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RECOMMENDATIONS

All patients

➤ Level 2

- Patients at low risk for VTE require only early ambulation
- Patients at moderate to high VTE risk should receive intermittent pneumatic compression devices (IPC) and chemical prophylaxis as soon as clinically safe
- Hold chemical prophylaxis for a platelet count <50,000/mm³
- Interruption of chemical prophylaxis for procedures should be avoided
- Prophylactic inferior vena cava (IVC) filters are not recommended (see IVC Filter guideline)
- Subcutaneous unfractionated heparin (LDUH) 5000 mg q 8 hrs is preferred for patients with end stage renal disease or creatinine clearance (CrCl) <30 mL/min

➤ Level 3

- For patients receiving low molecular weight heparin (LMWH), dosing adjustment and/or anti-Xa monitoring (target peak level 0.2-0.5 IU/mL) should be considered for weight < 45 kg, body mass index (BMI) >30 kg/m², or suspected augmented renal clearance.

Surgery

➤ Level 1

- Standard dose enoxaparin (LMWH) 40 mg q 24 hrs or LDUH should be initiated in patients with moderate to high risk VTE

Trauma / Burns

➤ Level 1

- LMWH 40 mg q 12 hrs should be initiated in patients with moderate to high risk VTE

➤ Level 2

- Consider LMWH 30 mg BID, for patients age > 65 yrs, weight < 50 kg, or CrCl < 60

Obesity

➤ Level 2

- When LMWH is indicated, consider weight-based dosing of 0.5 mg/kg q 12 hrs if BMI ≥ 30
 - In patients over 160 kg, limit *initial* enoxaparin dose to 80 mg q 12 hrs; any subsequent dose adjustments should be based on anti-Xa monitoring
- When LDUH is indicated, consider increasing dose to 7500 mg q 8 hrs if BMI ≥ 35 and total body weight ≥ 120 kg (excluding TBI patients)

Traumatic Brain Injury

➤ Level 2

- Patients with documented repeat stable computed tomography (CT) of the head may be initiated on VTE prophylaxis (LDUH or LMWH) within 24 hours of hospital admission or craniotomy / craniectomy
- *Initial* doses greater than 40 mg q12 (regardless of BMI) are discouraged; any subsequent dose adjustments based on anti-xa monitoring

➤ Level 3

- VTE prophylaxis may be safely used in patients with intracranial pressure (ICP) monitors

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended as a general statement regarding appropriate patient care practices based on the medical literature and clinical expertise at the time of development. They should not be considered protocol or policy nor are intended to replace clinical judgment or dictate care of individual patients.

SUMMARY

Critically ill patients are at significant risk for venous thromboembolism (VTE) due to inactivity, immobilization, vascular injury, and/or hypercoagulable states. Appropriate VTE prophylaxis varies based on the patient's risk factors and physiologic state.

INTRODUCTION

Venous thromboembolism (VTE) is associated with significant morbidity and mortality as well as economic burden. The incidence of hospitalization-associated hospital VTE in high income countries is estimated to be 3.3 per 100 hospitalizations equating to 3.9 million annual cases of VTE in high income countries. Incidence is nearly double in low and middle income countries. VTEs account for the highest number of hospital-associated DALYs (Disability-adjusted life year) (1). A 2021 American Heart Association report estimates 1.2 million annual cases of VTE in the United States, 30% of which involve pulmonary embolism (PE) (2). Hospitalization for an acute medical illness increases the risk of VTE approximately 100-fold (3). The REITE registry, established in 2001 is the world's largest data base of information from patients with VTE. Based on May 2023 interactive data in the registry, the 30-day mortality from a deep vein thrombus (DVT) is 2.57% from lower limb DVT, 3.35% from upper limb DVT, and 5.08% from pulmonary embolism (PE). Mortality significantly increases with age >65 (4). The annual economic burden of VTE on the US healthcare system is estimated to be between \$7-10 billion per year for every 375,000-425,000 newly diagnosed medically treated VTE cases (5).

The overall incidence of DVT in surgical patients is 19-29% with patients with malignancy being at highest risk. PE is clinically recognized in 1.6% of patients with an additional 0.9% being recognized only post-mortem. Knowledge of specific risk factors forms the basis for appropriate prophylaxis. The rationale for thromboprophylaxis is based on the high prevalence of DVT among hospitalized patients, the clinically silent nature of the disease in the majority of patients, and the morbidity, costs, and potential mortality associated with DVT (6,7).

PE is the third most common cause of death in trauma patients who survive beyond the first day (8). Without prophylaxis, patients with multi-system or major trauma have a risk for DVT that exceeds 50%, and a risk of fatal PE of approximately 0.4-2.0% (9-12). The traumatically injured are at high risk for developing DVT and PE due to endothelial injury and prolonged immobility. DVT is seen in 69% of lower extremity fractures, 62% of spine fractures, 54% of major head injuries, and 40% of patients with blunt thoracoabdominal trauma (8). Patients with single-system, non-orthopedic injuries have a lower risk of DVT than those with multiple injuries or with lower extremity fractures.

Clinical risk factors for DVT and PE in the surgical patient

- Prolonged immobility
- Age > 40 years
- Stroke
- Paralysis
- Previous DVT
- Malignancy and its treatment
- Major surgery (particularly involving the abdomen, pelvis, and lower extremities)
- Obesity
- Spinal cord injury
- Lower extremity or pelvic fracture
- Need for a surgical procedure
- Duration of hospital stay
- Increasing age
- Varicose veins
- Cardiac dysfunction
- Indwelling central venous catheters
- Inflammatory bowel disease
- Nephrotic syndrome
- Pregnancy or estrogen use
- Congenital and acquired thrombophilic disorders (Factor V Leiden, lupus anticoagulant, protein C/S deficiency, etc...)
- Femoral venous line or major venous repair

In many patients, multiple risk factors may be present with the total risk being cumulative. For surgical patients, the incidence of DVT is proportional to the risk factors present and the risk associated with the procedure itself. Procedure-related risks include: the location, technique, and duration of the procedure; the type of anesthetic; the presence of infection; and the degree of postoperative immobilization.

Despite appropriate DVT prophylaxis, surgical patients may still develop both DVT and PE. A 2014 case-control study identified five independent predictors of in-hospital DVT despite chemoprophylaxis. These included hospitalization for cranial surgery, intensive care unit admission, admission leukocyte count $>13,000/\text{mm}^3$, presence of an indwelling central venous catheter, and admission from a long-term care facility. In the presence of such risk factors, aggressive efforts to achieve DVT prophylaxis should be maintained (13).

LITERATURE REVIEW

VTE prophylaxis in surgical patients

In 2012, the American College of Chest Physicians (ACCP) published updated comprehensive guidelines for VTE prophylaxis in trauma and surgical patients. The guidelines used the Rogers and Caprini risk stratification systems and the PICO format to generate clinical questions to guide the literature reviews used in developing the guidelines (14). SAGES (Society of American Gastrointestinal and Endoscopic Surgeons) has adopted and follows the recommendations of the ACCP (15).

For general and abdominal surgery patients, ACCP makes the following recommendations based on patient risk as determined by the Rogers and Caprini scores:

- Very low risk patients: recommend early ambulation
- Low risk patients: suggest mechanical prophylaxis over no prophylaxis
- Moderate risk patients without risk for major bleeding: suggest low-molecular-weight heparin (LMWH), low-dose unfractionated heparin (LDUH), or mechanical prophylaxis over no prophylaxis.
- Moderate risk patients with risk for major bleeding: suggest mechanical prophylaxis over no prophylaxis.
- High risk patients without risk for major bleeding: recommend low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin (LDUH), and mechanical prophylaxis.
- Moderate risk patients with risk for major bleeding: suggest mechanical prophylaxis over no prophylaxis.
- High risk patients undergoing surgery for cancer: recommend extended duration (4 weeks) LMWH over limited duration
- The ACCP recommended against using IVC filters as primary VTE prevention in surgical patients

The American Society of Hematologists used similar methods for its 2019 guidelines in patients undergoing major surgery (16).

- Use pharmacological or mechanical prophylaxis over no prophylaxis
- For those receiving pharmacological prophylaxis, use combined pharmacologic and mechanical prophylaxis over pharmacologic alone
- For those receiving pharmacological prophylaxis use LMWH or LDUH
- For mechanical prophylaxis use intermittent compression devices over compression stockings
- Recommend against using IVC filters for prophylaxis

VTE prophylaxis in trauma patients

LDUH is not effective in the trauma patient. In the 1996 Geerts et al. seminal study comparing LDUH to LMWH in trauma patients, LMWH heparin was shown to be superior to LDUH for VTE prophylaxis in trauma patients. LDUH was shown to be equivalent to no prophylaxis in high-risk trauma patients. (17).

In March 2022, the AAST and ACS sought to optimize and standardize VTE prophylaxis strategies for adult trauma patients across all trauma centers. The AAST/ACS committee on trauma reviewed guidelines from the Western Trauma Association, AAST, EAST, ACS, ACCP, NICE and ASH to arrive at the following standardized clinical protocol (18):

- Initiate VTE prophylaxis promptly and continuously unless the patient is ambulatory and expected length of stay is less than 24 hours
- Enoxaparin (LMWH) is the first choice for pharmacologic VTE prophylaxis
 - Enoxaparin 40 mg BID should be initiated for most patients
 - Enoxaparin 30 mg BID should be initiated in patients > 65 , less than 50 kg or with creatinine clearance of 30-60 mL/min
 - Prophylaxis should not be interrupted for mild to moderate thrombocytopenia or $(50,000-100,000/\text{mm}^3)$
 - Interruption of dosing for orthopedic or other procedures should be avoided

- For patients with BMI > 30, enoxaparin can be dosed at 0.5 mg/kg BID
- Patients who are young and thin with high creatinine clearance may require higher dosing
- After initial dosing, adjustments can be made according to anti-Xa levels with a target of 0.2-0.4 for peak levels. If obtained, levels should be drawn 3-4 hours after the fourth dose
- Subcutaneous unfractionated heparin (LDUH) is the preferred choice for patients with end stage renal disease or creatinine clearance <30 mL/min
 - 5000 units every 8 hours is the preferred dose and timing
 - 7500 units every 8 hours can be used for patients with BMI ≥ 35 or total body weight (TBW) ≥120 kg
- Consider lower extremity screening duplex in asymptomatic patients only if they are considered high risk for VTE
- Prophylactic IVC filters are not recommended
- Special circumstances
 - Blunt solid organ injury
 - Early VTE (within 24-48 hours) is recommended. Prophylaxis should be initiated in high grade (IV, V) injuries once bleeding is stabilized.
 - Traumatic Brain Injury (TBI)
 - Patients should be risk stratified using the Modified Berne-Norwood Criteria
 - Low risk: Initiate prophylaxis within 24 hours if CT is stable
 - Moderate risk: Initiate prophylaxis at 72 hours if CT is stable
 - High risk: Consider screening lower extremity duplex or IVC filter placement
 - At Orlando Regional Medical Center, the neurosurgical team advocates early use of LDUH 5000 U q 8 hours at the time of admission (in the absence of active intracranial hemorrhage) for the first seven (7) days of prophylaxis after which time the patient may be switched to LMWH. LDUH is initiated when intracranial hemorrhage is deemed stable on repeat imaging.
 - Spine fracture/SCI
 - Initiate prophylaxis within 48 hours of injury or spine surgery

REFERENCES

1. Raskob GE, Angchaisuksiri P, Blanco AN, et al. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol* 2014; 34(11):2363-2371.
2. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics-2021 Update: A report from the American Heart Association. *Circulation* 2021; 143(8):e254-e743.
3. Lutsey PL, Zakai NA Epidemiology and prevention of venous thromboembolism. *Nat Rev Cardiol* 2023; 20:248–262.
4. Riete. www.rieteregistry.com/graphics-interactives/dead-30-days. Accessed 18 June 2023.
5. Grosse SD, Nelson RE, Nyarko KA, Richardson LC, Raskob GE. The economic burden of incident venous thromboembolism in the United States: A review of estimated attributable healthcare costs. *Thromb Res* 2016; 137:3-10.
6. Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota AJ. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133(6 Suppl):454S
7. Clagett, GP, Reisch, JS. Prevention of VTE in general surgical patients: result of a meta-analysis. *Ann Surg* 1988; 208:227-240.
8. Pasquale M, Fabian TC, and the EAST Ad Hoc Committee on Practice Management Guideline Development. Practice management guidelines for trauma from the Eastern Association for the Surgery of Trauma. *J Trauma* 1998; 44:941-957.
9. Huber O, Bounameaux H, Borst F, et al. Postoperative pulmonary embolism after hospital discharge: an underestimated risk. *Arch Surg* 1992; 127:310-313.
10. Montgomery KD, Geerts WH, Potter HG, et al. Practical management of VTE following pelvic fractures. *Orthop Clin North Am* 1997; 28:397-404.
11. Hoyt DR, Simons RK, Wincell RJ, et al. A risk analysis of pulmonary complications following major trauma. *J Trauma* 1993; 35:524-531.

12. Frezza EE, Siram SM, Van Thiel DH, et al. VTE after penetrating chest trauma is not a cause of early death. *J Cardiovasc Surg* 1996; 37:521-524.
13. Wang TF, Wong CA, Milligan PE, Thoenke MS, Woeltje KF, Gage BF. Risk factors for inpatient venous thromboembolism despite thromboprophylaxis. *Thromb Res* 2014; 133:25-29.
14. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, Samama CM. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141(2 Suppl):e227S-e277S.
15. Richardson WS, Hamad GG, Stefanidis D et al. SAGES VTE prophylaxis for laparoscopic surgery guidelines: an update. *Surg Endosc* 2017; 31:501–503.
16. Anderson D, Morgano G, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. *Blood Adv* 2019; 3(23):3898–3944.
17. Geerts WH, Jay RM, Code KI, et al. A comparison of low –dose heparin with low-molecular weight heparin as prophylaxis against VTE after major trauma. *N Engl J Med* 1996; 335:701-707.
18. Rappold JF, Sheppard FR, et al. Venous thromboembolism prophylaxis in the trauma intensive care unit: an American Association for the Surgery of Trauma Critical Care Committee Clinical Consensus Document. *Trauma Surg Acute Care* 2021; 24:6(1):e000643.