American Association for the Surgery of Trauma/American College of Surgeons Committee on Trauma clinical protocol for postdischarge venous thromboembolism prophylaxis after trauma

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ABSTRACT: Trauma patients are at an elevated risk for developing venous thromboembolism (VTE), which includes pulmonary embolism and deep vein thrombosis. In the inpatient setting, prompt pharmacologic prophylaxis is utilized to prevent VTE. For patients with lower extremity fractures or limited mobility, VTE risk does not return to baseline levels postdischarge. Currently, there are limited data to guide postdischarge VTE prophylaxis in trauma patients. The goal of these postdischarge VTE prophylaxis guidelines are to identify patients at the highest risk of developing VTE after discharge and to offer pharmacologic prophylaxis strategies to limit this risk. (*J Trauma Acute Care Surg.* 2024;96: 980–985. Copyright © 2024 Wolters Kluwer Health, Inc. All rights reserved.)

KEY WORDS: Deep vein thrombosis; pulmonary embolism; lovenox; enoxaparin; aspirin.

Trauma patients are at an elevated risk for developing venous thromboembolism (VTE), including both deep vein thrombosis (DVT) and pulmonary embolism (PE).[1–3] For this reason, trauma patients are routinely treated with pharmacologic VTE prophylaxis during their hospitalization with several consensus, standardized protocols already established (Table 1).[4–8] For many patients with severe traumatic injuries, the risk of VTE remains high even at the time of hospital discharge.[9,10] Therefore, postdischarge pharmacologic VTE prophylaxis is recommended in select patients at high risk for developing VTE after discharge.[11]

Protocol Rationale and Goals

Extended-duration VTE prophylaxis has shown efficacy in patients undergoing major orthopedic procedures as well as those requiring abdominopelvic surgery for cancer.[12,13] Currently, there are limited data to guide postdischarge VTE prophylaxis in trauma patients. Prolonged immobility, limited weight-bearing status, and an ongoing prothrombotic state can place trauma patients at an increased risk of VTE events that persists after discharge. The goal of these postdischarge VTE prophylaxis guidelines are to identify patients at the highest risk of developing VTE after discharge and to offer pharmacologic prophylaxis strategies that are safe, limit VTE risk, and promote patient adherence.

Members from the American Association for the Surgery of Trauma (AAST) and the American College of Surgeons Committee on Trauma (ACS-COT) with a clinical and/or research interest in optimizing VTE prophylaxis established a working group to develop this postdischarge VTE prophylaxis protocol. A comprehensive literature review on the topic was performed to identify peer-reviewed publications, guidelines, and protocols related to postdischarge VTE prophylaxis in trauma and orthopedic surgery patients. These studies were reviewed by work group members over a series of virtual meetings and the elements of the postdischarge VTE prophylaxis protocol were proposed for review by the group. After the workgroup came to consensus on the recommendations, the protocol was reviewed by the AAST Patient Assessment Committee and the ACS-COT Performance Improvement and Patient Safety (PIPS) leadership. The final clinical protocol was reviewed and approved by the AAST Board of Managers and the ACS-COT Executive Committee (Supplemental Digital Content, http://links.lww.com/TA/D655).

EVIDENCE BASE: BRIEF SUMMARY

Patient Selection

Longitudinal, postdischarge data in trauma patients with high risk injury patterns have demonstrated VTE rates of 10% in the first 3 months postinjury.[10] Therefore, we recommend continuation of VTE prophylaxis beyond the time of discharge in select, high-risk patients. Patients at increased risk of VTE after discharge include those with pelvic fractures, lower extremity fractures, spinal cord injury (SCI), or those unable to ambulate independently because of their injuries (Table 1).[11] Patients with other conditions increasing their risk of VTE, such as prior thrombotic events or malignancy, should undergo individualized risk assessment and extended prophylaxis may be considered.

Medication Choice

Numerous agents have been studied for extended-duration VTE prophylaxis in the orthopedic literature including low molecular weight heparin (LMWH), warfarin, direct oral anticoagulants (DOACs) and aspirin. Most studies have focused on total hip arthroplasty (THA), total knee arthroplasty (TKA), or hip fracture fixation.[14,15] Current orthopedic guidelines are based upon initial studies and subsequent meta-analyses that report a significant reduction in VTE without a significant increase in risk of major bleeding within the first 14–35 days postoperatively, which correlates with the highest risk period for VTE.[16–18] While current orthopedic clinical practice guidelines

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TABLE 1. National and International Guidelines

Organization	Guideline	References
American College of Surgeons–Committee on Trauma	American College of Surgeons–Committee on Trauma Best Practices Guidelines: Spine Injury	Trauma Quality Programs Best Practices Guidelines: Spine injury. American College of Surgeons. March 2022; Accessed: July 16, 2023. Available at: https://www.facs.org/-/media/files/quality-programs/trauma/tqip/spine_injury_guidelines.ashx.
Western Trauma Association	Updated guidelines to reduce venous thromboembolism in trauma patients: A Western Trauma Association critical decisions algorithm.	Ley EJ, Brown CVR, Moore EE, et al. Journal of Trauma and Acute Care Surgery: November 2020;89:971–981
American Association for the Surgery	American Association for the Surgery of Trauma / American College of Surgeons–Committee on Trauma Clinical Protocol for Inpatient Venous Thromboembolism Prophylaxis after Trauma	Yorkgitis BK, Berndtson AE, Cross A, et al. J Trauma Acute Care Surg. 2022;82:597–604.
Eastern Association for the Surgery of Trauma	Practice management guidelines for the prevention of VTE in Trauma Patients: The EAST practice management guidelines workgroup.	Rogers FB, Cipolle MD, Velmahos G, et al. J Trauma. 2002;53:142–164.
American Society of Hematology	American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients	Anderson DR, Morgano GP, Bennett C, et al. Blood Adv. 2019;3:3898–3944

recommend extended-duration prophylaxis postdischarge, the medication of choice is evolving.[19] LMHW is favored by many studies and is the first-line prophylactic medication recommended in the most recent CHEST guidelines for orthopedic surgery VTE prophylaxis[20–22]; however, many recent studies have shown that oral agents, such as aspirin and DOACs, are efficacious and may have increased patient compliance.[23] The decreased cost of aspirin compared with LMWH or DOACs is another important factor that may enhance compliance postdischarge.

Utilizing aspirin for postdischarge prophylaxis was initially supported by a study in 398 orthopedic surgery patients comparing an initial 10 days of LMWH (dalteparin) after THA followed by randomization to daily aspirin 81 mg versus ongoing daily LMWH (dalteparin 5000 units) for an additional 28 days. This study demonstrated no difference in rates of VTE (1.3% dalteparin vs. 0.3% aspirin) or major bleeding, suggesting that aspirin is noninferior to LMWH and offers a safe and effective approach to postdischarge VTE prophylaxis.[24] Because of these data, improved compliance and relatively low cost, there has been increased use of aspirin for postdischarge VTE prophylaxis after joint surgery.[25,26] Recently, the landmark study by the Major Extremity Trauma Research Consortium (METRC) compared aspirin versus LMWH for thromboprophylaxis in trauma patients with an extremity fracture treated operatively or any pelvic/acetabular fracture.[27] This multicenter, pragmatic study enrolled 12,211 patients who were randomized to either receive aspirin 81 mg twice daily versus LMWH 30 mg twice daily starting in the inpatient setting. Postdischarge prophylaxis was at the discretion of the treating physician; however, the median duration of thromboprophylaxis postdischarge was 21 days and did not differ between treatment groups. The primary outcome of the study was death at 90 days, which was not different between groups. DVT rates were low in this study population overall, but more frequent in patients who had received aspirin than in those who had received heparin (2.5% vs. 1.7%), although the difference was not statistically significant. There was no difference in PE or bleeding complications between patients treated with aspirin versus LMWH. This is the best evidence to date that aspirin is noninferior to LMWH for patients with pelvic and operative extremity fracture and its use is associated with low VTE rates.

Direct oral anticoagulants (DOACs) have also been considered for postdischarge VTE prophylaxis in orthopedic surgery patients. Previous studies comparing DOACs versus LMWH for extended prophylaxis in patients undergoing THA or TKA have demonstrated mixed results. A randomized, double blinded, non-inferiority trial of 3,494 patients compared daily dabigatran (150 mg or 220 mg) versus daily LMWH (enoxaparin 40 mg) after THA with a median treatment duration of 33 days. They found no difference in the primary endpoint of VTE or death from all causes between groups (enoxaparin 6.7%, dabigatran 150 mg 8.6%, dabigatran 220 mg 6.0%), as well as no difference in major bleeding events.[28] They concluded that both doses of dabigatran were noninferior to enoxaparin for VTE prevention. Conversely, a pooled analysis of the ADVANCE-2[29] and ADVANCE-3[30] randomized trials compared twice daily apixaban 2.5 mg daily versus daily LMWH (enoxaparin 40 mg) for patients following THA or TKA. This study evaluated 8,464 patients demonstrating a significant reduction in VTE events in patients treated with apixaban (0.7% vs. 1.5%) with no difference in major bleeding events.[31] A retrospective cohort study of 29,684 patients who underwent THA or TKA demonstrated that choice of prophylaxis agent (DOAC vs. aspirin) did not alter VTE risk; however postoperative bleeding risk was lower in patients treated with aspirin.[32] Several studies have demonstrated that DOAC use is safe and efficacious in limiting VTE risk in orthopedic and select orthopedic trauma patients.[33–35] Based on the widespread use of DOACs for other indications, DOAC use for VTE prophylaxis after major orthopedic surgery and in trauma patients is increasing.[26,36,37] Use of DOACs for postdischarge prophylaxis is an acceptable approach to decrease VTE risk; however, because there are limited data directly comparing DOACs to LMWH or aspirin for high-risk orthopedic trauma or polytrauma patients, we currently do not recommend DOACs for routine postdischarge prophylaxis in trauma patients.[38]

Aspirin Dosing

The dose of aspirin utilized in different trials assessing its efficacy for VTE prophylaxis is highly variable, with reports including aspirin 81 mg daily or BID, 100 mg daily, 150 mg daily, 160 mg daily, 300 mg daily or BID, and 325 mg daily, BID, or TID.[24,39] Older studies from the 1970s and 1980s even included doses as high as 650 mg BID. This significant variability in dosing has frequently been noted as a limitation in the study of aspirin as appropriate postoperative VTE prophylaxis, impairing efforts at comparing studies or performing subsequent meta-analyses.[40] Due to this, prior position papers such as the CHEST guidelines for Prevention of VTE in Orthopedic Surgery Patients[21] generally have not recommended specific aspirin doses. In contrast, the CHEST guidelines for Prevention of VTE in Nonorthopedic Surgical Patients[41] specifically recommend that when aspirin is used for prophylaxis it should be "low-dose" due to the uncertain risks and benefits of high-dose aspirin in this patient population (due to lack of data). The only current trial in trauma patients, the METRC trial, utilized aspirin 81 mg BID.[27] Given that trauma patients often have more injuries than fractures alone, bleeding risk in major trauma patient is likely higher than in the total hip arthroplasty, total knee arthroplasty, and isolated hip fracture patients on which most orthopedic studies were performed; therefore, as there is very limited data on higher-dose aspirin (>81 mg BID) in trauma patients we recommend following the example of the METRC study as the most appropriate existing literature.

Postdischarge VTE Prophylaxis Recommendations

Postdischarge VTE prophylaxis should consider the risk of VTE, as well as the risk of postinjury hemorrhage. The medication choice and duration of prophylaxis should be tailored to the specific injury patterns present (Fig. 1).

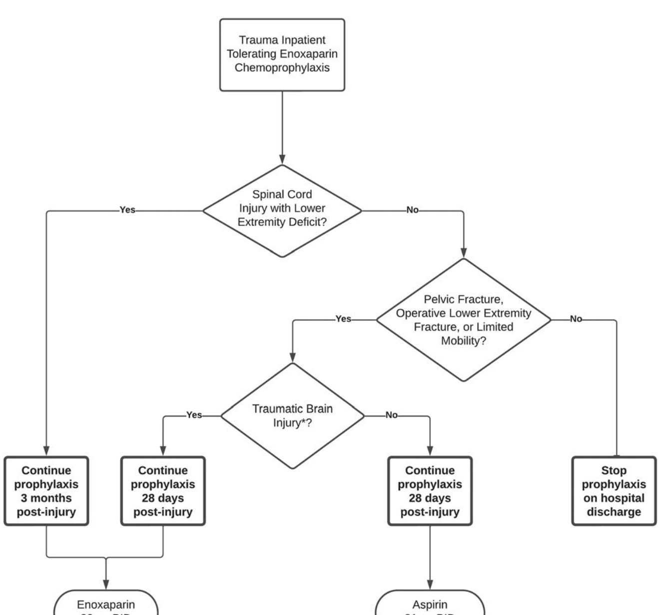

Figure 1. Postdischarge VTE prophylaxis algorithm.

Pelvic Fracture and/or Lower Extremity Fracture

In most high-risk patients, we recommend an additional 4 weeks of pharmacologic prophylaxis from the time of injury. These recommendations are based on the orthopedic literature where extended prophylaxis is recommended for 35 days postoperatively in patients undergoing major orthopedic surgery (THA, TKA, and hip fracture surgery).[21] While varying doses of aspirin have also been evaluated, we recommend 81 mg twice daily as it is the most commonly studied and has the best results in patients with orthopedic trauma injuries.[27,42] In patients with any pelvic fracture, or those with an extremity fracture treated operatively, we recommend postdischarge treatment with aspirin 81 mg twice daily for 28 days postoperatively.

Limited Mobility With Traumatic Brain Injury

In the inpatient setting, enoxaparin 40 mg twice daily or weight-based enoxaparin dosing with anti-Xa adjustment has become the standard of care for prophylaxis in most trauma patients.[5,6] It is currently recommended that TBI patients with intracranial hemorrhage are treated with enoxaparin 30 mg twice daily once their intracranial hemorrhage is stable.[5] VTE prophylaxis with LMWH has been shown to be safe in the inpatient setting following TBI,[43] while oral medications including aspirin have insufficient data to support routine recommendation. The inability to routinely monitor renal function and measure anti-Xa levels in the outpatient setting, and the potential risk of bleeding, has led to most guidelines suggesting a postdischarge enoxaparin dose of 30 mg twice daily.[21,41] Patients with contraindications to LMWH, including renal dysfunction, should receive subcutaneous unfractionated heparin. We recommend that patients with TBI with limited mobility or TBI patients with lower extremity fracture be treated with enoxaparin 30 mg twice daily for 28 days postinjury.

Spinal Cord Injury

Patients with SCI and resultant motor dysfunction are at particularly high risk of developing VTE, and therefore require a longer duration of VTE prophylaxis postdischarge.[44] Data on extended prophylaxis in this subset of patients are extremely limited; however, one study of postdischarge prophylaxis in SCI patients demonstrates that LMWH is more efficacious than unfractionated heparin during the rehabilitation phase.[45] Current consensus guidelines, including the American College of Surgeons – Committee on Trauma Best Practice Guidelines for Spine Injury,[46] recommend ongoing VTE prophylaxis for at least 3 months postinjury.[47] Therefore, we recommend that patients with SCI should be treated with enoxaparin 30 mg twice daily for a minimum period of 3 months postinjury.

Limitations

High quality data defining the optimal duration of postdischarge VTE prophylaxis and the appropriate medication selection in trauma patients are limited. Current studies on postdischarge VTE prophylaxis were evaluated after an extensive literature review and discussed by work group members; however, neither a formal evaluation of the level of evidence nor the strength of recommendations provided are included as part of this clinical protocol. These recommendations are likely to evolve in the future as new data is published.

CONCLUSION

High-risk trauma patients, including those with pelvic fracture, operative lower extremity fracture, SCI, or those unable with limited mobility after TBI should receive postdischarge VTE prophylaxis. Additional studies defining the optimal VTE prophylaxis strategy and duration in polytrauma trauma patients are needed.

AUTHORSHIP

A.E.B., L.N., T.W.C. participated in the study design. A.E.B., B.K.Y., A.C., R.K., C.T., G.T.T., D.G.J., D.W.A., E.J.L., L.N., T.W.C. participated in the drafting of guidelines. A.E.B., T.W.C. participated in the drafting of article. B.K.Y., A.C., R.K., C.T., G.T.T., D.G.J., D.W.A., E.J.L., L.N.. participated in the critical revision of article.

DISCLOSURE

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