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

**Abnormalities of Blood Flow**

**Vessel Wall Abnormalities**

**Abnormalities of Clotting Components**

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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

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Anticoagulants for VTE Prophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Dosage Frequency</th>
<th>Route</th>
<th>NBPD Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfractionated heparin</td>
<td>Inactivation of factor Xa and thrombin</td>
<td>BID-TID</td>
<td>SC</td>
<td>AEFGV</td>
</tr>
<tr>
<td>Low molecular weight heparin</td>
<td>Factor Xa inhibition</td>
<td>Once daily</td>
<td>SC</td>
<td>AEF18x-VW</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Factor Xa inhibitor</td>
<td>Once daily</td>
<td>SC</td>
<td>No</td>
</tr>
<tr>
<td>Danaparoid</td>
<td>Factor Xa inhibition &gt; thrombin inhibition</td>
<td>BID</td>
<td>SC</td>
<td>No</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Vitamin K antagonist</td>
<td>Once daily</td>
<td>PO</td>
<td>AEFGVW</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Direct thrombin inhibitor</td>
<td>BID</td>
<td>PO</td>
<td>No</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Factor Xa inhibitor</td>
<td>Once daily</td>
<td>PO</td>
<td>AEFVW</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Factor Xa inhibitor</td>
<td>BID</td>
<td>PO</td>
<td>No</td>
</tr>
</tbody>
</table>
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
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

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

- Need to decide whether net benefit is optimized by administering or withholding antithrombotic prophylaxis
- Relevant nonfatal events in medical and surgical prophylaxis include:
  - PE/DVT
  - GI/surgical site bleeding
- Importance of these events rated and judged to be of similar importance (DVT slightly less important)
  - If antithrombotic regimen prevents more VTE events than it causes bleeding events compared with an alternative, it will be recommended
  - If therapy causes more bleeding events than it prevents VTE events, recommendations will favor withholding (or administering less aggressive) prophylaxis
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
    - 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 PE's 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>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</td>
<td>5</td>
</tr>
<tr>
<td>Previous VTE (with the exclusion of superficial veins)</td>
<td>3</td>
</tr>
<tr>
<td>History of vascular disease</td>
<td>3</td>
</tr>
<tr>
<td>History of thrombophlebitis</td>
<td>3</td>
</tr>
<tr>
<td>History of previous hospitalization with potential risk factors</td>
<td>2</td>
</tr>
<tr>
<td>History of trauma and/or surgery</td>
<td>2</td>
</tr>
<tr>
<td>History of major hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>History of active bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Active neoplastic disease or leukemia</td>
<td>1</td>
</tr>
<tr>
<td>Active infection or septic shock</td>
<td>1</td>
</tr>
<tr>
<td>History of recent surgery or trauma</td>
<td>1</td>
</tr>
<tr>
<td>History of chronic bleeding disorders</td>
<td>1</td>
</tr>
<tr>
<td>Ongoing hormonal treatment</td>
<td>1</td>
</tr>
</tbody>
</table>

Risk score ≥ 4 is considered high risk
Risk score < 4 is considered low risk

Medical (Non-Surgical) Patients: Risk Factors for 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 10^9/L
A Note on the Strength of Recommendations

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

• 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)

• 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)
### VTE Risk Assessment

<table>
<thead>
<tr>
<th>VTE Risk Category</th>
<th>Patient Population</th>
<th>Estimated baseline risk in absence of prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>&lt;7 Rogers Score</td>
<td>0.1%</td>
</tr>
<tr>
<td>Low</td>
<td>7-10 Rogers Score</td>
<td>0.4%</td>
</tr>
<tr>
<td>Moderate</td>
<td>&gt;10 Rogers Score</td>
<td>1.5%</td>
</tr>
<tr>
<td>High</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Symptomatic VTE

### Bleeding Risk Assessment

- General/abdominal-pelvic surgery: 1.2% (baseline risk 1.8 x higher in high-risk patients)
- Vascular Surgery: 1.2%
- Plastic/reconstructive surgery: Average risk
- Bariatric surgery: List of potential risk factors provided as guide
- Cardiac surgery: High risk
- Craniotomy: ~1.1%
- Spinal surgery: <0.5% (potentially severe complications)
- Trauma: 3.4-4.7%
### 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; IVC filters not suggested for primary VTE prevention (2C)
  - Surveillance with venous compression ultrasound not suggested (2C)

- **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)

- **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)

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Orthopedic Surgery Patients


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Orthopedic Surgery Patients: Baseline VTE Risk

Table 2—Estimated Unfalsified, Symptomatic VTE Rates After Major Orthopedic Surgery

<table>
<thead>
<tr>
<th>Initial Prophylaxis</th>
<th>Extended Prophylaxis</th>
<th>Cumulative Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Days 0-14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days 15-35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days 0-35</td>
</tr>
<tr>
<td>No prophylaxis</td>
<td>VTE 3.4%</td>
<td>VTE 1.3%</td>
</tr>
<tr>
<td></td>
<td>(PE 1.0%, DVT 1.9%)</td>
<td>(PE 0.5%, DVT 0.9%)</td>
</tr>
<tr>
<td>LMWH</td>
<td>VTE 1.5%</td>
<td>VTE 1.5%</td>
</tr>
<tr>
<td></td>
<td>(PE 0.3%, DVT 1.2%)</td>
<td>(PE 0.3%, DVT 1.2%)</td>
</tr>
</tbody>
</table>
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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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

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Thank you!

Questions?