minutes**
- **DOES NOT break down clots, prevents further formation of clots**
- **Measure effect with aPTT.**

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http://www.stoptheclot.org

Coagulation Cascade

Retrieved from www.thrombosisadviser.com

LDUH

- **Advantages of UFH**
- Rapidly enters the blood stream and acts swiftly to prevent clot formation
- Rapidly wears off when the infusion or injections are stopped (short half life)
- Rapidly reversed by protamine, a UFH antidote, if serious side effects occur
- Inexpensive compared with other heparin formulations ($1.11/dose)
- **Disadvantages of UFH**
- Variable anticoagulant effect due to significant protein binding.
- Frequent blood tests are necessary to ensure correct dosage
- IV administration requires hospitalization usually for 5-10 days after blood-clot diagnosis

Retrieved from *http://www.stoptheclot.org*

LDUH

- **Potential Side Effects of UFH**
- Uncontrolled bleeding (most serious side effect)
- Injection site reactions such as redness and irritation
- Loss of bone strength (osteoporosis?)
- Elevated liver enzymes
- Heparin induced thrombocytopenia (HIT)

*****NOT EFFECTIVE IN THE TRAUMA PATIENT!!*****

Retrieved from
http://www.stoptheclot.org

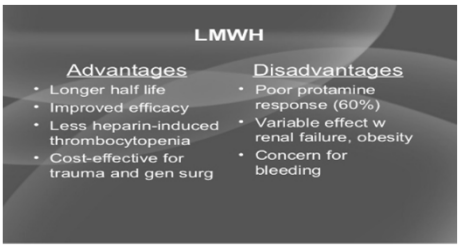
Low Molecular Weight Heparin (LMWH)

Enoxaparin (lovenox, $5.90/dose), dalteparin

ACTION

- Anti-factor Xa
  - ******Levels <0.2units/ml are considered sub-therapeutic and require and increase in enoxaparin dosing (0.1mg/kg). ******
  - ******Levels >0.6 units/ml require decrease in enoxaparin dosing (0.1mg/kg).******

LMWH



LMWH (AUMC Trauma Protocol; Adult)

- Should be started w/I 12 hours of hospital admission unless special cohort (discussed later). Dosing 0.5mg/kg q 12hr.
- Do not hold chemoprophylaxis prior to surgery per *CHEST guidelines;* if must be held due to nature of procedure, not before 12 hours. ***Resume 12 hours post-op!***
- Monitor Anti-Xa levels routinely.
  - -Maximum Anti-Xa effect occurs 3-5 hours after SQ injection.
  - -Half-life of the Anti-Xa effect is ~7 hours.
- Not to be used with CrCl <30 ml/min.

(Rogers, F., et. Al., 2002)

Special Cohorts w/ VTE dosing

Pediatrics
Trauma
Cancer
TBI
Solid Organ Injury
SCI

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Pediatrics

- VTE is rare in pediatric population.
- Incidence rises in trauma population. <1% with a mortality rate of 2.2%. Morbidity associated high however, 50%.
- 2016: A panel of expert panelists from various pediatric specialties concluded that it was recommended that those <12 years of age should not receive chemoprophylaxis. Those >/ 13 years of age who are mobile but have noted risk factors, chemoprophylaxis should be considered.

(Thompson, A., et. Al., 2013)

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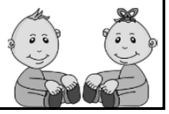

LMWH (AUMC Trauma Pediatric Protocol)

- Enoxaparin 0.5mg/kg q 12 when appropriate.
- Do not hold chemoprophylaxis prior to surgery per *CHEST guidelines;* if must be held due to nature of procedure, not before 12 hours. ***Resume 12 hours post-op!***
- Anti-Xa level monitoring not required. Draw level in event VTE is diagnosed.
- If there is a change in renal status or weight, do not use enoxaparin. Use LDUH.
- Not to be used with CrCl <30 ml/min.

Trauma

- 8th edition of American College of Chest Physicians recommend LMWH for trauma patients.
- Eastern Association for the Surgery of Trauma (EAST) states LDUH inferior to LMWH for VTE prophylaxis. LMWH is standard of choice: 40mg daily or 30mg q 12 (Rogers, F. , et. Al., 2002).
- Weight based dosing? *0.5mg/kg of actual body weight to determine dosing in obese patients, q 12 hours*

(Singer, G. , et. Al., 2016)

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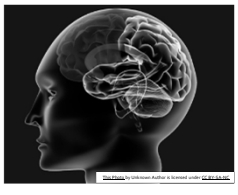
Traumatic Brain Injury (TBI)



- Head injury is an independent factor for VTE (Carney, N., et. Al., 2016).
- Brain Trauma Foundation currently states that LMWH or LDUH should be used along with mechanical prophylaxis; there is no standardized recommendation for preserved agent, dosing, or timing.
- Parkland Protocol- TBI risk stratification:
  1. Low risk
  2. Medium risk/high risk
  3. IVC filter use removed (AUMC still uses)

Cancer

- Cancer associated thrombus- recommend using LMWH over VKA (Grade 2b)

  1mg/kg/dose BID enoxaparin

- Treatment duration – extended tx recommended over 3 months
- Parenteral anticoagulation not given before rivaroxaban and apixaban. Is overlapped w VKA therapy.
- In patients w/ DVT of the leg or PE and active cancer, recommend extended therapy over 3 months
- DOACS?

(Kearon, et. Al., 2016)

Solid Organ Injury

- VTE incidence very low (1.2%).
- No contraindications for use of chemoprophylaxis in patients without signs of active hemorrhage, coagulopathy, hemodynamic instability, or hypothermia.
- Studies varied with what type used.

(Joseph, B., et. Al., 2015)

Spinal Cord Injury (SCI)

- Spine fractures, SCI
- VTE after spine surgery incidence 31%.

  ?lack of chemoprophylaxis after surgery- *incidence of post-op spinal hematoma <1%**

  -Studies report decreased VTE when prophylaxis is started <48 hrs post op without bleeding complications (Kim, D., et. Al., 2015).

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Vitamin K Antagonist

- Warfarin (Coumadin)
  1. Dosing must be individualized for patient INR AND condition being treated.
  2. Full anticoagulation effect not achieved for several days. Antithrombotic effect may not be seen for 5 days.
  3. Frequent monitoring first week of therapy crucial.
  4. Medication Interactions.
  5. Food Interactions

*
https://depts.washington.edu/anticoag

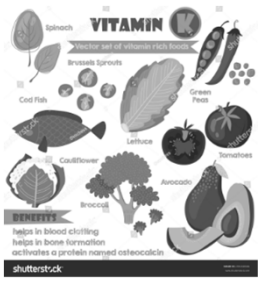
Lab Monitoring Schedule

- **Maintenance Therapy**
- Dose held today in patient with significant over anticoagulation: In 1 - 2 days
- Dosage change today: Within 1 - 2 weeks
- Dosage change < 2 weeks ago: Within 2 - 4 weeks
- Routine follow-up of medically stable & reliable patients: Every 4 - 8 weeks
- Routine follow-up of medically unstable or unreliable patients: Every 1 - 2 weeks
- **After Hospital Discharge**
- if patient or therapy is unstable: in 1-3 days
- if patient or therapy is stable: in 3-7 days

https://depts.washington.edu/anticoag

Medication Interactions

Food Interactions



Direct Oral Anticoagulants (DOACS)

- DOACS have changed anticoagulation therapy tremendously.
- Comparable efficacy, lower bleeding risk; SAFE
- Patient selection
- Parenteral therapy bridging needed w edoxaban, dabigatran; Rivaroxaban and apixaban monotherapy.
- Do not need to routinely measure DOAC activity.
- Temporary interruption of therapy for procedures
- Reinitiation of DOACS post procedure

(Burnett, et. Al., 2016)

Chest Guidelines 2016

Anthrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis (9th ed.): American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

(Kearon, C., et. Al., 2016) doi: http://dx.doi.org/10.1016/j.chest.2015.11.026

Updates

- For VTE and no cancer- DOACS over VKA therapy; VKA over LMWH
- For VTE and Cancer- LMWH over VKA, DOACS (no direct comparisons have been made w which one)
- No changes made on cessation timing of anticoagulation.
- Recommend AGAINST an IVC filter while on anticoagulation.
- Compression stockings are not routinely used to prevent post-thrombotic syndrome (PTS)

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