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Updated Guidelines to Reduce Venous Thromboembolism in Trauma Patients: A Western Trauma Association Critical Decisions Algorithm

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INTRODUCTION

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 (Figure 1) and accompanying comments represent a safe and sensible approach to reducing VTE in trauma patients. The aim for this approach is to provide updated guidelines which 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

VTE, 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 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 subcutaneous enoxaparin 30mg twice daily performed better than subcutaneous heparin 5000u twice daily at reducing DVT in moderate to severely injured trauma patients (31% v. 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 less than 10 are at lower VTE risk and may not require pharmacologic prophylaxis.¹³⁻¹⁵ As 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 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 due to 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 due to 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 benefits 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 two 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 (PT) more than 3 seconds above control or a platelet count of less than 50,000 per cubic millimeter.⁴ More recent studies indicate that PT 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 (TIC) 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 to 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 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 which 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 VTE², 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 preoperatively³⁴ 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,}

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 prophylaxis¹⁶, 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 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 due to a lower threshold for ordering a venous compression duplex.

G Pharmacologic prophylaxis should 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 to 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 due to active bleeding, coagulopathy, hemodynamic instability, solid organ injury, traumatic brain injury, or

spinal trauma. In most cases pharmacologic prophylaxis may be started in under 24 hours and in almost every case pharmacologic prophylaxis may be started in under 72 hours.

Pharmacologic prophylaxis is often held due to pending surgery despite the evidence that it may be initiated prior to 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 six hours prior to 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 prior to 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 due to its increased bioavailability, longer plasma-half life, and more predictable pharmacokinetics and pharmacodynamics compared to 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, and does not have the associated osteoporosis observed with heparin treatment.⁴⁶

When choosing the initial dose, enoxaparin 40mg twice daily should be considered the standard for most trauma patients as 30mg twice daily frequently results in inadequate pharmacologic prophylaxis.⁴⁷⁻⁵⁵ Therefore, patients 18 to 65 years with weight above 50kg, and a creatinine clearance above 60mg/dl should be started on enoxaparin 40mg 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 30-60mg/dl should continue to receive initial dosing at enoxaparin 30mg twice daily.

The initial enoxaparin dose for trauma patients with a normal creatine clearance may also be based on weight. Options include 0.5mg/kg twice daily^{51, 52}, 0.6mg/kg twice daily⁵³, or 30mg for 50-60kg patients, 40mg for 61-99kg patients, and 50mg for patients greater than 100kg.⁵⁴ Patients who are initiated on higher doses of enoxaparin based upon weight should be monitored by anti Xa levels due to 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 5000u three times daily based in part on a randomized trial that suggested this regimen might be noninferior and cost effective compared to enoxaparin 30mg twice daily.⁵⁶ This practice should be reconsidered as the trial was underpowered due to 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% v. enoxaparin 5.1%, p=0.2).^{45, 56} In addition, the study was not powered to detect a difference in the rate of pulmonary embolism or heparin induced thrombocytopenia, both of which impact the complication rate and health care costs.^{45, 57} More recently, enoxaparin 30mg twice daily was established as superior to unfractionated heparin 5000u three times daily at the prevention of VTE and PE.⁴⁵

Unfractionated heparin for renal failure

In the presence of end stage renal disease or a creatinine clearance <30mg/dl, subcutaneous unfractionated heparin at 5000u every eight hours may be initiated.² As 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 FDA approved for use in dialysis patients. Providing lower enoxaparin doses in the setting of a creatinine clearance <30mg/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 under 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 enoxaparin 30 mg 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 due to 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 enoxaparin 30mg twice daily titrated by anti Xa levels targeting a peak range of 0.2-0.4 IU/ml or a trough range of 0.1-0.2 IU/ml. For pregnant patients who weigh more than 90kg initiating enoxaparin 40mg 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 due to 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, rivaroxaban 10mg once daily and apixaban 2.5 mg twice daily, both which are direct oral factor Xa inhibitors. Most orthopedic trials that compare rivaroxaban or apixaban to enoxaparin demonstrate 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 rate⁶⁹ and a lower bleeding rate.⁷⁰ As only retrospective analyses have examined the use of DOACs for pharmacologic prophylaxis after trauma, randomized controlled trials are necessary prior to 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. Due to 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 40mg or more, and 18% required doses of 50mg or more.⁴⁷ Adjusting enoxaparin by anti Xa peak or trough levels appears to lead to a lower 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 0.2–0.4 IU/mL for peak

levels or 0.1-0.2 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 which utilized 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 81mg daily with the possibility of increasing the dose to 325mg 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 was established decades ago, over 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 doses have 8.5 times higher DVT risk compared to 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 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 to 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 heparin induced thrombocytopenia and these are expanded upon below.

Acute thrombus

Although routine VTE surveillance is not indicated for all trauma patients², weekly duplex scanning may be warranted in those at high VTE risk.³⁹ Selective venous ultrasound 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 ultrasound 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 IVC filter should be considered as detailed in section K.¹

Pending surgery

As discussed in section G, routinely holding pharmacologic prophylaxis due to 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 prophylaxis⁸³ 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 prior to resumption.^{9, 10} If enoxaparin is scheduled at 10am and 10pm, the morning dose may be held for 10am epidural catheter placement/removal to allow for the necessary 12-hour interval without pharmacological prophylaxis. At 10pm 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 prior to epidural catheter placement/removal followed by a 4-hour to 12-hour interval prior to 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 four to six-hour interval is

recommended prior to epidural placement/removal followed by a one-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 due 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 to 0% with prophylactic enoxaparin.^{7, 87} The clinical diagnosis of HIT may be predicted by assigning scores that includes 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 due to the irreversible nature of these anticoagulants and the difficulties with dosing and maintaining their therapeutic levels.^{7, 88, 89}

K Inferior vena cava (IVC) filters may be considered in the setting of proximal DVT or pulmonary embolism 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 post discharge 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 one-year required until the VTE rate returns to that of the general population.^{95, 97} VTE related readmissions account for 1.2% of 1-year trauma readmissions at a cost of \$250M annually.⁹⁹

Post discharge 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 post discharge pharmacologic prophylaxis following abdominal or pelvic surgery for malignancy or inflammatory bowel disease was associated with a decrease in VTE events.⁹⁸ As the optimal post discharge dose and duration of enoxaparin after trauma are not well studied, doses above 30mg twice daily should be avoided and the duration of

pharmacologic prophylaxis may be considered for up to four 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 post discharge pharmacologic prophylaxis for high VTE risk trauma patients as it has been shown to be as effective as enoxaparin with less bleeding complications, better post discharge adherence, and is not limited by the constraints of insurance oversight.^{98, 100} DOACs may also be considered for post discharge 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 has clearly been associated with decreased rates of VTE events.

AUTHOR CONTRIBUTION

All authors contributed to the conception and design. E.J.L contributed to the data acquisition. All authors contributed to the data interpretation. E.J.L, CVB, EEM, MJM contributed to the article preparation. All authors contributed to the critical revisions.

DISCLOSURES

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ACCEPTED

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FIGURE LEGEND

Figure 1: The Western Trauma Association algorithm for VTE Prophylaxis after Trauma. Circled letters correspond to sections in the associated manuscript. Algorithm circle-bubbles represent patient criteria, algorithm square-bubbles represent expert recommendations. CrCl, creatinine clearance; DVT, deep venous thrombosis; Hb, hemoglobin; HIT, heparin induced thrombocytopenia; LMWH, enoxaparin; Mg/dl, milligrams per deciliter; PE, pulmonary embolism; q8h, every eight hours; q12h, every twelve hours; TBI, traumatic brain injury; UFH, unfractionated heparin; VTE, venous thromboembolism

Figure 1

