What's New in Antithrombotic Treatment of VTE Disease: ACCP (CHEST) Guidelines Update 2021

Thursday | November 11, 2021 | 12:00 – 1:00pm ET

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Moderators:
Geoffrey Barnes, MD, MSc | Andrea Van Beek, RN, DNP, AGPCNP-BC
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Disclosures

The speakers have the following relevant financial relationships with commercial interests:

Deborah Siegal, MD, MSc
Aspen Pharma | Bayer | BMS/Pfizer Alliance | LEO Pharma | Novartis | Portola | Servier

Philip Wells, MD
Bayer | BMS/Pfizer Alliance | Janssen | Sanofi

Geoffrey Barnes, MD, MSc
Pfizer/Bristol-Myers Squibb | Janssen | Portola | AMAG Pharmaceuticals
National Certification Board of Anticoagulation Providers

Andrea Van Beek, RN, DNP, AGPCNP-BC
None
Antithrombotic Therapy for VTE Disease
Second Update of the CHEST Guideline and Expert Panel Report

Scott M. Stevens, MD  Scott C. Woller, MD  Lisa Baumann Kreuziger, MD  ...  Janine R.E. Vintch, MD  Philip S. Wells, MD  Lisa K. Moores, MD  Show all authors

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## Guideline Summary

<table>
<thead>
<tr>
<th>Background</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 2nd update to 9th edition</td>
<td>• GRADE methodology</td>
<td>• 29 guidance statements</td>
</tr>
<tr>
<td>• Recommendations on 17 PICO questions (4 new)</td>
<td>• Strong and weak recommendations based on certainty of evidence</td>
<td>• 4 new statements</td>
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<td></td>
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<td>• 8 modified statements</td>
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Questions that form the basis for recommendations are defined using PICO framework.

<table>
<thead>
<tr>
<th>P</th>
<th>Population</th>
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<tbody>
<tr>
<td>I</td>
<td>Intervention</td>
</tr>
<tr>
<td>C</td>
<td>Comparator</td>
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<tr>
<td>O</td>
<td>Outcomes</td>
</tr>
</tbody>
</table>
Guideline Structure

- Whether to treat
- Interventional and adjunctive treatments
- Initiation phase (~5 to 21 days)
- Treatment phase (3 months)
- Extended phase (3 months to no planned stop date)
# Evidence-to-Decision Framing

| Certainty of Evidence | Our confidence that the effect estimate is adequate to support a recommendation (high, moderate, low, very low)  
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>Reflects strengths and limitations of the evidence (study design, risk of bias, imprecision, inconsistency, indirectness, publication bias)</td>
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| Strength of Recommendations | Extent to which we can be confident that the desirable effects of an intervention outweigh its undesirable effects  
<table>
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<tbody>
<tr>
<td></td>
<td>Categorized as strong or weak</td>
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</table>
### Strength of Recommendations

**“How patients and clinicians should use these recommendations”**

<table>
<thead>
<tr>
<th></th>
<th>STRONG recommendation (&quot;We recommend...&quot;)</th>
<th>WEAK recommendation (&quot;We suggest...&quot;)</th>
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<tbody>
<tr>
<td><strong>For patients</strong></td>
<td>Most individuals would want the intervention.</td>
<td>A majority would want the intervention, but many would not.</td>
</tr>
<tr>
<td><strong>For clinicians</strong></td>
<td>Most individuals should receive the intervention.</td>
<td>Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making.</td>
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</tbody>
</table>
Four Areas of Uncertainty

- Isolated Distal DVT
- Isolated Subsegmental PE
- Cerebral Vein Thrombosis
- Extended Phase Therapy
Case 1

• 52-year-old man
• No past medical history, no major VTE risk factors
• Hemodynamically stable, BMI 32
• Normal laboratory investigations
• Acute thrombosis of left posterior tibial vein

PICO Question

Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated distal DVT?
# Isolated Distal DVT: Evidence Profile

## Selected Summary of Findings

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Absolute Effect (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE at 3 months</td>
<td>60 fewer events per 1000 cases (from 77 fewer to 21 fewer)</td>
</tr>
<tr>
<td>Major bleeding at 3 months</td>
<td>2 fewer events per 1000 cases (from 7 fewer to 29 more)</td>
</tr>
<tr>
<td>Overall mortality at 3 months</td>
<td>0 fewer events per 1000 cases (from 0 fewer to 0 more)</td>
</tr>
</tbody>
</table>
Isolated Distal DVT

PICO Question

Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated distal DVT?

In patients with isolated distal DVT of the leg...

WITHOUT severe symptoms or risk factors for extension, we suggest serial imaging of the deep veins for 2 weeks over anticoagulation

*weak recommendation, moderate-certainty evidence*

WITH severe symptoms or risk factors for extension, we suggest anticoagulation over serial imaging of the deep veins

*weak recommendation, low-certainty evidence*

Other Guidelines:
ASH 2018: no specific guidance
NICE 2020: recommendations for proximal only
Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated distal DVT?

In patients with isolated distal DVT of the leg who are managed with serial imaging...

- We recommend no anticoagulation if the thrombus does not extend.
  - **strong recommendation, moderate-certainty evidence**

- We suggest anticoagulation if thrombus extends but remains confined to distal veins.
  - **weak recommendation, very low-certainty evidence**

- We recommend anticoagulation if thrombus extends into the proximal veins.
  - **strong recommendation, moderate-certainty evidence**

Other Guidelines:
- ASH 2018: no specific guidance
- NICE 2020: recommendations for proximal only
Additional Considerations

- Positive D-dimer
- Extensive thrombosis
- Close to proximal veins
- No reversible provoking factor
- Active cancer
- History of VTE
- Hospitalized patient
- COVID-19 diagnosis
- Highly symptomatic
- Prefer to avoid repeat imaging

Favor choosing anticoagulation

- Thrombosis of muscular veins (e.g. soleus, gastrocnemius)
- Moderate or high risk for bleeding
- Prefer to avoid anticoagulation

Favor choosing serial imaging
Case 2

- 68-year-old woman
- Dyslipidemia, hypothyroidism, no VTE risk factors
- Assessed in ED for chest discomfort
- CTPA: single subsegmental pulmonary embolism RLL
- Bilateral compression ultrasound negative

PICO Question

Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated subsegmental pulmonary embolism?
Isolated Subsegmental PE

**PICO Question**
Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated subsegmental pulmonary embolism?

In patients with subsegmental PE (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs...

- **LOW RISK** for recurrent VTE, we suggest **clinical surveillance over anticoagulation**
  - *weak recommendation, low-certainty evidence*

- **HIGH RISK** for recurrent VTE, we suggest **anticoagulation over clinical surveillance**
  - *weak recommendation, low-certainty evidence*

**Other Guidelines:**
ESC 2019: further imaging to confirm PE when isolated subsegmental filling defects are seen on CT pulmonary angiogram
Additional Considerations

More Likely to be “True Positive"
- High quality CTPA with good opacification of distal pulmonary arteries
- Multiple intraluminal defects
- Defects involve more proximal subsegmental arteries (i.e. are larger)
- Defects on >1 image
- Defects surrounded by contrast Patients are symptomatic
- High clinical pretest probability
- Elevated D-dimer

Risk Factors for Recurrence/Progression and/or Adverse Outcomes
- Hospitalized
- Reduced Mobility
- Active cancer
- No reversible risk factor
- Low cardiopulmonary reserve
- Marked symptoms
- Moderate or high risk for bleeding
- Prefer to avoid anticoagulation
Case 3

- 60-year-old woman
- Persistent severe headache x 2 weeks
- CT venogram: left frontal cortical vein thrombosis with subarachnoid hemorrhage
- No medical history, no family history VTE, no VTE risk factors

PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with cerebral vein thrombosis?
Cerebral Vein Thrombosis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Absolute Effect (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall mortality at 90 days</td>
<td>108 fewer events per 1000 cases (from 162 fewer to 47 more)</td>
</tr>
<tr>
<td>New ICH or PE at 90 days</td>
<td>69 fewer events per 1000 cases (from – fewer to 83 more)</td>
</tr>
</tbody>
</table>
Cerebral Vein Thrombosis

In patients with cerebral vein/venous sinus thrombosis...

We recommend anticoagulation therapy for at least the treatment phase (first 3 months) over no anticoagulant therapy.

Strong recommendation, low-certainty evidence

Other Guidelines:
ACCP 2016: similar
ACC/AHA 2014: similar

Comments:
- Dose-adjusted heparin or low molecular weight heparin can be used
- Parenteral therapy until clinically stabilized
- Treatment phase less well defined than DVT or PE (studies 3 to 12 months)
- Extended anticoagulation in the absence of hormonal or other provoking factors, or persistent risk factors for recurrent VTE
### Scenario 1
- 74-year-old man
- Bilateral PE after hip replacement surgery
- Completed 3 months of anticoagulation

### Scenario 2
- 74-year-old man
- Bilateral PE after flight to New Zealand
- Completed 3 months of anticoagulation

### Scenario 3
- 74-year-old man
- Bilateral PE in the absence of provoking factors
- Completed 3 months of anticoagulation

**PICO Question**

Should extended-phase anticoagulant therapy vs no extended-phase anticoagulant therapy be provided to patients with VTE who have completed the treatment phase of therapy?
Extended-Phase Therapy

- **Major transient risk factor**
  - Recommend AGAINST OFFERING extended-phase anticoagulation
  - Strong recommendation, moderate-certainty evidence

- **Minor transient risk factor**
  - Suggest AGAINST OFFERING extended-phase anticoagulation
  - Weak recommendation, moderate-certainty evidence

- **Absence of transient provocation (unprovoked or persistent risk factor)**
  - Recommend OFFERING extended-phase anticoagulation with a DOAC
  - Strong recommendation, moderate-certainty evidence

- **Absence of transient risk factor (unprovoked or persistent risk factor) and cannot receive DOAC**
  - Suggest offering extended-phase anticoagulation with a VKA
  - Weak recommendation, moderate-certainty evidence
## Selected Summary of Findings

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<thead>
<tr>
<th>Outcome</th>
<th>Absolute Effect (95% CI)</th>
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<tbody>
<tr>
<td>Recurrent VTE at 7 to 48 months</td>
<td>64 fewer events per 1000 cases (from 80 fewer to 37 fewer)</td>
</tr>
<tr>
<td>Major bleeding at 7 to 48 months</td>
<td>6 more events per 1000 cases (from 1 more to 14 more)</td>
</tr>
<tr>
<td>All-cause mortality at 7 to 48 months</td>
<td>4 fewer events per 1000 cases (from 10 fewer to 5 more)</td>
</tr>
</tbody>
</table>
Case 4

- 74-year-old man
- Bilateral PE in the absence of provoking factors
- Completed 3 months of anticoagulation with DOAC
- Offered extended-phase therapy and agrees

**PICO Question**

Should reduced-dose Xa inhibitor (apixaban or rivaroxaban) vs full-dose Xa inhibitor (apixaban or rivaroxaban) be provided to patients with VTE who have been selected to receive extended-phase anticoagulant therapy?
### Selected Summary of Findings

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Absolute Effect (95% CI)</th>
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<tbody>
<tr>
<td>Recurrent symptomatic VTE at 12 months</td>
<td>2 more events per 1000 cases (from 5 fewer to 12 more)</td>
</tr>
<tr>
<td>Major or CRNMB at 12 months</td>
<td>10 fewer events per 1000 cases (from 18 fewer to 2 more)</td>
</tr>
<tr>
<td>Mortality</td>
<td>Not estimable</td>
</tr>
</tbody>
</table>
In patients offered extended-phase anticoagulation...

We suggest the use of reduced-dose apixaban or rivaroxaban over full-dose apixaban or rivaroxaban. 

Weak recommendation, very low-certainty evidence.

Considerations:
- Choice of drug and dose is informed by multiple variables (BMI, renal function, adherence to dosing regimen, cost)
4 Areas of Uncertainty

- Isolated Distal DVT
- Isolated Subsegmental PE
- Cerebral Vein Thrombosis
- Extended Phase Therapy
Questions?
How to Claim Credit

1) Go to: http://acf.cmecertificateonline.com/
2) Select “What's New in Antithrombotic Treatment of VTE Disease: ACCP (CHEST) Guidelines Update 2021”
3) Evaluate the program
4) Print certificate for your records

This program is accredited for Physicians, Pharmacists, and Nurses for enduring accreditation for 1.0 hours
Online Literature Update

- **Features:**
  - Most important articles starred
  - Searchable
  - Abstract can be read on site
  - View by date range
  - Includes ACF authored papers

- **Links to our new Rapid Recap Newsletter**

Thank you, Dr. Bishoy Ragheb and Elaine Whalen, for this vision!
Where are these resources?

- Literature update created 1\textsuperscript{st} & 3\textsuperscript{rd} Mondays, monthly
- Rapid Recap one month following by several editorial teams
AC Forum Resources

- Guidance for Treatment of Various VTE – update in progress
- Guidance for Management of Acute VTE During Pregnancy
- Guidance for Management of Peripartum VTE Prophylaxis
- VTE Prophylaxis in Acutely Ill Medical Patients
- Treatment of Cancer-Associated VTE
- Oral Anticoagulation for Primary VTE Prevention in Ambulatory Patients with Active Cancer
- Presentation - “22 Practical Teaching Points about DVT, PE, Anticoagulation, & Thrombophilia” - Dr. Stephan Moll
View presentations on your own schedule through **January 15, 2022**, including recorded versions of our Live Q&A’s and Presidents’ Panel!

- Up to 13.75 hours of Enduring CE available!
Health Disparities & Patient Care: Could I Have Prevented a Stroke?

Thursday | December 16, 2021 | 12:00pm EST

**Presenters:** April Allen, PharmD, CACP | Danielle Jenkins, RN, BSN | Julia Mulheman, PharmD

**Moderators:** Sara Vazquez, PharmD, BCPS, CACP | Terri Wiggins, MS
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