PA TQIP Collaborative Best Practice Management Guideline for VTE Prophylaxis

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Protocol

1. Scope:

Clinical providers caring for injured patients at Pennsylvania Trauma Systems Foundation (PTSF) Accredited Trauma Centers.

2. Purpose:

The PA TQIP Collaborative has identified significant variation statewide in institution specific protocols for VTE Chemoprevention. Recent PA-TQIP Collaborative data have shown Pennsylvania trauma centers to have an elevated incidence of VTE when compared with centers nationwide. This document is intended to serve as a resource document to aid PA centers in formulating optimal institutional specific VTE preventions protocols.

3. Background:

Trauma patients, especially those admitted to the intensive care unit, are at an increased risk for venous thromboembolism (VTE). The major complication of deep venous thromboembolism (DVT), pulmonary embolism (PE), accounts for as many as 200,000 deaths annually.

Injured patients in whom prophylactic strategies are not employed may have an incidence of DVT approaching 40% and an incidence of PE of nearly 20%[1]. Equally important, delays in initiating prophylaxis or missed doses may also increase the incidence significantly when compared with receiving timely interventions strategies[2]. Recently 14 centers within the PA TQIP Collaborative retrospectively chart reviewed all cases of pulmonary embolus in the Pennsylvania Trauma Outcomes Study (PTOS) registry for the calendar years of 2016-2108. This analysis revealed that 31.8% of the 179 cases identified had missed doses with the majority being held around orthopedic procedural interventions[3].

The optimal timing for the initiation of venous thromboembolism (VTE) prophylaxis in certain injured sub-populations such as traumatic brain injury (TBI) or orthopedics is currently controversial. National guidelines are frustratingly vague in these areas. The American College of Chest Physicians Guidelines are not specific as they suggest that mechanical prophylaxis be used until the risks of bleeding expansion are felt to have abated. The existing neurosurgical literature suggests that TBI is a heterogeneous population of injuries regarding the risk of spontaneous progression of intracranial injury[4]. If the risk for expansion of hemorrhage is heterogeneous, it stands to reason that the time to stabilization of hemorrhage may vary with the type and size of the hemorrhagic lesion. Such controversies, particularly in the fields of orthopedic surgery and neurosurgery, are contributing significantly to delays in initiation chemoprophylaxis or breaks in the chemotherapeutic regiment around procedural interventions in these patient populations.

The primary goal of this best practice protocol is thus to help PA trauma centers identify and deploy the most appropriate evidence-based treatment strategies appropriate for their unique institutional needs. We recognize that each center will have different institutional capabilities, processes, resources, and patient populations which will necessitate customizing their institutional protocol. This document will serve as a “toolbox” of available evidenced base therapies as well as guidance on which of these options is likely to be most effective. It is our hope that this document will facilitate implementation of more effective prophylactic strategies which will reduce the state incidence of VTE which significantly impacts short and long-term outcomes of injured patients in Pennsylvania (PA).

4. General Considerations

a. Applicable Patient Population

A variety of scoring systems have been developed for use in the trauma population to assess the risk of venous thromboembolism (VTE) in the individual patient with the RISK Assessment Profile (RAP)[5] and Trauma Embolic Scoring System (TESS)[6] being the most well validated. Such scoring systems have also been used to assess risk benefit calculations for patients potentially benefiting from IVC filter placement

as well as to assess value of prolonged VTE prophylaxis post-discharge. Injured patients requiring hospitalization beyond 24 hours almost universally fall into moderate or high-risk populations, and therefore all trauma patients should receive both intermittent compression devices (ICD) and chemoprophylaxis unless contraindicated.

Observations patients present a unique challenge to many centers, particularly where the prevalence of geriatric patients is high. These patients are often unpredictable with regard to their ambulatory capability and length of stay and such centers may consider deploying VTE prophylaxis strategies to the observation population in order to simplify decision-making of admitting providers and minimize risk of fallout when patients stay beyond the expected 23 hours of observation.

All patients should be mobilized as soon as safely able. Mobility alone is not adequate VTE prophylaxis in the high-risk trauma patients. ICDs should be placed preferentially on the lower extremities. Where there may be a contraindication to lower extremity ICDs, the upper extremity placement is an acceptable alternative. Thromboembolism deterrent stockings (TEDs) and ICDs can be used together in spinal cord injury patients as they may provide additional benefit in reducing VTE and ameliorate peripheral vasodilatory effects of this injury. Strong evidence for routine simultaneous use of TEDs concurrently with ICD's is lacking and should be left to the discretion of the individual institution.

The following are considered contraindications to lower extremity ICD application:

- Bilateral lower extremity amputees
- Presence of bilateral external fixators or orthopedic casts/splints.
- Presence of bilateral lower extremity fasciotomy
- Presence of repaired or unrepaired soft tissue injuries in the calf region that would preclude the application of calf SCDs due to pain or suboptimal healing secondary to intermittent compression.
- Presence of abscess or cellulitis in the region of the calf SCD application.
- Presence of a graft or flap at the calf region that has not been documented to have completely healed.
- Presence of a unilateral external fixator, fasciotomy, etc. will not be considered a contraindication to placement of lower extremity ICD in the contralateral limb.

Lower extremity ICDs that apply therapy to the foot only may be a viable option in some of the above patient scenarios.

Patients expected to be hospitalized < 24 hours are excluded from this practice management guideline (PMG) due to their generally low risk for VTE. Such patients may be placed on this protocol at the providers discretion if they are deemed to be at high risk for VTE or there is a significant possibility that their hospital stay will exceed 24 hours.

b. Preferred Chemoprophylactic Agents and Dosing

Enoxaparin is the preferred pharmacologic agent as it has the best overall performance in the injured patient population[7]. Unfractionated heparin (UFH) is an acceptable alternative for patients with compromised creatinine clearance (CrCl) or situations in which a contraindication to low molecular weight heparin (LMWH) exists. Allergic reaction to heparinoids or known or suspected heparin induced thrombocytopenia should be considered absolute contraindications to both LMWH and UFH.

Manufacturer suggested Food and Drug Administration approved dosing for enoxaparin has been 30mg subcutaneously (SQ) every 12 hours (h) or 40mg SQ daily. However, several recent publications suggest chemoprophylaxis with such "traditional" dosing regimens result in subtherapeutic Anti-factor-Xa (Anti-Xa) levels below the suggested prophylactic target range between 0.2 and 0.5 IU/mL in as many as 70-90% of patients[8,9,10]. Obese patients may be at particular risk for this phenomenon. Multiple studies have demonstrated weight-based enoxaparin markedly improves the percentage of patients with Anti-Xa levels in the target range for prophylaxis and are thus recommended for utilization as per the protocol below[11,12]. Centers with very low rates of VTE may consider utilizing standard or "traditional" dosing as benefit from

weight-based dosing in these centers may be minimal while potentially incurring an increased risk of bleeding complications.

CrCl ≥30ml/min:
0.5mg/kg actual body weight rounded to the nearest 10mg/kg/dose SQ every 12h[#].
Enoxaparin dose is based on actual body weight with a maximum dose of 150mg SQ every 12h.

CrCl > 10 but <30 ml/min:
Enoxaparin 0.5mg/kg SQ Daily rounded to the nearest 10mg/dose.

Dialysis or CrCl <10 ml/min:
BMI<40: Heparin SQ 5000u SQ every 8 hours
BMI>40: Heparin 7500u every 8 hours

[#]For dosing accuracy and patient safety, consideration can be made to round all doses to the nearest 10mg. Enoxaparin syringes are available in the following strengths: 30mg, 40mg, 60mg, 80mg, 100mg, 120mg, and 150mg. Where the dose is between commercially available syringes, a partial dose is administered.

Absolute contraindication to prophylactic anticoagulation
Clinically evident bleeding requiring emergent surgical or interventional control
Actively expanding spinal or intracranial hemorrhage requiring surgical/procedural intervention.

Relative contraindications to chemoprophylaxis mostly revolve around patient specific injures and are discussed in detail in under Section 5: Important Patient Subpopulations).

Known remote history of Heparin Induced Thrombocytopenia (HIT) or heparin allergy will necessitate use of an alternative agent. Prophylaxis with Fondaparinux[13] is a safe and effective alternative in this situation. In cases where HIT develops as an acute sequela to initiation of chemoprophylaxis with LMWH or UFH, immediate discontinuation is recommended with concurrent testing to confirm the diagnosis. In such cases, transition to an alternative agent with full therapeutic anticoagulation is recommended due to the exceedingly high incidence of both venous and arterial thromboembolic phenomenon that commonly occur in patients developing acute onset of HIT.

c. Timing:

Patients without bleeding risk should have chemoprophylaxis instituted as soon as is deemed safe. Missed or delayed doses have been documented to increase patient risk of VTE[14]. In many patients this may be as early as at the time of hospitalization (i.e. ED or trauma bay). Missed doses due to the patient being off floor for studies or procedures or unnecessary awakening of the patient are common reasons for lack of compliance with VTE protocols. We therefore recommend standardized dosing intervals in order to minimize these events. In our discussions within the PA TQIP Collaborative, 0600 and 1800 appear to be the most commonly used dosing interval both for the reasons outlined above and that it allows holding the 0600 dose where morning procedural interventions are needed and for which prophylaxis through the procedure is not appropriate. Each institution will need to develop methodologies which transition patients presenting in off hours over to such standardized timing. One possible method could be to give pharmacy staff the authority to transition dose timing in the first 24-48 hours. Another method may be to start all trauma patients at the next available standardized dosing interval regardless of the initial timing of the order to initiate chemoprophylaxis Standardized order sets can also minimize provider variations in time as well. Each institution will have to weigh these and other options and develop a customized plan unique to their needs. Dose timing has been a common source of non-compliance with chemoprophylaxis in PA.

d. Anti-Xa Monitoring and Dosage Adjustment

Recent availability of cost effective, on-site, Anti-Xa assays for LMWH now enables dose optimization of in the individual patient when enoxaparin is the agent utilized for chemoprophylaxis. Such protocols have

been shown to significantly improve the percentage of patients who reach the appropriate target range for prophylaxis[9,15]. Some recent studies have documented a reduction or trend toward reduction in VTE[16,17] incidence where Anti-Xa monitoring and dose adjustment are utilized but definitive evidence is currently lacking. Institutions having this capability should strongly consider Anti-Xa monitoring to confirm their institution's dosing protocol successfully achieves target prophylactic Anti-Xa levels in a majority of patients, while simultaneously minimizing the number of patients who are supratherapeutic.

Each institution will have to weigh the cost and potential benefit of this technology and decision-making is likely to be affected by local institutional incidence of both VTE and bleeding complications of chemoprophylaxis. Anti-Xa monitoring can be targeted to subpopulations as well such as obese patients where subtherapeutic levels are common.

Where Anti-Xa monitoring is utilized, pharmacists in this working group currently recommend Anti-Xa levels should be drawn after the 4th sequential dose of enoxaparin. The level should be drawn as a peak level 4 hours after the dose. The adequate dosing for prophylaxis is indicated by an Anti-Xa level of 0.2-0.5 IU/mL. If the level is found to be less than 0.2 IU/mL, then the enoxaparin dose should be increased by 10mg q 12 hours, and a repeat Anti-Xa level should be repeated after the fourth dose post increase.

Dose adjustment tailored to Anti-Xa level should occur according to the algorithm below:

ANTI-Xa LEVEL (units/mL)	HOLD NEXT DOSE	DOSAGE CHANGE	NEXT ANTI-Xa LEVEL
<0.2	NO	Increase each dose by 10 mg.	4 hrs. after the 4th dose of the new dosing regimen
0.2 – 0.5	NO	NO	Next day, then within 1 week
>0.5 – 0.7	NO	Decrease dose by 10mg.	4 hrs. after the 4th dose of the new dosing regimen
>0.7 – 1.0	NO	Decrease dose by 20 mg.	4 hrs. after the 4th dose of the new dosing regimen
>1.0	Until anti-Xa level less than 0.6 units/mL	Decrease 40%	Before next dose and q 12h until anti-Xa level less than 0.5 units/mL

In certain patient subpopulations, UFH may be deemed a safer alternative to LMWH. Heparin Anti-Xa assay therapeutic windows and dose adjustment strategies are currently much less well studied. We therefore do not recommend Heparin Anti-Xa monitoring in patients for whom UFH is employed as their prophylactic agent.

e. Screening:

Screening of asymptomatic patients should not be routinely performed as it has not been shown to be beneficial[18]. Symptomatic patients (i.e. leg swelling) can be investigated with Duplex Ultrasound for exclusion of extremity VTE with good sensitivity and specificity. Screening assessments as TESS have been utilized at some centers to identify "very high risk" injured patients for which screening may have some benefit but is not recommended for routine use[6]. Symptomatic PE is most commonly ruled out by performing CTA chest. VQ scan, and in rare cases, pulmonary angiography are viable alternatives.

f. Vena cava filters:

Current treatment recommendations have discouraged use of prophylactic IVC filters due to their association with increased rates of lower extremity DVT, complications associated with migration and

potential for promulgating thrombosis of the vena cava, as well as the lack of evidence that they reduce rates of symptomatic PE or 90-day mortality[19,20].

Therapeutic IVC filters remain a treatment option in the following circumstances:

- Recurrent PE despite therapeutic anticoagulation.
- PE/central DVT with absolute contraindication to anticoagulation lasting longer than 7 days[20].

In the absence of confirmed central DVT or PE, prophylactic IVC filter placement is not recommended.

g. Protocol Maintenance:

Little evidence exists currently in the literature as to the optimal method of VTE chemoprophylaxis institution and maintenance by providers, but it is intuitive that the providers prescribing chemoprophylaxis should have a clear overall picture of the patient's physiologic condition, injuries and current treatment plan in order to make cogent decision with respect to withholding or ordering chemoprophylaxis. In the case of the injured patient, the trauma service providers best achieve this objective. In the interest of patient safety, we therefore recommend all orders for VTE prophylaxis be written by trauma providers after conferring with subspecialists as indicated. Likewise, bedside nursing questions revolving around potential need to hold chemoprophylaxis should be referred to the trauma providers. In level 4 centers, the trauma provider may be a hospitalist.

Daily review of each patient's eligibility and active orders for VTE chemoprevention should be performed by trauma team providers to ensure compliance with the institutions VTE prevention protocol. Incorporating such efforts int patient rounds, morning and evening report, or multidisciplinary rounds can all be effective methodologies for ensuring such review occurs. Electronic medical record indicators or "traffic lights" have been used successfully in several PA institutions during morning and evening sign-out to ensure patient orders and nursing administration are consistent with team treatment plan.

Missed doses:

Unauthorized missed doses should be tracked by the PI process. Where incidence is high, a plan for feedback to the administrating nurse provider may be warranted. Some institutions have employed scripted patient counseling or educational videos to minimize patient refusal[21].

h. Recommendations for Extended Prophylaxis Post Discharge:

As many as 70% of VTE's may be diagnosed post-discharge[22]. Patients remain at risk for about 3 months[23], particularly when they are non-ambulatory, most commonly secondary to orthopedic injury. Currently patients who are being discharged home or to destinations where subcutaneous prophylaxis is not feasible are at the highest risk. Such non-ambulatory patients should receive home prophylaxis with LMWH, UFH, or prophylactic dose novel anticoagulant (NOAC) for 35 days. ASA has been shown to be an effective alternative in some orthopedic populations. Frequently the patient's insurance coverage can factor in to feasibility and compliance with such therapy.

i. Protocol Education and Surveillance:

Protocol education should be widespread any time the protocol is revised. Educational efforts should include TS providers, residents, bedside nursing, operating room staff and treating subspecialists.

The institution's protocol should be actively surveilled daily by treating trauma providers. The centers performance improvement program should track compliance. Deviation from institutional target rates of compliance should be reported to the centers Trauma Operations Committee (or equivalent) and actively tracked until compliance is verified. A graduated protocol for counseling patients real-time by both nursing and TS providers should be in place if therapy is refused.

5. Important Trauma Patient Subpopulations

a. Isolated Orthopedic Trauma

Patients who sustain isolated orthopedic injury are at significant risk for VTE and should have chemoprophylaxis initiated as soon as it is deemed safe. Where bleeding risk is deemed to be low, VTE chemoprophylaxis should begin no later than the first available standardized dosing time occurring after initiation of chemoprophylaxis.

Traditional recommendations for elective orthopedic surgery have suggested that prophylaxis should be held in the 6-12 hours preceding and following orthopedic procedures in order to minimize risk of bleeding or wound healing complications[24].Unfortunately, the uncertainty surrounding the scheduling of urgent and emergent orthopedic interventions frequently leads to prolonged delays or missed doses in this population at high risk for VTE.

Although controversial, currently several Pennsylvania trauma centers (8 Level 1 and 5 Level II centers) have moved to continuous prophylaxis throughout the perioperative window in trauma patients with isolated orthopedic injuries to reduce their locally high institutional rates of VTE. Although conclusive evidence of the safety such protocols is currently lacking, the experience from these centers have not shown increased rates of bleeding or wound complications continuous perioperative chemoprophylaxis. Institutions within the state where VTE incidence is high, and bleeding complication rates are low, may consider adopting continuous uninterrupted chemoprophylaxis or narrowing the prohibited perioperative window in the orthopedic trauma population.

In circumstances in which the treating orthopedic surgeon and trauma surgeon agree bleeding risk is prohibitive, chemoprophylaxis may be held or delayed as deemed appropriate. In such cases, communication should occur attending to attending with orders placed by the trauma service and rationale for deviation from protocol documented in the patient's chart.

b. Neurotrauma Patients

This patient population has high untreated rates of VTE due to hypercoagulability and extended immobility[25]. ICDs should be instituted on admission in all patients where a contraindication does not exist[26]. At the current time there remains significant variation amongst Pennsylvania trauma centers statewide as to the preferred agent for chemoprophylaxis in the setting of TBI. Neurosurgical expert opinion in this area is highly varied and evidence-based data in this area remains sparse and widely debated.

The most salient controversies have surrounded both the agent of choice, and the safe timing of initiation. Expansion of traumatic hemorrhagic lesions is rare when chemoprophylaxis is begun after confirmation of stability with CT imaging and ranges from 1 to 4%[4,27]. Although hemorrhage expansion is rare it does on occasion require intervention[27] Anecdotal experiences surrounding such events often impacts local institutional discussions regarding VTE chemoprophylaxis protocols with many trauma surgeons and neurosurgeons preferring to manage patients on a case by case basis. Although such opinions are at times strongly held, this working group recommends utilization of a local institutional standardized protocol rather than case by case individualized management in the majority of neurotrauma patients, as this is the only way produce sustained reductions in VTE incidence . The primary goal of the institutional protocol for chemoprophylaxis in the setting of TBI should be to facilitate initiation as early as possible to minimize the risk of VTE, while also mitigating the risk of hemorrhage expansion.

An increasing body of literature suggest that early initiation of chemoprophylaxis in the first 72 hours post injury is both safe and effective. The American College of Surgeons (ACS) Trauma Quality Improvement Program (TQIP) Best Practice Guideline on traumatic brain injury now advocates initiation of LMWH within 72 hours of injury in patients with stable CT imaging.[28] This guideline recommends stratifying TBI bleeding risk per the Modified Parkland Protocol which is a commonly employed protocol in neurotrauma. This protocol is based on a modification of injury patterns initially described by Berne and Norwood[25] and classifies TBI patients as low, moderate, or high risk for hemorrhage progression based on hemorrhage morphology (Figure 1). Small low risk lesions can be started at 24 hours as long a f/u imaging does not show progression. Early initiation for these low risk TBI hemorrhagic lesion is critical to reducing overall VTE

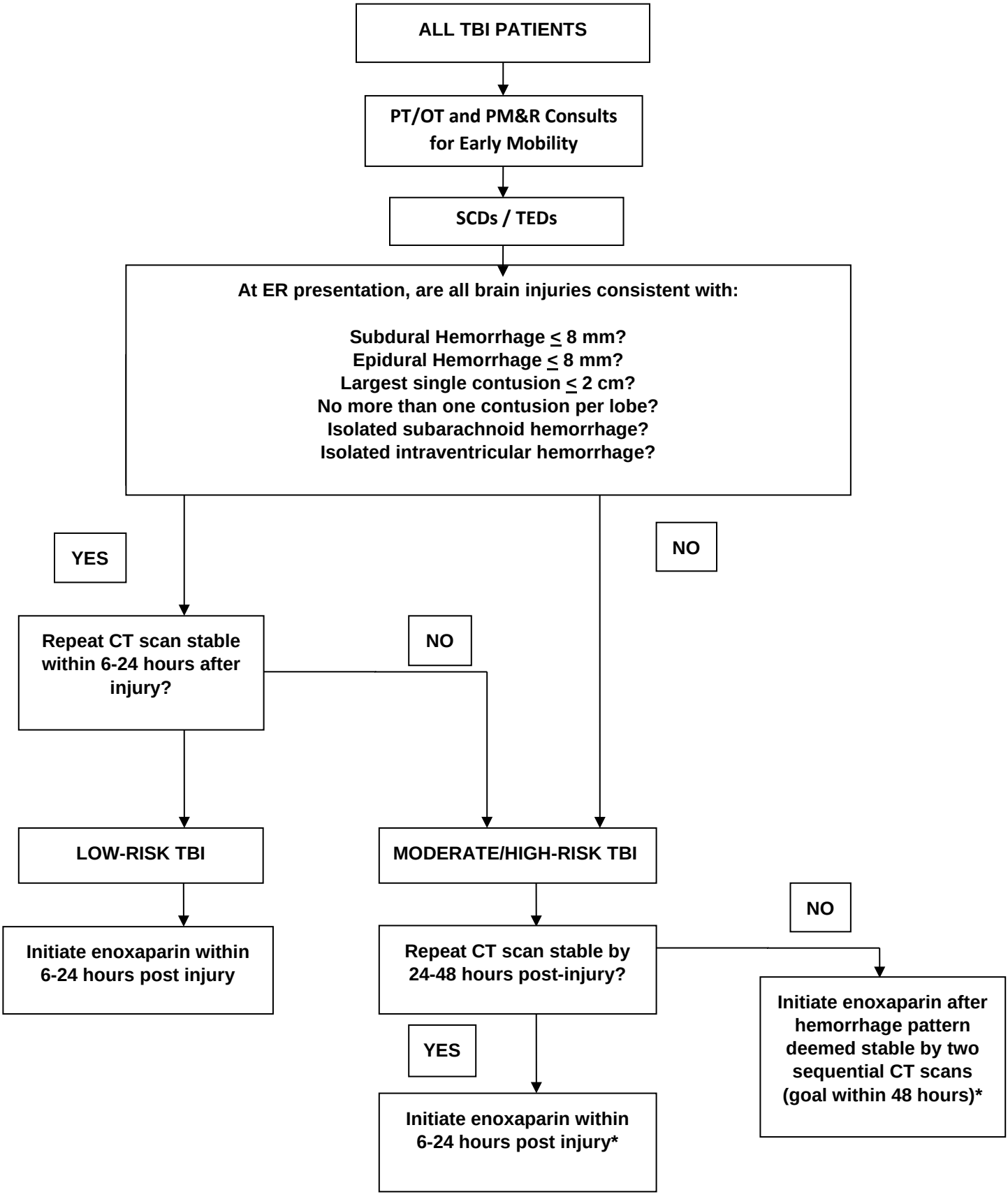
incidence as they often have coexistent orthopedic injuries for which delays in initiation may significantly increase risk for VTE. Moderate and high-risk lesions for progression should can be observed for longer prior to initiation but should be started no later than 72 hours as long as 24 hours of stability on imaging is confirmed. Where progression has been demonstrated, chemoprophylaxis should be held for 24 hours and reassessed.

This recommendation is reinforced by a recent propensity-matched cohort study performed using the TQIP registry demonstrating a reduced risk of both PE OR 0.48; (5% CI, 0.25-0.91), and DVT OR 0.51; 95% CI, 0.36-0.72) when chemoprophylaxis was initiated before 72 hours when con compared with after. This risk reduction was observed without increase risk of late neurosurgical intervention or death.

Local institutional compliance with protocols in these patients can be monitored via TQIP Benchmark reporting which gives specific comparative data on the local institution's agent of choice as well as timing of initiation of chemoprophylaxis stratified by cohort.

Another factor complicating protocol decision-making is the current paucity of literature that specifically examines the safety and efficacy of weight-based dosing in the setting of traumatic brain injury. We therefore recommend patients receiving Enoxaparin for prophylaxis in the setting of neurotrauma should commence therapy with a "traditional" dosing regimen of Enoxaparin. In institutions where VTE rates in the neurotrauma population are high, consideration may be made for moving toward weight based dosing in the individualized patient after a period of image stability is confirmed utilizing "traditional dosing" when dose monitoring reveals subtherapeutic levels of Anti-Xa.

The Modified Parkland Protocol is recommended to assist decision-making regarding the timing of chemoprophylaxis.



***UFH can be substituted for enoxaparin but has inferior performance with respect to LMWH in preventing VTE and is therefore not recommended.**

Special Considerations

Peri-procedural Dosing in TBI

- Where non-emergent operative or procedural intracranial interventions are planned, the 0600 dose should be held prior to procedure.
- Where emergent operative intervention is required, chemoprophylaxis is immediately discontinued and is resumed no earlier than 24 hours post procedure, provided there has been clinical stability of the patient's neuro exam and post-operative imaging shows stability of any coexistent hemorrhage.

Spinal Cord Injury

- Similar to TBI, current consensus opinion is that LMWH should be within 72 hours in patients sustaining spinal cord injury[29, 30-34]. After 72 hours, untreated patients with paraplegia or quadriplegia carry risk of VTE that exceeds 50% [35, 36].
- Both thigh-high TEDS and SCDs may be of benefit in the setting of spinal cord injury. This recommendation stems from their markedly elevated risk of VTE. In addition, TEDs can reduce venous capacitance and increase cardiac pre-load, frequently preventing the hypotension observed in neurogenic shock.
- Initiate chemoprophylaxis on admission if no surgical intervention is planned and no epidural hematoma is present.
- Prophylactic IVC filters are not recommended unless both ICDs and pharmacologic measures are contraindicated.
- If mobility is expected to remain impaired for > 2 weeks, extended prophylaxis post discharge should be initiated with therapeutic anticoagulation for at least 3 months[35,36] .

Tubes and Drains

- In most cases insertion of EVD/monitor occurs shortly after admission and chemoprophylaxis has not yet been started.
- In the case where acute change requires emergent placement of EVD/monitor, enoxaparin should be discontinued at the time of decision to proceed with placement.
- Chemoprophylaxis therapy around EVD/monitor removal is identical to the regiment for neuraxial therapy (see below).

Neuraxial Anesthesia

- Wherever possible, peripheral nerve blocks are preferred to neuraxial anesthesia as they do not impede institution of chemoprophylaxis in injured patients.
- Patients who undergo neuraxial anesthesia should receive chemoprophylaxis in accordance with the American Society of Regional Anesthesia (ASRA) guidelines outlined below[37]:

Prior to Insertion:

Heparin 5000u SQ q 12h or q 8 hours:

Hold for at least 4 hours prior to placement.

Enoxaparin 30mg SQ BID or 40mg SQ once daily:

Hold for at least 12 hours prior to placement.

During neuraxial therapy:

Heparin 5000ug SQ q 12 hours or q 8 hours:

May be resumed no less than 4-6 hours post neuraxial procedure. Prior to removal of indwelling catheter/device, heparin SQ should be held for 4-6 hours. Heparin chemoprophylaxis may be resumed after 1 hour after discontinuation/removal.

Enoxaparin 40mg once daily (only):

May be resumed no less than 12 hours post neuraxial procedure. In the event of traumatic neuraxial placement, the first dose of Enoxaparin should be given 24 hours post procedure. Discontinuation of neuraxial therapy/ removal of any indwelling device should be done 12 hours after last dose of Enoxaparin. Indicated chemoprophylaxis may be resumed 4 hours after discontinuation/removal. Concomitant use of anti-platelet therapy should be avoided while indwelling catheter is in place.

Procedure for Deviation from Protocol when deemed appropriate by treating Neurosurgeon (NS)

Deviation from the above protocol can occur in situations where the treating attending TS and attending NS both agree that the risk outweighs benefit of chemoprophylaxis. Such deviations from protocol should only occur after an attending to attending conversation, and with documentation in the record as to the rationale. Except in emergent circumstances, all orders placed should be placed by TS providers.

c. Solid Organ injury

Patients with solid organ injury should have chemoprophylaxis started at 24-48 from arrival where clinical stability is confirmed. Qualifying patients should have stable vital signs, clinical exam and H&H over the preceding 24 hours.[38-43] Similarly, chemoprophylaxis can be resumed in the immediate post-operative period where the bleeding source has been definitively addressed (i.e. splenectomy). Where bleeding risk continues, chemoprophylaxis can be instituted at 24-48 hours post procedure when stability is confirmed.

d. Pediatric Trauma

Injured patients with **age ≥13** years requiring hospitalization ≥24 hours who are **non-ambulatory** secondary to their injuries should receive ICD's and chemoprophylaxis (unless contraindicated)[44-47].

Examples of Injuries include:

- Pelvic fracture
- Long bone fracture
- Spinal Cord Injury
- intubated with CVC

Injured patients with **age ≥13** years requiring hospitalization ≥24 hours who remain **ambulatory** should receive ICD's. Chemoprophylaxis should be instituted only if they have any of the following:

- Personal or family history of VTE
- Known hypercoagulable state
- Femoral vein central line
- Complex pelvic fracture or complex lower extremity fracture
- Obese (>95% BMI)
- Current use of exogenous estrogens

Injured patients with **age ≤12** years do not routinely require VTE chemoprophylaxis unless they have a personal/family history of VTE or a known hypercoagulable state **AND** ≥1 of the other above risk factors. Consultation with hematology is recommend when considering chemoprophylaxis in children ≤12 years.

Where chemoprophylaxis is indicated, enoxaparin is the preferred agent. The preferred dosing regimen is 0.5mg/kg (max 30mg) SQ BID or q12hr.

Mechanical prophylaxis either alone or in combination with pharmacologic prophylaxis should be used when appropriately sized device available.

e. Multi-system Trauma:

Multisystem trauma prophylaxis will be determined by the subpopulation category with the most restrictive protocol.

f. Pregnant trauma patients:

There is a paucity of data for enoxaparin in pregnancy. It has historically been difficult to dose due to unpredictable volume of distribution between the fetus. Emerging data supports its use and in the setting of monitoring anti-Xa levels, it is considered safe[24,48,49]. Standard weight-based dosing of enoxaparin 0.5mg/kg SQ every 12 hours with monitoring of anti-Xa levels is recommended[24,48,49].

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