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Updated guidelines to reduce venous thromboembolism in trauma patients: A Western Trauma Association critical decisions algorithm

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This is a recommended evaluation and management algorithm from the Western Trauma Association (WTA) Algorithms Committee focused on the management of pharmacologic prophylaxis for venous thromboembolism (VTE) prevention in trauma patients. Because there are few related published prospective, randomized clinical trials that have generated class I data on this topic in the trauma population, these recommendations are based primarily on published prospective and retrospective cohort studies, and expert opinion of the WTA members. The final algorithm is the result of an iterative process including an initial internal review and revision by the WTA Algorithm Committee members, and then final revisions based on input during and after presentation of the algorithm to the full WTA membership.

Goals

The algorithm (Fig. 1) and accompanying comments represent a safe and sensible approach to reducing VTE in trauma patients. The aim for this approach was to provide updated guidelines that apply to most patients, most of the time. We recognize that there will be multiple factors that may warrant or require deviation from any single recommended algorithm and that no algorithm can completely replace expert bedside clinical judgment. We encourage institutions and clinicians to use this algorithm as a general framework in the approach to trauma patients and to customize and adapt it to better suit the specifics of that program or location.

Burden of Disease

Venous thromboembolism, including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a potentially preventable complication after trauma. The focus of this algorithm is on optimizing the delivery of pharmacologic prophylaxis to prevent VTE and minimize any associated complications. For those trauma patients diagnosed with a DVT or PE, including distal upper extremity or calf thrombosis, specific treatments are addressed in other guidelines and will not be covered in this algorithm.[1,2]

Without pharmacologic prophylaxis, a 1994 study determined that the DVT rate was 58% in severely injured trauma patients who undergo serial impedance plethysmography with lower extremity contrast venography.[3] In a landmark, 1996 *New England Journal of Medicine* publication 30 mg of subcutaneous enoxaparin twice daily performed better than 5,000 U of subcutaneous heparin twice daily at reducing DVT in moderate to severely injured trauma patients (31% vs. 44%, $p = 0.04$).[4] The risk of major bleeding was low regardless of therapy, and importantly, the first dose of pharmacologic prophylaxis was initiated within 36 hours of the injury and continued through all surgical procedures except spinal fixation when a single preoperative dose was held.[4] This study established that early, uninterrupted enoxaparin was superior to heparin at reducing VTE after trauma. In the last decade, a number of reviews and societal recommendations focused on improving the guidelines to reduce the rate of VTE and related complications after trauma.[1,2,5–11]

Despite this progress, debate persists regarding optimal dosing and timing of enoxaparin, including when to initiate, hold, and resume it before and after surgery or epidural placement. Trauma patients frequently receive a delayed, suboptimal dose of enoxaparin, which is then held for any potential surgical procedure despite substantial evidence that encourages early, uninterrupted pharmacologic prophylaxis. An updated algorithm on the appropriate management of VTE prophylaxis is therefore indicated.

ALGORITHM

The following lettered sections correspond to the letters identifying specific sections of the algorithm shown in Figure 1. In each section, we provide a brief summary of the important aspects and options that should be considered at that point in the evaluation and management process.

A

This algorithm is designed for adult trauma patients 18 years and older.

Importantly, although younger children have a significantly lower VTE risk, older children and adolescents have a VTE risk that approaches their adult counterparts.[12] Guidance for VTE prophylaxis in children can be found in the joint practice management guideline from the Pediatric Trauma Society and the Eastern Association for the Surgery of Trauma, which recommends, "pharmacologic prophylaxis be considered for children older than 15 years old and in younger postpubertal children with Injury Severity Score (ISS) greater than 25."[11]

B

Assessment of VTE risk will assist in determining which patients require pharmacologic prophylaxis.

In general, an ISS of 10 or more suggests that pharmacologic prophylaxis should be initiated as soon as possible, whereas patients with an ISS of less than 10 are at lower VTE risk and may not require pharmacologic prophylaxis.[13–15] Because ISS is not calculated in real time, the Greenfield Risk Assessment Profile or the Trauma Embolic Scoring System can assist with calculating VTE risk.[13–15] Patients with spine or pelvic fractures, repair of venous injury, a history of VTE, or inherited clotting disorders have increased VTE risk and should be considered for pharmacologic prophylaxis.[2,13,14] Among

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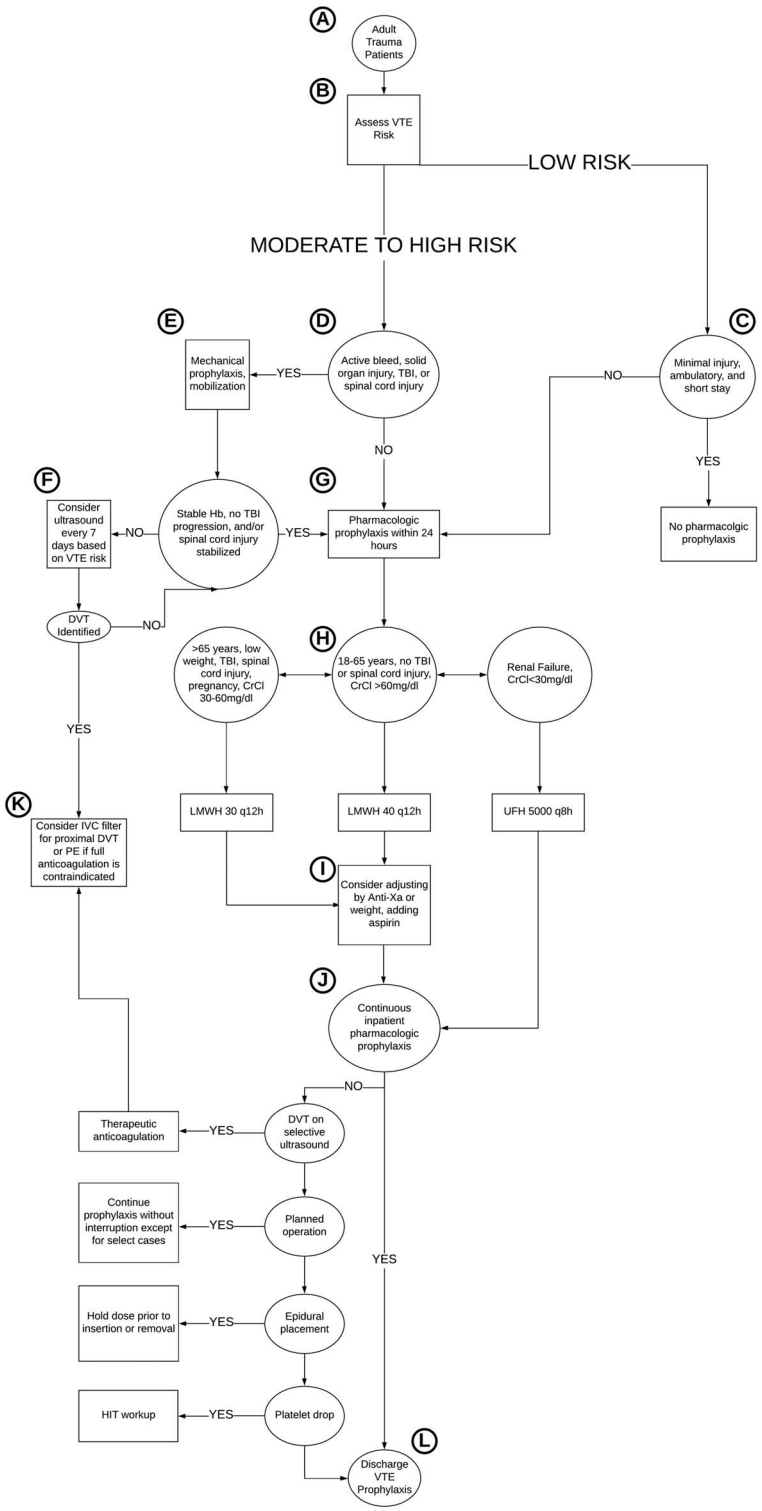

Figure 1. The WTA algorithm for VTE prophylaxis after trauma. Circled letters correspond to sections in the associated article. Algorithm circle-bubbles represent patient criteria; algorithm square-bubbles represent expert recommendations. CrCl, creatinine clearance; Hb, hemoglobin; LMWH, enoxaparin; q8h, every 8 hours; q12h, every 12 hours; UFH, unfractionated heparin.

trauma patients with minor injuries, independent predictors of increased VTE risk are increased age, obesity, and lower extremity fractures; any combination of these three characteristics should encourage initiation of pharmacologic prophylaxis.[13]

C

Patients with minor trauma may not require pharmacologic prophylaxis.

Given the related pain with injection, potential for hematoma at the injection site, cost for the medication, and nursing costs for administration, avoiding pharmacologic prophylaxis may be indicated for select low-risk patients after minor trauma. The Trauma Embolic Scoring System can be used to assess VTE risk, as patients with a low score require no pharmacologic prophylaxis because of their low VTE rate.[13] Ambulatory patients with minor injuries and short hospital stays may not require pharmacologic prophylaxis. Trauma patients capable of ambulation but confined to bed because of intoxication, restraints, or other reasons should receive pharmacologic prophylaxis. In general, trauma patients who require hospital admission for more than 24 hours require pharmacologic prophylaxis, whereas those hospitalized for less than 24 hours do not. For the patients who do not receive pharmacologic prophylaxis, mechanical prophylaxis and/or aspirin are low cost and low morbidity options, although their benefit is uncertain given the low VTE rate.[13–16]

D

Appropriate delays in pharmacologic prophylaxis may occur for those patients with an active bleed, coagulopathy, hemodynamic instability, solid organ injury, traumatic brain injury (TBI), or spinal trauma.

Quantifying the risk and benefit of initiating pharmacologic prophylaxis for each patient is a challenge that is best determined by the trauma team at bedside. Detailing every indication where a delay may be indicated is outside the scope of these guidelines; several are described below. However, it is important to note that the guidance in both the literature and clinical practice supports very short delays to the initiation of pharmacologic prophylaxis, even among these cohorts.

Active Bleeding, Coagulopathy, or Hemodynamic Instability

Control of active bleeding is necessary before starting pharmacologic prophylaxis. In the presence of hemodynamic instability, a hemoglobin drop of greater than 2 g/dL in under 12 hours or ongoing blood transfusion is an appropriate indication to delay the initiation of pharmacologic prophylaxis.[2,4] Systemic coagulopathy was previously proposed as a reason to delay pharmacologic prophylaxis with one study holding pharmacologic prophylaxis for an elevated prothrombin time of more than 3 seconds above control or a platelet count of less than 50,000 per cubic millimeter.[4] More recent studies indicate that prothrombin time and platelet count are not as reliable at predicting systemic coagulopathy as viscoelastic hemostatic assays, which may demonstrate hypocoagulability and hypercoagulability after trauma.[2,17–19] The hypocoagulability due to trauma largely resolves within 24 hours, after which hypercoagulability becomes prevalent. In this setting, pharmacologic prophylaxis may be considered after the initial resuscitation is complete.[17,20] Deferring the initiation of pharmacologic prophylaxis during trauma-induced coagulopathy is associated with an increased VTE rate such that the initiation of pharmacologic prophylaxis is encouraged if the hypocoagulable state is expected to resolve and there are no signs of ongoing bleeding.[17]

Solid Organ Injury

Delays occur in the initiation of pharmacologic prophylaxis for patients with solid organ injury. Several studies indicate that patients with solid organ injury who received early pharmacologic prophylaxis had lower DVT and PE rates without increased risk of failure of nonoperative management, bleeding complications, or mortality; these risks did not increase when pharmacologic prophylaxis was started within 24 hours compared with within 48 hours.[20–23] Early pharmacologic prophylaxis within 12 to 24 hours appeared to be safe across moderate American Association for the Surgery of Trauma injury grade and type of solid organ injury (liver, spleen, and/or kidney), without an increased risk of bleeding that necessitated intervention or blood transfusion.[21] Although those with grade IV and V injuries should be approached with caution, pharmacologic prophylaxis may be initiated within 24 hours for most patients with solid organ injury.[21–23]

Traumatic Brain Injury

Concern for progression of TBI is a common reason for the delay in initiation of pharmacologic prophylaxis. This delay is dependent on the type of TBI; those with "cerebral contusion, localized petechial hemorrhages, or diffuse axonal damage" may safely receive pharmacologic prophylaxis without delay.[4] When pharmacologic prophylaxis is appropriately delayed, the follow-up computed tomography (CT) after TBI diagnosis is an important indicator for when to initiate pharmacologic prophylaxis.[24] For patients with TBI progression on the follow-up CT, exposure to pharmacologic prophylaxis is a predictor for further progression, and it should be held until a follow-up CT demonstrates no progression.[24] In contrast, if the follow-up CT demonstrates no TBI progression, then pharmacologic prophylaxis should be initiated.[24] Importantly, progression of TBI occurs in about 10% of patients with a stable follow-up CT, regardless of whether pharmacologic prophylaxis is provided or not.[24] Those trauma centers that provide pharmacologic prophylaxis within 24 hours after TBI have significantly lower rates of VTE with no difference in rates of late neurosurgical intervention.[23,25–30] Even in the setting of combat related penetrating TBI, initiating pharmacologic prophylaxis 24 hours after injury for those patients with a stable CT was safe, with similar progression rates regardless of pharmacologic prophylaxis.[29] The majority of TBI patients with a stable CT may be initiated on enoxaparin within 24 hours, and nearly all TBI patients should receive pharmacologic prophylaxis within 72 hours of the time of injury.[23,28,31]

Spinal Trauma

In the absence of pharmacologic prophylaxis, patients who undergo spine surgery or those with spine trauma, fracture, or cord injury have a high incidence of VTE,[2] and delays longer than 72 hours lead to a substantial increase in the VTE rate.[32]

Pharmacologic prophylaxis must be initiated as soon as possible after spine surgery or any spine injury.[32,33] Regimens that provide pharmacologic prophylaxis preoperatively[34] or immediately after operative fixation are considered safe.[4,34] When a departmental protocol was implemented that required pharmacologic prophylaxis preoperatively or the same day of spine surgery, the VTE rate decreased and the rate of spinal hematoma was unchanged.[34] Similarly, pharmacologic prophylaxis initiated within 48 hours of operative fixation of traumatic spine fractures did not increase the risk of bleeding, progression of neurological injury, or postoperative complications including spinal hematoma.[23,33]

E

Mechanical prophylaxis for moderate to high VTE risk patients is encouraged regardless of concurrent pharmacologic prophylaxis.

For patients who are not started immediately on pharmacologic prophylaxis, mechanical prophylaxis with intermittent pneumatic compression and mobilization, when possible, should be encouraged. Intermittent pneumatic compression lowers the DVT incidence if no pharmacologic prophylaxis is initiated and therefore is recommended for patients with a contraindication to pharmacologic prophylaxis.[2,35,36] In contrast, the addition of intermittent pneumatic compression in critically ill patients who received pharmacologic prophylaxis did not lead to a reduction in the DVT rate, although the study had a low DVT rate and only 8% of the population were trauma patients.[16] Combining mechanical prophylaxis with pharmacologic prophylaxis is therefore encouraged for moderate to high VTE risk patients in part because those who received the combination had a lower incidence of symptomatic PE.[35] Compression stockings do not appear to reduce the VTE rate in the presence of pharmacologic prophylaxis,[16] but thigh high compression stockings may provide a benefit to those trauma patients who cannot be started on pharmacologic prophylaxis.[2]

Mobility is also an important component for VTE prevention, as early mobility leads to a reduction in VTE.[37] A mobility protocol is safe in trauma patients and may reduce patient deconditioning besides decreasing the rate of VTE.[37] Prolonged maintenance of spinal precautions is associated with an increased DVT rate and should be avoided to allow early mobility.[38]

F

Weekly venous compression duplex should be considered in patients at high VTE risk who cannot be started or maintained on pharmacologic prophylaxis.

Although debate persists, routine surveillance with venous compression duplex is not indicated or feasible for all trauma patients.[2] Routine surveillance duplex after trauma does not decrease the risk of PE or fatal PE, and false-positive results lead to unnecessary therapeutic anticoagulation.[2] In trauma patients at low VTE risk, the high cost and low yield of acute, clinically relevant findings suggest that the practice may be avoided. Some institutions advocate for routine surveillance in low-risk trauma patients to identify both acute and preexisting DVT, which may help identify and treat the related complications such as venous insufficiency, venous stasis ulcers, or pain with ambulation.[39] For trauma patients at high VTE risk, routine surveillance duplex is associated with a reduced PE rate.[39] The Greenfield Risk Assessment Profile can identify which trauma patients may benefit from routine surveillance.[14,39] Weekly duplex scanning may be particularly beneficial in high VTE risk patients who cannot be started or maintained on pharmacologic prophylaxis. Whatever the institutional guidelines, identification of DVT should not be a hospital-reported outcome. Institutions that routinely screen all trauma patients have higher rates of DVT, and those centers with comprehensive quality improvement efforts that do not routinely screen will also have higher DVT rates because of a lower threshold for ordering a venous compression duplex.

G

Pharmacologic prophylaxis must be initiated as soon as possible and for most trauma patients may be initiated within 24 hours.

When high VTE risk trauma patients who receive enoxaparin within 24 hours of admission are compared with those who receive only mechanical prophylaxis, minor and major bleeding events do not differ.[40] As detailed in section E, appropriate delays may occur in the initiation of pharmacologic prophylaxis because of active bleeding, coagulopathy, hemodynamic instability, solid organ injury, TBI, or spinal trauma. In most cases, pharmacologic prophylaxis may be started in less than 24 hours, and in almost every case, pharmacologic prophylaxis may be started in less than 72 hours.

Pharmacologic prophylaxis is often held because of pending surgery despite the evidence that it may be initiated before most surgical procedures.[4,41–43] Trauma patients who require an operation are unique in that their first operation may occur within minutes of arrival or days into the hospitalization. Increasingly, pharmacologic prophylaxis is delayed or skipped for pending surgery, which leads to an increased VTE rate.[40] Preoperative dosing of pharmacologic prophylaxis is not unique to trauma. In other patient populations at high risk for VTE, the use of preoperative pharmacologic prophylaxis decreased the DVT rate without increasing the complication rate.[41,42] Guidelines for perioperative care in gynecologic/oncology recommend, "Prophylaxis should be initiated pre-operatively and continued post-operatively."[44] Patients who underwent elective hip surgery who received low molecular weight heparin approximately 6 hours before surgery had a lower rate of proximal DVT without increasing major, minor, or trivial bleeding rates.[43] This benefit was not observed when low molecular weight heparin was provided 12 hours or more preoperatively.[43] We believe that the common and somewhat reflexive process of withholding pharmacologic prophylaxis for 12 to 24 hours before planned surgical procedures is almost always unnecessary and will result in an increased VTE risk without an accompanying decrease in the risk of bleeding events.

H

After deciding to start pharmacologic prophylaxis, the specific anticoagulant and initial dose should be determined for each patient. Enoxaparin is the recommended choice for most trauma patients with higher doses now considered the standard of care.

The preferred agent for pharmacologic prophylaxis is the low molecular weight heparin enoxaparin because of its

increased bioavailability, longer plasma-half life, and more predictable pharmacokinetics and pharmacodynamics compared with unfractionated heparin.[4,45] Enoxaparin interacts less with platelets, which may reduce bleeding complications compared with unfractionated heparin; has a lower incidence of heparin-induced thrombocytopenia (HIT); and does not have the associated osteoporosis observed with heparin treatment.[46]

When choosing the initial dose, 40 mg of enoxaparin twice daily should be considered the standard for most trauma patients, as 30 mg twice daily frequently results in inadequate pharmacologic prophylaxis.[47–55] Therefore, patients 18 to 65 years with weight of more than 50 kg and a creatinine clearance of more than 60 mg/dL should be started on 40 mg of enoxaparin twice daily, as this dose is safe and reduces the VTE rate.[47–55] Patients who are older than 65 years, weigh less than 50 kg, or who have a creatinine clearance of 30 to 60 mg/dL should continue to receive initial dosing at 30 mg of enoxaparin twice daily.

The initial enoxaparin dose for trauma patients with a normal creatine clearance may also be based on weight. Options include 0.5 mg/kg twice daily,[51,52] 0.6 mg/kg twice daily,[53] or 30 mg for 50 to 60 kg patients, 40 mg for 61 to 99 kg patients, and 50 mg for patients greater than 100 kg.[54] Patients who are initiated on higher doses of enoxaparin based upon weight should be monitored by anti-Xa levels because of the fluctuations in creatinine clearance after trauma that might lead to changes in the enoxaparin dose.[50]

Although enoxaparin is preferable to heparin for pharmacologic prophylaxis, some institutions continue to dose unfractionated heparin at 5,000 U three times daily based in part on a randomized trial that suggested that this regimen might be noninferior and cost-effective compared with 30 mg of enoxaparin twice daily.[56] This practice should be reconsidered as the trial was underpowered because of an assumed DVT rate of 44% for unfractionated heparin versus 31% for enoxaparin, and a 10% noninferiority margin for the power calculation. The actual difference in the VTE rate was 3.1%, which favored enoxaparin without reaching significance (unfractionated heparin, 8.2% vs. enoxaparin, 5.1%; $p = 0.2$).[45,56] In addition, the study was not powered to detect a difference in the rate of PE or HIT, both of which impact the complication rate and health care costs.[45,57] More recently, 30 mg of enoxaparin twice daily was established as superior to 5000 U of unfractionated heparin three times daily at the prevention of VTE and PE.[45]

Unfractionated Heparin for Renal Failure

Quantifying the risk and benefit of the type and initial dose of pharmacologic prophylaxis for each patient is a challenge best determined by the trauma team at bedside. As noted, 40 mg of enoxaparin twice daily is the recommended initial pharmacologic prophylaxis for most trauma patients. Detailing every indication where an alternative therapeutic or dose may be indicated is outside the scope of these guidelines; several are described below.

In the presence of end-stage renal disease or a creatinine clearance of <30 mg/dL, subcutaneous unfractionated heparin at 5000 U every 8 hours may be initiated.[2] Because enoxaparin is excreted by the kidneys, its administration to patients with renal failure may lead to increased bleeding complications and should be avoided.[2] Enoxaparin has not been Food and Drug Administration approved for use in dialysis patients. Providing lower enoxaparin doses in the setting of a creatinine clearance of <30 mg/dL while closely monitoring anti-Xa levels may be possible in the future, but additional research is necessary before this recommendation can be made. In most other settings, enoxaparin is preferable to unfractionated heparin, as enoxaparin leads to lower VTE rates without increased bleeding complications.[4,45]

Brain and Spine Trauma

For TBI patients, enoxaparin is associated with less VTE and higher survival than unfractionated heparin with no difference in the progression of brain lesions, regardless if the dose was delivered in less than 24 hours after admission, between 24 to 48 hours, or after 48 hours.[26] Similarly, those patients with spine trauma should preferentially receive early enoxaparin.[32,33] Patients with brain and spine trauma should be initiated on 30 mg of enoxaparin twice daily and considered for dose adjustment by anti-Xa level.[4,47]

Pregnant Patients

Pregnant patients require specific dose recommendations for pharmacologic prophylaxis after trauma because of the progressive hypercoagulability,[58] as well as the increase in renal clearance and weight changes that occur over the course of pregnancy.[59] These variables generally require higher enoxaparin doses with more frequent dosing. Neither unfractionated heparin nor enoxaparin crosses the placenta, and both are considered safe to use in pregnancy.[58–60] As such, during an admission for trauma, pregnant patients should receive 30 mg of enoxaparin twice daily titrated by anti-Xa levels targeting a peak range of 0.2 to 0.4 IU/mL or a trough range of 0.1 to 0.2 IU/mL. For pregnant patients who weigh more than 90 kg, initiating 40 mg of enoxaparin twice daily is recommended with similar anti-Xa level titration.[58–60]

Isolated Orthopedic Injuries and Direct Oral Anticoagulants

Pharmacologic prophylaxis with direct oral anticoagulants (DOACs) or aspirin should not be a primary choice for pharmacologic prophylaxis for most trauma patients because of the lack of related clinical trials. The use of DOACs or aspirin may be considered in the setting of isolated orthopedic injuries, but only if the patient declines injection with enoxaparin or unfractionated heparin.[5,61–66] Two DOACs are approved for pharmacologic prophylaxis after elective orthopedic surgery, 10 mg of rivaroxaban once daily, and 2.5 mg of apixaban twice daily, both which are direct oral factor Xa inhibitors. Most orthopedic trials that compare rivaroxaban or apixaban to enoxaparin demonstrate that DOACs have equal to better VTE rates with similar to higher bleeding rates.[62–64,66–68] In contrast, other analyses conclude that enoxaparin has a lower VTE rate[69] and a lower bleeding rate.[70] Because only retrospective analyses have examined the use of DOACs for pharmacologic prophylaxis after trauma, randomized controlled trials are necessary before DOACs becoming a primary agent for trauma patients.[66,71,72]

The use of low dose aspirin may also be considered for pharmacologic prophylaxis in trauma patients with isolated orthopedic injuries who decline injection.[2,5,69,73] For those trauma patients started on a DOAC for pharmacologic prophylaxis, aspirin may replace the DOAC after 5 days with similar prevention of VTE.[74]

I

Many trauma patients require dose adjustment after initiating enoxaparin.

Because of the variations in renal clearance, weight, bioavailability, and coagulation cascade, monitoring enoxaparin by anti-Xa levels is necessary. In one series, 84% of trauma patients required doses of 40 mg or more, and 18% required doses of 50 mg or more.[47] Adjusting enoxaparin by anti-Xa peak or trough levels appears to lower the VTE rate without increasing bleeding complications in moderate to severely injured patients, trauma patients who require ICU admission, burn injuries, and surgical oncology patients.[47–49,75] Although some debate exists on the appropriate target for anti-Xa levels, consensus suggests targeting 0.2 to 0.4 IU/mL for peak levels or 0.1 to 0.2 IU/mL for trough levels.[47–50,55,75,76] Anti-Xa monitoring should also be considered for those patients who receive weight-based enoxaparin.[50,53,76]

Although thromboelastography (TEG) has not been validated for monitoring pharmacologic prophylaxis, TEG with platelet mapping may assist with monitoring platelet inhibition. A randomized trial that used TEG as an adjunct to identify inadequate enoxaparin doses did not observe lower rates of VTE with the TEG-guided enoxaparin dosing.[77] In contrast, TEG with platelet mapping may help determine if a hypercoagulability is due to platelet function, which encourages the addition of aspirin to the pharmacologic prophylaxis regimen.[78] If aspirin is added, the initial recommended dose is 81 mg daily with the possibility of increasing the dose to 325 mg daily depending on subsequent TEG with platelet mapping results.[18,19]

J

The continuous, uninterrupted dosing of pharmacologic prophylaxis should be the standard for most trauma patients throughout their hospital stay.

Although the safety and benefit of uninterrupted pharmacologic prophylaxis were established decades ago, more than half of trauma patients encounter interruptions.[79,80] A direct correlation is observed between the number of missed doses and DVT risk such that patients who miss two to four doses have 8.5 times higher DVT risk compared with those with no missed doses.[80] For TBI patients who are started on pharmacologic prophylaxis, interrupted dosing causes an approximately 600% increase in the VTE rate.[81]

The following are common reasons for missed pharmacologic prophylaxis: pending invasive procedure (41.6%), none (27.1%), patient was absent from the room (11.7%), concern for bleeding (12.1%), epidural catheter removal (5.9%), and physician/nursing error (1.6%).[80] When holding pharmacologic prophylaxis, the rate of bleeding with pharmacologic prophylaxis is no different than without it.[40] If nonfatal VTE events are compared with nonfatal bleeding complications, the risk/benefit ratio favors continuing pharmacologic prophylaxis.[82] Every effort should focus on continuing pharmacologic prophylaxis without interruption. The appropriate indications for holding or altering pharmacologic prophylaxis include acute thrombus, craniotomy, spinal surgery, epidural placement, or HIT, and these are expanded upon below.

Acute Thrombus

Although routine VTE surveillance is not indicated for all trauma patients,[2] weekly duplex scanning may be warranted in those at high VTE risk.[39] Selective venous compression duplex should be performed promptly for symptomatic evidence of DVT such as unexpected leg swelling or pain.[6] For those trauma patients with significant injuries and gaps in pharmacologic prophylaxis, weekly venous compression duplex may be considered.[39] If a DVT or PE is identified, then therapeutic anticoagulation is necessary per current guidelines, and if it is contraindicated, then an inferior vena cava (IVC) filter should be considered as detailed in section K.[1]

Pending Surgery

As discussed in section G, routinely holding pharmacologic prophylaxis because of pending surgery is only indicated, with few exceptions, for brain or spine surgery.[4] Given the delays and cancellations of cases that may occur during trauma patient care, holding pharmacologic prophylaxis preoperatively can cause days of missed pharmacologic prophylaxis. Preoperative pharmacologic prophylaxis is safe for trauma patients[2,4] and leads to a lower VTE rate.[43] The preoperative administration of pharmacologic prophylaxis is also encouraged for surgical patients in other specialties who have a high VTE risk and leads to a lower DVT rate without increasing the complication rate.[4,41–43] The lower VTE rate is lost if pharmacologic prophylaxis is provided more than 12 hours preoperatively.[43]

Epidural Catheter

Epidural catheters reduce morbidity and mortality in trauma patients sustaining chest injuries and are often a component of multimodal pain strategies. Patients who require an epidural catheter increasingly have interruptions in pharmacologic prophylaxis[83] such that epidural catheter placement is now associated with an increased VTE rate[84,85] whereas previously this was not the case.[86] Regional Anesthesia Guidelines recommend a 12-hour interval between enoxaparin dose and epidural placement/removal followed by a 4-hour to 12-hour interval before resumption.[9,10] If enoxaparin is scheduled at 10 AM and 10 PM, the morning dose may be held for 10 AM epidural catheter placement/removal to allow for the necessary 12-hour interval without pharmacological prophylaxis. At 10 PM, the scheduled enoxaparin dosing may resume, so only one dose is missed. If higher doses of enoxaparin are required for pharmacologic prophylaxis, Regional Anesthesia Guidelines recommend a 24-hour interval for therapeutic enoxaparin before epidural catheter placement/removal followed by a 4-hour to 12-hour interval before resumption,[9,10] indicating that, at most, two doses of enoxaparin should be missed for any enoxaparin therapy. Anti-Xa–guided enoxaparin doses are encouraged with limited interruption to reverse the higher VTE rate associated with epidural use.[84,85] For unfractionated heparin, a 4 to

6-hour interval is recommended before epidural placement/removal followed by a 1-hour interval before unfractionated heparin is resumed, which allows for uninterrupted dosing.

Heparin-Induced Thrombocytopenia

Selective platelet monitoring should be considered for those trauma patients who receive pharmacologic prophylaxis because of the risk of heparin-induced thrombocytopenia (HIT). Platelet monitoring is recommended for patients who are considered high risk for HIT approximately every 3 days from day 4 to day 14 or until pharmacologic prophylaxis is stopped.[7] Trauma patients who are exposed only to enoxaparin may be considered low risk for HIT and may not require routine platelet monitoring, as the rate of clinical HIT was 2.7% with prophylactic heparin compared with 0% with prophylactic enoxaparin.[7,87] The clinical diagnosis of HIT may be predicted by assigning scores that include thrombocytopenia, timing, thrombosis, and alternative causes.[7,88,89] Once diagnosed, the heparin anticoagulants must be replaced with nonheparin anticoagulants, such as the direct thrombin inhibitor argatroban, which can create challenges for trauma patients suspicious for HIT because of the irreversible nature of these anticoagulants and the difficulties with dosing and maintaining their therapeutic levels.[7,88,89]

K

Inferior vena cava filters may be considered in the setting of proximal DVT or PE when there is a contraindication to appropriate therapeutic anticoagulation.

The use of IVC filters is variable among trauma centers although their placement is decreasing without a documented change in PE rates, so prophylactic placement is not recommended.[90] In a randomized controlled trial of high VTE risk trauma patients who were unable to receive pharmacologic prophylaxis during the first 72 hours of admission, a prophylactic IVC filter did not lower the incidence of PE or mortality, which established the lack of utility of early prophylactic placement of an IVC filter in this population.[91] The placement of an IVC filter does not impact mortality regardless of whether a DVT is present or absent.[92,93] While consensus guidelines provide conflicting recommendations and most studies have been observational, among patients diagnosed with an acute proximal DVT or PE who cannot receive adequate therapeutic anticoagulation, an IVC filter should be considered to reduce the rate of recurrent PE without altering the mortality rate.[94]

L

Trauma patients with TBI, orthopedic or spine injuries, and those who undergo major surgery are at particular VTE risk and should be considered for postdischarge pharmacologic prophylaxis.

Pharmacologic prophylaxis after discharge for high VTE risk trauma patients is supported by evidence that demonstrates the practice is efficacious, safe, and cost-effective and may be considered for patients with TBI, orthopedic or spine injuries, and those who undergo major surgery.[2,95–98] The highest VTE risk occurs during the first 3 months after injury with approximately 1 year required until the VTE rate returns to that of the general population.[95,97] Venous thromboembolism–related readmissions account for 1.2% of 1-year trauma readmissions at a cost of US $250 million annually.[99]

Postdischarge pharmacologic prophylaxis with enoxaparin is efficacious, associated with a low rate of clinically relevant bleeding complications, and is cost-effective in patients at high VTE risk.[2,96] The introduction of postdischarge pharmacologic prophylaxis following abdominal or pelvic surgery for malignancy or inflammatory bowel disease was associated with a decrease in VTE events.[98] Because the optimal postdischarge dose and duration of enoxaparin after trauma are not well studied, doses more than 30 mg twice daily should be avoided, and the duration of pharmacologic prophylaxis may be considered for up to 4 weeks after the date of admission.[2] For those who undergo major orthopedic surgery, pharmacologic prophylaxis may be extended up to 35 days from the date of surgery.[5] Aspirin may be initiated for postdischarge pharmacologic prophylaxis for high VTE risk trauma patients, as it has been shown to be as effective as enoxaparin with less bleeding complications and better postdischarge adherence, and is not limited by the constraints of insurance oversight.[98,100] Direct oral anticoagulants may also be considered for postdischarge pharmacologic prophylaxis after isolated orthopedic injury.[74]

SUMMARY AND CONCLUSIONS

This algorithm was designed to provide comprehensive and clear guidance aimed at reducing the VTE rate after trauma. Although there are multiple factors that will lead to deviations from the presented algorithm, most trauma patients should be initiated on early and higher doses of enoxaparin that often should be adjusted by anti-Xa levels. For most trauma patients, pharmacologic prophylaxis should continue uninterrupted throughout the hospital stay and at times after discharge. Avoiding preventable and non–evidence-based delays to the initiation and missed doses of pharmacologic prophylaxis should be a best-practice focus of all trauma centers, and it has clearly been associated with decreased rates of VTE events.

AUTHORSHIP

All authors contributed in the conception and design. E.J.L. contributed in the data acquisition. All authors contributed in the data interpretation. E.J.L., C.V.R.B., E.E.M., and M.J.M. contributed in the article preparation. All authors contributed in the critical revisions.

DISCLOSURE

The authors declare no conflicts of interest.
The results and opinions expressed in this article are those of the authors and do not reflect the opinions or official policy of any of the listed affiliated institutions, the United States Army, or the Department of Defense (if military coauthors).

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