



ASH CLINICAL PRACTICE GUIDELINES
VENOUS THROMBOEMBOLISM (VTE)



Prevention of Venous Thromboembolism in Surgical Hospitalized Patients

An Educational Slide Set

American Society of Hematology 2019 Guidelines
for Management of Venous Thromboembolism

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Clinical Guidelines

American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients

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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

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

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

Example: PICO question

“Should mechanical prophylaxis vs. no prophylaxis be used for patients undergoing major surgery?”

EVIDENCE SYNTHESIS

Evidence summary generated for each PICO question via systematic review of health effects plus:

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

MAKING RECOMMENDATIONS

Recommendations made by guideline panel members based on evidence for all factors.

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 .



Objectives

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

1. Describe recommendations for VTE prophylaxis after major surgery, including common orthopedic procedures
2. Approach VTE prophylaxis in patients with major trauma
3. Describe recommendations for VTE prophylaxis after neurosurgical procedures



VTE is common following major surgical procedures

Surgery accounts for 25% of VTE in the community, even with current prophylaxis strategies

Post-op VTE risk **variable by procedure**; *higher risk* in joint arthroplasty, neurosurgery, vascular surgery, others

Post-op VTE may cause over 50,000 deaths annually in the United States

VTE after surgery often occurs **after hospital discharge** (particularly with shorter hospital admissions)

Patient groups addressed in this chapter

Patients undergoing
major surgical procedures
Includes cancer- and non-
cancer-related procedures

Patients hospitalized
for **major trauma**
Includes trauma patients
who did or did not undergo
surgical procedures

There are two major modalities applied for the prevention of post-operative VTE

Pharmacologic Prophylaxis

- Anticoagulants
(LMWH, UFH, direct oral anticoagulants, Vitamin K antagonists)
- Antiplatelet agents
(ASA)

Mechanical Prophylaxis

- Graduated compression stockings
- Intermittent Pneumatic compression devices
- IVC filters

What clinical outcomes were considered by the panel as critical to decision-making?

Where possible, questions were addressed with studies that reported symptomatic outcomes:

- Mortality
- Symptomatic VTE: *PE, proximal DVT, severe distal DVT*
- Major bleeding
- Reoperation

Less emphasis on asymptomatic VTE events (those detected on screening surveillance tests)

If symptomatic events not distinguished from asymptomatic, **modeling** was performed to estimate proportion of asymptomatic VTE that would become clinically important



The structure of these guidelines

Some recommendations are applicable to **specific types of surgery:**

- Pharmacological prophylaxis vs. no pharmacological prophylaxis
- Type of pharmacological prophylaxis

Other recommendations are applicable **across different types of major surgery, in general**

- Pharmacological prophylaxis vs. mechanical prophylaxis
- Duration of pharmacological prophylaxis
- Timing of pharmacological prophylaxis

Case 1: Total Hip Arthroplasty

69 year old male

Past Medical History: Diabetes, Hypertension, Osteoarthritis

Medications: Metformin, Ramipril, Lasix

Surgery:

- Elective total hip arthroplasty yesterday under spinal anesthesia
- Estimated blood loss 100 cc
- Surgical site looks clean and dry today



Your patient is post-operative day #1 following an elective total hip arthroplasty. He has no prior history of thrombosis, and is on no regular antithrombotic therapy.

What would you recommend today for post-operative VTE prophylaxis?

- A. Aspirin
- B. Direct oral anticoagulant
- C. Low molecular weight heparin (LMWH)
- D. Unfractionated heparin (UFH)
- E. Warfarin

Recommendation

For patients undergoing total hip arthroplasty or total knee arthroplasty, the panel suggests using **either ASA or anticoagulants** (*conditional recommendation, very low certainty*)

Aspirin compared with anticoagulants:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with ANTICOAGULANTS	Risk difference with ASPIRIN
● Mortality	RR 2.32 (0.15 to 36.90)	1 per 1,000	1 more death per 1,000 (1 fewer to 33 more)
● Symptomatic PE	RR 1.49 (0.37 to 6.09)	6 per 1,000	3 more PE per 1,000 (4 fewer to 29 more)
● Symptomatic proximal DVT	RR 1.49 (0.51 to 4.34)	6 per 1,000	3 more DVT per 1,000 (3 fewer to 30 more)
● Major bleeding	RR 2.63 (0.64 to 10.79)	4 per 1,000	6 more bleeds per 1,000 (1 fewer to 35 more)

Very low certainty evidence for any net health benefit or harm

Studies are ongoing comparing these options using clinically relevant endpoints



Recommendation

For patients undergoing total hip arthroplasty or total knee arthroplasty **where anticoagulants are used**, the panel suggests using **DOACs over LMWH** (*conditional recommendation, moderate certainty*)

DOACs compared with LMWH:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with <i>LMWH</i>	Risk difference with <i>DOACs</i>
● Mortality	RR 0.94 (0.53 to 1.66)	1 per 1,000	0 fewer deaths per 1,000 (1 fewer to 1 more)
● Symptomatic PE	RR 0.74 (0.50 to 1.10)	6 per 1,000	1 fewer PE per 1,000 (3 fewer to 1 more)
● Symptomatic proximal DVT	RR 0.56 (0.39 to 0.79)	6 per 1,000	3 fewer DVT per 1,000 (4 fewer to 1 fewer)
● Major bleeding	RR 1.03 (0.79 to 1.35)	10 per 1,000	0 fewer bleeds per 1,000 (2 fewer to 4 more)

Use of routine, out-of-hospital prophylaxis favored DOACs over LMWH given the need for parenteral administration of LMWH

If you decide to use an anticoagulant, any of the approved DOACs are reasonable options

Recommendation

For patients undergoing surgery, the panel suggests using any of the DOACs approved for use (*conditional recommendation, low certainty*)

There are no studies comparing:

- Different DOACs from the same class
- DOACs from different classes to each other (e.g. Xa inhibitor vs. direct thrombin inhibitor)

Benefits and harms appear to be similar for each DOAC, when potential differences were tested by analyzing for subgroup effects.

It's unclear how quickly antithrombotic prophylaxis should be started after major surgery, in general

Recommendation

For patients undergoing major surgery, the panel suggests using **either early or delayed** antithrombotic prophylaxis (*conditional recommendation, very low certainty*)

Early (<12 hours) compared with **Delayed**:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with <i>Delayed</i>	Risk difference with <i>Early</i>
● Symptomatic PE	RR 0.63 (0.23 to 1.72)	8 per 1,000	3 fewer PE per 1,000 (6 fewer to 6 more)
● Symptomatic proximal DVT	RR 0.88 (0.40 to 1.96)	19 per 1,000	2 fewer DVT per 1,000 (10 fewer to 16 more)
● Major bleeding	RR 1.63 (0.81 to 3.29)	7 per 1,000	5 more bleeds per 1,000 (1 fewer to 17 more)
● Reoperation	RR 1.84 (0.89 to 3.80)	2 per 1,000	2 more re-operation per 1,000 (0 fewer to 6 more)



After hearing about the evidence, your patient would prefer to take a DOAC, which is started in the morning of post-operative day 1.

How long should he receive post-operative pharmacologic prophylaxis for?

- A. In hospital only
- B. Short-term duration (4 to 14 days)
- C. Extended duration (19 to 42 days)
- D. Indefinite anticoagulation therapy



Recommendation

- For patients undergoing major surgery, the panel suggests using **extended prophylaxis over short-term prophylaxis** (*conditional recommendation, very low certainty*)
- “Extended” – beyond 3 weeks (19-42 days); “Short-term” – up to 2 weeks (4 -14 days)

Extended compared with Short-term antithrombotic prophylaxis:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with <i>Short-term</i>	Risk difference with <i>Extended</i>
● Mortality	RR 0.94 (0.64 to 1.39)	16 per 1,000	1 fewer death per 1,000 (6 fewer to 6 more)
● Symptomatic PE	RR 0.44 (0.22 to 0.85)	8 per 1,000	4 fewer PE per 1,000 (6 fewer to 1 fewer)
● Symptomatic proximal DVT	RR 0.30 (0.21 to 0.42)	16 per 1,000	12 fewer DVT per 1,000 (13 fewer to 10 fewer)
● Major bleeding	RR 1.00 (0.59 to 1.70)	8 per 1,000	0 fewer bleeds per 1,000 (3 fewer to 6 more)

These data are largely limited to two high-risk surgical scenarios (hip and knee arthroplasty, cancer general surgical procedures)

More studies are needed in other surgical scenarios.



Case 1: Conclusion

Your patient is discharged on low-dose DOAC for 5 weeks.

He is seen in follow-up by his surgeon at 5 weeks and has done well, with no thrombotic or bleeding complications.

Case 2: Trauma

74 year old female falls down the stairs and strikes her head

Past Medical History: diabetes, hypertension

Medications: gliclazide, ramipril, amlodipine

Clinical Course

- CT head: moderate subdural hemorrhage, 2 x 3 cm, mild mass effect
- No neurologic deficits, normal mental status, hemodynamics stable
- Admitted to the Trauma Intensive Care Unit for observation, with no plans for surgical intervention



This patient has been admitted with a moderate-sized subdural hemorrhage to the critical care unit. The neurosurgical team feels she is at high bleeding risk. There are no plans for surgery.

What would you recommend for thromboprophylaxis at this juncture?

- A. No prophylaxis is indicated as she is at low thrombotic risk
- B. Mechanical prophylaxis only
- C. Pharmacologic prophylaxis only
- D. Combined (mechanical and pharmacologic) prophylaxis



Recommendation

For patients experiencing major trauma, the panel suggests:

If LOW to MODERATE risk of bleeding, **suggest pharmacological prophylaxis**

If HIGH risk of bleeding, **suggest against pharmacological prophylaxis**

(conditional recommendation, very low certainty)

Pharmacologic compared with **NO pharmacologic** prophylaxis:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with NO pharmacologic	Risk difference with Pharmacologic
● Mortality	RR 0.95 (0.84 to 1.07)	71 per 1,000	4 fewer death per 1,000 (11 fewer to 5 more)
● Symptomatic PE	RR 0.49 (0.33 to 0.72)	15 per 1,000	3 fewer PE per 1,000 (5 fewer to 2 fewer)
● Symptomatic proximal DVT	RR 0.51 (0.38 to 0.69)	13 per 1,000	7 fewer DVT per 1,000 (9 fewer to 4 fewer)
● Major bleeding	RR 1.24 (1.12 to 1.37)	24 per 1,000	14 more bleeds per 1,000 (7 more to 21 more)

Must re-evaluate **bleeding risk** periodically as patients recover from trauma

Trauma patients should receive mechanical prophylaxis while anticoagulants are contraindicated.

Recommendation

For patients undergoing major surgery who do not receive pharmacologic prophylaxis, the panel suggests using **mechanical prophylaxis over no mechanical prophylaxis** (*conditional recommendation, very low certainty*)

- **This recommendation in the guidelines applies to surgical patients**
- However, in the absence of specific contraindications (including lower limb injuries), *trauma patients should also receive mechanical prophylaxis if anticoagulants cannot be given safely*



72 hours later the patient remains stable. Her repeat CT head shows no change in the size of her hemorrhage. She is still in the intensive care unit and has limited mobility. The neurosurgical team feels she can receive pharmacologic prophylaxis safely now.

What would you recommend at this juncture?

- A. Continue mechanical prophylaxis only
- B. LMWH
- C. UFH
- D. Prophylactic inferior vena cava filter insertion

Recommendation

For patients experiencing major trauma in whom pharmacological prophylaxis is used, the panel suggests using **either LMWH or UFH** (*conditional recommendation, low certainty*)

LMWH prophylaxis compared with UFH prophylaxis:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with UFH prophylaxis	Risk difference with LMWH prophylaxis
● Mortality	RR 1.32 (0.14 to 12.39)	5 per 1,000	2 more deaths per 1,000 (4 fewer to 54 more)
● Symptomatic PE	RR 1.04 (0.11 to 9.92)	3 per 1,000	0 fewer PE per 1,000 (6 fewer to 61 more)
● Symptomatic proximal DVT	RR 0.57 (0.25 to 1.31)	7 per 1,000	3 fewer DVT per 1,000 (5 fewer to 2 more)
● Major bleeding	RR 2.40 (0.53 to 10.78)	14 per 1,000	20 more bleeds per 1,000 (7 more to 138 more)



Case 2: Conclusion

Your patient is started on prophylactic LMWH for VTE prophylaxis.

There are no signs of recurrent bleeding and she is discharged from the intensive care unit to the neurosurgical ward in stable condition.

While in hospital she does not develop VTE and is subsequently discharged to rehabilitation.

Case 3: Neurosurgery

35 year old female with 4 x 4 cm meningioma causing mild mass effect

Past Medical History: healthy

Medications: none

Exam: Normal vital signs. Surgical site clean and dry. Weight 70 kg.

Clinical Course

- Undergoes uneventful neurosurgical resection of this benign tumour
- Admitted to neurosurgical ward post-operatively
- Transferring out of bed and walking to bathroom independently



You are seeing this patient on post-operative day #1 following her meningioma resection. She is ambulating and is expected to be in hospital for the next 5 to 7 days while she recovers. She has no prior history of thrombosis.

What should she receive for post-operative VTE prophylaxis?

- A. No pharmacologic prophylaxis
- B. LMWH
- C. UFH
- D. Prophylactic IVC filter insertion



Recommendation

For patients undergoing major neurosurgical procedures, the panel **suggests against using pharmacological prophylaxis** (*conditional recommendation, very low certainty*)

Pharmacologic compared with **No Pharmacologic** prophylaxis:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with <i>No Pharmacologic</i>	Risk difference with <i>Pharmacologic</i>
● Mortality	RR 1.27 (0.57 to 2.86)	35 per 1,000	9 more deaths per 1,000 (15 fewer to 65 more)
● Symptomatic PE	RR 0.84 (0.03 to 27.42)	2 per 1,000	0 fewer PE per 1,000 (2 fewer to 53 more)
● Symptomatic proximal DVT	RR 0.50 (0.30 to 0.84)	12 per 1,000	6 fewer DVT per 1,000 (8 fewer to 2 fewer)
● Major bleeding	RR 1.57 (0.70 to 3.50)	17 per 1,000	10 more bleeds per 1,000 (5 fewer to 43 more)
● Re-operation	RR 0.43 (0.06 to 2.84)	31 per 1,000	18 fewer re-OR per 1,000 (29 fewer to 57 more)

These risk estimates, and the panel's recommendations, are based on RCT data.

Patients undergoing neurosurgery will also routinely receive mechanical prophylaxis methods.

Why is pharmacologic prophylaxis not routinely recommended after neurosurgical procedures?

- Benefit of pharmacological prophylaxis after neurosurgical procedures is likely small
 - While observational data favor pharmacologic prophylaxis, randomized data suggest lower risk reduction in VTE
 - Benefits of pharmacological prophylaxis often seen in asymptomatic DVT using screening venography, which may not be as clinically important
- Harms of major bleeding from pharmacologic prophylaxis are moderate due to greater potential for morbidity from this surgical site
- Effective prophylaxis can be provided via mechanical methods



You are seeing another patient on the same day who also had meningioma resection the day before. *This patient is 78 years old, has obesity, and Parkinson's Disease.* He is expected to be in hospital for 5 to 7 days post-operatively but has limited mobility.

What would you suggest for post-operative VTE prophylaxis?

- A. No pharmacologic prophylaxis
- B. LMWH
- C. UFH
- D. Direct oral anticoagulant
- E. Prophylactic IVC filter insertion

Either of these choices is reasonable as there is very low certainty in the evidence

However, pharmacological prophylaxis **may be considered** in the following circumstances (*including this case*):

- Subgroups of patients at higher thrombosis risk, including those with *prolonged immobility after surgery*
- Neurosurgical procedures with *lower risk of major bleeding*
- Persistent mobility restriction *after immediate post-surgical bleeding risk has subsided*



Recommendation

- For the **subset of patients** undergoing major neurosurgical procedures for whom pharmacologic prophylaxis is used, the panel suggests using **LMWH over UFH** (*conditional recommendation, very low certainty*)

LMWH prophylaxis compared with UFH prophylaxis:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with UFH Prophylaxis	Risk difference with LMWH Prophylaxis
● Mortality	RR 0.34 (0.04 to 3.21)	5 per 1,000	3 fewer death per 1,000 (5 fewer to 11 more)
● Symptomatic PE	RR 0.20 (0.01 to 4.03)	2 per 1,000	2 fewer PE per 1,000 (2 fewer to 6 more)
● Symptomatic proximal DVT	RR 1.00 (0.14 to 6.91)	12 per 1,000	0 fewer DVT per 1,000 (10 fewer to 71 more)
● Major bleeding	RR 0.76 (0.20 to 2.95)	22 per 1,000	5 fewer bleeds per 1,000 (18 fewer to 43 more)

Although there was very low certainty, the net benefit was judged to favor LMWH over UFH



What about prophylactic IVC filter insertion? Not recommended before major surgery, including this case

Recommendation

- For patients undergoing major surgery, the panel **suggests against using IVC filters** for prophylaxis of VTE (*conditional recommendation, very low certainty*)

IVC Filter compared with No IVC Filter:

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with No IVC Filter	Risk difference with IVC filter
● Mortality	RR 1.38 (0.81 to 2.37)	11 per 1,000	4 more deaths per 1,000 (2 fewer to 15 more)
● Symptomatic PE	RR 0.29 (0.11 to 0.80)	11 per 1,000	8 fewer PE per 1,000 (10 fewer to 2 more)
● Symptomatic proximal DVT	RR 2.19 (1.07 to 4.50)	26 per 1,000	31 more DVT per 1,000 (2 fewer to 92 more)

High rates of DVT and trend towards higher mortality with filters **outweigh potential reduction in risk of PE**

Recommendations also did not consider **potential harms of filter insertion** (e.g. IVC perforation, filter embolization)

Should this patient also receive mechanical prophylaxis? Two additional recommendations

Recommendation

- For patients undergoing major surgery who receive pharmacologic prophylaxis, the panel suggests **using combined prophylaxis** with mechanical and pharmacologic methods over pharmacologic agents alone (*conditional recommendation, very low certainty*)
 - **REMARK:** for patients at high risk for VTE, combined prophylaxis is particularly favored over either mechanical or pharmacologic alone
-
- **There may be a reduction in the risk of PE** (RR 0.40, 95% CI 0.26-0.65) in favor of combined prophylaxis but net health benefit is uncertain
 - Panel unable to assess for potential drawbacks of mechanical prophylaxis (e.g. falls, skin complications) which are often unmeasured

Should this patient also receive mechanical prophylaxis? Two additional recommendations

Recommendation

- For patients undergoing major surgery who receive mechanical prophylaxis, the panel suggests using **intermittent pneumatic compression devices over graduated compression stockings** (*conditional recommendation, very low certainty*)
- There may be no difference in symptomatic PE, but **risk of symptomatic DVT may be reduced with pneumatic compression** (RR 0.48, 95% CI 0.25-0.93)
- In settings where pneumatic compression devices are not available, graduated compression stockings are an acceptable and feasible option



Case 3: Conclusion

Your first patient (**35 year old, mobile**) receives **graduated compression stockings** as pneumatic compression devices are not available on your ward. **She does not receive pharmacologic prophylaxis.** She is encouraged to ambulate and is discharged after 5 days.

Your second patient (**78 year old, immobile**) receives **combined prophylaxis with graduated compression stockings and LMWH.** He does not experience any bleeding or thrombotic complications and is discharged to rehabilitation after 8 days in hospital.

Other procedure-specific recommendations

Surgery type	The panel suggests (rec. number)	Comment or Rationale
Hip fracture repair	Pharmacological prophylaxis over no pharmacological prophylaxis (14); using either LMWH or UFH (15)	Small increase in bleeding risk with prophylaxis outweighed by moderate reductions in PE and DVT
Major general surgery	Pharmacological prophylaxis over no pharmacological prophylaxis (16); using either LMWH or UFH (17)	Small increase in bleeding risk with prophylaxis outweighed by moderate reductions in PE and DVT
Laparoscopic cholecystectomy	Panel suggests <u>against</u> using pharmacologic prophylaxis (18)	Very low baseline VTE risk. Specific high risk groups (thrombophilia, prior VTE, cancer) may benefit
Cardiac and vascular surgery	Either pharmacologic or no pharmacologic prophylaxis (25)	Possible reductions in VTE, and increases in bleeding with pharmacologic prophylaxis. Possible harms including development of HIT, particularly with UFH

Other procedure-specific recommendations

Surgery type	The panel suggests (rec. number)	Comment or Rationale
Gynecologic	Pharmacological prophylaxis over no pharmacological prophylaxis (29); using either LMWH or UFH (30)	Reduction in VTE outweighs small increase in major bleeding risk
TURP	Panel suggests <u>against</u> using pharmacologic prophylaxis (21)	Very low baseline VTE risk after this procedure
Radical prostatectomy	Panel suggests against using pharmacologic prophylaxis (23)	Assuming average patient undergoing robotic laparoscopic procedures. Risk may be higher if open procedure or extensive nodal dissection

Identified Areas of Future Investigation

- Benefit of combined prophylaxis compared with pharmacologic alone
- Extended prophylaxis outside of orthopedics and cancer surgery
- Optimal duration of extended pharmacologic prophylaxis
- Timing of initiating prophylaxis in higher-risk bleeding procedures
- Comparison of different prophylaxis strategies for hip fracture surgery
- Benefits and risks of pharmacologic prophylaxis after neurosurgery, using clinically important endpoints
- Use of delayed pharmacologic prophylaxis in trauma patients with major bleeding, including intracranial hemorrhage



Back to our Objectives

1. Describe recommendations for VTE prophylaxis after major surgery, including common orthopedic procedures
 - Recommendations for arthroplasty and other elective procedures
2. Approach VTE prophylaxis in patients with major trauma
 - Initiation of pharmacologic prophylaxis after assessing bleeding risk
3. Describe recommendations for VTE prophylaxis after neurosurgical procedures
 - Potential morbidity of post-operative bleeding often outweighs potential benefit; take thrombotic risk (including post-operative mobility) into account



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