

The Management of Anticoagulation for Venous Thromboembolism in the Hospitalized Adult

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Anticoagulation for patients with venous thromboembolism (VTE) is associated not only with considerable benefits, including prevention of pulmonary embolus and thrombus extension, but also with potential significant risks, such as life-threatening bleeding.¹ Hospitalized patients may require anticoagulation to treat new VTE or for secondary prevention of prior events. Hospital admission is a high-risk time for anticoagulation control.² Additionally, anticoagulation has become an increasingly complex decision as the number of therapeutic agents on the market has significantly increased, coupled with medication interactions and dosing intricacies. Management is multifaceted and associated with wide variation in practice patterns.³ Thus, further evidence-based guidance for providers is necessary for the care of the hospitalized patient with VTE.

KEY RECOMMENDATIONS FOR THE HOSPITALIST

The following are 16 selected guideline recommendations most relevant to adult hospitalists.⁴ Recommendations were graded as “strong” if most individuals should follow the recommended course of action and “conditional” if different choices are appropriate for different patients.

Initial Anticoagulant Dosing, Monitoring, and Medication Interactions

(for all recommendations—evidence quality: low certainty; recommendation strength: conditional)

Recommendation 1. In obese patients receiving low molecular weight heparin (LMWH), determine the initial dose based on actual body weight rather than a fixed or “capped” maximum dose.

Recommendation 2. For obese patients or those with renal dysfunction receiving LMWH, avoid dosing based on serum antifactor Xa levels. Instead, adjust dosing based on product labeling, with appropriate dose reduction in patients with chronic kidney disease.

Recommendation 3. For patients receiving direct oral anticoagulant (DOAC) therapy, avoid measuring the anticoagulation effect during management of bleeding as there is no

evidence to support a beneficial effect, and it may result in a delay in treatment.

Recommendation 4. For patients requiring administration of inhibitors or inducers of P-glycoprotein or cytochrome P450 enzymes, use LMWH or vitamin K antagonists (VKA) rather than a DOAC.

Recommendation 5. When transitioning from a DOAC to a VKA, the medications should overlap until the international normalized ratio (INR) is therapeutic instead of bridging with a heparin agent.

Recommendations for Ongoing Outpatient Monitoring upon Discharge from the Hospital

Recommendation 6. Use point-of-care INR testing by patients at home, with self-adjustment of VKA dose (evidence quality: low certainty; recommendation strength: strong).

Recommendation 7. Patients should be referred for specialized anticoagulation management rather than to their primary care provider (PCP) (evidence quality: very low certainty; recommendation strength: conditional).

Recommendation 8. Supplementary education, in addition to basic education, should be made available to patients to help improve outcomes (evidence quality: very low certainty; recommendation strength: conditional).

Hospitalists are often responsible for the coordination of care upon discharge from the hospital, including discharge teaching, subspecialty referrals, and determination of patient suitability for home monitoring and dose adjustment. The follow-up plan may depend on local systems and access. A PCP can manage anticoagulation if performed in a systematic and coordinated fashion.⁵

Recommendations for Patients on Anticoagulation Undergoing Procedures

Recommendation 9. For patients with a low or moderate risk of recurrent VTE on VKA therapy undergoing procedures, periprocedural bridging with heparin or LMWH should be avoided. This excludes patients at high risk for recurrent VTE, defined as those with recent VTE (<3 months); having a known thrombophilic abnormality such as antiphospholipid syndrome, protein C/S deficiency, or antithrombin deficiency; or high-risk patient populations by expert consensus and practice guidelines^{4,6} (evidence quality: moderate certainty; recommendation strength: strong).

Recommendation 10. For patients on DOACs undergoing procedures, measurement of the anticoagulation effect of the

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DOAC should be avoided (evidence quality: very low certainty; recommendation strength: conditional).

Recommendations for Patients on Anticoagulation Suffering from Supratherapeutic Levels or Bleeding Complications

(for all recommendations—evidence quality: very low certainty; recommendation strength: conditional)

Recommendation 11. If a patient on VKA therapy has an INR between 4.5 and 10 *without* clinically relevant bleeding, the use of vitamin K therapy can be avoided in favor of temporary cessation of VKA alone.

Recommendation 12. If a patient on VKA therapy has life-threatening bleeding, four-factor prothrombin complex concentrate (PCC) should be used in addition to the cessation of VKA therapy and initiation of vitamin K therapy, over the use of fresh frozen plasma, because of the ease of administration and minimal risk of volume overload.

Recommendation 13. If a patient has life-threatening bleeding on a Xa inhibitor, the panel recommends discontinuation of the medication and the option to administer either PCC or recombinant coagulation factor Xa, as there have been no studies comparing these two strategies.

Recommendation 14. If life-threatening bleeding occurs in a patient on dabigatran, idarucizumab should be administered, if available.

Recommendation 15. In patients with bleeding while on heparin or LMWH, protamine should be administered.

Recommendation 16. Following an episode of life-threatening bleeding, anticoagulation should be resumed within 90 days, provided that the patient is at moderate to high risk for recurrent VTE, is not at high risk for recurrent bleeding, and is willing to continue anticoagulation.

CRITIQUE

Methods in Preparing Guidelines

The panel was funded by the American Society of Hematology (ASH), a nonprofit medical specialty society.⁴ The panel is multidisciplinary, including physicians and providers as well as patient representatives, and is supported by the McMaster University GRADE Center, which conducted new and updated systematic reviews of the evidence according to the “Cochrane Handbook for Systematic Reviews of Interventions.” The panel members agreed on 25 recommendations and two good practice statements. The recommendations were made available to external review by stakeholders and addressed. Comments made by 10 individuals or organizations were subsequently incorporated.

Sources of Potential Conflict of Interest

Panel members, other than patient representatives, did not receive funding, and the majority of the panel had no conflicts of interest to report. Given the minimal influence of outside parties including pharmaceutical companies, and the wide

diversity of opinions sought in the creation of the guidelines, concern for conflict of interest is low.

Generalizability

These guidelines assume that the decision to anticoagulate a patient, and which agent to use, has already been made and thus do not offer further guidance on this decision. These guidelines also do not address optimal choices for anticoagulation in specific patient populations, such as patients with cancer. They are limited in scope to exclude the treatment of specific thromboembolic disease processes such as subsegmental pulmonary emboli, superficial venous thrombus, or distal vein thrombosis. Unfortunately, challenging decisions made by hospitalists frequently fall into one of these categories. Coincident with these guidelines, ASH introduced comprehensive guidelines to support basic diagnostic decisions.⁷

AREAS IN NEED OF FUTURE STUDY

More evidence is needed to better understand optimal monitoring practices for patients on anticoagulation therapy, including the ideal INR monitoring frequency for patients on VKA therapy. Additionally, there is a need to better understand the difference in clinical outcomes and resources utilization when care is provided by an anticoagulation specialist as compared with a PCP. Finally, while guidelines suggest that anticoagulation should be resumed within 90 days of a life-threatening bleed, there is a need to better understand the optimal timing of a restart, as well as the patient factors to be considered in this decision.

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References

1. Nutescu EA, Burnett A, Fanikos J, Spinler S, Wittkowsky A. Pharmacology of anticoagulants used in the treatment of venous thromboembolism [published correction appears in *J Thromb Thrombolysis*. 2016;42(2):296-311]. *J Thromb Thrombolysis*. 2016;41(1):15-31. <https://doi.org/10.1007/s11239-015-1314-3>.
2. van Walraven C, Austin PC, Oake N, Wells PS, Mamdani M, Forster AJ. The influence of hospitalization on oral anticoagulation control: a population-based study. *Thromb Res*. 2007;119(6):705-714.
3. Rodwin BA, Salami JA, Spatz ES, et al. Variation in the use of warfarin and direct oral anticoagulants in atrial fibrillation and associated cost implications. *Am J Med*. 2019;132(1):61-70. <https://doi.org/10.1016/j.amjmed.2018.09.026>.
4. Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Adv*. 2018;2(22):3257-3291. <https://doi.org/10.1182/bloodadvances.2018024893>.
5. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [published correction appears in *Chest*. 2012;142(6):1698-1704]. *Chest*. 2012;141(2 suppl):e419S-e496S. <https://doi.org/10.1378/chest.11-2301>.
6. Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008;133(6 suppl):299S-339S. <https://doi.org/10.1378/chest.08-0675>.
7. Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. *Blood Adv*. 2018;2(22):3226-3256. <https://doi.org/10.1182/bloodadvances.2018024828>.