

PENNSYLVANIA

Trauma Quality Improvement Program

(PA-TQIP)



p e n n s y l v a n i a
**TRAUMA
SYSTEMS**
f o u n d a t i o n

PA-TQIP Collaborative

Best Practice Management Guideline

for VTE Prophylaxis

Original 2020

Updated December 2022

PA TQIP Collaborative Best Practice Management Guideline for VTE Prophylaxis

Panel of Contributors

Neurosurgical Work Group:

Michelle Budzyn, Pharm D., BCPS

Geisinger Wyoming Valley
Assistant Director of Pharmacy

Julie Donnelly, MSN, RN, TCRN

Thomas Jefferson University Hospital
Trauma Program Manager

Forrest B. Fernandez, MD

Reading Hospital
Division Chief, Trauma and Acute Care Surgery

Carol Fox, RN, MA, CNRN

Lehigh Valley Health Network
Trauma Program Director

Richard Lopez, DO, FACS, FACOS*

Geisinger Wyoming Valley Medical Center
Trauma Program Medical Director

David O. Okonkwo, MD, PhD

UPMC Presbyterian
Neurosurgeon

Andrew Tsen, MD

Lehigh Valley Health Network
Neurosurgeon

James V. Yuschak, MD

Jefferson Abington Hospital
Trauma Program Medical Director

#TQIP Leadership Liaison

*Workgroup Lead

General and Monitoring Work Group:

Cynthia Anthony, MSN, RN, TCRN

AHN Forbes Hospital
Trauma Performance Improvement Coordinator

John Gallagher, DNP, RN-C#

Penn Presbyterian Medical Center
Trauma Program Manager

Cheryl MacDonald-Sweet, RN, CEN, CPEN, TCRN

Wilkes-Barre General Hospital
Trauma Program Administrator

Michelle Budzyn, Pharm D.

Geisinger Wyoming Valley Medical Center
Clinical Pharmacist

Megan Rapp, MD*

Geisinger Medical Center
Trauma Surgeon

Maureen L. Small, BSN, RN

Jefferson Abington Hospital
Trauma Program Manager

#TQIP Leadership Liaison

*Workgroup Lead

Orthopedic Work Group:

Deborah Clark, MSN, RN

Geisinger Community Medical Center
Trauma Program Manager

Cynthia Fusco, DO*

Jefferson Torresdale Hospital
Trauma Program Medical Director

Bree Harrison, BSN, RN, TCRN

Lehigh Valley Health Network
Trauma Program Manager

Scott Lovenstein

Jefferson Torresdale Hospital
Pharmacist

Jo Ann Miller, CRNP, MSN, CCRN-K, TCRN

Lancaster General Health, Penn Medicine
Trauma Program Manager

Donna Titus, MSN, RN, CEN, TCRN#

Jefferson Torresdale Hospital
Trauma Program Manager

Olga Woloszczuk, RPH

Jefferson Health
Pharmacist

#TQIP Leadership Liaison

*Workgroup Lead

Solid Organ Work Group:

Eric Bradburn, DO*

Lancaster General Health, Penn Medicine
Trauma Program Medical Director

Linda DiBello, BSN, RN, JD

Paoli Hospital
Trauma Performance Improvement Coordinator

Karen M. Frock, PharmD, BCPS, BCCCP

York Hospital
Clinical Pharmacy Specialist
Trauma/Surgical/Neurosurgical Critical Care

Denise Torres, MD#

Geisinger Health System/Geisinger Medical Center
Director of Acute Care Surgery/Director of Trauma
Surgery

Jill Volgraf, BA, RN

Temple University Hospital
Trauma Program Manager

#TQIP Leadership Liaison

*Workgroup Lead

Pediatric Work Group:

Melinda Gallagher, MS, BSN, RN

UPMC Children's Hospital of Pittsburgh
Trauma Nurse Coordinator

Carol A. Hanson, MSN, RN

Geisinger Janet Weis Children's Hospital
Trauma Program Manager

Alfred P. Kennedy, MD

Geisinger Janet Weis Children's Hospital
Trauma Program Medical Director

Richard L. Lambert, MD

Geisinger Janet Weis Children's Hospital
PCCM Director

Loreen Meyer, MSN, RN

St. Christopher's Hospital
Trauma Program Manager

Gary Nace, MD*

Children's Hospital of Philadelphia
Trauma Surgeon

Christine Perlick, BSN, RN

UPMC Children's Hospital of Pittsburgh
Trauma Program Manager

Diane Perks, DNP, CRNP

Children's Hospital of Philadelphia
Trauma Program Manager

Terry Snavely, MSN, RN#

Pennsylvania Trauma Systems Foundation
Manager of Performance Improvement

Bryan Snook, PharmD, BCPPS

Geisinger Janet Weis Children's Hospital
Clinical Pharmacist - Pediatric Team Leader

#TQIP Leadership Liaison

*Workgroup Lead

Other Contributors:

Roman Gokhman, Pharm.D.

Reading Hospital
Critical Care Pharmacy Clinical Specialist

Atif K. Ahmed, MD

Jefferson – Torresdale
Director of Orthopedic Trauma

Daniel S. Horwitz, MD

Geisinger Health System and Geisinger
Commonwealth School of Medicine
Professor and Chief Orthopaedic Trauma

George Koenig, Jr. DO, MS, FACS

Thomas Jefferson University Hospital
Trauma Program Medical Director

Anthony Martin, BSN, RN, TCRN

Reading Hospital
Trauma Program Manager

Other Contributors (Continued):

Alison Muller, MLS, MSPH

Reading Hospital
Research Coordinator

Saqib Rehman, MD, MBA

Temple University Hospital
Medical Director, Physician Assistant Program
Vice Chair and Professor, Orthopaedic Surgery and
Sports Medicine

Eric M. Slotkin, DO, FAAOS

Reading Hospital
Division Chief, Orthopedic Surgery

Gabrielle Wenger, RHIT, CPC, CAISS, CSTR

Pennsylvania Trauma Systems Foundation
Trauma Registry Auditor

[#]TQIP Leadership Liaison

^{*}Workgroup Lead

Endorsers:

Pennsylvania Trauma Medical Directors

Pennsylvania Trauma Program Managers

Spinal Column Work Group (Added December 2022):

Russell Dumire, MD

Anthony Martin, MBA, RN, BSN, TCRN

Denise Torres, MD

Forrest B. Fernandez, MD

Raquel Forsythe, MD

Karen Frock, PharmD

Michael H. Haak, MD

Alan S. Hilibrand, MD

Jack Jallo, MD, PhD

Herman C. Lawson, MD

David O. Okonkwo, MD, PhD Dr. Shaw, UPMC

Jeremy D. Shaw, MD

James M. Schuster, MD, PhD

Andrew R. Tsen, MD

Alexander R. Vaccaro, MD, PhD, MBA

Rebecca Geyer, MSN, RN, TCRN

Gabrielle Wenger, RHIT, CPC, CAISS, CSTR

Conemaugh Health System

Reading Hospital

Geisinger Health System

Grand View Health

University of Pittsburgh Medical Center

WellSpan Health

Geisinger Health System

Thomas Jefferson University Hospital

Thomas Jefferson University Hospital

Reading Hospital

University of Pittsburgh Medical Center

University of Pittsburgh Medical Center

University of Pennsylvania

Lehigh Valley Health Network

Thomas Jefferson University Hospital

Pennsylvania Trauma Systems Foundation

Pennsylvania Trauma Systems Foundation

Outline

1. Scope	Page 7
2. Purpose	Page 7
3. Background	Page 7
4. General Considerations	Page 8
a. Applicable Patient Population	Page 8
b. Preferred Chemoprophylactic Agents and Dosing	Page 8
c. Timing	Page 9
d. Anti-Xa Monitoring and Dosage Adjustment	Page 10
e. Screening	Page 10
f. Vena Cava Filters	Page 11
g. Protocol Maintenance	Page 11
h. Recommendations for Extended Prophylaxis Post Discharge	Page 11
i. Protocol Education and Surveillance	Page 11
5. Important Patient Subpopulations	Page 12
a. Isolated Orthopedic Trauma	Page 12
b. Neurotrauma	Page 12
i. Traumatic Brain Injury (TBI)	Page 13
ii. Spinal Column Injury	Page 13
c. Solid Organ Injury	Page 15
d. Pediatric Trauma	Page 15
e. Multi-system Trauma	Page 15
f. Pregnant Trauma Patients	Page 15
6. Attachment A Modified Parkland Protocol	Page 16
7. Attachment B VTE Prophylaxis Guideline for Spinal Column Injury*	Page 17
8. References	i
9. Attachment B References*	v

****Updated December 2022***

Protocol

1. Scope:

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

2. Purpose:

The PA TQIP Collaborative identified significant variation statewide in institution specific protocols for VTE Chemoprevention. Recent PA-TQIP Collaborative data show Pennsylvania trauma center patients have elevated incidence of venous thromboembolism (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 VTE. The major complication of deep venous thromboembolism (DVT), pulmonary embolism (PE), accounts for as many as 200,000 deaths annually.

When prophylactic strategies are not employed, injured patients 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 strategies². Fourteen centers within the PA TQIP Collaborative retrospectively chart reviewed all cases of pulmonary embolism 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 interventions³.

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 use of mechanical prophylaxis 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 injury⁴. 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, contribute 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 were 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. Observation patients present a unique challenge to many centers, particularly where the prevalence of geriatric patients is high. These patients are often unpredictable regarding their ambulatory capability and length of stay and such centers may consider deploying VTE prophylaxis strategies to the observation population 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 population⁷. 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 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 injuries and are discussed in detail in 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 Fondaparinux¹³ 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 VTE¹⁴. 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 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 with 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 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 DOSE	NEXT DOSE	DOSAGE CHANGE	NEXT ANTI-Xa LEVEL
<0.2	NO		Increase each dose by 10 mg.	4 hrs. after the 4 th 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 4 th dose of the new dosing regimen
>0.7 – 1.0	NO		Decrease dose by 20 mg.	4 hrs. after the 4 th 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 beneficial¹⁸. 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 use⁶. 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 days²⁰.

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 IV 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 into 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 administering nurse provider may be warranted. Some institutions have employed scripted patient counseling or educational videos to minimize patient refusal²¹.

h. Recommendations for Extended Prophylaxis Post Discharge

As many as 70% of VTE's may be diagnosed post-discharge²². Patients remain at risk for about three months²³, 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 into 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 complications²⁴.

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

This patient population has high untreated rates of VTE due to hypercoagulability and extended immobility²⁵. ICDs should be instituted on admission in all patients where a contraindication does not exist²⁶. 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 intervention²⁷. 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 to 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, within 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 the first 72 hours post injury in patients with stable CT imaging.²⁸ This guideline recommends stratifying TBI bleeding risk per the Modified Parkland Protocol (see Attachment A) which is a commonly employed protocol in neurotrauma. This protocol is based on a modification of injury patterns initially described by Berne and Norwood²⁵ 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 can be observed for longer prior to initiation but should be started within the first 72 hours post injury 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; (95% CI, 0.25-0.91), and DVT OR 0.51; 95% CI, 0.36-0.72) when chemoprophylaxis was initiated within the first 72 hours post injury when compared with after. This risk reduction was observed without increased risk of late neurosurgical intervention or death⁵⁰. 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.

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 Column Injury Cohort (See Attachment B and Attachment B References)

- After 72 hours, untreated patients with paraplegia or quadriplegia carry risk of VTE that exceeds 50%.^{6,10,11}
- Effective VTE prevention in this cohort requires a multidisciplinary collaborative approach. Early consultation of physiatry, and physical and occupational therapy are recommended.
- Intermittent pneumatic compression (IPC) sleeves or graduated compression stockings should be applied on admission unless contraindicated.⁷ Although less effective than pharmacologic thromboprophylaxis, compression devices are thought to reduce venous capacitance and increase cardiac pre-load, frequently preventing the hypotension observed in neurogenic shock.
- Low molecular weight heparin (LMWH) has been found more effective in preventing VTE than unfractionated heparin (UFH) in the setting of major trauma while not significantly increasing the risk of bleeding in the setting of neurotrauma.^{4,5,8,12,16,17,21}
- Like TBI, current consensus opinion is that LMWH should begin within 72 hours of spinal cord injury.^{2,3,9}
- Initiate pharmacologic thromboprophylaxis on admission if no surgical intervention is planned and no epidural hematoma is present.
- For patients undergoing immediate decompressive spinal surgery, LMWH should be started within 48 hours of surgery.^{16,24}

- Patients expected to undergo non-emergent spinal stabilization should begin prophylactic treatment with LMWH (preferred) or UFH upon admission.
 - Enoxaparin should be held for 12hrs pre-operatively and Heparin held the morning of surgery.
 - Prophylaxis should resume within 24hrs of the operation.
- Prophylactic IVC filters should only be considered if both compression devices and pharmacologic measures are contraindicated.¹⁴
- If mobility is expected to remain impaired for > 2 weeks, extended prophylaxis post discharge should be initiated with therapeutic anticoagulation for at least 8 weeks as the risk of VTE is highest during the 3-month period after injury.^{6,13,23}

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 below³⁷:

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

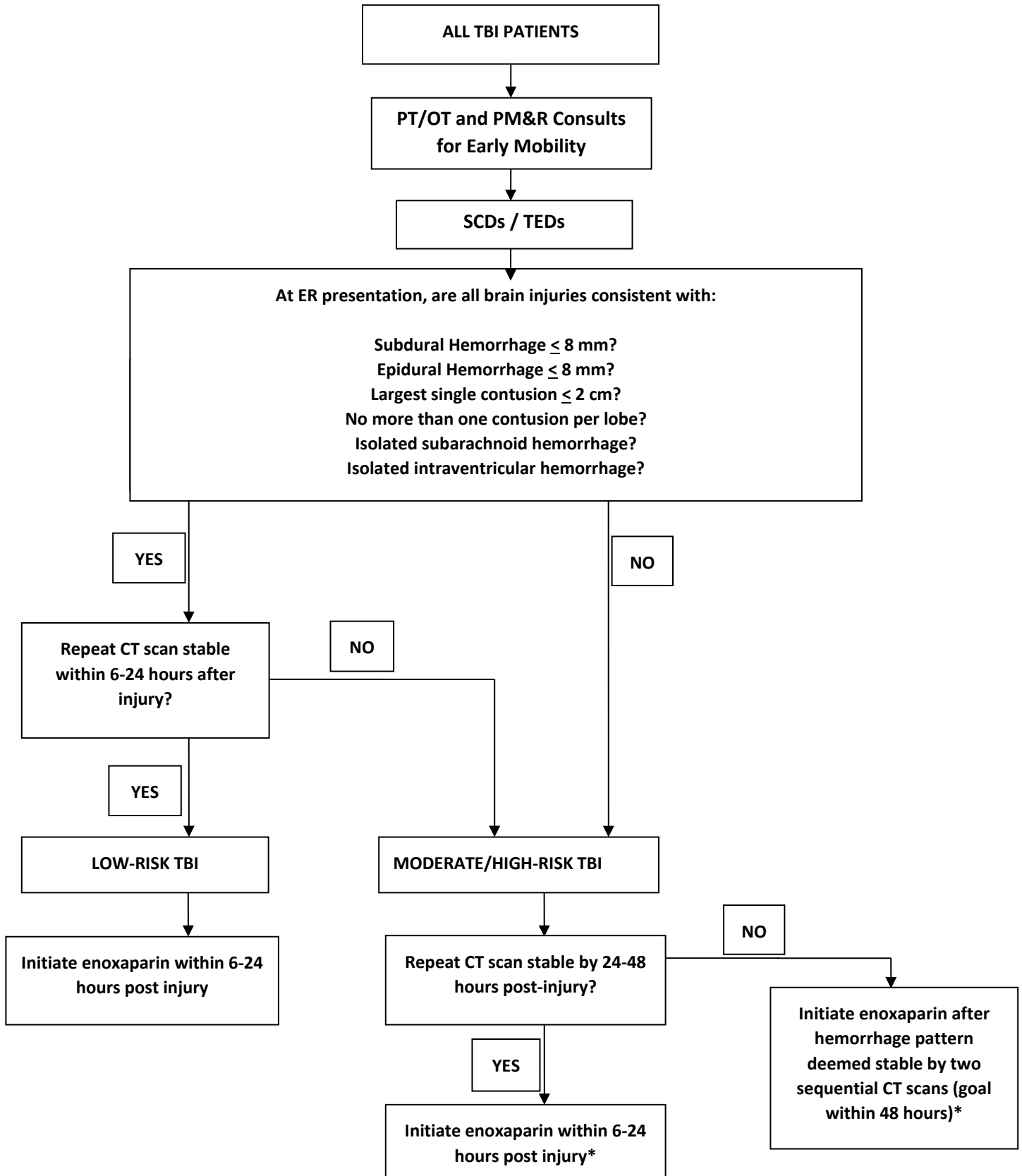
Multisystem trauma prophylaxis will be determined by the subpopulation category with the most restrictive protocol.

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}.

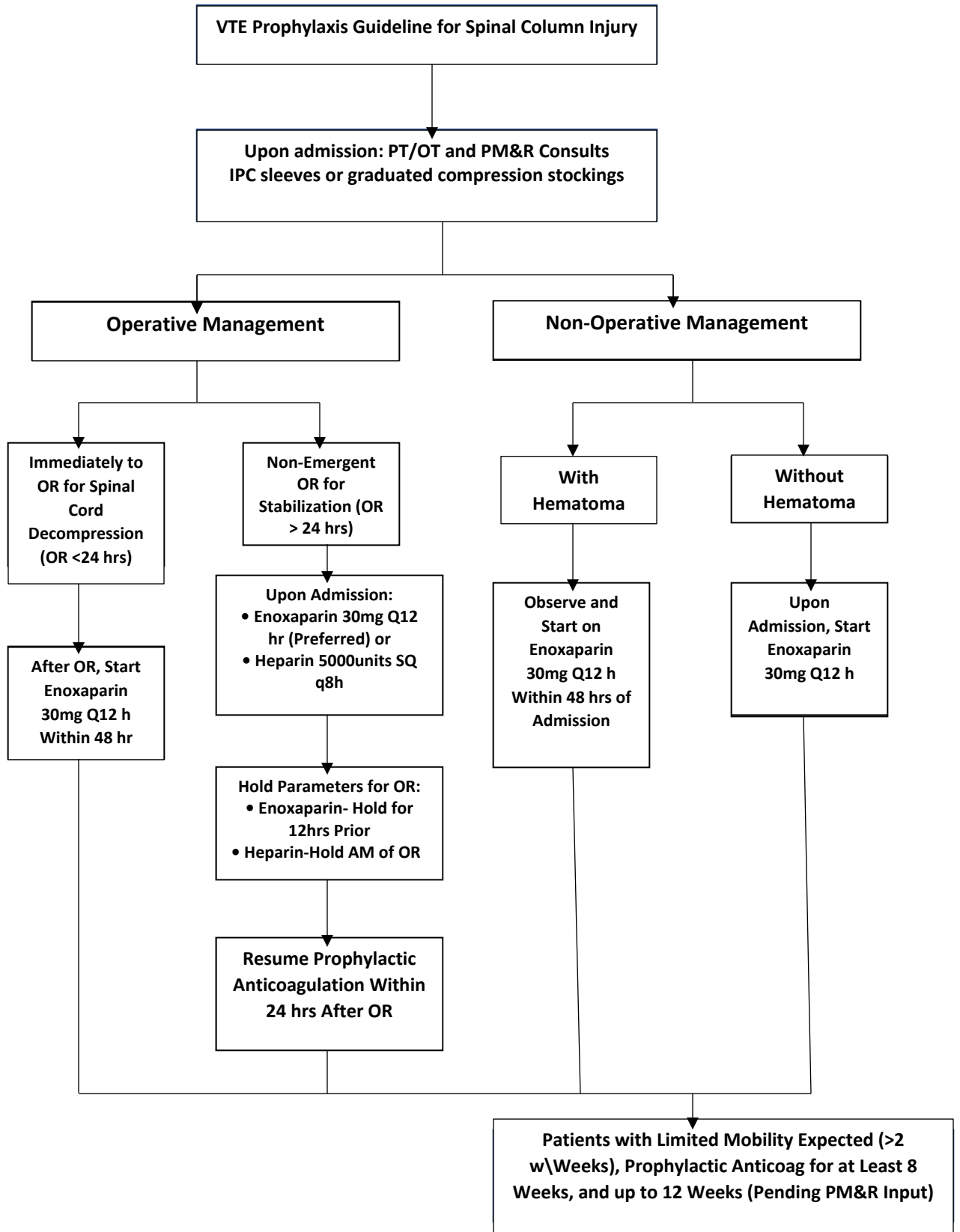
6. ATTACHMENT A

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.

7. ATTACHMENT B*
VTE Prophylaxis Guideline for Spinal Column Injury**



*Please Consult the Attachment B Reference List

8. REFERENCES

1. Montero RE, Baldominos UG, Lopez AJ, Santolaya PR. Effectiveness, and safety of thromboprophylaxis with enoxaparin in medical inpatients. *Thromb Res.* 2011;128(5):440-445.
2. Hemmila MR, Cain Nielsen AH, Jakubus JL, Mikhail JN, Dimick JB. Association of Hospital Participation in a Regional Trauma Quality Improvement Collaborative with Patient Outcomes. *JAMA Surg.* 2018;153(8):747-756. doi:10.1001/jamasurg.2018.0985.
3. PA TQIP Collaborative analysis of patients sustaining PE in PTOS data registry years 2016-2018. Unpublished raw data.
4. Norwood SH, Berne JD, Rowe SA, Villarreal DH, Ledlie JT. Early venous thromboembolism prophylaxis with enoxaparin in patients with blunt traumatic brain injury. *J Trauma.* 2008;65(5):1021–1027.
5. Greenfield LJ, Proctor MC, Rodriquez JL, Luchette FA, Cipolle MD, Cho J. Posttrauma thromboembolism prophylaxis. *J Trauma* 1997;42(1):100-103.
6. Rogers FB, Shackford SR, Horst MA, Miller JA, Wu D, Bradburn E, Rogers A, Krasne M. Determining venous thromboembolic risk assessment for patients with trauma: The Trauma Embolic Scoring System. *J Trauma Acute Care Surg.* 2012;73(2):511-515.
7. Geerts WH, Jay RM, Code KI, Chen E, Szalai JP, Saibil EA, Hamilton PA. A comparison of low-dose heparin with low-molecular weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med* 1996;335(10):701-7.
8. Freeman A, Homer T, Pendleton RC, Rondina MT. Prospective comparison of three enoxaparin dosing regimens to achieve target anti-factor Xa levels in hospitalized, medically ill patients with extreme obesity. *Am J Hematol* 2012;87(7):740-3.
9. Imran JB, Madni TD, Clark AT, Rizk P, Huang E, Minshall CT, Taveras LR, Cunningham HB Eastman AL, Koshy JP, Kacir CD, Cripps MW. Inability to predict subprophylactic anti-factor xa levels in trauma patients receiving early low-molecular-weight heparin. *J Trauma Acute Care Surg.* 2018;85(5):867-872.
10. Berndtson AE, Costantini TW, Lane J, Box K, Coimbra R. If some is good, more is better: An enoxaparin dosing strategy to improve pharmacologic venous thromboembolism prophylaxis. *J Trauma Acute Care Surg.* 2016;81(6):1095-1100.
11. Pannucci CJ, Hunt MM, Fleming KI, Prazak AM. Weight-based dosing for once-daily enoxaparin cannot provide adequate anticoagulation for venous thromboembolism prophylaxis. *Plast Reconstr Surg.* 2017;140(4):815-822.
12. Sanofi-Aventis, Bridgewater, NJ. Prescribing information for Lovenox (enoxaparin sodium injection) for subcutaneous and intravenous use. Available at: <http://products.sanofi.us/Lovenox/Lovenox.pdf>. Accessed October 4, 2019.
13. GlaxoSmithKline, Research Triangle Park, NC. Prescribing information for Arixtra (fondaparinux). Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/021345s010lbl.pdf2017. Accessed August 2019.
14. Louis SG, Sato M, Geraci T, Anderson R, Cho SD, Van PY, Barton JS, Riha GM, Underwood S, Differding J, Watters JM, Schreiber MA. Correlation of missed doses of enoxaparin with increased incidence of deep vein thrombosis in trauma and general surgery patients. *JAMA Surg.* 2014;149(4):365-70.
15. Costantini TW, Min E, Box K, Tran V, Winfield RD, Fortlage D, Doucet J, Bansal V, Coimbra R. Dose adjusting enoxaparin is necessary to achieve adequate venous thromboembolism prophylaxis in trauma patients. *J Trauma Acute Care Surg.* 2013; 74:128-135.

16. Ko A, Harada MY, Barmparas G, Chung K, Mason R, Yim DA, Dhillon N, Marguiles DR, Gewertz BL, Ley EJ. Association between enoxaparin dosage adjusted by anti-factor Xa trough level and clinically evident venous thromboembolism after trauma. *JAMA Surg.* 2016;151(11):1006-1013.
17. Kay AB, Majercik S, Sorensen J, Woller SC, Stevens SM, White TW, Morris DS, Baldwin M, Bledsoe JR. Weight-based enoxaparin dosing and deep vein thrombosis in hospitalized trauma patients: a double-blind, randomized, pilot study. *Surgery.* 2018; pii: S0039-6060(18)30094-1. doi: 10.1016/j.surg.2018.03.001. [Epub ahead of print].
18. Cipolle MD, Wojcik R, Seislove E, Wasser TE, Pasquale MD. The role of surveillance duplex scanning in preventing venous thromboembolism in trauma patients. *J Trauma* 2002;52(3):453-462.
19. Hemmila MR, Osborne NH, Henke PK, Kepros JP, Patel SG, Cain Nielsen AH, Birkmeyer NJ. Prophylactic inferior vena cava filter placement does not result in a survival benefit for trauma patients. *Ann Surg* 2015;262(4):577-585.
20. Kwok MH, Rao Sudhakar, Honeybul S, Zellweger R, Wibrow B, Lipman J, Holley J, Kop A, Geelhoed E, Corcoran T, Misur P, Edibam C, Baker, RI, Chamberlain J, Forsdyke C, Rogers FB. A multicenter trial of vena cava filters in severely injured patients. *N Engl J Med.* 2019;381(4):328-337.
21. Haut ER, Aboagye JK, Shaffer DL, Wang J, Hobson DB, Yenokyan G, Sugar EA, Kraus PS, Farrow NE, Canner JK, Owodunni OP, Florecki KL, Webster KLW, Holzmueller CG, Pronovost PJ, Streiff MB, Lau BD. Effect of real-time patient centered education bundle on administration of venous thromboembolism prevention in hospitalized patients. *JAMA Netw Open.* 2018;1(7):e184741. Doi: 10.001/jamanetworkopen.2018.4741
22. Park MS, Perkins SE, Spears GM, Ashrani AA, Leibson CL, Boos CM, Harmsen WS, Jenkins DH, Bailey KR, Ballman KV, Heit JA. Risk factors for venous thromboembolism after acute trauma: A population-based case-cohort study. *Thromb Res.* 2016; 144:40-45.
23. Godat LN, Kobayashi L, Chang DC, Coimbra R. Can we ever stop worrying about venous thromboembolism after trauma? *J Trauma Acute Care Surg* 2015;78(3):475-480.
24. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, Ortel TL, Pauker SG, Colwell Jr., CW. Prevention of VTE in orthopedic surgery patients. *Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence Based Clinical Practice Guidelines.* *Chest.* 2012;141(2 Suppl): e278S-e325S.
25. Pastorek RA, Cripps MW, Bernstein IH, Scott WW, Maden CJ, Rickert KL, Wolf SE, Phelan HA. The Parkland Protocol's modified Berne-Norwood criteria predict two tiers of Risk for traumatic brain injury progression. *J Neurotrauma* 2014;31(20):1737-1743.
26. Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS, Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, Manley GT, Nemecek A, Newell DW, Rosenthal G, Schouten J, Shutter L, Timmons SD, Ullman JS, Videtta W, Wilberger JE, Wright DW. Guidelines for the management of severe traumatic brain injury. V. Deep vein thrombosis prophylaxis. *J Neurotrauma* 2007;24 Suppl 1:S32-6.
27. Norwood SH, McAuley CE, Berne JD, Vallina VL, Kerns DB, Grahm TW, Short K, McLarty JW. Prospective evaluation of the safety of enoxaparin prophylaxis for venous thromboembolism in patients with intracranial hemorrhagic injuries. *Arch Surg.* 2002;137(6):696-702.
28. American College of Surgeons. ACS TQIP Best Practices in the management of traumatic brain injury. https://www.facs.org/-/media/files/quality-programs/trauma/tqip/tbi_guidelines.ashx Accessed Nov 5, 2019.

29. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW. Prevention of venous thromboembolism: American College of Chest Physicians Evidence Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008;133(6 suppl):381S-453S.
30. Dhall SS, Hadley MN, Aarabi B, et al. Deep venous thrombosis, and thromboembolism in patients with cervical spinal cord injuries. *Neurosurgery* 2013; 72 Suppl 2:244.
31. Christie S, Thibault-Halman G, Casha S. Acute pharmacological DVT prophylaxis after spinal cord injury. *J Neurotrauma* 2011; 28:1509.
32. Teasell RW, Hsieh JT, Aubut JA, et al. Venous thromboembolism after spinal cord injury. *Arch Phys Med Rehabil* 2009; 90:232.
33. Van PY, Schreiber MA. Contemporary thromboprophylaxis of trauma patients. *Curr Opin Crit Care* 2016; 22:607.
34. Phelan HA. Pharmacologic venous thromboembolism prophylaxis after traumatic brain injury: a critical literature review. *J Neurotrauma* 2012;29(10):1821–1828.
35. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J. Med.* 1994;331(24):1601.
36. Fujii Y, Mammen EF, Farag A, Muz J, Saliccioli GG, Weingarden ST. Thrombosis in spinal cord injury. *Thromb Res.* 1992;68(4-5):357.
37. Horlocker TT, Vandermeulen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. *American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition. Reg Anesth Pain Med* 2018; 43:263-309.
38. Wooster ME, Spalding MC, Betz JA, Sellers S, Moorman ML, O'Mara MS. Non-operative management of blunt hepatic injury: Early return to function, chemical prophylaxis, and elucidation of Grade III injuries. *Int J Acad Med.* 2018; 4:271-7. <http://www.ijam-web.org/text.asp?2018/4/3/271/248336> [accessed 2019 Sep 24].
39. Skarupa D, Hanna K, Zeeshan M, Madbak F, Hamidi M, Haddadin Z, Northcutt A, Gries L, Kulvatunyou N, Joseph B. Is Early Chemical Thromboprophylaxis in Patients with Solid Organ Injury a Solid Decision? *J Trauma Acute Care Surg.* 2019;2163-0755. doi:10.1097/TA.0000000000002438. [Publish Ahead of Print.]
40. Coleman JR, Kay AB, Moore EE, Moore HB, Gonzalez E, Majercik S, Cohen MJ, White T, Pieracci FM. It's sooner than you think: Blunt solid organ injury patients are already hypercoagulable upon hospital admission - Results of a bi-institutional, prospective study. *Am J of Surg.* 2019;10: pii: S0002-9610(19)30345-9.[Epub ahead of print].
41. Rostas JW, Manley J, Gonzalez RP, Brevard SB, Ahmed N, Frotan MA, Mitchell E, Simmons JD. The safety of low molecular-weight heparin after blunt liver and spleen injuries. *Am J Surg.* 2015;210(1):31-34.
42. Joseph B, Pandit V, Harrison C, Lubin D, Kulvatunyou N, Zangbar B, Tang A, O'Keeffe T, Green DJ, Gries L, Friese RS, Rhee P. Early thromboembolic prophylaxis in patients with blunt solid abdominal organ injuries undergoing nonoperative management: is it safe? *Am J Surg.* 2015;209(1):194-198.
43. Schellenberg, M, Inaba K, Biswas S, Heindel P, Benjamin E, Strumwasser A, Matsushima K, Lam L, Demetriades D. When is it safe to start VTE prophylaxis after blunt solid organ injury? A prospective study from a level I trauma center. *World J Surg.* 2019;43(11):2797-2803. doi: 10.1007/s00268-019-05096-7. [Epub ahead of print].

44. Bigelow AM, Flynn-O'Brien KT, Simpson PM, Dasgupta M, Hanson SJ. Multicenter review of current practices associated with venous thromboembolism prophylaxis in pediatric patients after trauma. *Pediatr Crit Care Med*. 2018;19(9):e448-e454.
45. Carrillo LA, Kumar A, Harting MT, Pedroza C, Cox CS Jr. Venous thromboembolism risk factors in a pediatric trauma population. *Pediatr Surg Int*. 2019;35(4):487-493.
46. Hanson SJ, Faustino EV, Mahajerin A, O'Brien SH, Streck CJ, Thompson AJ, Petrillo TM, Petty JK. Recommendations for venous thromboembolism prophylaxis in pediatric trauma patients: A national, multidisciplinary consensus study. *J Trauma Acute Care Surg*. 2016;80(5):695-701.
47. Mahajerin A, Petty JK, Hanson SJ, Thompson AJ, O'Brien SH, Streck CJ, Petrillo TM, Faustino EV. Prophylaxis against venous thromboembolism in pediatric trauma: A practice management guideline from the Eastern Association for the Surgery of Trauma and the Pediatric Trauma Society. *J Trauma Acute Care Surg*. 2017;82(3):627-636.
48. Alshwabkeh L, Economy KE, Valente AM. Anticoagulation during pregnancy: Evolving strategies with a focus on mechanical valves. *J Am Coll Cardiol*. 2016;68(16):1804-1813.
49. Villani M, Ageno W, Grandone E, Dentali F. The prevention and treatment of venous thromboembolism in pregnancy. *Expert Rev Cardiovasc Ther*. 2017;15(5):397-402.
50. James P Byrne, Stephanie A Mason, David Gomez, Christopher Hoeft, Haris Subacius, Wei Xiong, Melanie Neal, Farhad Pirouzmand, Avery B Nathens. Timing of Pharmacologic Venous Thromboembolism Prophylaxis in Severe Traumatic Brain Injury: A Propensity-Matched Cohort Study. *Observational Study J Am Coll Surg*. 2016 Oct; 223(4):621-631.e5. doi: 10.1016/j.jamcollsurg.2016.06.382. Epub 2016 Jul 21.

9. Attachment B Reference List (Added December 2022)

1. American College of Surgeons. ACS TQIP Best Practices Guidelines - Spine Injury. https://www.facs.org/media/k45gikqv/spine_injury_guidelines.pdf. Accessed April 16, 2022.
2. Alquist S, Park HY, et al. Venous Thromboembolism Chemoprophylaxis Within 24 Hours of Surgery for Spinal Cord Injury: Is It Safe and Effective? *Neurospine* 2020;17(2):407-416.
3. Arnold PM, Harrop JS, Merli G, et al. Efficacy, safety, and timing of anticoagulant thromboprophylaxis for the prevention of venous thromboembolism in patients with acute spinal cord injury: A systematic review. *Global Spine Journal*. 2017
4. Benjamin E, Recinos G, Aiolfi A, Inaba K, Demetriades D. Pharmacological Thromboembolic Prophylaxis in Traumatic Brain Injuries: Low Molecular Weight Heparin Is Superior to Unfractionated Heparin. *Ann Surg*. 2017 Sep;266(3):463-469. doi: 10.1097/SLA.0000000000002359. PMID: 28650361. <https://pubmed.ncbi.nlm.nih.gov/28650361/>
5. Christie et al. Acute Pharmacological DVT Prophylaxis after Spinal Cord Injury. *Journal of Neurotrauma* 28:1509–1514
6. Chung WS, Lin CL, Chang SN, et al. Increased risk of deep vein thrombosis and pulmonary thromboembolism in patients with spinal cord injury: A nationwide cohort prospective study. *Thromb Res*. 2014; 133(4): 579–584.
7. Consortium for Spinal Cord Medicine. Prevention of venous thromboembolism in individuals with spinal cord Injury: Clinical practice guidelines for health care providers, 3rd ed. *Top Spinal Cord Inj Rehabil*. 2016 Summer; 22(3): 209–240 <https://pubmed.ncbi.nlm.nih.gov/29339863/>
8. DiGeorgio et al. Safety and effectiveness of early chemical deep venous thrombosis prophylaxis after spinal cord injury: pilot prospective data. *Neurosurg Focus* 43 (5):E21, 2017
9. Fehlings MG, Tetreault LA, Aarabi B, et al. A clinical practice guideline for the management of patients with acute spinal cord injury: Recommendations on the type and timing of anticoagulant thromboprophylaxis. *Global Spine Journal*. 2017; 7(3 Suppl): 212S–220S. <https://pubmed.ncbi.nlm.nih.gov/29164026/>
10. Fujii Y, Mammen EF, Farag A, Muz J, Saliccioli GG, Weingarden ST. Thrombosis in spinal cord injury. *Thromb Res*. 1992;68(4-5):357
11. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J. Med*. 1994;331(24):1601.
12. Geerts WH, Jay RM, Code KI, Chen E, Szalai JP, Saibil EA, Hamilton PA. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med*. 1996 Sep 5;335(10):701-7. doi: 10.1056/NEJM199609053351003. PMID: 8703169. <https://pubmed.ncbi.nlm.nih.gov/8703169/>
13. Giorgi-Pierfranceschi M, Donadini MP, Dentali F, et al. The short- and long-term risk of venous thromboembolism in patients with acute spinal cord injury: A prospective cohort study. *Thromb Haemost*. 2013; 109(1): 34–38.
14. Gorman, P. H., Qadri, S. F. A., & Rao-Patel, A. (2009). Prophylactic Inferior Vena Cava (IVC) Filter Placement May Increase the Relative Risk of Deep Venous Thrombosis After Acute Spinal Cord Injury. *Journal of Trauma: Injury, Infection & Critical Care*, 66(3), 707–712. <https://doi.org/10.1097/ta.0b013e318188beba>

15. Hamidi et al. Operative spinal trauma: Thromboprophylaxis with low molecular weight heparin or a direct oral anticoagulant. *J Thromb Haemost*. 2019;17:925–933.
16. Kim DY, Kobayashi L, Chang D, et al. Early pharmacological venous thromboembolism prophylaxis is safe after operative fixation of traumatic spine fractures. *Spine*. 2015 Mar 1; 40(5): 299–304.
17. Lin Z et al. The effectiveness and safety of LMWH for preventing thrombosis in patients with spinal cord injury: a meta-analysis. *Journal of Orthopaedic Surgery and Research* (2021) 16:262
18. PA TQIP Collaborative analysis of patients sustaining PE in PTOS data registry years 2016-2018. Unpublished raw data.
19. Raksin, PB, Harrop, JS, Anderson, PA, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the evaluation and treatment of patients with thoracolumbar spine trauma: Prophylaxis and treatment of thromboembolic events. *Neurosurgery*. 2019; 84: E39–E42
20. Thomas Jefferson University Hospital (TJUH) Trauma SCI/VTE Prophylaxis Guideline 2021. Unpublished.
21. Tran A, Fernando SM, Carrier M, et al. Efficacy and safety of low molecular weight heparin versus unfractionated heparin for prevention of venous thromboembolism in trauma patients: A systematic review and meta-analysis. *Ann Surg*. 2021 Aug 13. doi:10.1097/ SLA.0000000000005157. Epub ahead of print. PMID: 34387202 <https://pubmed.ncbi.nlm.nih.gov/34387202/>
22. UAMS Department of Physical Medicine and Rehabilitation / Trauma Rehabilitation Resources Program Spinal Cord Injury Guidelines 2020. <https://medicine.uams.edu/pmr/wp-content/uploads/sites/3/2021/02/Guidelines-SCI-Deep-Vein-Thrombosis-2020.pdf>. Accessed May 5, 2022.
23. Weidner et al. Prevention of thromboembolism in spinal cord injury -S1 guideline. *Neurological Research and Practice* (2020) 2:43
24. Zeeshan et. Al. Optimal timing of initiation of thromboprophylaxis in spine trauma managed operatively: A nationwide propensity-matched analysis of trauma quality improvement program. *J Trauma Acute Care Surg* Volume 85, Number 2 <https://pubmed.ncbi.nlm.nih.gov/29613956/>