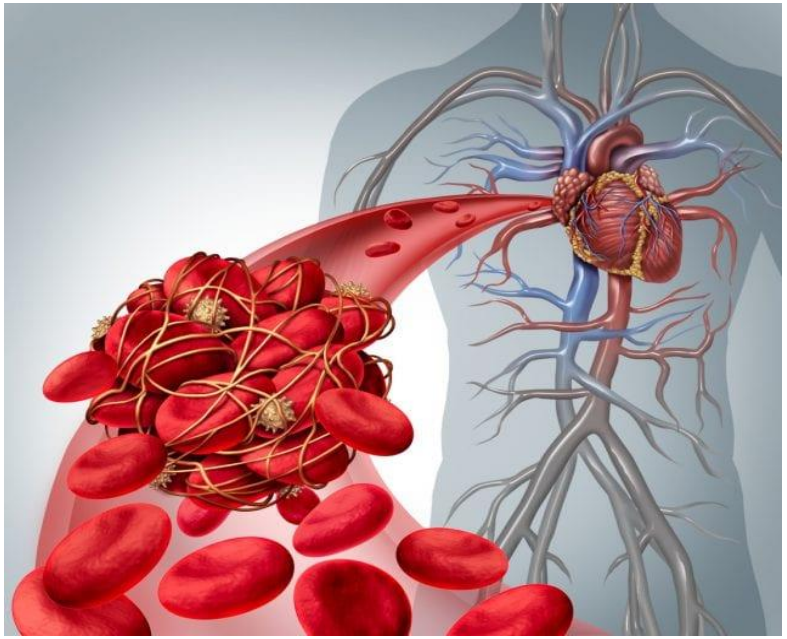
Venous Thromboembolism Prophylaxis in Hospitalized Obese Patients: Dose it Matter?



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https://www.europeanpharmaceuticalreview.com/news/42756/vte-therapeutics-market-3-billion-2025/

Disclosure

I have no actual or potential conflict of interest in relation to this presentation.

Learning Objectives

Pharmacists:

- Assess risk factors for venous thromboembolism (VTE) to determine if VTE prophylaxis is indicated in hospitalized patients
- List dosing of anticoagulants for VTE prophylaxis in hospitalized obese and non-obese patients
- Evaluate dosing and frequency of anticoagulants for VTE prophylaxis in hospitalized obese patients

Pharmacy Technicians:

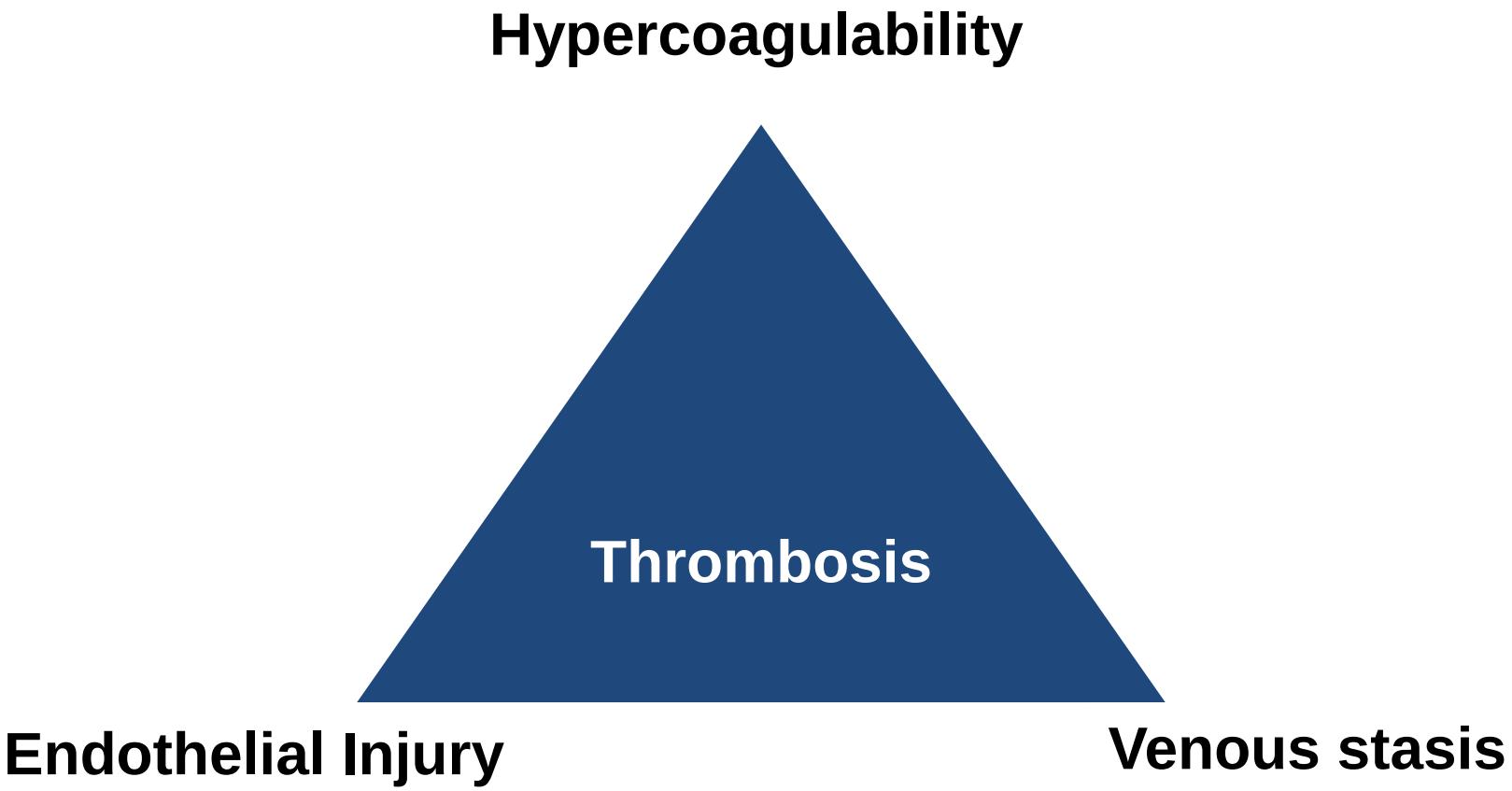
- Identify risk factors for which venous thromboembolism (VTE) prophylaxis is indicated in hospitalized patients
- List anticoagulants that are used for VTE prophylaxis in hospitalized patients
- Recall dosing and frequency of anticoagulants for VTE prophylaxis in hospitalized obese patients

Epidemiology

- VTE occurs in ~1% of hospitalized patients every year (15-20% without prophylaxis)
- 2008: Call to Action released by Surgeon General to reduce nosocomial VTE
- VTE prophylaxis: common core measure by The Joint Commission

J Thromb Haemost. 2007 Mar;5(3):632-4.
JAMA. 2005 Feb 9;293(6):715-22.
Br J Haematol. 2005 Feb;128(3):291-302.

Virchow's Triad



Cancers (Basel). 2018 Oct 11;10(10).
J Thromb Haemost. 2003 Dec;1(12):2463-5.
Clin Med Insights Oncol. 2014 Dec 4;8:129-37.
J Transl Med. 2011 Oct 20;9:179.

VTE Risk Assessment Methods

- Padua Risk Score
- Geneva risk score (see appendix)
- IMPROVE VTE score (see appendix)

Padua Score

Padua VTE Risk Score	
Active cancer, previous VTE, reduced mobility, thromboembolic condition	+3
Trauma or surgery < 1 mo.	+2
Age ≥ 70 years, heart or respiratory failure, acute MI or stroke, acute infection or rheumatologic disorder, BMI > 30 kg/m^2, ongoing hormonal treatment	+1

Padua VTE Risk Score Interpretation	
Total Risk Score	Interpretation
< 4 points	Prophylaxis is NOT indicated
≥ 4 points	Prophylaxis is indicated

VTE Chemoprophylaxis: History

- Chemoprophylaxis: implemented in the 1970s
- Absolute risk reduction (ARR) of VTE with chemoprophylaxis vs. no prophylaxis: up to 18%

Samama, et al. *N Engl J Med* 1999; 341:793-800. (MEDENOX).			
Population	**Intervention**	**Comparator**	**Outcomes (40mg vs. placebo)**
Non-ICU patients with expected LOS ≥ 6 days	Enoxaparin 20mg (n=287) or 40mg (n=291)	Placebo (n=288)	VTE on day 1-14: 5.5% vs. 14.9% (p=<0.001) Hemorrhage (major + minor): 8.6% vs. 12.6% (NS)

VTE Chemoprophylaxis: Dosing and Monitoring

Standard Dosing for VTE Prophylaxis	
Enoxaparin	**Heparin**
40mg SQ q24h	5000 units q12h or q8h

Enoxaparin Goal Anti-Xa Levels	
Prophylaxis	**Treatment**
0.2-0.5 IU/mL	0.5-1.0 IU/mL (q12h dosing) 1.0-2.0 IU/mL (q24h dosing)

Review Question #1

Which of the following is a VTE risk assessment tool to evaluate VTE risk in hospitalized patients?

A. HAS-BLED score

B. Padua score

C. MELD score

D. CHA_2DS_2-VASc score

Review Question #1

Which of the following is a VTE risk assessment tool to evaluate VTE risk in hospitalized patients?

A. HAS-BLED score

B. Padua score

C. MELD score

D. CHA_2DS_2-VASc score

Obesity

- The proportion in the U.S. is steadily increasing
- 6-fold increased risk for VTE
- Pharmacokinetic changes: Increased Vd, Reduced tissue perfusion
- Enoxaparin and heparin poorly distribute into adipose tissue
  - As little as 0.7 mg/kg to achieve therapeutic anti-Xa levels

Review Question #2

Which of the following characteristics about obesity are true?

A. Decreased risk for VTE
B. Decreased volume of distribution
C. Increased blood flow into adipose tissue
D. Poor distribution of heparin into adipose tissue

Review Question #2

Which of the following characteristics about obesity are true?

A. Decreased risk for VTE
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C. Increased blood flow into adipose tissue
D. Poor distribution of heparin into adipose tissue

Controversy

- Studies that assessed VTE prophylaxis dosing in obese patients investigated a plethora of doses and demonstrated conflicting results
- No consensus on dosing recommendations, especially in obese patients

Controversy

2018 ASH Guidelines	2012 Chest Guidelines
VTE Prophylaxis Recommendations – LMWH preferred over UFH – LMWH preferred over DOACs **Research Priorities Identified** – Determining optimal dosing of chemoprophylaxis – Should dosing be increased in obese patients?	**VTE Prophylaxis Recommendations** – LMWH preferred over UFH – Heparin BID preferred over TID – No discussion of dosing in obese patients

Clinical Controversy

What is the most appropriate dosing of anticoagulants for VTE prophylaxis in hospitalized obese patients?

Clinical considerations

- Prophylaxis dosing: syringe size increments (i.e., no wasting)
- Pharmacokinetic changes in obesity

Beall J, et al.

Efficacy and safety of high-dose subcutaneous unfractionated heparin prophylaxis for the prevention of venous thromboembolism in obese hospitalized patients.

Hosp Pharm. 2016;51(5):376-381.

Beall, et al.
Study Design

- Retrospective, single-center, cohort study
- Study Groups:
  - Conventional-Dose: Heparin 5000 units SQ three times daily
  - High-Dose: Heparin 7500 units SQ three times daily

Hosp Pharm. **2016;51(5):376-381.**

Inclusion Criteria

Inclusion Criteria	Exclusion Criteria
▪ Obese patients, identified by ICD-9 codes ▪ 3 or more doses of heparin administered	▪ Age < 18 years old ▪ VTE or bleeding on admission ▪ Receipt of enoxaparin during hospitalization ▪ Receipt of therapeutic anticoagulation on admission or during hospitalization ▪ Pregnancy or peripartum ▪ Imprisonment ▪ Paraplegia ▪ Major surgery ▪ Inpatient rehabilitation ▪ History of heparin-induced thrombocytopenia

Hosp Pharm. 2016;51(5):376-381.

Outcomes

Primary outcomes identified by ICD-9 codes:

- Nosocomial VTE—No VTE on admission or within 30 days of previous admission
- Bleeding— bleeding not present at the time of admission and occurring after 24h of UFH
- Major bleeding—per ISTH definitions
  - (See appendix

Hosp Pharm. **2016;51(5):376-381.**

Statistical Analysis

- Unpaired Student's t test: continuous, parametric variables
- Chi-square test: categorical variables
- Mann-Whitney U test: nonparametric data
- Alpha significance: < 0.05 for all statistical tests

Hosp Pharm. **2016;51(5):376-381.**

Baseline Characteristics

Patient Characteristics	Conventional-Dose N=2182	High-Dose N=196	p Value
Age (yrs)–mean(SD)	58 (14.3)	54 (13.3)	<0.0001
Female	61.8%	46.9%	<0.0001
LOS—median (range)	4 (1—188)	7 (1—136)	<0.0001
CKD	31.7%	41.8%	0.004
ICU Admission	17.3%	43.4%	<0.0001
Active Cancer	5.7%	2%	0.03
Respiratory failure	13.5%	48.5%	<0.0001
History of VTE	3.5%	3.6%	0.98

Hosp Pharm. 2016;51(5):376-381.

Outcomes

Outcomes	Conventional-Dose N=2182	High-Dose N=196	P Value
Nosocomial VTE	5 (0.23%)	2 (1.02%)	0.05
DVT	3	2	
PE	2	0	
Bleeding	2 (0.09%)	0 (0)	0.67

Hosp Pharm. 2016;51(5):376-381.

Critique

Author's Conclusion: "This study failed to demonstrate a statistically significant reduction in the rate of nosocomial VTE in obese patients who received high-dose heparin thromboprophylaxis."

Strengths	Limitations	Other
• **Relatively large sample size** • **Appropriate definitions for outcomes** • **Appropriate inclusion/exclusion criteria** • **Analyzed appropriate comorbidities and characteristics**	• **Retrospective design** • **Outcomes identified by ICD-9 codes** • **Differences in baseline characteristics** • **Difference in sample size**	• **Low rates of VTE**

Hosp Pharm. **2016;51(5):376-381.**

Beal, et al.
Take Home Points

- High dose heparin neither decreased risk of VTE nor increased risk of bleeding compared to conventional dosing
- Limited by differences in baseline characteristics, particularly LOS

Joy M, et al.

Safety and efficacy of high-dose unfractionated heparin for prevention of venous thromboembolism in overweight and obese patients.

Pharmacotherapy. 2016;36(7):740-748.

Study Design

- Single-center, retrospective observational cohort study
- Study Groups:
  - Low-Dose (LD): Heparin 5000 units SQ every 8 hours
  - High-Dose (HD): Heparin 7500 units SQ every 8 hours

Pharmacotherapy. 2016;36(7):740-748.

Joy, et al.

Inclusion Criteria	Exclusion Criteria
• Age ≥ 18 years old • Weight > 100 kg • Heparin prophylaxis at above doses during hospitalization	• LOS <48 hours • Patients who were admitted with VTE • Patients who required anticoagulation • History of or diagnosed with atrial fibrillation during their hospitalization • Received enoxaparin for VTE prophylaxis at any time during hospitalization

Pharmacotherapy. 2016;36(7):740-748.

Outcomes

- Primary outcome: Confirmed VTE
  - DVT diagnosed by LE US
  - PE diagnosed by CT chest
- Secondary Outcomes:
  - Major and minor bleeding (ISTH definitions)
  - Mortality

Pharmacotherapy. 2016;36(7):740-748.

Statistical Analysis

- To meet power:
  - Effect size of 9.3% in the high-dose group
  - Effect size of 5.7% in the low-dose group
  - 1788 patients included
- Chi-squared test: categorical variables an
- Student t test: continuous variables
- Multivariable logistic regression model: To identify risk factors for VTE occurrence
- 2-tailed test of statistical significance: $p<0.05$

Pharmacotherapy. 2016;36(7):740-748.

Patient Characteristics

Patient Characteristics	BMI 25–29.9		BMI 30–34.9		BMI 35–39.9		BMI ≥ 40	
	HD (n=23)	LD (n=41)	HD (n=144)	LD (n=123)	HD (N=152)	LD (n=171)	HD (n=432)	LD (n=239)
Weight—mean (SD)	106±6	102±11	109±7	106±7	117±13	114±11	147±31	135±25
BMI—mean (SD)	29±0.9	29±1.3	33±1.4	33±1.4	38±1.3	37±1.4	51±11	48±8
Major surgery	22%	20%	33%	18%	16%	30%	15%	37%
ICU upon admission—%	61%	27%	56%	36%	49%	28%	40%	13%
PMH—%								
VTE	4%	7%	0.7%	2%	2%	1%	4%	4%
Cancer	9%	10%	8%	3%	0.7%	1%	6%	7%
Heart Failure	17%	10%	8%	6%	8%	14%	19%	9%
LOS—median (IQR)	7 (4-9)	3 (2-7)	5 (3-10)	4 (2-8)	6 (3-12)	3 (2-6)	5 (3-11)	3 (2-6)
Total days of heparin received—median (IQR)	5 (3-9)	3 (2-6)	5 (3-8)	3 (2-6)	5 (3-9)	3 (3-5)	5 (3-10)	3 (2-5)

Pharmacotherapy. 2016;36(7):740-748.

Outcomes

Outcomes	High-Dose (N=751)	Low-Dose (N=584)	P Value
VTE	3%	1.5%	0.14
DVT	2.3%	1.4%	0.43
PE	0.9%	0.2%	0.08
Bleeding—all patients			
≥ 2-g/dl Hgb drop in 24-hr period	10%	7%	**<0.01**
≥ 2-g/dl Hgb drop from admission	27%	18%	0.09
≥ 2 units of pRBCs transfused	11%	8%	**0.04**
Bleeding—floor patients			
≥ 2-g/dl Hgb drop in 24-hr period	9%	5%	0.07
≥ 2-g/dl Hgb drop from admission	21%	14%	**0.02**
≥ 2 units of pRBCs transfused	10%	4%	**<0.01**
Bleeding—floor patients with BMI ≥ 40			
≥ 2-g/dl Hgb drop in 24-hr period	7%	4%	0.17
≥ 2-g/dl Hgb drop from admission	20%	10%	**0.01**
≥ 2 units of pRBCs transfused	10%	3%	**0.02**

Pharmacotherapy. 2016;36(7):740-748.

Outcomes

Outcomes	BMI 25–29.9		BMI 30–34.9		BMI 35–39.9		BMI ≥ 40	
	HD (n=23)	LD (n=41)	HD (n=144)	LD (n=123)	HD (N=152)	LD (n=171)	HD (n=432)	LD (n=239)
VTE	4%	2%	1%	1.5%	4%	1%	3%	2%
DVT	4%	2%	—	1%	3%	1%	3%	2%
PE	—	—	1%	1%	2%	—	0.5%	—
≥ 2-g/dl Hgb drop in 24 hr	13%	5%	15%	11%	11%	8%	7%	8%
≥ 2-g/dl Hgb drop from ad.	17%	20%	31%	28%	30%	18%	25%	12%
≥ 2 units of pRBCs trans.	9%	3%	13%	9%	19%	11%	11%	5%

Pharmacotherapy. 2016;36(7):740-748.

Critique

Author's Conclusion: ""This study failed to demonstrate a statistically significant reduction in the rate of nosocomial VTE in obese patients who received high-dose heparin thromboprophylaxis."

Strengths	Limitations	Other
• **Large sample size** • **Appropriately defined outcomes** • **Analyzed appropriate comorbidities and characteristics** • **Stratification of outcomes by heparin dose and by BMI category**	• **Retrospective design** • **Failed to meet power** • **LOS, ICU admission, and respiratory failure significantly higher in high-dose group**	• **High rates of bleeding in both groups** • **Larger numbers of VTE in BMI < 40 group** • **No assessment of symptomatic vs. incidental VTE**

Pharmacotherapy. 2016;36(7):740-748.

Joy et al.
Take-Home Points

- High dose heparin was not associated with a decreased risk of VTE, but an increased risk of bleeding.
- Limited by the study's failure to meet power and differences in patient characteristics.

Borkgren-Okonek MJ, et al**.**
Enoxaparin thromboprophylaxis in gastric bypass patients: extended duration, dose stratification, and antifactor Xa activity.
Surg Obes Relat Dis. 2008;4(5):625-631.

Study Design

- Prospective, open-label trial
- Study Groups:
  - BMI ≤ 50 kg/m2 : enoxaparin 40mg every 12 hours
  - BMI > 50 kg/m2 : enoxaparin 60mg every 12 hours
- Enoxaparin started 12 hours after surgery, through hospitalization, and for 10 days after discharge
- Sequential compression devices were applied throughout hospitalization
- Ambulation initiated day of or day after surgery

Surg Obes Relat Dis. 2008;4(5):625-631.

Borkgren-Okonek, et al.

Inclusion Criteria	Exclusion Criteria
– ≥ 18 years old – Bariatric surgery candidate and was to receive Roux-en-Y gastric bypass (RYGB) surgery	• SCr > 1.6 mg/dL • Chronic warfarin use • Contraindication to UFH or LMWH • History of VTE or hypercoagulable state

Surg Obes Relat Dis. 2008;4(5):625-631.

Outcomes

- Primary outcomes:
  - Efficacy: clinically evident VTE within 3 months post-surgery
    - Lower extremity US or CT Chest performed in symptomatic patients
  - Safety: major bleeding (ISTH definition)

Surg Obes Relat Dis. 2008;4(5):625-631.

Baseline Characteristics

Patient Characteristics	BMI ≤ 50 (n=124)	BMI > 50 (n=99)
Age (years)—mean (SD)	44.7 (10.1)	44.3 (10.6)
Weight, kg—mean (SD)	125.5 (18.5)	161.4 (27.3)
BMI—mean (SD)	44.9 (3.7)	57.4 (6.4)
Length of Stay (LOS)—median	3.4 (1.5)	3.6 (1.9)
Female—no.	96	72
VTE Risk Factors—no.		
DM	36	30
OSA	53	76

Surg Obes Relat Dis. 2008;4(5):625-631.

Outcomes

Anti-Xa (IU/mL)	All (n=206)	40mg Q12H (n=109)	60mg Q12H (n=97)
<0.18	18%	21%	14.4%
0.18—0.44	74.3%	79%	69.1%
>0.44	7.8%	—	16.5%

- VTE: n=1
- Major bleeding: n=5 (n=4 in 40mg arm)

Surg Obes Relat Dis. 2008;4(5):625-631.

Critique

Author's Conclusion: ""This BMI-stratified, extended enoxaparin dosing regimen provided well-tolerated, effective prophylaxis against venous thromboembolism in patients undergoing gastric bypass surgery."

Strengths	Limitations	Other
• **Large sample size** • **Prospective design** • **Analysis of anti-Xa levels**	• **No mention of statistical analyses** • **Small number of included patients**	• **Short LOS** • **Low rates of VTE** • **Low rates of bleeding** • **Small number of outcomes** • **Use of SCDs throughout hospitalization** • **Utilized thromboprophylaxis after discharge** • **Only included patients undergoing gastric bypass surgery**

Surg Obes Relat Dis. 2008;4(5):625-631.

Take-Home Points

- Low rates of both VTE and bleeding associated with the use of BMI-stratified enoxaparin dosing
- Definitive BMI categories used for dosing strengthen the results of this study

Additional Heparin Studies

Study	Study Des.	Population	Interv.	Sample Size	Baseline Char.	Outcomes
Lee, et al. 2017	Retro. Cohort Study	Critically ill non-obese and obese patients	Heparin 5000u BID or TID	Non-obese: N=2813 Obese: N=243	<u>Weight (kg)</u> Non-obese: 78.57 ± 18.07 Obese: 134.11 ± 31.55 <u>BMI (kg/m^2)</u> Non-obese: 27.15 ± 5.15 Obese: 47.75 ± 9.18	VTE: 2.1% vs. 3%; P=0.11
Pantanwala, et al. 2018	Retro. Cohort Study	Hospital. obese and non-obese patients	Heparin 5000u q8h	Non-obese: n=3437 Obese: n=1673	<u>BMI</u> Avg. Obese: 37 ± 8 Non-obes.: 24 ± 4	VTE: 0.6% vs. 0.7%; P=0.7 Intracranial bleeding: 0.1% vs. 0.2%; P=0.34 GI bleeding: 0.4% vs. 0.4%; P>0.99

Heart Vessels. 2019 Apr;34(4):678-687.
J Oncol Pharm Pract. 2018 Apr;24(3):185-189.

Additional Heparin Studies

Study	Study Design	Population	Interv.	Sample Size	Baseline Charact.	Outcomes
Peters, et al. 2016	Retro. chart review	MICU patients	Heparin 5000 units TID	BMI < 30: n=285 BMI > 30: n=276	Avg. BMI: < 30: 24.8 ± 3.3 >30: 38.8 ± 8.8	VTE: 12 vs. 18; p=0.222
Cotter, et al. 2005	Retro. cohort study	Morbidly obese patients undergoing gastric bypass	Heparin 5000 units q8h	N=107	Avg. BMI: 51.3 (37-82) Avg. LOS: 4.3 (3-7) Avg. Risk factors for VTE: 3.4 (2-7)	VTE: n=1 (16 days post-operatively)
Miller, et al. 2004	Retro. review	Roux-en-Y Gastric Bypass Surgery	Heparin 5000 or 7500 units q8h	N=255	Avg. BMI: 50 Avg. Weight: 138 kg LOS: 2.2 days (1-94)	VTE: n=2 Postoperative bleeding: n=6

Additional Enoxaparin Studies

Study	Study Des.	Pop.	Interv.	Sample Size	Baseline Char.	Outcomes
Miranda, et al. 2017	RCT	Hosp. obese patients	40mg or 60mg SQ daily	40mg: N=45 60mg: N=46	Weight 100 kg [90—111 or 114] BMI 35-37 [33-40]	**Therapeutic aXa**: 31% vs. 69%; P=0.007 **Minor bleeding:** 4% vs. 4%
Alnatsheh, et al. 2019	Retro. Cohort Study	Hosp. obese and non-obese patients	30mg BID or 40mg daily	Non-obese: N=118 Overweight: N=112 Obese: N=198	Weight (kg): 62 vs. 80 vs. 102 BMI: 22.1 vs. 27.4 vs. 36.6 Median LOS—days 6 (4–9) vs. 5 (4–9 vs. 5 (4-8)	VTE (no.): 3 vs. 2 vs. 3; P=0.81
Al Otaib, et al. 2017	Prosp. cohort study	Hosp. obese surgical patients	0.5mg/kg daily	N=50	BMI: 40.5 ± 5 (range: 35-55) Weight: 101 ± 18 (range: 74-150) Average dose: 50 ± 9.8 mg LOS: 11 ± 7 days	**Reached target aXa level (0.2-0.6):** 88% No VTE or bleeding

Additional Enoxaparin Studies

Study	Study Design	Pop.	Interv.	Sample Size	Baseline Char.	Outcomes
Rondina, et al. 2010	Prosp. cohort study	Morbidly obese hosp. patients	0.5 mg/kg daily	N=26	BMI: 48.1 ± 11.1 Weight: 135.6 ± 25.3 kg Avg. LOS: 3 days Avg. dose: 67mg ± 12 mg	No bleeding events No VTE Avg. aXa level peak: 0.25 +/- 0.11
Steib,et al. 2015	RCT	Gastric bypass patients	40mg daily vs. 60mg daily vs. 40mg BID	40mg daily: n=44 60mg daily: n=44 40mg BID: n=47	Average BMI: 40mg daily: 49 ± 1 60mg daily: 48 ± 1 40mg BID: 47 ± 1	No thromboembolic events Bleeding events: n=1,2,6 Ther. anti-Xa: 12.8%, 56.4%, 27.3%; P<0.001
Scholten, et al. 2002	Pros. cohort study	Morbidly obese bariatric surgery patients	30mg BID vs. 40mg BID	N=481 (30 BID: n=92; 40 BID: 389)	Avg. BMI: 51.7 vs. 50.4 Avg. LOS: 5.67 vs. 3.81 days (P < 0.05)	LOS: 5.67 vs. 3.81 days; P<0.05 Post-operative DVT: 5.4% vs. 0.6%; P<0.01 Treated hemorrhage: n=1 vs. 1

Additional Enoxaparin Studies

Study	Study Design	Pop.	Interv.	Sample Size	Baseline Char.	Outcomes
Scholten, et al. 2002	Prosp. cohort study	Morbidly obese patients undergoing bariatric surgery	Enoxaparin 30mg BID vs. enoxaparin 40mg BID	N=481 (30 BID: n=92; 40 BID: 389)	Avg. BMI: 51.7 vs. 50.4 Avg. LOS: 5.67 vs. 3.81 d (P < 0.05)	LOS: 5.67 vs. 3.81 days; P<0.05 Post-operative DVT: 5.4% vs. 0.6%; P<0.01 Treated hemorrhage: n=1 vs. 1
Steele, et al. 2015	RCT	Bariatric surgical patients	40mg BID vs. fondaparinux 5mg daily	N=198 (enox, n=98; fonda, n=100)	Avg. BMI: 45.4 ± 5.4	Ther. aXa: 32.4% vs. 74.2% DVT: 2.4% vs. 2.2% Minor bleeding: 5.1% vs. 3.0% (NS)
Brunetti, et al. 2019	Retro. Cohort Study	Obese patients undergoing sleeve gastrectomy	40mg SQ BID vs. heparin	Enoxaparin: n=16 Hep 5000: n=7 Hep 7500: n=37	Avg. Weight 124.3 ± 25.5 vs. 140.6 ± 21.2 Avg. BMI 41.8 ± 5.9 vs. 45.8 ± 6.9	aXa >0.1: 93.8% vs. 4.5%; P<0.0001 VTE: none Major bleeding: n=1 Minor bleeding: 87.5% vs. 27.3%; P<0.0001

Additional Enoxaparin Studies

Study	Study Design	Pop.	Interv.	Sample Size	Baseline Char.	Outcomes
Bickford, et al. 2013	Prosp. cohort study	Obese trauma patients	0.5mg q12h	N=86 BMI	Avg. BMI: 35.3 ± 9.8 Avg. Weight: 113.3 ± 30 Avg. LOS: 9.5 ± 1.0	Achieved target aXa: n=74 VTE: n=18 (16 before enoxaparin was initiated)
Ludwig, et al. 2011	Retro. cohort study	Obese SICU patients	0.5mg q12h	N=23	BMI: 46.4 [36-77] Weight: 136 kg [97-267] LOS 15.8 days [4-39]	Therapeutic aXa: 91% Bleeding: n=1 Minor bleeding: n=1

Direct oral anticoagulant (DOAC) studies

Goldhaber SZ, et al. Apixaban versus enoxaparin for thromboprophylaxis in medically ill patients (ADOPT). *N Engl J Med.* 2011 Dec 8;365(23):2167-77.				
Population	**Intervention**	**Comparator**	**Baseline Char.**	**Outcomes(apixaban vs. enoxaparin)**
Hospitalized, medically ill patients	Apixaban 2.5mg PO BID	Enoxaparin 40mg SQ daily for 7 ± 4 days	BMI > 30 kg/m2: 44.5% vs. 44.3%	VTE or VTE-related death at 10 days: 2.71% vs. 3.06%; P=0.44 Major bleeding: 0.47% vs. 0.19%; P=0.04

Cohen AT, et al. Rivaroxaban for thromboprophylaxis in acutely ill medical patients (MAGELLAN). *N Engl J Med*. 2013 Feb 7;368(6):513-23.				
Population	**Intervention**	**Comparator**	**Baseline char.**	**Outcomes (rivaroxaban vs. enoxaparin)**
Hospitalized, medically ill patients	Rivaroxaban 10mg PO daily for 35 ± 4 days	Enoxaparin 40mg SQ daily	Mean weight: 77.5kg vs. 77.3kg Mean BMI: 28.2 vs. 28.2	VTE or VTE-related death: 2.7% vs. 2.7%; P=0.003 for non-infer. Clinically relevant bleeding: 2.8% vs. 1.2%; P<0.001

Recommendations

- In patients with a CrCl < 30 mL/min:
  - If BMI < 50 kg/m2 or weight < 150 kg → UFH 5000 units q8h.
  - If BMI ≥ 50 kg/m2 or weight ≥ 150 kg → UFH 7500 units q8h.

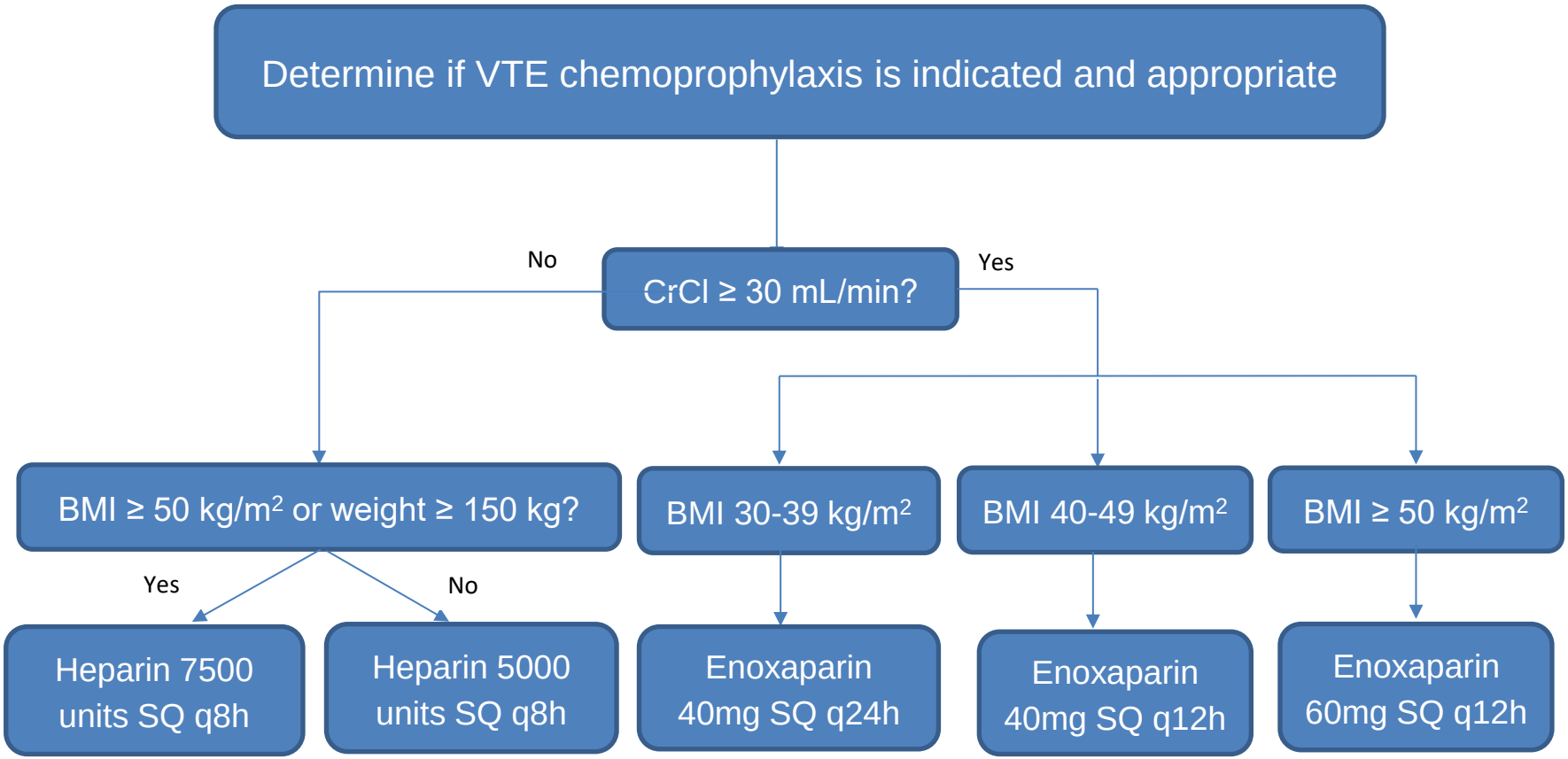
Recommendations

- In patients with a CrCl ≥ 30 mL/min:
  - If BMI 30-40 kg/m2 → enoxaparin 40mg SQ q24h.
  - If BMI 40-50 kg/m2 → enoxaparin 40mg SQ q12h.
  - If BMI ≥ 50 kg/m2 → enoxaparin 60mg SQ q12h.

Recommendations

- I recommend the use of LMWH or UFH over the use of DOACs in this population.
- I recommend against the routine use of anti-Xa level monitoring for VTE prophylaxis.

Treatment Algorithm



Summary

- Nosocomial VTE remains a concern in hospitalized patients
- More research into optimal dosing for VTE prophylaxis in obese patients is needed

Reference for Pharmacists

1. Schünemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Adv*. 2018 Nov 27;2(22):3198-3225.

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- Amanda Kitten, PharmD, MSc

Post-Test Question #1

Which of the following is a risk factor for developing hospital-acquired VTE?

A. Active cancer
B. Chronic obstructive pulmonary disease (COPD)
C. Cirrhosis
D. Underweight (BMI < 18.5 kg/m2)

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Post-Test Question #2

Which of the following reflects standard dosing of enoxaparin for VTE prophylaxis in non-surgical, hospitalized patients?

A. Enoxaparin 30mg SQ every 24 hours
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Post-Test Question #3

The heparin dosing regimens that have been most studied for VTE prophylaxis in hospitalized obese patients are ____ and ____.

A. 2500 units SQ q8h; 7500 units SQ q8h
B. 5000 units SQ q24h; 5000 units SQ q12h
C. 5000 units SQ q12h; 7500 units SQ q8h
D. 5000 units SQ q8h; 7500 units SQ q8h

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Post-Test Question #4

MB is a 75-year-old male with a PMH of VTE, type 2 DM, HTN, and heart failure with reduced ejection fraction (HFrEF) who is admitted to the medical ward for HF exacerbation treatment. The patient's weighs 125 kg (BMI 35 kg/m^2) and has a creatinine clearance of 120 mL/min (SCr at baseline). Which of the following enoxaparin regimens for VTE prophylaxis are most appropriate for MB?

A. Enoxaparin 30mg SQ q24h
B. Enoxaparin 40mg SQ q24h
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Post-Test Question #4

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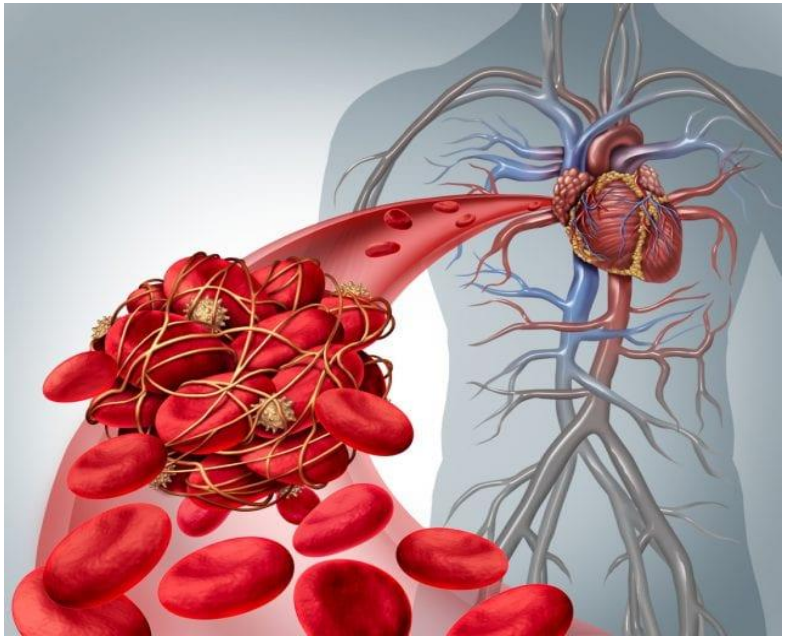
Venous Thromboembolism Prophylaxis in Hospitalized Obese Patients: Dose it Matter?



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https://www.europeanpharmaceuticalreview.com/news/42756/vte-therapeutics-market-3-billion-2025/