IN THE NAME OF GOD

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Venous Thromboembolism Prophylaxis In Surgical Patients

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INTRODUCTION

- An estimated **one-third of the 150,000 to 200,000 VTE-related deaths** per year in the United States occur following surgery.
- About **50% of VTE** occur in current or **recently hospitalized patients,** especially if they are admitted for surgery
- The **Virchow triad** of **stasis**, **hypercoagulable state**, and **vessel injury** is present in most surgical patients.
- Patients who undergo major general surgical, gynecologic, urologic, and neurosurgical procedures without thromboprophylaxis **have a significant incidence of perioperative DVT**.

INTRODUCTION

- The **goal of prophylaxis** is to reduce the **mortality and morbidity associated with VTE**.

- The **first manifestation of VTE** may be a **life-threatening PE** , and as indicated earlier, clinical evaluation to detect DVT before PE is unreliable.

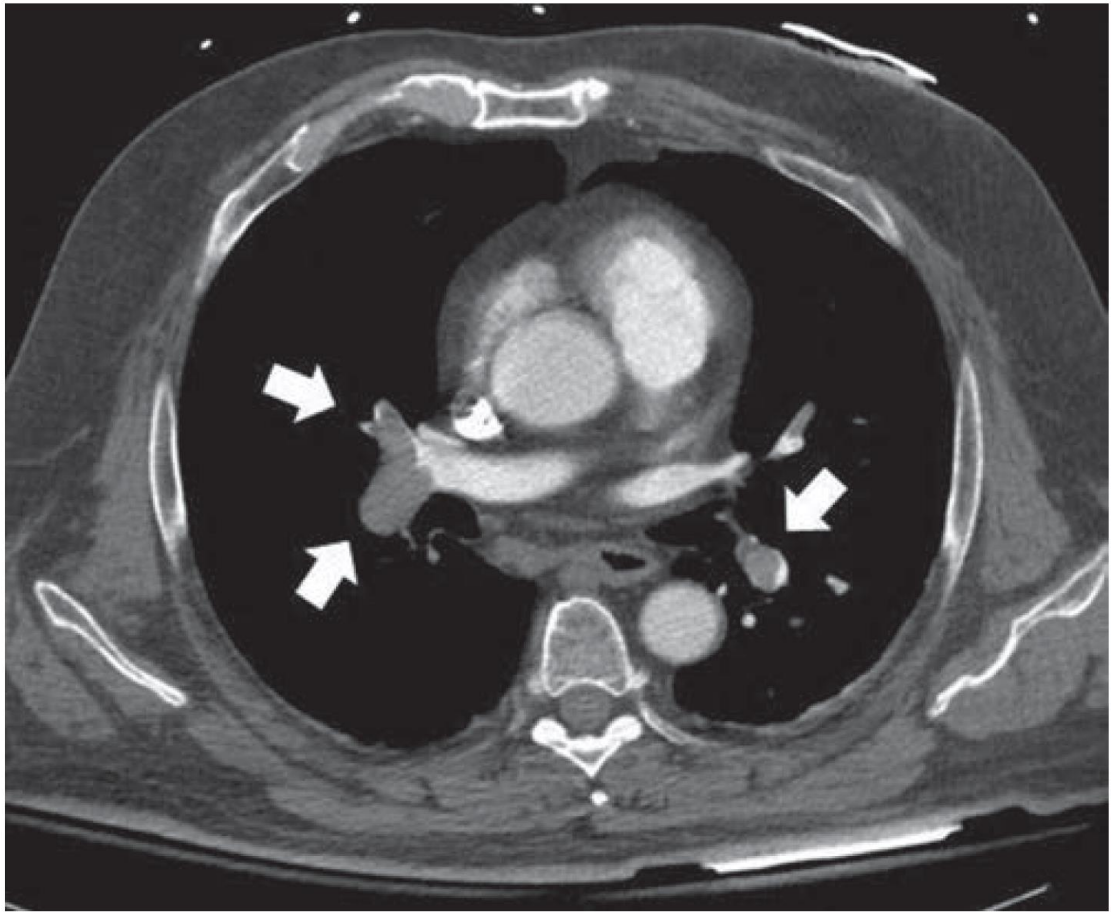

Figure 24-11. Computed tomography angiogram showing multiple pulmonary embolisms (*arrows*). *(Used with permission from Dr. Scott Ambruster.)*

PROPHYLAXIS

- **Effective methods of VTE prophylaxis** involve the use of **one or more pharmacologic or mechanical modalities**.

- Currently available **pharmacologic agents** include **low-dose UFH**, **LMWH**, **synthetic pentasaccharides**, and **vitamin K antagonists**.

- **Mechanical methods** include **intermittent pneumatic compression (IPC)** and **graduated compression stockings**.

- There is **insufficient evidence to consider aspirin alone as adequate DVT prophylaxis**.

PROPHYLAXIS

- The **risk for VTE associated with a surgical procedure** depends on
  - the type of **operation**,
  - type of **anesthesia**,
  - **duration of surgery**, and
  - **Patient related risk factors**, such as patient **age**, presence of **cancer**, **prior VTE, obesity**, presence of **infection**, and known **thrombophilic disorders**.

PROPHYLAXIS

- **VTE risk can be stratified** according to the previously mentioned **risk assessment models**, the **Caprini score** and **Rogers score**.
- These risk assessment models are included in the prophylaxis guidelines for nonorthopedic surgery (Tables 24-5 and 24-6). A composite score is created using assigned values for each risk factor. The cumulative score for each patient is then used to predict thrombosis risk and provide recommendations regarding VTE prophylaxis.

PROPHYLAXIS

- Patients at **very low risk (<0.5%; Rogers score <7; Caprini score 0)** who undergo **general or abdominopelvic procedures do not require pharmacologic or mechanical pro-phylaxis**; however, **early ambulation is required**.

Caprini risk assessment model

1 POINT	2 POINTS	3 POINTS	5 POINTS
Age 41–60	Age 61–74	Age ≥75	Stroke (<1 month)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m^2	Major open surgery (> 45 minutes)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen legs	Laparoscopic surgery (> 45 minutes)	Factor V Leiden	Acute spinal cord injury (<1 month)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (>72 hours)	Lupus anticoagulant	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibody	
Oral contraceptives of hormone replacement	Central venous access	Elevated serum homocysteine	
Sepsis (<1 month)		Heparin-induced thrombocytopenia	
Serious lung disease, including pneumonia (<1 month)		Other congenital or acquired thrombophilia	
Abnormal pulmonary function test			
Acute myocardial infarction			
Congestive heart failure			
History of inflammatory bowel disease			
Medical patient at bed rest			

Risk assessment model from the Patient Safety in Surgery Study

RISK FACTOR	RISK SCORE POINTS
Operation type other than endocrine	
Respiratory and hernia	9
Thoracoabdominal aneurysm, embolectomy/thrombectomy, venous reconstruction, and endovascular repair	7
Aneurysm	4
Mouth, palate	4
Stomach, intestines	4
Integument	3
Hernia	2
ASA, physical status classification	
3,4, or 5	2
2	1
Female sex	1
Work RVU	
>17	3
10–17	2
Two points for each of these conditions	2
Disseminated cancer	
Chemotherapy for malignancy within 30 days of operation	
Preoperative serum sodium >145 mmol/L	
Transfusion >4 units packed RBCs in 72 hours before operation	
Ventilator dependent	
One point for each of these conditions	1
Wound class (clean/contaminated)	
Preoperative hematocrit ≤38%	
Preoperative bilirubin >1 mg/dL	
Dyspnea	
Albumin ≤3.5 mg/dL	
Emergency	
Zero points for each of these conditions	0
ASA physical class of 1	
Work RVU <10	
Male sex	

PROPHYLAXIS

- Patients at **low risk** (<1.5%; Rogers score 7–10; Caprini score 1–2) should receive **mechanical prophylaxis**.

Caprini risk assessment model

1 POINT	2 POINTS	3 POINTS	5 POINTS
Age 41–60	Age 61–74	Age ≥75	Stroke (<1 month)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m^2	Major open surgery (> 45 minutes)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen legs	Laparoscopic surgery (> 45 minutes)	Factor V Leiden	Acute spinal cord injury (<1 month)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (>72 hours)	Lupus anticoagulant	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibody	
Oral contraceptives of hormone replacement	Central venous access	Elevated serum homocysteine	
Sepsis (<1 month)		Heparin-induced thrombocytopenia	
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Medical patient at bed rest			

Risk assessment model from the Patient Safety in Surgery Study

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Disseminated cancer	
Chemotherapy for malignancy within 30 days of operation	
Preoperative serum sodium >145 mmol/L	
Transfusion >4 units packed RBCs in 72 hours before operation	
Ventilator dependent	
One point for each of these conditions	1
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Preoperative hematocrit ≤38%	
Preoperative bilirubin >1 mg/dL	
Dyspnea	
Albumin ≤3.5 mg/dL	
Emergency	
Zero points for each of these conditions	0
ASA physical class of 1	
Work RVU <10	
Male sex	

PROPHYLAXIS

- Patients at **moderate risk** (3%; **Rogers score >10**; **Caprini score 3–4**) should receive **LMWH** at recommended doses, **low-dose UFH**, **or** **mechanical prophylaxis**.

Caprini risk assessment model

1 POINT	2 POINTS	3 POINTS	5 POINTS
Age 41–60	Age 61–74	Age ≥75	Stroke (<1 month)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m^2	Major open surgery (> 45 minutes)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen legs	Laparoscopic surgery (> 45 minutes)	Factor V Leiden	Acute spinal cord injury (<1 month)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (>72 hours)	Lupus anticoagulant	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibody	
Oral contraceptives of hormone replacement	Central venous access	Elevated serum homocysteine	
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Serious lung disease, including pneumonia (<1 month)		Other congenital or acquired thrombophilia	
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Risk assessment model from the Patient Safety in Surgery Study

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Transfusion >4 units packed RBCs in 72 hours before operation	
Ventilator dependent	
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Preoperative bilirubin >1 mg/dL	
Dyspnea	
Albumin ≤3.5 mg/dL	
Emergency	
Zero points for each of these conditions	0
ASA physical class of 1	
Work RVU <10	
Male sex	

PROPHYLAXIS

- Patients at **high risk** (6%; **Caprini score ≥5**) should receive **LMWH** at recommended doses **or low-dose UFH and mechanical prophylaxis**.

Caprini risk assessment model

1 POINT	2 POINTS	3 POINTS	5 POINTS
Age 41–60	Age 61–74	Age ≥75	Stroke (<1 month)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m^2	Major open surgery (> 45 minutes)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen legs	Laparoscopic surgery (> 45 minutes)	Factor V Leiden	Acute spinal cord injury (<1 month)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (>72 hours)	Lupus anticoagulant	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibody	
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Risk assessment model from the Patient Safety in Surgery Study

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Operation type other than endocrine	
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Thoracoabdominal aneurysm, embolectomy/thrombectomy, venous reconstruction, and endovascular repair	7
Aneurysm	4
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Stomach, intestines	4
Integument	3
Hernia	2
ASA, physical status classification	
3,4, or 5	2
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Female sex	1
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>17	3
10–17	2
Two points for each of these conditions	2
Disseminated cancer	
Chemotherapy for malignancy within 30 days of operation	
Preoperative serum sodium >145 mmol/L	
Transfusion >4 units packed RBCs in 72 hours before operation	
Ventilator dependent	
One point for each of these conditions	1
Wound class (clean/contaminated)	
Preoperative hematocrit ≤38%	
Preoperative bilirubin >1 mg/dL	
Dyspnea	
Albumin ≤3.5 mg/dL	
Emergency	
Zero points for each of these conditions	0
ASA physical class of 1	
Work RVU <10	
Male sex	

PROPHYLAXIS

- **Thromboprophylaxis** should **continue until discharge**,
- select **high-risk patients with malignancy** in whom **extended-duration prophylaxis (up to 4–6 weeks**) may be beneficial.
- Patients with **significant risk for bleeding** should **receive mechanical prophylaxis** until this **risk subsides**.

PROPHYLAXIS

- Overall, **low-dose UFH and LMWH reduce** the risk for **symptomatic and asymptomatic VTE by 60% to 70%.**

- **Lower dosages of LMWH appear to be associated with less bleeding risk than low-dose UFH,**
- **but UFH produces less bleeding risk than higher prophylactic dosages of LMWH**.

- **Other advantages of LMWH** include **once-daily dosing** protocols and a **lower rate of heparin-associated** antibody formation.

UNFRACTIONATED HEPARIN (UFH)

- Unfractionated heparin (**UFH**) **binds to antithrombin** via specific 18-saccharide sequence. **This increases antithrombin activity over a thousandfold.**
- The **antithrombin-heparin complex** primarily **inhibits factor IIa** (thrombin) and **factor Xa** and, to **lesser degree, factors IXa, XIa, and XIIa of the coagulation cascade**. In addition, UFH also binds to tissue factor pathway inhibitor, which **inhibits the conversion of factors X to Xa, and factors IX to IXa**.
- Finally, UFH catalyzes the inhibition of thrombin by heparin cofactor II via a mechanism independent antithrombin.

UNFRACTIONATED HEPARIN (UFH)

- **Nonorthopedic surgery:**
  - **Patients with active cancer**:
    - **SUBQ**: **5,000** units **2 to 4 hours prior to surgery**, then **5,000 units every 8 to 12 hours started ~6 to 24 hours after surgery**.
    - Note: The optimal duration of prophylaxis has not been established, but it **is usually given for a minimum of 7 to 10 days; extending for up to 4 weeks may be reasonable in those undergoing major abdominal or pelvic surgery** (Ref).
  - **Patients without cancer:**
    - SUBQ: **5,000 units every 8 to 12 hours**, with **initial dose given ≥2 hours prior to surgery**.
    - **Alternatively**, may **postpone pharmacologic prophylaxis until after surgery** (eg, **high bleeding risk**) when it is safe to initiate.
    - **Continue until fully ambulatory** and **risk of VTE has diminished (typically up to 10 days**) .
- **Low-weight patients (eg, <50 kg)** may be more sensitive to routine prophylactic doses, increasing the potential for higher than intended levels of anticoagulation; **consider adhering to every-12-hour dosing interval** (Ref).

UNFRACTIONATED HEPARIN (UFH)

- **Orthopedic surgery** (eg, hip fracture surgery, total hip arthroplasty, total knee arthroplasty):
  - **SUBQ**: **5,000 units every 8 to 12 hours**, with **initial dose administered ≥12 hours preoperatively** or **≥12 hours postoperatively once hemostasis is achieved**;
  - **optimal duration** of prophylaxis is **unknown**, but it is usually given for a **minimum of 10 to 14** days and **can be extended for up to 35 days**;
  - **some experts suggest** a duration in the lower end of the range (**10 to 14 days) for total knee** arthroplasty or higher end of the range (~**30 days) for total hip arthroplasty** (Ref).
  - For **extended duration of prophylaxis**, may **transition to an oral anticoagulant or alternative SUBQ anticoagulant with less frequent dosing** (Ref).

UNFRACTIONATED HEPARIN (UFH)

- **Pregnancy**:
- **Prophylactic dose** (also referred to as intermediate dose to account for weight gain during pregnancy):
  - **First trimester**: SUBQ: **5,000 to 7,500 units every 12** hours (Ref).
  - **Second trimester**: SUBQ: **7,500 to 10,000 units every 12 hours** (Ref).
  - **Third trimester**: SUBQ: **10,000 units every 12 hours** (**reduce dose if the aPTT becomes elevated**) (Ref).

LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- are derived from the **depolymerization of porcine UFH**. Like UFH, **LMWHs bind to antithrombin** via a specific pentasaccharide sequence to expose an active site for the neutralization of factor Xa.
- In comparison to UFH, LMWHs **have increased bioavailability (>90% after SC injection**), **longer half-lives** (approximately **4 to 6 hours**) (half life of of UFH is about 60 to 90 minutes), and **more predictable elimination rates**.

LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- **Most patients treated** with weight-based once- or twice-daily SC LMWH injections **do not require laboratory monitoring** for anticoagulant effect, a distinct advantage over continuous IV infusions of UFH.
- Patients who do require monitoring include those with **significant renal insufficiency**, **pediatric** patients, **obese** patients greater than 120 kg, and **pregnant** patients.
- **Monitoring may be performed using anti-Xa activity** assays.

ENOXAPARIN

- **Prophylactic** enoxaparin = 40mg/day
  - **Dose adjustment** required/precaution advised for **CrCl < 30mL/min**
  - Dose adjustment required/precaution advised for **obese** patients with a BMI ≥ 40
  - Dose adjustment in pediatrics:

Prophylactic Dose	Patients <2mths of age Or < 20kg	20 to 50kg	> 50kg
	Consult Clinical Haematology	20mg once daily	40mg once daily > 100kg, consult Clinical Haematology

ENOXAPARIN

- **BMI 30 to 39 kg/m^2:**
  - Use **standard prophylaxis dosing (40 mg once daily)**.[2] Some experts **use weight-based dosing (ie, 0.5 mg/kg based on TBW once or twice daily**, depending upon level of VTE risk).Δ[3,4]
- **BMI ≥40 kg/m^2:**
  - Empirically **increase standard prophylaxis dose by 30%** (ie, from **30 mg every 12 hours to 40 mg every 12 hours**).◊[2] Some experts use weight-based dosing (ie, **0.5 mg/kg based on TBW** once or twice daily, depending upon level of VTE risk).Δ[3-7]
- **High VTE-risk bariatric surgery with BMI ≤50 kg/m^2:** 40 mg every 12 hours.§[8,9]
- **High VTE-risk bariatric surgery with BMI >50 kg/m^2:** 60 mg every 12 hours.§[9]

IVC FILTER PLACEMENT

- **IVC filter insertion is not recommended for primary prophylaxis**.

- Prophylactic **insertion of retrievable IVC filters** has been **suggested for *VTE prophylaxis*** in **high-risk young trauma** patients, **bariatric surgical patients**, and some patients with **malignancy** or **hypercoagulable states** **who cannot receive anticoagulation therapy for a short period of time**.

- Careful follow-up is required to assure all potentially removable filters are in fact removed.

THANKS FOR YOUR KIND ATTENTION