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GUIDELINE UPDATE I: VENOUS THROMBOEMBOLISM (VTE) MANAGEMENT

An update of the CHEST guideline on VTE management was published in August 2021 and contains guidance relevant to hospitalists.¹ Pertinent updates include the management of distal deep vein thrombosis (DVT), subsegmental pulmonary embolism (PE), and anticoagulation duration.

Deep and Superficial Venous Thrombosis

For patients with acute, isolated, distal (i.e., below-the-knee) lower extremity DVT with severe symptoms or risk factors for extension,^a anticoagulation is suggested (weak recommendation).¹ For patients with superficial venous thrombosis and risk factors for clot progression (including above-the-knee location or involving the greater saphenous vein),^a 45 days of fondaparinux 2.5mg is advised (weak recommendation). Rivaroxaban 10mg daily is an appropriate alternative (weak recommendation, new guidance).¹

Take away: Many hospitalized patients diagnosed with an acute distal DVT will have risk factors for clot extension;^a therefore Direct Oral Anticoagulant (DOAC) therapy should be considered. Similarly, superficial venous thromboses may be managed with daily low dose rivaroxaban for 45 days if the thrombosis is in the thigh or the greater saphenous vein, or if traditional VTE risk factors are present.^a

Subsegmental Pulmonary Embolism (SSPE)

In patients with an isolated subsegmental PE and no DVT who are deemed low risk for recurrent VTE,^a clinical surveillance is suggested (weak recommendation).¹ Characteristics that might prompt anticoagulation, in addition to the risk factors below,^a include multiple intra-

luminal defects, visible clot on multiple images/projections, an elevated d-dimer, severe symptoms, or a high pre-test probability for PE. In the setting of a “low-risk” PE, outpatient treatment is recommended (strong recommendation).¹ A simplified Pulmonary Embolism Severity Index (sPESI) score of zero can help support the decision for outpatient treatment but is not required. Conversely, right ventricular dysfunction or elevated cardiac biomarkers should dissuade outpatient management.

Take away: Most inpatients with an isolated SSPE will warrant anticoagulation based on either risk factors,^a imaging findings, or the results of a lower extremity venous ultrasound. In hemodynamically stable patients without significant comorbidities and with appropriate access to medical care, outpatient management of low-risk PE is favored.

Cancer-associated VTE

Oral Xa inhibitors are now recommended over low molecular weight heparin (LMWH) in the setting of cancer-associated VTE (strong recommendation).¹ Apixaban or LMWH is preferred with luminal gastrointestinal tract cancers.

Take-away: In patients with cancer-associated VTE, apixaban is the drug of choice.

Duration of Anticoagulation

If the acute VTE is unprovoked, or the risk factor for VTE^a is expected to persist, extended anticoagulation with reduced-dose direct-acting oral anticoagulant beyond three months is recommended (strong recommendation regarding duration).¹

Take-away: In patients with an unprovoked VTE or VTE with a persistent risk factor,^a ongoing anticoagulation with a low-dose DOAC should be considered after at least three months of full treatment. This decision should

account for patient preference, bleeding risk, and should be re-evaluated yearly or with any change in clinical status.

VTE risk factors^a

- **Major risk factors** within three months before VTE diagnosis:
 - Surgery > 30 minutes with general anesthesia
 - Hospitalized with acute illness for > 2 days and significantly reduced mobility
 - Cesarean section
 - Major trauma
- **Minor risk factors** within two months before VTE diagnosis:
 - Surgery < 30 minutes with general anesthesia
 - Hospitalized with acute illness for < 3 days
 - Estrogen therapy
 - Pregnant or peri-partum
 - Bedbound with an acute illness out of hospital for > 2 days
 - Prolonged car or air travel
 - Leg injury with reduced mobility > 2 days
- **Persistent risk factors**
 - Example: Active cancer, Antiphospholipid syndrome

5-10mg (“strong opioid;” n=59) four times daily or codeine/acetaminophen 8mg/500mg-16mg/1000mg four times daily (“mild opioid;” n=61) for up to three weeks.

The primary outcome, mean daily pain score days 1 to 7 post-discharge, was 4.04 (95% CI, 3.67 to 4.41) in the strong opioid group and 4.54 (95% CI, 4.17 to 4.90) in the mild opioid group. The difference was not statistically significant (−0.50 [95% CI, −1.11 to 0.12]; p = 0.11). The daily oral morphine equivalent was 32.9mg in the strong opioid group versus 5.5mg in the mild opioid group, a 6-fold difference. The mean number of tablets used was not statistically different between groups.

Other investigators have also shown benefits with weak opioids. A 2009 Cochrane review found significant analgesic effect in a variety of post-operative patients with codeine 30-60mg/300-1000mg acetaminophen.³ Another study examining post-operative oral surgery pain found significant benefit of codeine 30mg/acetaminophen 300mg compared to placebo.⁴ Taken together, these studies suggest that weak opioids such as codeine/acetaminophen are effective for post-operative pain and can reduce the opioid burden.

Take away: In patients with a surgically managed tibia fracture, a discharge pain control regimen that includes codeine/acetaminophen would be appropriate.

GUIDELINE UPDATE 2: IS CODEINE/ACETAMINOPHEN APPROPRIATE FOR PAIN CONTROL AFTER A FRACTURE?

Case: A 40-year-old male sustains a mid-shaft tibia fracture in a motor vehicle accident. He is managed with surgical fixation, acetaminophen, ibuprofen, and oxycodone. What should he be prescribed for pain upon discharge?

A recent, double-blind, randomized controlled trial from a single major trauma hospital in Sydney, Australia sought to answer this question.² Investigators enrolled 120 patients (75% men, mean age 37 years) with one or more acute, non-pathologic fracture(s) of a long bone, the pelvis, or foot, managed with surgical fixation. Post-operative pain was treated at the discretion of the inpatient team. At discharge, the mean pain score was 4 out of 10. Patients were randomized to receive oxycodone

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Conflicts of Interest

The author has no conflicts of interest to disclose.



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REFERENCES

1. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. *Chest*. 2021;160(6):e545-e608. [doi:10.1016/j.chest.2021.07.055](https://doi.org/10.1016/j.chest.2021.07.055)
2. Jenkin DE, Naylor JM, Descallar J, et al. Effectiveness of Oxycodone Hydrochloride (Strong Opioid) vs Combination Acetaminophen and Codeine (Mild Opioid) for Subacute Pain After Fractures Managed Surgically: A Randomized Clinical Trial. *JAMA Network Open*. 2021;4(11):e2134988. [doi:10.1001/jamanetworkopen.2021.34988](https://doi.org/10.1001/jamanetworkopen.2021.34988)
3. Toms L, Derry S, Moore RA, et al. Single Dose Oral Paracetamol (Acetaminophen) with Codeine for Postoperative Pain in Adults. *Cochrane Database of Systematic Reviews*. 2009;(1). [doi:10.1002/14651858.cd001547.pub2](https://doi.org/10.1002/14651858.cd001547.pub2)
4. Forbes JA, Bates JA, Edquist IA, et al. Evaluation of Two Opioid-Acetaminophen Combinations and Placebo in Postoperative Oral Surgery Pain. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy - Wiley Online Library*. 1994;14:139-146. [doi:10.1002/j.1875-9114.1994.tb02800.x](https://doi.org/10.1002/j.1875-9114.1994.tb02800.x)