



Update on Venous Thromboembolism Prophylaxis



Disclosure

- No conflicts of interest to declare



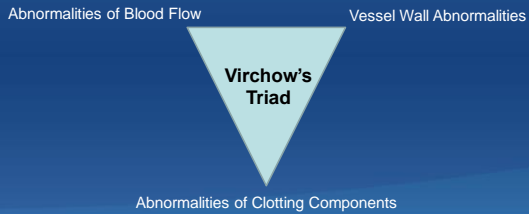
Learning Objectives

- After completion of this presentation, participants should be able to:
 - Define venous thromboembolism, its risk factors, and methods of prevention of VTE
 - Summarize the changes and recommendations in the 2012 CHEST guidelines
 - Understand the basics of the new Accreditation Canada Required Organizational Practice for VTE prophylaxis
 - Use the SaferHealthcareNow! VTE prophylaxis initiative for help implementing a VTE prophylaxis program at their institution



Venous Thromboembolism (VTE)

- Includes deep vein thrombosis (DVT) and pulmonary embolism (PE)
- **Virchow's Triad:** 3 primary factors influence formation of pathological clots





Risk Factors for VTE

- History of VTE
- Active or previous malignancy
- Recent major orthopedic surgery
- Venous compression
- Severe hemiparesis, paralysis, or immobility prior to hospitalization
- Acute neurologic disease
- Severe sepsis or post-op infection
- Extensive or lower-extremity burn
- Inherited or acquired thrombophilia
- Trauma or acute spinal cord injury
- Age > 60 years
- Obesity
- Use of estrogen-containing OCs or HRT
- Pregnancy/Postpartum
- Varicose veins
- Inflammatory bowel disease
- Heart failure
- Acute respiratory disease
- Nephrotic syndrome
- Type of anesthesia (general > epidural/spinal)
- Central venous catheterization



Anticoagulants for VTE Prophylaxis

Drug	MOA	Dosing Frequency	Route	NBPDP Benefit?
Unfractionated heparin	Inactivation of factor Xa and thrombin	BID-TID	SC	AEFGV
Low molecular weight heparin	Factor Xa inhibition > thrombin inhibition	Once daily	SC	AEF18+VW
Fondaparinux	Factor Xa inhibitor	Once daily	SC	No
Danaparoid	Factor Xa inhibition >> thrombin inhibition	BID	SC IV	No
Warfarin	Vitamin K antagonist	Once daily	PO	AEFGVW
Dabigatran	Direct thrombin inhibitor	BID	PO	No
Rivaroxaban	Factor Xa inhibitor	Once daily	PO	AEFVW
Apixaban	Factor Xa inhibitor	BID	PO	No



Rationale for VTE Prophylaxis

- Hospitalization for acute medical illness is associated with an eightfold increased risk for VTE
- Almost every hospitalized patient has at least one risk factor for VTE and most have multiple risk factors
- VTE is associated with substantial morbidity and mortality, but is also a major resource burden on the healthcare system
- VTE is one of the most common causes of preventable death in hospitalized patients
 - 30-day case fatality rate for DVT is 5% and for PE is 33%
- Long-term complications include bleeding related to anticoagulant therapy, increased risk of recurrent VTE, and post-thrombotic syndrome (30-50%)



Accreditation Canada

- ROP:
 - The team identifies medical and surgical clients at risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) and provides appropriate thromboprophylaxis.
- Tests for Compliance:
 - The organization has a written thromboprophylaxis policy or guideline.
 - The team identifies clients at risk for VTE and provides appropriate, evidence-based VTE prophylaxis.
 - The team establishes measures for appropriate thromboprophylaxis, audits implementation of appropriate thromboprophylaxis, and uses this information to make improvements to their services.
 - The team identifies major orthopedic surgery clients (hip and knee replacements, hip fracture surgery) who require post-discharge prophylaxis and has a mechanism in place to provide appropriate post-discharge prophylaxis to such patients.
 - The team provides information to health professionals and clients about the risks of VTE and how to prevent it.



Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: ACCP Evidence-Based Clinical Practice Guidelines

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**Introduction to the Ninth Edition :
Antithrombotic Therapy and Prevention of
Thrombosis, 9th ed: American College of
Chest Physicians Evidence-Based Clinical
Practice Guidelines**

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ACCP Guidelines (9th Edition)

Table 1—Major Innovations in AT9

1. Unconflicted methodologists as topic editors. Conflicted experts did not participate in final process of making recommendations.
2. Many evidence profile and summary of finding tables.
3. New insights into evidence (asymptomatic thrombosis, aspirin).
4. Quantitative specification of values and preferences based on systematic review of relevant evidence and formal preference rating exercise.
5. Article addressing diagnosis of DVT.

AT9 = Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.



Patient Values and Preferences: Systematic Review

- Recommendations involve trade-offs between benefits and risks of treatment
- Patient values and preferences are **HIGHLY** variable
 - Heterogeneity of results leaves considerable uncertainty
 - Variability and uncertainty suggests that strong recommendations should only be made when the benefits of an intervention **substantially** outweigh the risks
- Conclusions related to VTE:
 - Patients unwilling to accept small increase in risk of death to avoid post-thrombotic syndrome
 - Warfarin therapy does not have important negative impact on QOL
 - Aversion to warfarin may decrease over time after treatment initiated
 - Injection treatments well tolerated
 - Compression stockings also well tolerated, but less preferred vs. injection treatments

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Approach to Outcome Measurement in the Prevention of Thrombosis in Surgical and Medical Patients

- Provides rationale for approach to making recommendations used in VTE prophylaxis guidelines
- Reduction in asymptomatic events not an appropriate outcome
 - Estimate of frequency of symptomatic VTE and bleeding and their consequences are necessary for making appropriate recommendations
- Reviews the merits/limitations of 4 approaches to estimating the reduction in symptomatic thrombosis
 - Direct measurement of symptomatic VTE
 - Use of asymptomatic events for relative risks and symptomatic events from RCTs for baseline risk
 - Use of baseline risk estimates from studies that did not perform surveillance and relative effect from asymptomatic events in RCTs
 - Use of available data to estimate the proportion of asymptomatic events that will become symptomatic

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Medical (Non-Surgical) Patients: Methodology

- Patient values and preferences (trade-offs)
 - 1:1 ratio of symptomatic VTE to major extracranial bleeding
 - 2.5:1 ratio of symptomatic VTE to intracranial bleeding
- Estimation of baseline risk for VTE
 - Hospitalized medical patients: Padua Prediction Score
 - 11% in high-risk patients
 - Combination of DVT (6.7%), nonfatal PE (3.9%), and fatal PE (0.4%)
 - 0.3% in low-risk patients
 - Critically ill patients: 2 approaches
 - DVT: direct data for symptomatic events from trials
 - PE: derived from symptomatic PEs reported in 3 observational studies
- Estimation of baseline risk for bleeding (0.4%)
 - Derived from control arm of trials of thromboprophylaxis in medical patients



Medical (Non-Surgical) Patients: Risk Stratification

Table 2—Risk Factors for VTE in Hospitalized Medical Patients^a

Risk Factor	Points
Active cancer ^a	3
Previous VTE (with the exclusion of superficial vein thrombosis)	3
Reduced mobility ^b	3
Already known thrombophilic condition ^c	3
Recent (\leq 1 mo) trauma and/or surgery	2
Elderly age (\geq 70 y)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI \geq 30)	1
Ongoing hormonal treatment	1

Risk score \geq 4 is considered high risk
Risk score $<$ 4 is considered low risk



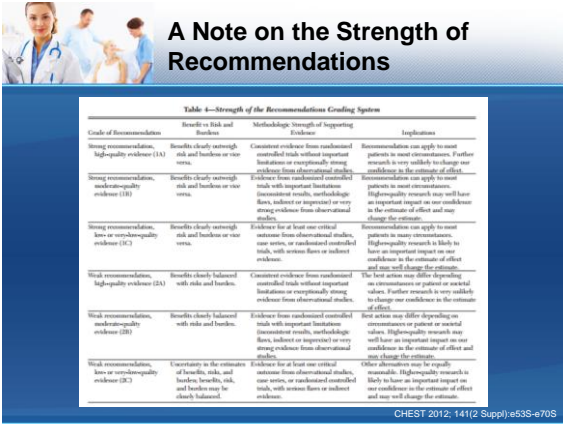
Medical (Non-Surgical) Patients: Risk Factors for Bleeding

Table 3—Independent Risk Factors for Bleeding in 10,890 Hospitalized Medical Patient^a

Risk Factor	Total Patients, No. (%) (N = 10,890)	OR (95% CI)
Active gastroduodenal ulcer	238 (2.2)	4.15 (2.21-7.77)
Bleeding in 3 mo before admission	211 (2.2)	3.64 (2.21-5.96)
Platelet count $<$ 50 x 10 ⁹ /L	179 (1.7)	3.37 (1.84-6.14)
Age \geq 85 y (vs $<$ 40 y)	1,178 (10.8)	2.96 (1.43-6.15)
Hepatic failure (INR $>$ 1.5)	219 (2.0)	2.15 (1.10-4.23)
Severe renal failure (CrCl $<$ 30 mL/min/1.73 m ²)	1,094 (11.0)	2.14 (1.44-3.20)
ICU or CCU admission	925 (8.5)	2.10 (1.42-3.10)
Central venous catheter	920 (7.5)	1.85 (1.18-3.00)
Bleomycin therapy	749 (6.9)	1.78 (1.09-2.90)
Current cancer	1,196 (10.9)	1.76 (1.20-2.61)
Male sex	5,387 (49.4)	1.48 (1.10-1.99)

Data shown were obtained by multiple logistic regression analysis for characteristics at admission independently associated with in-hospital bleeding (major bleeding and clinically relevant asymptomatic bleeding combined). CrCl = glomerular filtration rate; INR = international normalized ratio.
^aAlthough not specifically studied in medical patients, one would also expect dual antiplatelet therapies to increase the risk of bleeding.

- Patients considered to have excess risk of bleeding if they had multiple risk factors or had one of the three risk factors with the strongest association with bleeding:
 - Active gastroduodenal ulcer
 - Bleeding in 3 months prior to admission
 - Platelet count $<$ 50 x 10⁹/L

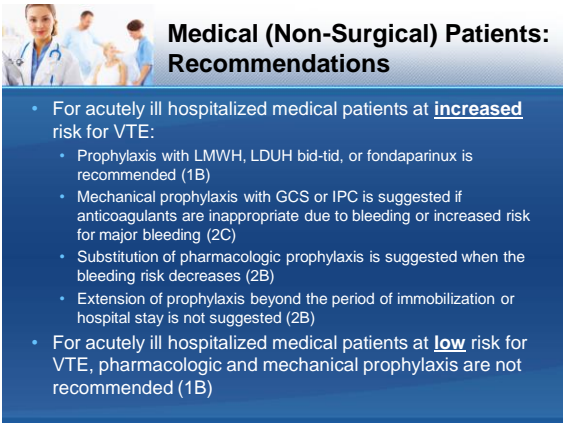


A Note on the Strength of Recommendations

Table 4—Strength of the Recommendations Grading System

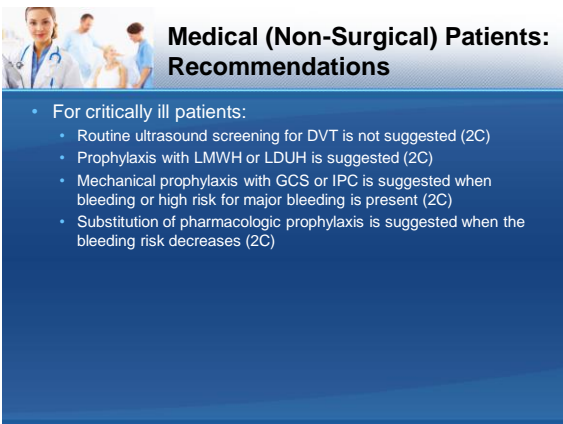
Grade of Recommendation	Benefit vs Risk and Burden	Methodologic strength of supporting evidence	Implications
Strong recommendation, high-quality evidence (1A)	Benefits clearly outweigh risks and burdens or vice versa.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change our confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risks and burdens or vice versa.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. High-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Strong recommendation, low or very-low-quality evidence (2C)	Benefits clearly outweigh risks and burdens or vice versa.	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Recommendation can apply to most patients in many circumstances. High-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits clearly balanced with risks and burdens.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	The best action may differ depending on circumstances or patient or societal values. Further research is unlikely to change our confidence in the estimate of effect.
Weak recommendation, moderate-quality evidence (2B)	Benefits clearly balanced with risks and burdens.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies.	The best action may differ depending on circumstances or patient or societal values. High-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation, low or very-low-quality evidence (2C)	Uncertainty in the estimate of benefit, risks, and burden may be clearly balanced.	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Other alternatives may be equally reasonable. High-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.

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Medical (Non-Surgical) Patients: Recommendations

- For acutely ill hospitalized medical patients at **increased** risk for VTE:
 - Prophylaxis with LMWH, LDUH bid-tid, or fondaparinux is recommended (1B)
 - Mechanical prophylaxis with GCS or IPC is suggested if anticoagulants are inappropriate due to bleeding or increased risk for major bleeding (2C)
 - Substitution of pharmacologic prophylaxis is suggested when the bleeding risk decreases (2B)
 - Extension of prophylaxis beyond the period of immobilization or hospital stay is not suggested (2B)
- For acutely ill hospitalized medical patients at **low** risk for VTE, pharmacologic and mechanical prophylaxis are not recommended (1B)



Medical (Non-Surgical) Patients: Recommendations

- For critically ill patients:
 - Routine ultrasound screening for DVT is not suggested (2C)
 - Prophylaxis with LMWH or LDUH is suggested (2C)
 - Mechanical prophylaxis with GCS or IPC is suggested when bleeding or high risk for major bleeding is present (2C)
 - Substitution of pharmacologic prophylaxis is suggested when the bleeding risk decreases (2C)



Medical (Non-Surgical) Patients: Recommendations

- For outpatients with cancer:
 - Routine prophylaxis with LMWH or LDUH is not suggested if there are no additional risk factors for VTE (2B)
 - Prophylactic use of VKA is not recommended in the absence of additional risk factors for VTE (1B)
 - Prophylaxis with LMWH or LDUH is suggested in those with solid tumors and additional risk factors for VTE (1B)
 - Prophylaxis with LMWH/LDUH (2B) or VKA (2C) is not suggested in those with indwelling central venous catheters



Medical (Non-Surgical) Patients: Recommendations

- For long-distance travelers at increased risk of VTE:
 - Frequent ambulation, calf muscle exercise, or sitting in an aisle seat are suggested (2C)
 - Use of properly fitted, below-knee GCS providing 15-30 mmHg of pressure at ankle is suggested during travel (2C)
- For long-distance travelers without risk factors for VTE, use of GCS is not suggested (2C)
- For ALL long-distance travelers, use of ASA or anticoagulants to prevent VTE is not suggested (2C)



Medical (Non-Surgical) Patients: Recommendations

- For chronically immobilized patients residing at home or in a nursing home, the routine use of VTE prophylaxis is not suggested (2C)
- Long-term daily use of mechanical or pharmacologic prophylaxis to prevent VTE is not recommended in patients with asymptomatic thrombophilia (1C)



Nonorthopedic Surgical Patients: Recommendations

- General and abdominal-pelvic surgery:
 - Very low risk: No prophylaxis recommended (1B and 2C)
 - Low risk: Mechanical prophylaxis with IPC suggested (2C)
 - *Moderate risk: LMWH, LDUH or IPC suggested (2B and 2C)
 - Moderate risk with high bleeding risk: IPC suggested (2C)
 - High risk: LMWH or LDUH recommended (1B); addition of GCS or IPC suggested (2C)
 - High risk with cancer: Extended-duration prophylaxis (4 weeks) with LMWH is recommended (1B)
 - High risk with high bleeding risk: IPC suggested until risk of bleeding decreased and pharmacologic prophylaxis can be started (2C)
 - High risk with contraindications to LDUH/LMWH: low-dose ASA, fondaparinux, or IPC suggested (2C)
 - IVC filters not suggested for primary VTE prevention (2C)
 - Surveillance with venous compression ultrasound not suggested (2C)




Nonorthopedic Surgical Patients: Recommendations

- Cardiac surgery:
 - Uncomplicated postoperative course: optimally applied IPC suggested (2C)
 - Prolonged hospital course due to complications: addition of LDUH or LMWH to mechanical prophylaxis suggested (2C)
- Thoracic surgery:
 - *Moderate risk: LDUH, LMWH, or optimally applied IPC suggested (2B and 2C)
 - High risk: LDUH or LMWH recommended (1B); addition of GCS or IPC suggested (2C)
 - High risk for major bleeding: optimally applied IPC suggested until bleeding risk decreased and pharmacologic prophylaxis can be started (2C)



Nonorthopedic Surgical Patients: Recommendations

- Craniotomy:
 - Mechanical prophylaxis with IPC suggested (2C)
 - Addition of pharmacologic prophylaxis suggested in patients at very high risk for VTE (malignancy) once adequate hemostasis is established (2C)
- Spinal Surgery:
 - Mechanical prophylaxis with IPC suggested (2C)
 - Addition of pharmacologic prophylaxis suggested in patients at very high risk for VTE (malignancy or combined anterior-posterior approach) once adequate hemostasis is established (2C)



Nonorthopedic Surgical Patients: Recommendations

- Major trauma:
 - LDUH, LMWH, or IPC suggested (2C)
 - Addition of mechanical prophylaxis to pharmacologic prophylaxis suggested in patients at high risk for VTE if not contraindicated by lower-extremity injury (2C)
 - Mechanical prophylaxis with IPC suggested in patients with contraindications to LMWH and LDUH (if no lower extremity injury), with addition of pharmacologic prophylaxis when the bleeding risk is decreased or contraindication to heparin resolves (2C)
 - Primary VTE prevention with an IVC filter is not suggested (2C)
 - Surveillance with venous compression ultrasound not suggested (2C)



Orthopedic Surgery Patients

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Prevention of VTE in Orthopedic Surgery Patients : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Yngve Falck-Ytter, Charles W. Francis, Norman A. Johanson, Catherine Curley, Ola E. Dahl, Sam Schulman, Thomas L. Ortel, Stephen G. Pauker and Clifford W. Colwell, Jr

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Orthopedic Surgery Patients: Baseline VTE Risk

Table 2—[Section 1.3.1] Estimated Nonfatal, Symptomatic VTE Rates After Major Orthopedic Surgery

	Initial Prophylaxis, Postoperative Days 0-14	Extended Prophylaxis, Postoperative Days 15-35	Cumulative, Postoperative Days 0-35
No prophylaxis	VTE 2.80% (PE 1.00%, DVT 1.80%)	VTE 1.50% (PE 0.50%, DVT 1.00%)	VTE 4.3% (PE 1.50%, DVT 2.80%)
LMWH	VTE 1.15% (PE 0.35%, DVT 0.80%)	VTE 0.65% (PE 0.20%, DVT 0.45%)	VTE 1.8% (PE 0.55%, DVT 1.25%)



Orthopedic Surgery Patients: Recommendations

- Total hip arthroplasty/total knee arthroplasty:
 - Prophylaxis with one of LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, LDUH, adjusted-dose VKA, ASA, or IPC is recommended for a minimum of 10 -14 days (1B and 1C)
 - LMWH is suggested in preference to other agents (2B and 2C)
- Hip fracture surgery:
 - Prophylaxis with one of LMWH, fondaparinux, LDUH, adjusted-dose VKA, ASA, or IPC is recommended for a minimum of 10-14 days (1B and 1C)
 - LMWH is suggested in preference to other agents (2B and 2C)



Orthopedic Surgery Patients: Recommendations

- All major orthopedic surgery:
 - Prophylaxis with LMWH should be started either 12 h or more preoperatively or 12h or more postoperatively (1B)
 - Extension of thromboprophylaxis in the outpatient period up to 35 days from the day of surgery is suggested (2B)
 - Dual prophylaxis with an anticoagulant and an IPC is suggested during the hospital stay (2C)
 - IPC or no prophylaxis is suggested in patients at increased risk of bleeding (2C)
 - Apixaban or dabigatran (alternatively rivaroxaban or adjusted-dose VKA if those unavailable) should be offered to patients refusing injections or IPC (1B)
 - IVC filter placement for primary prevention of VTE is not suggested in patients with contraindications to mechanical/pharmacologic prophylaxis (2C)
 - Doppler ultrasound screening is not recommended in asymptomatic patients prior to hospital discharge (1B)



Orthopedic Surgery Patients: Recommendations

- No prophylaxis is suggested in patients with isolated lower-leg injuries requiring leg immobilization (2C)
- No prophylaxis is suggested in patients undergoing knee arthroscopy without a history of prior VTE (2B)



SaferHealthcareNow! Initiative

- Objectives:
 - To increase the use of appropriate thromboprophylaxis in acute care hospitalized patients
 - To align with Accreditation Canada's Required Organizational Practice related to VTE prevention
- Inclusion: All acute care patients
- Exclusions:
 - Pediatrics (≤ 18 years of age)
 - Obstetrics
 - Psychiatry/mental health
 - Rehab
 - Long-term care

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SaferHealthcareNow! Initiative

- Measures:
 - Appropriate VTE prophylaxis
 - Use of order sets
 - Process of care measures linked to the recommended steps in implementing appropriate VTE prophylaxis
 - Clinical outcomes (optional)
- Included in the kit:
 - Rationale for VTE prophylaxis
 - Recommendations for appropriate prophylaxis
 - Recommendations for development of a formal process of VTE quality improvement
 - Recommendations and tools for implementation of a VTE prophylaxis program (e.g. organization-wide thromboprophylaxis policy, order sets)

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Local Initiatives in Vitalite Health Network

- Development of a regional policy for the prevention of VTE
- Development of a working group in Zone 6 (and maybe other zones??) for development of order sets for VTE prophylaxis