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CHEST

Antithrombotic Therapy for VTE Disease

CHEST Guideline and Expert Panel Report

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PODCAST

BACKGROUND: We update recommendations on 12 topics that were in the 9th edition of these guidelines, and address 3 new topics.

METHODS: We generate strong (Grade 1) and weak (Grade 2) recommendations based on high- (Grade A), moderate- (Grade B), and low- (Grade C) quality evidence.

RESULTS: For VTE and no cancer, as long-term anticoagulant therapy, we suggest dabigatran (Grade 2B), rivaroxaban (Grade 2B), apixaban (Grade 2B), or edoxaban (Grade 2B) over vitamin K antagonist (VKA) therapy, and suggest VKA therapy over low-molecular-weight heparin (LMWH; Grade 2C). For VTE and cancer, we suggest LMWH over VKA (Grade 2B), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C). We have not changed recommendations for who should stop anticoagulation at 3 months or receive extended therapy. For VTE treated with anticoagulants, we recommend against an inferior vena cava filter (Grade 1B). For DVT, we suggest not using compression stockings routinely to prevent PTS (Grade 2B). For subsegmental pulmonary embolism and no proximal DVT, we suggest clinical surveillance over anticoagulation with a low risk of recurrent VTE (Grade 2C), and anticoagulation over clinical surveillance with a high risk (Grade 2C). We suggest thrombolytic therapy for pulmonary embolism with hypotension (Grade 2B), and systemic therapy over catheter-directed thrombolysis (Grade 2C). For recurrent VTE on a non-LMWH anticoagulant, we suggest LMWH (Grade 2C); for recurrent VTE on LMWH, we suggest increasing the LMWH dose (Grade 2C).

CONCLUSIONS: Of 54 recommendations included in the 30 statements, 20 were strong and none was based on high-quality evidence, highlighting the need for further research.

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KEY WORDS: antithrombotic therapy; evidence-based medicine; GRADE approach; venous thromboembolism

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ABBREVIATIONS: AT9 = 9th Edition of the Antithrombotic Guideline; AT10 = 10th Edition of the Antithrombotic Guideline; CHEST = American College of Chest Physicians; CDT = catheter-directed thrombolysis; COI = conflict of interest; CTEPH = chronic thromboembolic pulmonary hypertension; CTPA = CT pulmonary angiogram; GOC = Guidelines Oversight Committee; INR = International Normalized Ratio; IVC = inferior vena cava; LMWH = low-molecular-weight heparin; NOAC = non-vitamin K oral anticoagulant; PE = pulmonary embolism; PTS = postthrombotic syndrome; RCT = randomized controlled trial; UEDVT = upper extremity deep vein thrombosis; US = ultrasound; VKA = vitamin K antagonist

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Choice of Therapy

- In patients with proximal DVT or pulmonary embolism (PE), we recommend long-term (3 months) anticoagulant therapy over no such therapy (Grade IB).
- Definitions:
- Long-term therapy = 3 months
- Extended therapy = indefinitely

- In patients with DVT of the leg or PE and no cancer, as long-term (first 3 months) anticoagulant therapy, we suggest dabigatran, rivaroxaban, apixaban, or edoxaban over vitamin K antagonist (VKA) therapy (all Grade 2B).
- For patients with DVT of the leg or PE and no cancer who are not treated with dabigatran, rivaroxaban, apixaban, or edoxaban, we suggest VKA therapy over low-molecular weight heparin (LMWH) (Grade 2C).
- IV given before d and e, not for r and a, overlap for VKA
- NOACs preferred due to reduced bleeding and convenience

NOACs

- Dabigatran - Pradaxa
- Rivaroxaban - Xarelto
- Apixaban - Eliquis
- Endoxaban - Savaysa

- In patients with DVT of the leg or PE and cancer ("cancer-associated thrombosis"), as long-term (first 3 months) anticoagulant therapy, we suggest LMWH over VKA therapy (Grade 2C), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 20), or edoxaban (Grade 2C).

- In patients with DVT of the leg or PE who receive extended therapy, we suggest that there is no need to change the choice of anticoagulant after the first 3 months (Grade 2C).
- May change due to circumstances or preferences

Duration of Therapy

- In patients with a proximal DVT of the leg or PE provoked by surgery, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade IB), (ii) treatment of a longer time-limited period (eg, 6, 12, or 24 months) (Grade IB), or (iii) extended therapy (no scheduled stop date) (Grade IB).

- In patients with a proximal DVT of the leg or PE provoked by a nonsurgical transient risk factor, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade IB) and (ii) treatment of a longer time-limited period (eg, 6, 12, or 24 months) (Grade IB). We suggest treatment with anticoagulation for 3 months over extended therapy if there is a low or moderate bleeding risk (Grade 2B), and recommend treatment for 3 months over extended therapy if there is a high risk of bleeding (Grade IB).

- In patients with an isolated distal DVT of the leg provoked by surgery or by a nonsurgical transient risk factor, we suggest treatment with anticoagulation for 3 months over treatment of a shorter period (Grade 2C), we recommend treatment with anticoagulation for 3 months over treatment of a longer time-limited period (eg, 6, 12, or 24 months) (Grade IB), and we recommend treatment with anticoagulation for 3 months over extended therapy (no scheduled stop date) (Grade IB).
- Not all patients will be treated

- In patients with an unprovoked DVT of the leg (isolated distal or proximal) or PE, we recommend treatment with anticoagulation for at least 3 months over treatment of a shorter duration (Grade IB), and we recommend treatment with anticoagulation for 3 months over treatment of a longer time-limited period (eg, 6, 12, or 24 months) (Grade IB).
- Not all patients may be treated
- Consider risk benefit of longer therapy if unprovoked

- In patients with a first VTE that is an unprovoked proximal DVT of the leg or PE and who have a (i) low or moderate bleeding risk (see text), we suggest extended anticoagulant therapy (no scheduled stop date) over 3 months of therapy (Grade 2B), and (ii) high bleeding risk (see text), we recommend 3 months of anticoagulant therapy over extended therapy (no scheduled stop date) (Grade IB).
- Reassess extended therapy annually

- In patients with a second unprovoked VTE and who have a (i) low bleeding risk (see text), we recommend extended anticoagulant therapy (no scheduled stop date) over 3 months (Grade IB);
(ii) moderate bleeding risk (see text), we suggest extended anticoagulant therapy over 3 months of therapy (Grade 2B); or (iii) high bleeding risk (see text), we suggest 3 months of anticoagulant therapy over extended therapy (no scheduled stop date) (Grade 2B).

- Reassess extended therapy annually

- In patients with DVT of the leg or PE and active cancer ("cancer-associated thrombosis") and who (i) do not have a high bleeding risk, we recommend extended anticoagulant therapy (no scheduled stop date) over 3 months of therapy (Grade IB), or (ii) have a high bleeding risk, we suggest extended anticoagulant therapy (no scheduled stop date) over 3 months of therapy (Grade 2B).
- Reassess extended therapy annually

- Risk of recurrence is reduced while patient remains on therapy of extended durations but risk of recurrence returns to baseline once the therapy is discontinued regardless of how long they were treated (6, 12, 18 or 24 months)

Aspirin

- In patients with an unprovoked proximal DVT or PE who are stopping anticoagulant therapy and do not have a contraindication to aspirin, we suggest aspirin over no aspirin to prevent recurrent VTE (Grade 2B).
- Aspirin is not an option in place of other therapy
- Remember resuming aspirin if it was stopped when other anticoagulation was started

Isolated Distal DVT

- In patients with acute isolated distal DVT of the leg and (i) without severe symptoms or risk factors for extension (see text), we suggest serial imaging of the deep veins for 2 weeks over anticoagulation (Grade 2C) or (ii) with severe symptoms or risk factors for extension (see text), we suggest anticoagulation over serial imaging of the deep veins (Grade 2C).
- Weigh risks and benefits of bleeding versus anticoagulation and reduced need for followup
- Extension risks – size, cancer, history VTE, inpatient

- In patients with acute isolated distal DVT of the leg who are managed with anticoagulation, we recommend using the same anticoagulation as for patients with acute proximal DVT (Grade IB).

- In patients with acute isolated distal DVT of the leg who are managed with serial imaging, we (i) recommend no anticoagulation if the thrombus does not extend (Grade IB), (ii) suggest anticoagulation if the thrombus extends but remains confined to the distal veins (Grade 2C), and (iii) recommend anticoagulation if the thrombus extends into the proximal veins (Grade IB).

Catheter Thrombolysis

- In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over CDT (Grade 2C).
- CDT may have benefit in reducing postthrombotic syndrome but may have increased cost and initial risk

IVC Filter

- In patients with acute DVT or PE who are treated with anticoagulants, we recommend against the use of an inferior vena cava (IVC) filter (Grade IB).
- IVC filter increases DVT, decreases PE and has no effect on mortality

Compression Stockings for PTS

- In patients with acute DVT of the leg, we suggest not using compression stockings routinely to prevent PTS (Grade 2B).
- Stockings will not reduce complications with prophylactic use but may be used if helps symptoms

Subsegmental PE

- In patients with subsegmental PE (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs who have a (i) low risk for recurrent VTE (see text), we suggest clinical surveillance over anticoagulation (Grade 20) or (ii) high risk for recurrent VTE (see text), we suggest anticoagulation over clinical surveillance (Grade 20).
- Consider serial ultrasound
- Surveillance better with high bleeding risk or good cardiopulmonary reserve
- Treatment better with cancer, low reserve, no risk factor

Out of Hospital PE

- In patients with low-risk PE and whose home circumstances are adequate, we suggest treatment at home or early discharge over standard discharge (eg, after the first 5 days of treatment) (Grade 2B).
- Good reserve, no bleeding risk, compliant

Systemic Thrombolysis for PE

- In patients with acute PE associated with hypotension (eg, systolic BP <90 mm Hg) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (Grade 2B).

- In most patients with acute PE not associated with hypotension, we recommend against systemically administered thrombolytic therapy (Grade IB).

- In selected patients with acute PE who deteriorate after starting anticoagulant therapy but have yet to develop hypotension and who have a low bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (Grade 2C).
- High risk patients need close monitoring to observe for clinical worsening
- RV evaluation not universally indicated

Catheter Removal of PE

- In patients with acute PE who are treated with a thrombolytic agent, we suggest systemic thrombolytic therapy using a peripheral vein over CDT (Grade 2C).
- Consider CDT for high bleeding risk and access to CDT

- In patients with acute PE associated with hypotension and who have (i) a high bleeding risk, (ii) failed systemic thrombolysis, or (iii) shock that is likely to cause death before systemic thrombolysis can take effect (eg, within hours), if appropriate expertise and resources are available, we suggest catheter- assisted thrombus removal over no such intervention (Grade 2C).

Thromboedarterectomy

- In selected patients with chronic thromboembolic pulmonary hypertension (CTEPH) who are identified by an experienced thromboendarterectomy team, we suggest pulmonary thromboendarterectomy over no pulmonary thromboendarterectomy (Grade 2C).

Thrombolysis of UE DVT

- In patients with acute upper extremity DVT (UEDVT) that involves the axillary or more proximal veins, we suggest anticoagulant therapy alone over thrombolysis (Grade 2C).

- In patients with UEDVT who undergo thrombolysis, we recommend the same intensity
and duration of anticoagulant therapy as in patients with UEDVT who do not undergo thrombolysis (Grade IB).

Recurrent VTE on Therapy

- In patients who have recurrent VTE on VKA therapy (in the therapeutic range) or on dabigatran, rivaroxaban, apixaban, or edoxaban (and are believed to be compliant), we suggest switching to treatment with LMWH at least temporarily (Grade 2C).
- Switch for at least 1 month then evaluate
- Consider true recurrence, compliance or malignancy

- In patients who have recurrent VTE on long-term LMWH (and are believed to be compliant), we suggest increasing the dose of LMWH by about one-quarter to one-third (Grade 2C).