Treatment of Deep Vein Thrombosis and Pulmonary Embolism

An Educational Slide Set

American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism

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Clinical Guidelines

American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism

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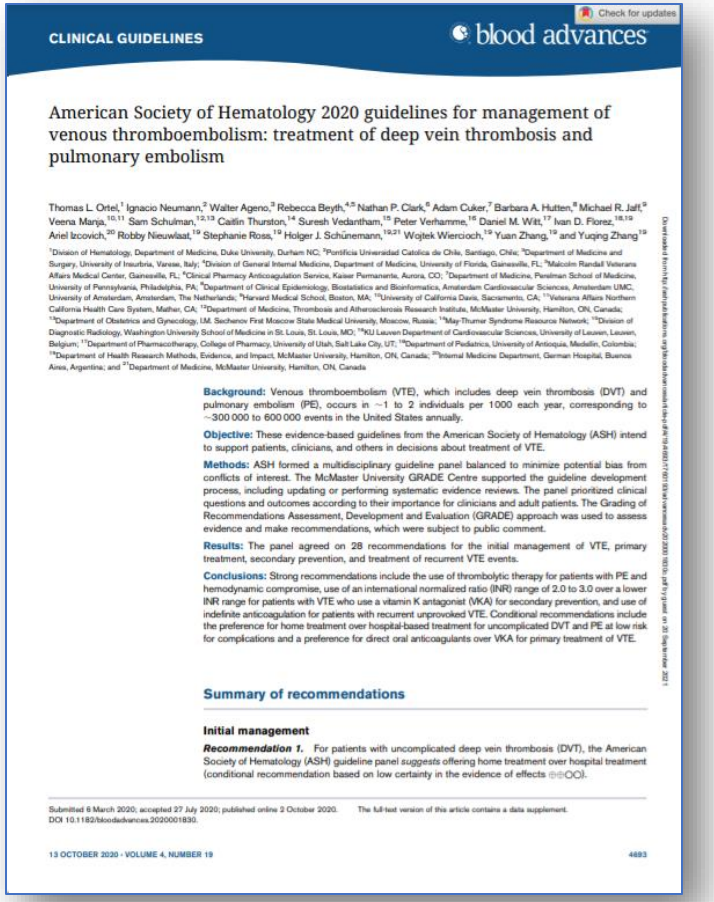

CLINICAL GUIDELINES

blood advances

American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism

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Background: Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), occurs in ~1 to 2 individuals per 1000 each year, corresponding to ~300 000 to 600 000 events in the United States annually.

Objective: These evidence-based guidelines from the American Society of Hematology (ASH) intend to support patients, clinicians, and others in decisions about treatment of VTE.

Methods: ASH formed a multidisciplinary guideline panel balanced to minimize potential bias from conflicts of interest. The McMaster University GRADE Centre supported the guideline development process, including updating or performing systematic evidence reviews. The panel prioritized clinical questions and outcomes according to their importance for clinicians and adult patients. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess evidence and make recommendations, which were subject to public comment.

Results: The panel agreed on 28 recommendations for the initial management of VTE, primary treatment, secondary prevention, and treatment of recurrent VTE events.

Conclusions: Strong recommendations include the use of thrombolytic therapy for patients with PE and hemodynamic compromise, use of an international normalized ratio (INR) range of 2.0 to 3.0 over a lower INR range for patients with VTE who use a vitamin K antagonist (VKA) for secondary prevention, and use of indefinite anticoagulation for patients with recurrent unprovoked VTE. Conditional recommendations include the preference for home treatment over hospital-based treatment for uncomplicated DVT and PE at low risk for complications and a preference for direct oral anticoagulants over VKA for primary treatment of VTE.

Summary of recommendations

Initial management

Recommendation 1. For patients with uncomplicated deep vein thrombosis (DVT), the American Society of Hematology (ASH) guideline panel *suggests* offering home treatment over hospital treatment (conditional recommendation based on low certainty in the evidence of effects ⊕◯◯◯).

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ASH Clinical Practice Guidelines on VTE

1. Prevention of VTE in Surgical Hospitalized Patients
2. Prevention of VTE in Medical Hospitalized Patients
3. **Treatment of Acute VTE (DVT and PE)**
4. Optimal Management of Anticoagulation Therapy
5. Prevention and Treatment of VTE in Patients with Cancer
6. Heparin-Induced Thrombocytopenia (HIT)
7. Thrombophilia
8. Pediatric VTE
9. VTE in the Context of Pregnancy
10. Diagnosis of VTE
11. Anticoagulation in Patients with COVID-19
12. Adaptation of ASH Management of VTE Guidelines for Latin America

How were these ASH guidelines developed?

PANEL FORMATION

Each **guideline panel** was formed following these key criteria:

- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of conflicts of interest

CLINICAL QUESTIONS

20 to 30 **clinically-relevant questions** generated in **PICO format** (population, intervention, comparison, outcome)

Example: PICO question

"Should thrombolytic therapy in addition to anticoagulation vs. anticoagulation alone be used for patients with extensive proximal DVT?"

EVIDENCE SYNTHESIS

Evidence summaries incorporated into Evidence to Decision (EtD) frameworks, which also addressed:

- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

MAKING RECOMMENDATIONS

Recommendations made by guideline panel members based on EtD frameworks.

ASH guidelines are reviewed annually by expert work groups convened by ASH. Resources, such as this slide set, derived from guidelines that require updating are removed from the ASH website.

How patients and clinicians should use these recommendations

	STRONG Recommendation ("The panel recommends…")	**CONDITIONAL Recommendation** ("The panel suggests…")
For patients	Most individuals would want the intervention.	A majority would want the intervention, but many would not.
For clinicians	Most individuals should receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use **shared decision making**.

Grading the quality of evidence

Objectives

By the end of this session, you should be able to

1. Describe the *initial management* of patients with deep vein thrombosis (DVT) and pulmonary embolism (PE)

2. Describe recommendations for *duration of anticoagulation* after venous thromboembolism (VTE)

3. Describe recommendations for management of *recurrent VTE*

VTE is a common and important cause of morbidity and mortality

VTE (including DVT and PE) occurs in 1-2 per 1,000 people per year

One third of patients with newly diagnosed VTE present with PE

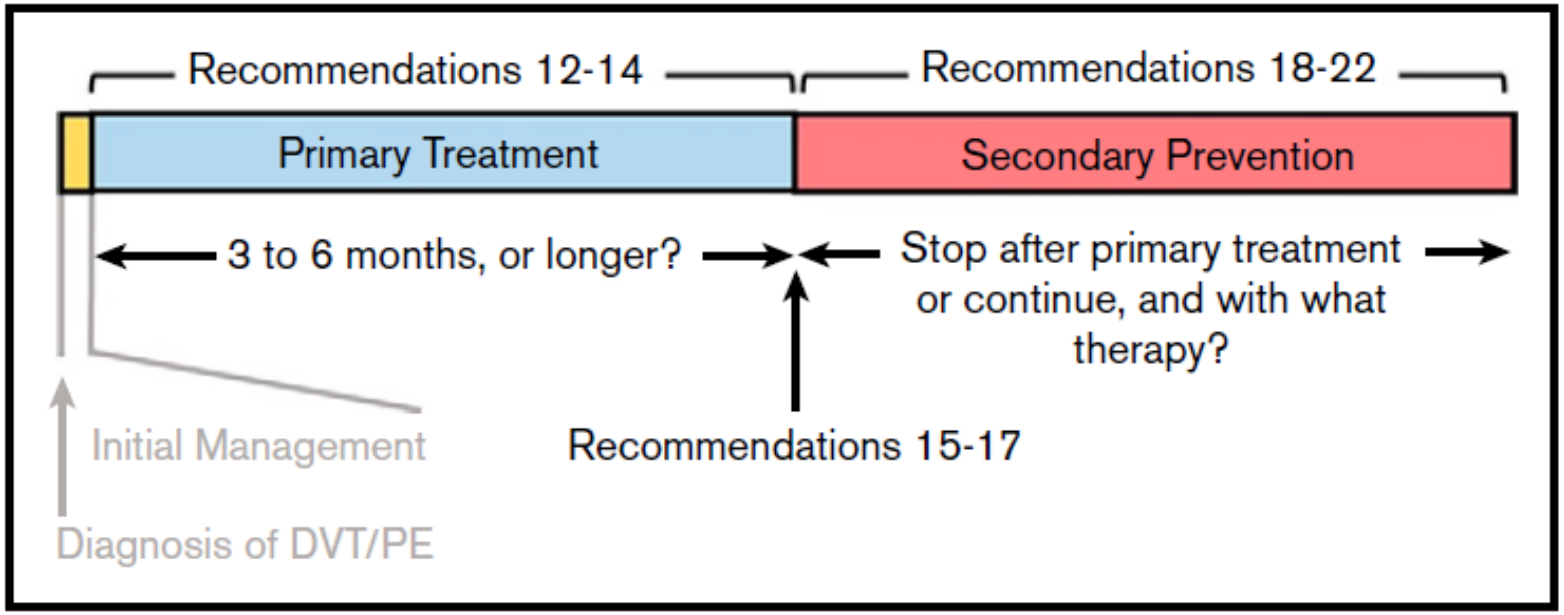
For patients with unprovoked VTE, risk of recurrence after completing a primary treatment course of anticoagulation is about 10% in two years

The incidence of VTE increases with age – as high as 1 in 100 in individuals above 80 years old

These guidelines

These guidelines are about managing VTE during:

- Initial stages (within 2 weeks)
- Primary treatment (3-6 months)
- Secondary prevention (beyond 6 months)



Case 1: Unprovoked DVT

48 year old male

Medical History: None

Medications: None

Seen in the Emergency Department with: left leg pain and swelling x 24 hours

Heart rate 80 beats per min
Respiratory rate 16 breaths per min
Oxygen saturation 99% on room air
Blood pressure 130/80
(+) Left calf swelling

D-dimer: 2,500 mcg/ml
Leg US: *distal external iliac vein, superficial femoral and popliteal vein non-compressible (occlusive DVT)*

What initial management plan would you recommend:

A. Anticoagulation only
B. Thrombolysis in addition to anticoagulation
C. Compression stockings in addition to anticoagulation
D. IVC filter insertion in addition to anticoagulation

Recommendation

In most patients with proximal DVT, the panel *suggests* **anticoagulation therapy alone** over thrombolytic therapy in addition to anticoagulation (conditional recommendation, low certainty)

Thrombolytic therapy + Anticoagulation compared with **Anticoagulation alone** in patients with extensive proximal DVT:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with Anticoagulation	*Risk difference with thrombolytic therapy + anticoagulation*
● Mortality	**0.77** (0.26-2.28)	9 per 1,000	**2 fewer deaths per 1,000** (7 fewer to 12 more)
● PTS	**0.71** (0.60 to 0.085)	641 per 1,000	**186 fewer PTS per 1,000** (96 fewer to 253 more)
● Major bleeding	**1.85** (1.41 to 2.44)	36 per 1,000	**31 more bleeds per 1,000** (15 fewer to 52 more)

Remarks:
Patients with limb threatening DVT may require thrombolysis

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Recommendation

For patients with DVT including those at increased risk of PTS, the panel *suggests against* the use of compression stockings (conditional recommendation, low certainty)

Anticoagulation alone compared with **compression stockings and anticoagulation** in patients with extensive DVT:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with VKA	*Risk difference with DOAC*
Mortality	**0.99** (0.72-1.36)	46 per 1,000	**0 fewer deaths per 1,000** (13 fewer to 17 more)
PE	**0.72** (0.31-1.70)	15 per 1,000	**4 fewer PE per 1,000** (10 fewer to 10 more)
DVT	**0.56** (0.12 to 2.70)	40 per 1,000	**18 fewer DVT per 1,000** (35 fewer to 68 more)
PTS	**0.62** (0.38 to 1.01)	213 per 1,000	**81 fewer cases of PTS per 1,000** (132 fewer to 2 more)

Remarks:
Stockings may still be considered for symptomatic relief in select patients

Quality of Evidence (GRADE): Low Moderate Strong

Treatment beyond anticoagulation for prevention of Post Thrombotic Syndrome (PTS)

- PTS may develop in 30% to 50% patients (5% to 10% severe)
- Adjunctive therapies can include compression stockings and thrombolysis:
  - Trend towards decreased PTS but not significant
  - No impact on mortality
  - For thrombolysis – increased bleeding risk
- There remains low certainty in the evidence and therapy may be considered for patients with:
  - Low risk of bleeding (thrombolysis)
  - Value rapid resolution of symptoms and prevention of PTS

Recommendation

In patients with VTE, the panel *suggests* using **DOACs over VKAs** (conditional recommendation, moderate certainty)

DOAC compared with **VKA** for VTE:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with VKA	*Risk difference with DOAC*
Mortality	**0.99** (0.85-1.15)	39 per 1,000	**0 fewer deaths per 1,000** (6 fewer to 6 more)
PE	**0.97** (0.77-1.23)	20 per 1,000	**1 fewer PE per 1,000** (5 fewer to 5 more)
DVT	**0.80** (0.59 to 1.09)	26 per 1,000	**5 fewer DVT per 1,000** (2 more to 11 fewer)
Major bleeding	**0.63** (0.47 to 0.84)	17 per 1,000	**6 fewer bleeds per 1,000** (3 fewer to 9 fewer)

Remarks:
May not be appropriate for all patient populations

The panel does not suggest one DOAC over another

Quality of Evidence (GRADE): Low Moderate Strong

Recommendation

For patients with **uncomplicated DVT**, the ASH guideline panel *suggests* offering **home treatment** over hospital treatment (conditional recommendation, low certainty)

Home treatment compared with **hospital treatment** in patients continuing on indefinite anticoagulation

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with hospital treatment	*Risk difference with home treatment*
● Mortality (10 days)	**Not estimable**	4 per 1,000	**Not estimable**
● PE	**0.64** (0.44 to 0.93)	68 per 1,000	**25 fewer PE per 1,000** (38 fewer to 5 fewer)
● DVT	**0.61** (0.42 to 0.90)	74 per 1000	**29 fewer DVT per 1,000** (43 fewer to 7 fewer)
● Major bleeding	**0.67** (0.33 to 1.36)	19 per 1,000	**6 fewer bleeds per 1,000** (13 fewer to 7 more)

Remarks:
Hospital treatment may benefit patients with limb threatening DVT or those at high risk of bleeding

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Case: back to our patient

Uncomplicated unprovoked VTE in previously well patient

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over VKA
  - Home treatment over hospital treatment

The patient receives 6 months of anticoagulation for primary treatment. What duration of anticoagulation do you recommend for secondary prevention?

A. 6-12 months
B. No secondary prevention is required
C. Indefinite
D. Will depend on use of prognostic scores

Recommendation

After primary treatment for patients with **unprovoked DVT or PE**, the panel *suggests* **indefinite antithrombotic therapy** (conditional, moderate certainty)

Indefinite anticoagulation compared with **stopping anticoagulation** in patients with unprovoked VTE after primary treatment:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with stopping	*Risk difference with indefinite anticoagulation*
Mortality	**0.75** (0.49-1.13)	18 per 1,000	**5 fewer deaths per 1,000** (9 fewer to 2 more)
PE	**0.29** (0.15 to 0.056)	29 per 1,000	**21 fewer PE per 1,000** (25 fewer to 13 more)
DVT	**0.20** (0.12 to 0.34)	63 per 1000	**50 fewer DVT per 1,000** (56 fewer to 42 fewer)
Major bleeding	**2.17** (1.40 to 3.35)	5 per 1,000	**6 more bleeds per 1,000** (2 more to 12 more)

Remarks:
Does not apply to patients who are at high risk of bleeding complication

Quality of Evidence (GRADE): Low Moderate Strong

Recommendation

For patients with unprovoked DVT and/or PE, the panel *suggests against* routine use of prognostic scores, D-Dimer testing or ultrasound to guide the duration of anticoagulation (conditional, low certainty)

Prognostic Scores	D-Dimer Testing	U/S
HERDOO2 VIENNA DASH	Persistently elevated D-Dimer	Residual vein thrombus

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Standard risk	*Risk difference with prognostic tools*
N/A: Insufficient evidence for treatment outcomes based on prognostic tools compared to standard approach			

Recommendation

For patients with DVT and/or PE who will continue with a DOAC for secondary prevention, the panel *suggests* using standard-dose DOAC or lower-dose DOAC (conditional recommendation, moderate certainty)

Lower-dose compared with **standard-dose DOAC** in patients continuing on indefinite anticoagulation

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with standard dose	*Risk difference with reduced dose DOAC*
Mortality	**0.68** (0.10-4.57)	6 per 1,000	**5 fewer deaths per 1,000** (9 fewer to 2 more)
PE	**1.25** (0.54 to 2.91	5 per 1,000	**21 fewer PE per 1,000** (25 fewer to 13 more)
DVT	**0.75** (0.36 to 1.53)	9 per 1000	**50 fewer DVT per 1,000** (56 fewer to 42 fewer)
Major bleeding	**0.97** (0.34 to 2.80)	4 per 1,000	**6 more bleeds per 1,000** (2 more to 12 more)

Lower dose DOAC regimens for secondary prevention of VTE

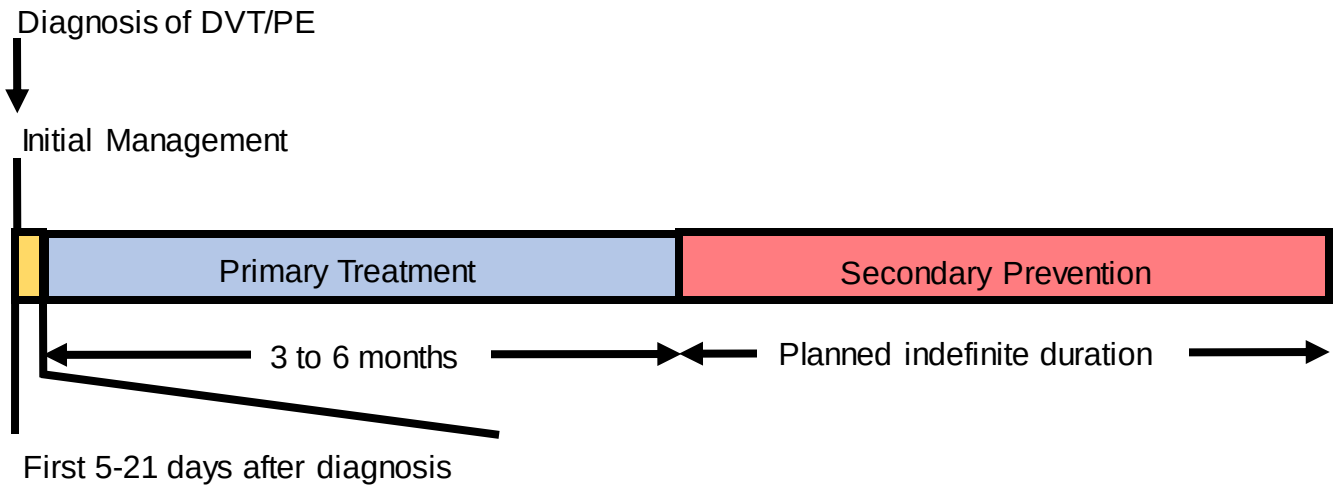
- **Apixaban 2.5 mg BID**
- **Rivaroxaban 10 mg OD**

Quality of Evidence (GRADE): Low Moderate Strong

Case Conclusion

Uncomplicated unprovoked VTE in previously well patient

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over warfarin
  - Home treatment over hospital treatment
- Duration:
  - Indefinite antithrombotic therapy
  - Standard or reduced dose DOAC



Case 2: Provoked DVT and PE (transient risk factor)

76 year old male

Medical History: CAD (MI 5 years earlier), HTN, Type 2 Diabetes

Medications: ASA, Amlodipine, Metformin, Rosuvastatin

Seen in the Emergency Department with: SOB and right leg pain x 48 hours. Underwent total hip replacement 1 week earlier and has not been taking prescribed DVT prophylaxis.

Heart rate 90 beats per min
Respiratory rate 22 breaths per min
Oxygen saturation 99% on RA
Blood pressure 150/90
(+) Right calf swelling

Right Leg US: *superficial femoral and popliteal vein non-compressible (occlusive DVT)*
CTPA: *Pulmonary embolism involving segmental arteries of the left lower lobe*

Recommendations

IVC filter insertion is not routinely recommended unless there is a contraindication to anticoagulation

For patients with proximal DVT and significant pre-existing cardiopulmonary disease, as well as for patients with PE and hemodynamic compromise, the panel suggests anticoagulation alone rather than anticoagulation plus insertion of an IVC filter *(conditional recommendation, low certainty)*

IVC filter in addition to anticoagulation versus **anticoagulation alone (NO FILTER)**:

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		*Risk with **NO FILTER***	*Risk difference using **FILTER***
● Mortality	**RR 1.15** (0.83 to 1.60)	60 per 1000	**9 more death per 1,000** (10 fewer to 36 more)
● PE	**RR 0.54** (0.22 to 1.33)	5 per 1000	**2 fewer PE per 1,000** (4 fewer to 2 more)
● DVT	**RR 1.64** (0.93 to 2.90)	5 per 1,000	**3 more DVT per 1,000** (0 fewer to 10 more)

If IVC filter is inserted (e.g., high bleeding risk) a retrievable filter is recommended with removal once patient can safely receive anticoagulant therapy

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Recommendation

For patients with DVT and/or PE with stable CVD, previously taking aspirin the panel *suggests* suspending aspirin for the duration of anticoagulation therapy (conditional, very low certainty)

Suspending ASA (Anticoagulation alone) compared with **Continuing ASA (ASA + anticoagulation)**

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with stopping ASA	*Risk with continuing ASA (ASA + Anticoagulation)*
Major bleeding	**1.26** (0.34 to 2.80)	29 per 1,000	**7 more bleeds per 1,000** (2 fewer to 21 more)

Remarks:
Does not apply to patients with recent coronary event or coronary intervention

Quality of Evidence (GRADE): Low Moderate Strong

Recommendation

In patients with pulmonary embolism (PE) with low risk of complications, the panel *suggests* home treatment over hospital treatment (conditional recommendation, very low certainty)

Home treatment compared with **hospital treatment** in patients continuing on indefinite anticoagulation

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with hospital treatment	*Risk difference with home treatment*
● Mortality (30 days)	**0.33** (0.01 to 7.98)	4 per 1,000	**3 fewer deaths per 1,000** (4 fewer to 30 more)
● PE	**2.95** (0.12 to 71.85)	0 per 1,000	**0 fewer PE per 1,000** (0 fewer to 0 fewer)
● DVT	**Not estimable**	0 per 1000	**Not estimable**
● Major bleeding	**6.88** (0.36 to 132.14)	0 per 1,000	**0 fewer bleeds per 1,000** (0 fewer to 0 fewer e)

Remarks:
Hospital treatment may benefit patients with submassive or massive PE, a high risk for bleeding or requiring IV analgesics

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Case: back to our patient

Provoked DVT and PE (transient risk factor) in patient with cardiopulmonary disease

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over warfarin
  - Suspend ASA
  - Home treatment over hospital treatment

The patient is shocked that this happened to him and asks what caused his blood clot.

Provoking Risk Factors for VTE

Transient Risk Factors
(resolve after provoked VTE)

MAJOR Risk Factor (occurs within 3 mth)
- Surgery, gen anesthesia > 30 min
- Confined to hospital bed ≥ 3 days with acute illness
- Cesarean section

MINOR Risk Factor (occurs within 2 mth)
- Estrogen therapy (OCP, HRT)
- Pregnancy, puerperium
- Confined to bed out of hospital ≥ 3 days with acute illness
- Leg injury, reduced mobilty ≥ 3 days

Chronic (Persistent) Risk Factors
(persistent after VTE occurs)

- Active cancer (ongoing chemo; recurrent or progressive disease)
- Inflammatory bowel disease
- Autoimmune disorder (e.g., antiphospholipid syndrome, rheumatoid arthritis)
- Chronic infection
- Chronic immobility (e.g., spinal cord injury)

The patient recovers well in hospital and is ready for discharge. In the absence of any major bleeding concerns, for how long should this patient be treated with anticoagulation?

A. 3-6 months
B. 6-12 months
C. Indefinite
D. 6 weeks

Recommendation

For primary treatment of deep venous thrombosis or pulmonary embolism, the panel suggests short term (3-6 months) over long term anticoagulation (6-12 months) (conditional recommendation, moderate certainty)

Long-term compared with **short-term** anticoagulation for patients with VTE provoked by transient risk factor

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with short-term	*Risk difference with long-term anticoagulation*
● Mortality	**1.38** (0.85 to 2.23)	18 per 1,000	**7 more deaths per 1,000** (3 fewer to 22 more)
● PE	**0.66** (0.29 to 1.151	50 per 1,000	**17 fewer PE per 1,000** (35 fewer to 25 more)
● DVT	**0.50** (0.27 to 0.95))	117 per 1000	**50 fewer DVT per 1,000** (24 fewer to 10 fewer)
● Major bleeding	**1.46** (0.78 to 2.73)	13 per 1,000	**6 more bleeds per 1,000** (3 fewer to 22 more)

Remarks:
For VTE provoked by transient risk factor, secondary prevention does not need to be considered

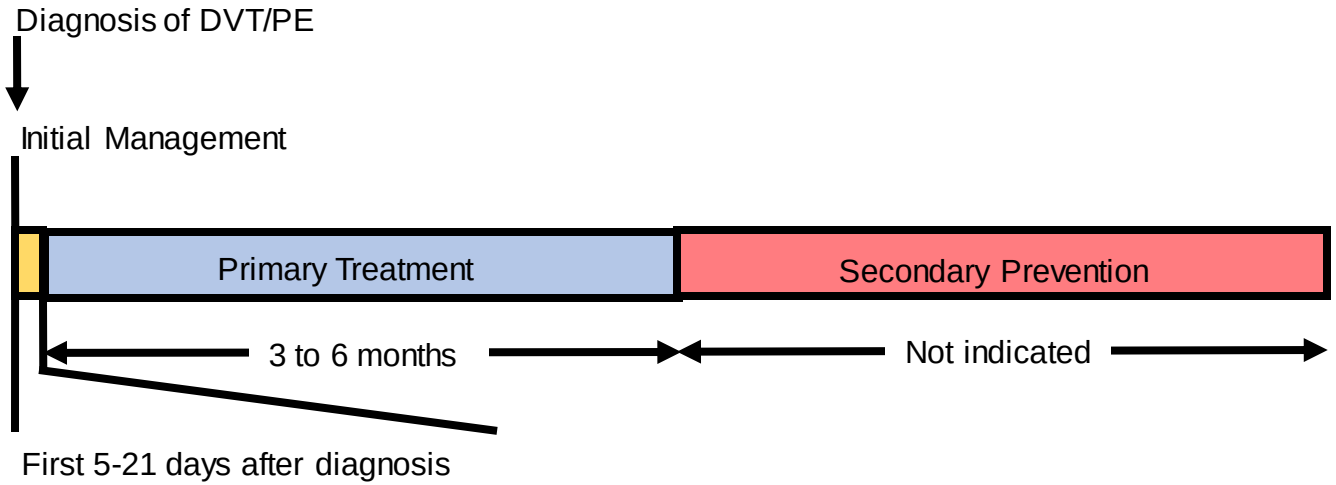
*Results based on approx. 2.5 year follow up

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Case: back to our patient

Provoked (transient risk factor) PE in patient with cardiopulmonary disease

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over warfarin
  - Suspend ASA
  - Home treatment over hospital treatment
- Duration:
  - 3-6 months
  - No secondary prevention
    - Can resume ASA if otherwise indicated



Case epilogue:

Three years later while on ASA only, the patient undergoes an appendectomy for appendicitis. Seven days after surgery, the patient has new leg swelling and is diagnosed with an acute left leg DVT. ASA is suspended and he is restarted on a DOAC for 3 months.

For how long should he be treated with anticoagulation?

A. 3-6 months
B. 6-12 months
C. Indefinite
D. 6 weeks

Recommendation

For patients who develop a DVT and/or PE provoked by a transient risk factor and have a history of a previous provoked thrombotic event the panel suggests stopping anticoagulation after completion of primary treatment (conditional recommendation, moderate certainty)

Long-term compared with **short-term** anticoagulation for patients with recurrent provoked VTE

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with short-term	*Risk difference with long-term anticoagulation*
Mortality	**0.75** (0.49 to 1.13)	18 per 1,000	**7 more deaths per 1,000** (3 fewer to 22 more)
PE	**0.29** (0.15 to 0.56)	29 per 1,000	**17 fewer PE per 1,000** (35 fewer to 25 more)
DVT	**0.20** (0.12 to 0.34)	117 per 1000	**50 fewer DVT per 1,000** (24 fewer to 10 fewer)
Major bleeding	**2.17** (1.40 to 3.35)	5 per 1,000	**6 more bleeds per 1,000** (3 fewer to 22 more)

Quality of Evidence (GRADE): Low Moderate Strong

Case Conclusion

Provoked PE (transient risk factor) in patient with pre-existing cardiopulmonary disease

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - DOAC over warfarin
  - Suspend ASA
  - Home treatment over hospital treatment
- Duration:
  - 3-6 months
  - No secondary prevention (can resume ASA if otherwise indicated)
- Recurrent VTE:
  - Reassess for initial management and primary treatment duration
  - No secondary prevention (in cases where first event is unprovoked, indefinite antithrombotic therapy is recommended

Case 3: Provoked submassive PE (chronic risk factor)

56 year old female

Medical History: Inflammatory Bowel Disease, CKD (CrCl 14 ml/min)

Medications: Infliximab

Seen in the Emergency Department with: Presyncope after 2 days of SOB and chest pain.

Heart rate 104 beats per min
Respiratory rate 22 breaths per min
Oxygen saturation 98% on 2L
Blood pressure 150/90

Troponin: *Troponin-T HS 250 ng/L*
CTPA: *Pulmonary embolism involving bilateral segmental arteries*
Bedside echo: *no clear evidence of right heart strain*

This patient has extensive bilateral PE with positive troponin and radiographic findings of right heart strain She is tachycardic but hemodynamically stable and responding well to IV fluids.

What initial management plan would you recommend:

A. Anticoagulation only
B. Systemic thrombolysis in addition to anticoagulation
C. Catheter-directed thrombolysis in addition to anticoagulation
D. IVC filter insertion in addition to anticoagulation

Recommendation.

For patients with PE with echocardiography and/or biomarkers compatible with right ventricular dysfunction but without hemodynamic compromise **(submassive PE)**, the panel suggests **anticoagulation alone** over the routine use of thrombolysis in addition to anticoagulation *(conditional recommendation, low certainty)*

Thrombolytic therapy in addition to anticoagulation versus **anticoagulation alone**:

Outcomes (Quality of Evidence)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with ***ANTICOAGULATION ALONE***	*Risk difference using* ***THROMBOLYSIS IN ADDITION TO ANTICOAG.***
● Mortality	**RR 0.61** (0.40 to 0.94)	133 out of 1,000 (13.3%)	**58 fewer death per 1,000** (9 fewer to 90 fewer)
● PE	**RR 0.56** (0.35 to 0.91)	16 out of 1,000 (1.6%)	**7 fewer PE per 1,000** (10 fewer to 2 fewer)
● Major bleeding	**RR 1.89** (1.46 to 2.46)	28 out of 1,000 (2.8%)	**31 more bleed per 1,000** (16 more to 51 more)
● Intracranial hemorrhage	**RR 3.17** (1.19-8.41)	3 per 1,000 (0.3%)	**7 more ICH per 1,000** (1 more to 21 more)

Remarks:

- Thrombolysis is reasonable to consider for younger patients with submassive PE at low risk for bleeding
- Patients with submassive PE should be monitored closely for hemodynamic compromise

Hemodynamic compromise: sBP < 90 mm Hg, or a decrease in sBP ≥ 40 mm Hg from baseline

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Patient is started on IV UFH and bridged to warfarin (preferred due to CKD), what do you recommend for duration and type of antithrombotic therapy?

A. 3-6 m*onths of anticoagulation then stop*

B. 3-6 months of anticoagulation, then continue anticoagulant therapy for secondary VTE prevention indefinitely

C. 3-6 months of anticoagulation then switch to ASA for secondary VTE prevention

D. 6-12 months of of anticoagulation then stop

Recommendation

After primary treatment for patients with DVT and/or PE **provoked by a chronic risk factor**, the panel *suggests* **indefinite antithrombotic therapy** over stopping anticoagulation (conditional recommendation moderate certainty)

Long-term compared with **short-term** anticoagulation for patients with VTE provoked by chronic risk factor

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with short- term	*Risk difference with long-term anticoagulation*
Mortality	**0.75** (0.49 to 1.13)	16 per 1,000	**4 fewer deaths per 1,000** (8 fewer to 2 more)
PE	**0.29** (0.15 to 0.56)	29 per 1,000	**21 fewer PE per 1,000** (25 fewer to 13 fewer)
DVT	**0.20** (0.12 to 0.34)	63 per 1000	**50 fewer DVT per 1,000** (56 fewer to 42 fewer)
Major bleeding	**2.17** (1.40 to 3.35)	5 per 1,000	**6 more bleeds per 1,000** (2 more to 12 more)

Chronic thrombotic risk factors include:

- Inflammatory bowel disease
- Autoimmune disease
- Active cancer
- Chronic immobility
- Chronic infections

*Results based on approx. 2 year follow up

Quality of Evidence (GRADE): Low Moderate Strong

Recommendation

For patients with DVT and/or PE who will continue to receive secondary prevention, the panel *suggests* using **anticoagulation over aspirin** (conditional recommendation, moderate certainty)

Aspirin compared with **anticoagulation** for patients with receiving secondary prevention for prior VTE

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with anticoagulation	*Risk difference with aspirin*
● Mortality	**0.86** (0.31 to 2.35)	7 per 1,000	**1 fewer deaths per 1,000** (5 fewer to 10 more)
● PE	**3.10** (1.24 to 7.73)	5 per 1,000	**11 more PE per 1,000** (1 more to 36 more)
● DVT	**3.15** (1.50 to 6.63)	8 per 1000	**17 more DVT per 1,000** (4 more to 46 more)
● Major bleeding	**0.49** (0.12 to 1.95)	5 per 1,000	**3 fewer bleeds per 1,000** (5 fewer to 5 more)

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Case Conclusion

Provoked submassive PE (chronic risk factor)

- Initial management:
  - Anticoagulation only (no thrombolysis, no compression stockings, no IVC filter)
  - Consider admission to hospital
- Duration of anticoagulation
  - Indefinite antithrombotic therapy with anticoagulation rather than ASA

Other guideline recommendations that were not covered in this session

- Home treatment vs hospital treatment for patients with PE and low risk for complication
- Thrombolytic therapy plus anticoagulation vs anticoagulation alone for patients with PE and hemodynamic compromise
- Systemic vs. catheter-directed thrombolysis for DVT, PE
- Breakthrough VTE
- INR intensity on warfarin when being used as the anticoagulant for secondary prophylaxis

Future Priorities for Research

- Which patients with DVT or PE would benefit most from thrombolytic therapy and optimal strategy for administration
- Which patient populations would benefit most from the incorporation of ≥1 of prognostic scores, D-dimer testing, and/or ultrasound into the decision-making process concerning whether anticoagulant therapy should be continued after completion of the primary treatment phase of therapy.
- Impact of different chronic risk factors on the rate of recurrent VTE
- Which patients can safely use a lower-dose DOAC for secondary prevention
- The evaluation and management of patients who sustain breakthrough thromboembolic events
- Which patients should continue antiplatelet therapy when anticoagulant therapy is initiated and which anticoagulant agent(s) and dose(s) are safest when coadministered with antiplatelet therapy.
- Which patients would potentially benefit from the use of compression stockings.

In Summary: Back to our Objectives

1. Describe the *initial management* of patients with deep vein thrombosis (DVT) and pulmonary embolism (PE)

2. Describe recommendations for *duration of anticoagulation* after venous thromboembolism (VTE)

3. Describe recommendations for management of *recurrent VTE*

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See more about the ASH VTE guidelines at www.hematology.org/VTEguidelines

Don’t miss our updated ASH VTE Guidelines Mobile App!