# JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)



# **Prevention of Venous Thromboembolism**

To establish guidance for anti-thrombotic therapy for the prevention of deep venous thrombosis and pulmonary embolism and the management of inferior vena cava filters placed in theater for primary or secondary prophylaxis of pulmonary embolism.

#### CONTRIBUTORS

MAJ Rachel Russo, MC, USAF MAJ Brian Gamble, MC, USA CAPT Matthew Bradley, MC, USN LCDR J. Michael Van Gent, MC, USN CAPT Matthew D. Tadlock, MC, USN Lt Col Remealle A. How, MC, USAF COL Jennifer M. Gurney, MC, USA

Previous Contributors: CDR Daniel Grabo, MC, USN; LTC Jason Seery, MC, USA; MAJ Scott Zakaluzny, MC, USAF; CDR Michel Kearns, MC, USN; CDR Nathaniel Fernandez, MC, USN

First Publication Date: 01 Jul 2006

Publication Date: 29 Mar 2024

Supersedes: 02 Aug 2016

# TABLE OF CONTENTS

BACKGROUND	3
RECOMMENDATIONS FOR VTE PROPHYLAXIS	3
SPECIAL POPULATIONS	4
Pending Surgery	4
Traumatic Brain Injury	5
Spine Trauma	5
Solid Organ Injury	
Patients with Indwelling Epidural and/or Paravertebral Catheters	6
Pregnant Patients	7
Pediatric Patients <sup>17</sup>	7
USE OF INFERIOR VENA CAVA FILTERS	
RETRIEVABLE INFERIOR VENA CAVA FILTERS (RIVCF)	8
AEROMEDICAL EVACUATION CONSIDERATIONS	8
PERFORMANCE IMPROVEMENT (PI) MONITORING	9
RESPONSIBILITIES	.0
REFERENCES1	0
ADDITIONAL REFERENCES	.3
APPENDIX A: VENOUS THROMBOEMBOLISM PREVENTION GUIDELINES	5
APPENDIX B: IVCF RECOMMENDATIONS	7
APPENDIX C: TELEMEDICINE / TELECONSULTATION	.8
APPENDIX D: INFORMATION REGARDING OFF-LABEL USES IN CPGS1	.9

#### SUMMARY OF CHANGES

- 1. The role of screening duplex ultrasounds for DVT in asymptomatic patients was changed from "not recommended" to "considered for patients with significant gaps in chemical VTE prophylaxis and periods of prolonged immobility."
- 2. Additional recommendations were included for special populations.

#### CPG ID: 36

# **PREVENTION OF VENOUS THROMBOEMBOLISM**

Published by the Joint Trauma System,



#### the DoD Center of Excellence for Trauma

Hypercoagulable state of trauma

Early transfusion (<24 hrs post injury)</p>

Transfusion of old blood (>28 days)

Immobility/prolonged transport time

Use of fresh frozen plasma with <4</p>

Solid Organ Injury

> AAST grade 1-3 liver, spleen,

kidney  $\rightarrow$  prophylaxis start

• Serial hemoglobin stable

Pre-puberty

• No hemodynamic instability

**Pediatric Patients** 

prophylaxis not

recommended

12-24 hours provided:

No ongoing blood

transfusion

units packed red blood cells

Multiple amputation/AKAs

> Traumatic Brain Injury

**Risk Factors** 

#### Venous Thromboembolism (VTE)

- Trauma patients have a 58% incidence rate
- > Trauma patients with burns have a 65% incidence rate
- Missing 2 doses of VTE prophylaxis increases the risk by 8.5x
- Do not hold chemical VTE prophylaxis for surgical procedures except brain, spine, and eye

Begin VTE prophylaxis in all trauma patients within 24 hours of injury in patients without coagulopathy or increased risk of bleeding. Every missed dose increases VTE risk.

#### R E C O M M E N D A T I O N S

- > Universal sequential compression devices
- > No direct oral anticoagulants or aspirin.
- Use if normal Creatinine clearance (CrCl) and able to monitor Anti-Xa: Enoxaparin 30mg SC BID
- Lower dose Enoxaparin or Heparin 5000u SC TID:
  - if > 65 yrs / < 50kg / CrCl < 30-60mg/Dl</li>
  - if CrCl < 30 mg/dL  $\rightarrow$  SC heparin 5000 U TID

IVC Filters – Retrievable are preferred. Limit duplex U/S to symptomatic patients only or a gap in pharmacologic prophylaxis for asymptomatic patients

#### SPECIAL POPULATIONS

#### Traumatic Brain Injury

- Stable 24-hour head CT prior to prophylaxis
- Consult neurosurgery
- Hold prophylaxis if IC hemorrhage or IC monitor
- interrupted prophylaxis increases VTE risk 6-fold

#### Epidural/Paravertebral Catheters

- 12 hr pre-procedure and 4-12-hour post-procedure
- Unfractionated heparin free: 4-6-hour pre-procedure and 1-hour post procedure
- Avoid missing doses of prophylaxis for epidural placement

#### **VTE Metrics**

- SCDs within 24 hours of injury
- Chemical VTE prophylaxis within 24 hours of injury or document contraindication
- Zero missed VTE prophylaxis doses

# <u>Spine Injury</u>

- > Consult spine surgeon
- Initiate VTE prophylaxis
   48–72-hour post-op or post injury
- Hold VTE prophylaxis for suspected spinal injury or focal neurologic deficits until imaging/consultation

MFTRICS

#### Pregnant Patients

- Enoxaparin & heparin –
- \*Considered SAFE for use\*
- Enoxaparin 30mg SC BID
- Enoxaparin 40mg SC BID (>90kg)

#### **IVC Filter Metrics**

Retrievable IVCs removed within 6 months

- ✓ Document:
  - Indication/exact location
  - Retrievable vs. Permanent
  - Manufacturer/Brand/Serial #/Lot #

#### 2

# BACKGROUND

Trauma patients are at high risk for Venous Thromboembolism (VTE) including Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE). Trauma patients can have up to 58% incidence of DVT.<sup>1</sup> Sevitt and Gallagher reported an even higher incidence (65%) in injured and burned patients and reported a 16.5% incidence of PE found at autopsy in this cohort of patients.<sup>2,3</sup>

In addition to the hypercoagulable state induced by severe injury in trauma, combat casualties have additional risk factors for DVT, including: <sup>1,4-8</sup>

- Early transfusion of blood products (≤24 hours)
- Transfusion of old blood (≥28 days)
- Multiple and/or above the knee amputations
- Immobility/prolonged air transport time
- Traumatic brain injury (TBI)

The use of Fresh Frozen Plasma (FFP) outside of large volume blood product transfusion (less than 4 U PRBC's) incurs an increased risk of VTE.<sup>9</sup> Early prophylaxis in this patient population is recommended provided hemostasis has been achieved.

Our deployed medical teams need to be prepared to care for injured children in the combat environment. While the incidence of DVT in pediatric trauma is much lower (6.2%) than that of adults in the civilian literature,<sup>10</sup> multiple risk factors including immobility and presence of central venous lines were associated with the development of DVT in pediatric trauma patients.

Prolonged airplane travel may also increase the occurrence of DVT, with one study noting a 10% prevalence of asymptomatic DVT in individuals undergoing flights of eight hours or more.<sup>11</sup> Combat casualties will often undergo prolonged evacuation, with long flights and immobility further increasing their risk of VTE. Thus, it is important to start VTE prophylaxis as soon as clinically possible.<sup>12</sup>

Different medical societies and working groups have published varying recommendations for chemical VTE prophylaxis. <sup>13-17</sup> The recommended clinical guidelines are based on supporting scientific evidence and expert consensus input. It is recommended to begin chemical VTE prophylaxis therapy as soon as coagulopathy is corrected in patients without an increased risk of bleeding.

# **RECOMMENDATIONS FOR VTE PROPHYLAXIS**

Unless contraindicated, all admitted trauma patients should receive Sequential Compression Device (SCD) therapy as primary VTE prophylaxis. **Chemical VTE prophylaxis should be initiated for all trauma patients 24 hours after injury unless contraindicated due to high risk of bleeding or in certain high risk special populations (see below)**. There are two options for chemical VTE prophylaxis:

- 1. Low Molecular Weight Heparin (LMWH).
  - a. Subcutaneous (SC) Enoxaparin 30 mg twice daily should be considered for most trauma patients with normal creatinine clearance (>30 mg/dL). Most patients in the austere deployed setting should continue with 30 mg twice daily, which has been shown to be superior to 5000 U of unfractionated heparin three times daily for the prevention of VTE in patients with normal creatinine clearance (CrCI). <sup>16,18</sup>

- b. Weight-based enoxaparin dosing is an acceptable alternative for trauma patients with a normal creatine clearance. Options include twice daily doses of 0.5-0.6 mg/kg,<sup>19-21</sup> or 30 mg for 50 to 60 kg patients, 40 mg for 61 to 99 kg patients, and 50 mg for patients greater than 100 kg.<sup>22</sup> Anti-Xa levels should be monitored when weight-based enoxaparin is administered because trauma patients experience fluctuations in creatinine clearance that might require dose adjustment.<sup>23</sup>
- c. Lower doses of enoxaparin can be considered in patients who weigh less than 50 kg. . For these patients, enoxaparin weight-based dosing (0.5-0.6 mg/kg) BID can be considered.
- d. Enoxaparin is renally excreted and should be avoided in patient with renal failure since it may lead to increased bleeding complications. <sup>24</sup> In this population heparin SQ 5000 U TID is recommended for **CrCl <30 mg/dL**.
- e. The rate of Heparin Induced Thrombocytopenia (HIT) after prophylactic enoxaparin is 0% compared to 2.7% with prophylactic unfractionated heparin.<sup>25,26</sup> Therefore, routine platelet monitoring is not required for trauma patients who are exposed only to enoxaparin.
- 2. Low dose Unfractionated Heparin (UFH)<sup>13-15</sup>
  - a. While enoxaparin is the preferred agent for chemical VTE prophylaxis in trauma patients with normal creatinine clearance, subcutaneous unfractionated heparin at 5000 U every 8 hours is preferred for patients with end-stage renal disease or a creatinine clearance of <30 mg/dL.<sup>24</sup>
  - b. In patients receiving UFH, platelet monitoring is recommended to monitor for HIT approximately every 3 days from day 4 to day 14 or until pharmacologic prophylaxis is stopped.<sup>25</sup> If HIT is diagnosed, heparin anticoagulants must be replaced with nonheparin anticoagulants (such as the direct thrombin inhibitor argatroban). These agents can be challenging to obtain and monitor in the deployed environment because these agents are irreversible and appropriate therapeutic levels are difficult to maintain.<sup>25,27,28</sup>

Pharmacologic prophylaxis with direct oral anticoagulants (DOACs) or aspirin should not be a primary choice for pharmacologic prophylaxis for most trauma patients because of the lack of related clinical trials.

Post discharge prophylaxis should be considered for patients with TBI, orthopedic or spine injuries and for those who underwent major surgery. Godat et al. reported that trauma patients who are at the highest risk to develop VTE (especially spinal cord injury with/without pelvic fracture) are at the greatest risk during the first three months after injury and that this risk decreases at six months post injury.<sup>3.23</sup>

# SPECIAL POPULATIONS

# Pending Surgery

Except for brain or spine surgery, holding chemical VTE prophylaxis prior to surgery is not indicated.

- 1. Routinely holding pharmacological prophylaxis prior to surgery may increase VTE risk without an accompanying decrease in the risk of bleeding. Many specialties with high DVT rates are now administering chemoprophylaxis at the start of surgery. <sup>29-32</sup>
- A pending invasive procedure is the most common reason for a patient missing a dose of chemoprophylaxis. Every missed dose increases VTE risk. Patients that miss two to four doses are at 8.5 times higher DVT risk compared with those with no missed doses.<sup>33</sup>

#### Traumatic Brain Injury

- 1. Enoxaparin 30mg SQ twice daily remains the dosing of choice.
- 2. Prior to starting chemical VTE prophylaxis in TBI patients:
  - a. Consult a neurosurgeon.
  - b. Obtain CT scan of the head 24 hours post injury to assess for intracranial hemorrhage stability.
- 3. Prophylaxis should be withheld in the setting of progression of intracranial hemorrhage or presence of an intracranial monitor.
- In patients with stable intracranial hemorrhage on repeat head CT, initiating chemical VTE prophylaxis 24-72 hours following traumatic brain injury does not increase the progression of intracranial hemorrhage.<sup>26,27</sup>
- 5. Initiating VTE chemical prophylaxis is recommended in TBI patients with a stable head CT 24 hours after injury. Even in the setting of combat related penetrating TBI, for those patients with a stable repeat head CT, initiating pharmacologic prophylaxis 24 hours after injury was safe, with similar rates of progression.<sup>34</sup> Caution should be taken in starting chemical VTE prophylaxis 24 hours post injury and discussion with neurosurgeon is recommended for TBI patients with the following conditions:
  - a. Polytrauma with or at risk for coagulopathy
  - b. Have intracranial monitor/drain in place.
  - c. Have one or more of the following TBI features that are "high risk" for progression according to the Norwood-Berne criteria:
    - SDH > 8mm
    - Epidural hemorrhage > 8mm
    - Largest single contusion > 2cm
    - More than one contusion per lobe
    - Diffuse or scattered subarachnoid hemorrhage.
    - Diffuse or scattered intraventricular hemorrhage.

For these patients, chemical VTE prophylaxis is typically restarted 72 hours post-injury or from last stable CT head, or as neurosurgeon recommends. <sup>35,36</sup>

6. Avoid interruptions in dosing for TBI patients who are started on chemical VTE prophylaxis. Interrupted dosing in this patient population causes a 600% increase in the VTE rate.<sup>37</sup>

#### Spine Trauma

- 1. Enoxaparin 30mg twice daily remains the recommended dosing.
- 2. Prior to starting chemical VTE prophylaxis, consult a spine surgeon.
- 3. Patients with traumatic spine injury or who undergo spine surgery should have VTE prophylaxis initiated within 48-72 hours after injury or after spine surgery.

- a. Chemical VTE prophylaxis initiated within 48 hours of operative fixation of traumatic spine fractures does not increase the risk of bleeding, progression of neurological injury, or postoperative complications including spinal hematoma. <sup>38</sup>
- b. Delays longer than 72 hours lead to a substantial increase in VTE rate. <sup>39</sup>
- 4. Patients with suspected traumatic spinal injury and neurologic deficits should have chemical VTE prophylaxis held until imaging and spinal surgical consultation are obtained.

# Solid Organ Injury

- 1. Chemical VTE prophylaxis should be initiated in patients with moderate (AAST grades 1-3- liver, spleen, kidney) solid organ injury in the absence of:
  - a. Hemodynamic instability
  - b. Hemoglobin drops greater than 2 g/dL in less than 12 hours
  - c. Ongoing blood transfusion after the initial resuscitation has been completed. <sup>24,29,40,41</sup>
- 2. Chemical VTE prophylaxis started within 12-24 hours of injury in this cohort decreased VTE rates without an increased risk of bleeding that required blood transfusion or intervention.<sup>42</sup>
- There is insufficient evidence on outcomes related to patients with grade 4 and 5 injuries because these patients often undergo operative management. All Grade 4 and 5 splenic injuries should undergo splenectomy. (See <u>JTS Blunt Abdominal Trauma, Splenectomy, and Post-Splenectomy Vaccination CPG</u>). Initiating chemical VTE prophylaxis post-operatively, in the absence of coagulopathy or other increased risk of bleeding, is considered safe.

# Patients with Indwelling Epidural and/or Paravertebral Catheters

Patients who require an epidural catheter increasingly have interruptions in pharmacologic prophylaxis <sup>45</sup> such that epidural catheter placement is now associated with an increased VTE rate <sup>46,47</sup> whereas previously this was not the case. <sup>48</sup>

- 1. The timing of administration for chemical VTE prophylaxis may need to be modified to accommodate the placement and/or removal of an epidural.
  - a. Regional Anesthesia Guidelines recommend a 12-hour interval between enoxaparin dose and epidural placement/removal followed by a 4-hour to 12-hour interval before resumption. <sup>43,44</sup>
  - b. For unfractionated heparin, a 4 to 6-hour interval is recommended before epidural placement/removal followed by a 1-hour interval before unfractionated heparin is resumed, which allows for uninterrupted dosing.
- 2. Avoid missing doses of VTE prophylaxis for epidural placement, if possible.
- In the combat casualty requiring an epidural pain catheter, modification of enoxaparin dosing to 40mg daily does not increase the incidence of venous thromboembolism.<sup>28</sup>

#### **Pregnant Patients**

- 1. Both unfractionated heparin and enoxaparin are considered safe in pregnancy as neither crosses the placenta. <sup>49-51</sup>
- 2. Pregnant trauma patients should receive an initial dose of 30 mg of enoxaparin twice daily titrated by anti-Xa levels, (if available) targeting a peak range of 0.2 to 0.4 IU/mL or a trough range of 0.1 to 0.2 IU/mL.

Pregnancy increases renal clearance, leads to changes in weight, and induces hormonal changes that result in hypercoagulability. All these factors influence drug dosing for chemoprophylaxis.

3. For pregnant trauma patients who weigh more than 90 kg, initiating 40 mg of enoxaparin twice daily is recommended with similar anti-Xa level titration.

#### Pediatric Patients <sup>17</sup>

- 1. There is insufficient high-quality evidence to make strong recommendations regarding the institution of chemical VTE prophylaxis in children hospitalized after trauma.
- 2. Based on the current recommendations of the Eastern Association for the Surgery of Trauma and the Pediatric Trauma Society, it is recommended that chemical VTE prophylaxis be considered for children older than 15 years who are at low risk of bleeding and for children younger than 15 years old who are post pubertal if they have an ISS greater than 25.
- 3. For prepubertal children, even with ISS greater than 25, routine chemical VTE prophylaxis is NOT recommended.

Refer to <u>Appendix A: Prevention of Venous Thromboembolism Guidelines</u> for specific guidance on different subsets of patients after various surgical procedures.

#### USE OF INFERIOR VENA CAVA FILTERS

Inferior Vena Cava Filter (IVCF) placement in the combat theater may be used for:

- 1. Primary prophylaxis (no evidence of VTE disease at the time of placement).
- 2. Secondary prophylaxis (documented DVT) of PE in the polytrauma patient.

Patients felt to be at particularly high risk for VTE development and who have a **clinical contraindication** to prophylactic anticoagulation are the most likely to have an IVCF placed.

Most series examining the use of IVCF placement for primary prophylaxis of PE in the trauma patient support a low rate of subsequent PE (1.6%), although the studies are of variable design and a strong consensus supporting this clinical practice cannot be made based upon available data.<sup>29</sup> There is no evidence that prophylactic use of IVCF is associated with a decreased PE rate or fatal PE rate. It should be noted that when IVCF are placed they are done so to prevent FATAL Pulmonary Emboli as DVT and PE still can occur.<sup>30-34</sup>

IVCF has no benefit in the prevention of DVTs and may be associated with the development of IVC and Deep Venous Thrombosis.<sup>14,37</sup>

The role of duplex ultrasound in the diagnosis of DVT should be reserved for the symptomatic patient. Serial screening duplex ultrasound for the diagnosis of DVT is not recommended.<sup>14</sup>

For those asymptomatic trauma patients with significant injuries and gaps in pharmacologic prophylaxis, venous compression duplex may be considered.<sup>52</sup> If a DVT or PE is identified, then therapeutic

# anticoagulation is necessary per current guidelines, and if it is contraindicated, then an inferior vena cava (IVC) filter should be considered.

Refer to <u>Appendix B</u> for additional recommendations regarding IVC filters.

#### **RETRIEVABLE INFERIOR VENA CAVA FILTERS (RIVCF)**

The vast majority of IVCF devices placed in the combat theater are Retrievable Inferior Vena Cava Filters (RIVCF). RIVCF are preferred to avoid some of the long-term complications of filter placement. Additionally, many patients only need this form of VTE prophylaxis for a defined period of time early after injury.

Combat injured patients from Operation Iraqi Freedom and Operation Enduring Freedom who had RIVCFs placed have an overall retrieval rate of 18%.<sup>54</sup> Despite successful removal of IVCF beyond 180 days and high success and low complication rate for attempted IVCF removal, rates of eventual removal of RIVCFs in multiple studies of trauma patients in the U.S. have been as low as 14% to 22%.<sup>36-39,53</sup>

It should be noted that the majority of patients was lost to follow up or did not have filters removed due to ongoing indications for use (82%). Therefore, the overall retrieval technical success rate may be much higher. Most series support removal of the most commonly used RIVCFs as early as they are no longer necessary and no later than approximately three months.<sup>42</sup> While it is possible to remove any of these later than this time period, the technical success declines significantly as potential complications associated with removal increase. Clear electronic documentation and a dedicated tracking system at the final continental U.S. (CONUS) medical treatment facility (MTF) must be in place to improve retrieval rates and minimize loss to follow up.<sup>43</sup>

# **AEROMEDICAL EVACUATION CONSIDERATIONS**

- 1. Aeromedical Evacuation (AE) from any area of responsibility to continental U.S. can require multiple flights over the course of days before the patient arrives at his or her final destination.
- 2. There is a clear association between long-distance travel and an increased risk of VTE, even in a "healthy traveler."
- Stresses of flight such as prolonged immobility and decreased humidity may contribute to VTE formation, especially in groups who already carry a high risk (trauma patients, recent surgeries, long bone fractures, smokers, pregnancy or post-partum, recent Myocardial Infarction, active cancer, presence of splint or cast, etc.).
- 4. Prophylaxis is essential to reduce the risk of VTE associated morbidity and mortality in all AE patients.
  - a. AE crews will encourage patient ambulation every 2 hours for patients whose condition allows.
  - b. SCD use should be universal for inpatients unless contraindicated by injury pattern. The Kendal SCD Express compression system is approved for use on military aircraft.
  - c. Chemical VTE prophylaxis is also recommended as above for all trauma or medical inpatients unless specifically contraindicated by the medical condition such as ongoing bleeding or coagulopathy.

- AE Patients with KNOWN acute VTE should be treated prior to flight unless there is a clear contraindication.
  - a. Treatment depends on the clinical situation, but may include low-molecular-weight Heparin, Fondaparinux, oral Xa inhibitors, or Unfractionated Heparin.
  - b. Oxygen and continuous pulse-oxygenation monitoring should be available during AE for patients with known VTE in case supportive measures are needed.
  - c. In the case of known or suspected Pulmonary Embolism, a Cabin Altitude Restriction should be considered to mitigate the effects of altitude on oxygenation and respiration.
  - d. Addition of a Critical Care Air Transport Team should also be considered in cases of PE with significant respiratory or hemodynamic compromise.

#### PERFORMANCE IMPROVEMENT (PI) MONITORING

#### POPULATION OF INTEREST

All trauma patients admitted to Role 2 or higher.

#### INTENT (EXPECTED OUTCOMES)

- 1. All patients in population of interest receive VTE prophylaxis with sequential compression device within 24 hours of injury.
- 2. All patients in population of interest start chemical VTE prophylaxis within 24 hours of injury or contraindication documented.
- 3. All ordered doses of chemical VTE prophylaxis are administered (no missed doses) or contraindication documented.
- 4. When IVCF is inserted, there is documentation in the medical record regarding the indication for procedure, whether the IVCF is retrievable, manufacturer, brand, serial number, lot number, and exact location of placement.
- 5. Retrievable IVC filters are removed within 6 months.

#### **PERFORMANCE / ADHERENCE METRICS**

- 1. Number and percentage of patients in the population of interest who start VTE prophylaxis with sequential compression device within 24 hours of injury.
- 2. Number and percentage of patients in the population of interest who receive chemical VTE prophylaxis within24 hours or have contraindication documented.
- 3. Number and percentage of patients in the population of interest who receive all ordered doses of chemical VTE prophylaxis or have contraindication documented.
- 4. Number and percentage of patients who receive IVC filter placement who have complete documentation of indication for procedure, whether the IVCF is retrievable, manufacturer, brand, serial number, lot number, and exact location of placement.
- 5. Number and percentage of retrievable IVC filters placed that are removed within 6 months.

#### DATA SOURCE

- Patient Record
- Department of Defense Trauma Registry (DoDTR)

#### SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed.

The system review and data analysis will be performed by the JTS Chief and the JTS PI Branch.

#### RESPONSIBILITIES

It is the trauma team leader's responsibility to ensure familiarity, appropriate compliance, and PI monitoring at the local level with this CPG.

All health care providers will:

- 1. Become familiar with the guidelines for the prevention of DVT (see <u>Appendix A</u>).
- 2. Appropriately manage patients who may be at risk of developing DVT.
- 3. Provide feedback on these guidelines and suggestions for changes to the CPG to the JTS Chief.

The senior surgeon and/or Intensivist at each Role 3 facility will:

- 1. Review all thromboembolic events in the Level III facility to assess ways to reduce the risk to the patient.
- 2. Coordinate with the JTS Performance Improvement Chief on the appropriateness of the guidelines being used and provide input for updates on an as needed basis.

# REFERENCES

- 1. Geerts WH, Code KJ, Jay RM, et al: A prospective study of venous thromboembolism after major trauma. N Engl J Med 1994;331(24):1601-1606.
- 2. Sevitt S, Gallagher N. Venous thrombosis and pulmonary embolism. A clinico-pathological study in injured and burned patients. Br J Surg 1961;48:475-489.
- 3. Godat LN Kobayashi L, Chang DC et al. Can we ever stop worrying about venous thromboembolism after trauma? J Trauma 2015;78(3):475-480.
- 4. Differding JA, Underwood SJ, Van PY, et al. Trauma induces a hypercoagulable state that is resistant to hypothermia as measured by thromboelastogram. Am J Surg 2011;201(5):587-591.
- 5. Gearhart MM, Luchette FA, Proctor MC, et al. The risk assessment profile score identifies trauma patients at risk for deep venous thrombosis. Surgery 2000;128(4):631-637.
- 6. Spinella PC, Carroll CL, Staff I, et al. Duration of red blood cell storage is associated increased incidence of deep venous thrombosis and in hospital mortality in patients with traumatic injuries. Critical Care 2009;13(5):R151.
- 7. Hutchinson TN, Krueger CA, Berry, JS, et al. Venous thromboembolism during combat operations: a 10-y review. J Surg Res 2014;187(2):625-630.
- 8. Knudson MM: Thromboembolism after trauma: an analysis of 1602 episodes from the American College of Surgeons National Trauma Data Bank. Ann Surg 2004: 490-496.

- 9. Zander AL, Olson EJ, Van Gent JM, et al. Does resuscitation with plasma increase the risk of venous thromboembolism? J Trauma 2015;78(1):39-43.
- 10. Hanson SJ, Punzalan RC, Greenup RA, et al. Incidence and risk factors for venous thromboembolism in critically ill children after trauma. J Trauma 2010;68(1):52-56.
- 11. Scurr JH, Machin SJ, Bailey-King S, et al. Frequency and prevention of symptom-less deep venous thrombosis in long haul flights: a randomized trial, Lancet 2001; 357:1485-1489.
- 12. Holley AB, Petteys S, Mitchell JD, et al. Thromboprophylaxis and VTE rates in soldiers wounded in Operation Enduring Freedom and Operation Iraqi Freedom. Chest 2013;144(3):966-973.
- 13. Rogers FB, Cipolle MD, Velmahos G, et al. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. J Trauma 2002;53(1):142-164.
- 14. Guyatt GH, Akl EA, Crowther M, et al. Antithrombotic therapy and prevention of thrombosis, 9th edition: American College of Chest Physicians evidence based clinical practice guidelines. Chest 2012;141(2):7S-47S.
- 15. Rappold JF, Sheppard FR, Carmichael II SP, et al. Venous thromboembolism prophylaxis in the trauma intensive care unit: an American Association for the Surgery of Trauma Critical Care Committee Clinical Consensus Document Trauma Surgery & Acute Care Open 2021;6:e000643.
- 16. Ley, EJ, Brown CVR, Moore EE, et al. Updated guidelines to reduce venous thromboembolism in trauma patients: A Western Trauma Association critical decisions algorithm, Journal of Trauma and Acute Care Surgery: Nov 2020. 89(5): 971-981.
- 17. Mahajerin A, Petty JK, Hanson, SJ, et al. MHS Prophylaxis against venous thromboembolism in pediatric trauma, Journal of Trauma and Acute Care Surgery: Mar 2017; 82(3): 627-636
- Jacobs BN, Cain-Nielsen AH, Jakubus JL, et al. Unfractionated heparin versus low-molecular-weight heparin for venous thromboembolism prophylaxis in trauma. J Trauma Acute Care Surg. 2017;83(1):151–158.
- 19. Walker CK, Sandmann EA, Horyna TJ, Gales MA. Increased enoxaparin dosing for venous thromboembolism prophylaxis in general trauma patients. Ann Pharmacother. 2017;51(4):323–331.
- 20. Bickford A, Majercik S, Bledsoe J, et al. Weight-based enoxaparin dosing for venous thromboembolism prophylaxis in the obese trauma patient. Am J Surg. 2013;206(6):847–851; discussion 851-2.
- 21. Nunez JM, Becher RD, Rebo GJ, Farrah JP, Borgerding EM, Stirparo JJ, Lauer C, Kilgo P, Miller PR. Prospective evaluation of weight-based prophylactic enoxaparin dosing in critically ill trauma patients: adequacy of AntiXa levels is improved. Am Surg. 2015;81(6):605–609.
- 22. 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.
- 23. Rodier SG, Bukur M, Moore S, et al. Weight-based enoxaparin with anti-factor Xa assay-based dose adjustment for venous thromboembolic event prophylaxis in adult trauma patients results in improved prophylactic range targeting. Eur J Trauma Emerg Surg. 2019.
- 24. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(S2):e227S–e277S.
- 25. Linkins LA, Dans AL, Moores LK, Bona R, Davidson BL, Schulman S, Crowther M. Treatment and prevention of heparin-induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(Suppl 2):e4955–e530S.

- Warkentin TE, Levine MN, Hirsh J, Horsewood P, Roberts RS, Gent M, Kelton JG. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med. 1995;332(20):1330–1335.
- 27. Berry C, Tcherniantchouk O, Ley EJ, et al. Overdiagnosis of heparin-induced thrombocytopenia in surgical ICU patients. J Am Coll Surg. 2011;213(1):10–17.
- 28. Harada MY, Hoang DM, Zaw AA, et al. Overtreatment of heparin-induced thrombocytopenia in the surgical ICU. Crit Care Med. 2017;45(1):28–34.
- 29. Geerts WH, Jay RM, Code KJ, et al. A comparison of low-dose heparin with low-molecular weight heparin as prophylaxis against venous thromboembolism after major trauma. New England Journal of Medicine 1996;335(10):701-707.
- 30. Whitworth JM, Schneider KE, Frederick PJ, et al. Double prophylaxis for deep venous thrombosis in patients with gynecologic oncology who are undergoing laparotomy: does preoperative anticoagulation matter? International Journal of Gynecologic Cancer 2011;21(6):1131-1134.
- Selby LV, Sovel M, Sjoberg DD, et al. Preoperative chemoprophylaxis is safe in major oncology operations and effective at preventing venous thromboembolism. J Am Coll Surg. 2016;222(2):129– 137.
- 32. Hull RD, Pineo GF, Stein PD, et al. Timing of initial administration of low-molecular-weight heparin prophylaxis against deep vein thrombosis in patients following elective hip arthroplasty: a systematic review. Arch Intern Med. 2001;161(16):1952–1960.
- 33. Louis SG, Sato M, Geraci T, et al. Correlation of missed doses of enoxaparin with increased incidence of deep vein thrombosis in trauma and general surgery patients. JAMA Surg. 2014;149(4):365–370.
- 34. Meyer RM, Larkin MB, Szuflita NS, et al. Early venous thromboembolism chemoprophylaxis in combat-related penetrating brain injury. J Neurosurg. 2017;126(4):1047–1055.
- 35. Pastorek R, Cripps M, Bernstein I, et al. The Parkland Protocol's modified Berne-Norwood criteria predict two-tiers of risk for traumatic brain injury progression. J of Neurotrauma 2014; 31: 1737-1743.
- 36. Phelan HA, Eastman AL, Madden CJ, et al. TBI risk stratification at presentation: A prospective study of the incidence and timing of radiographic worsening in the Parkland Protocol. Journal Trauma Acute Care Surgery 2012; 73: S122-S127.
- Salottolo K, Offner P, Levy AS, Mains CW, Slone DS, Bar-Or D. Interrupted pharmocologic thromboprophylaxis increases venous thromboembolism in traumatic brain injury. J Trauma. 2011;70(1):19–24; discussion 25-6.
- Kim DY, Kobayashi L, Chang D, Fortlage D, Coimbra R. Early pharmacological venous thromboembolism prophylaxis is safe after operative fixation of traumatic spine fractures. Spine. 2015;40(5):299–304.
- 39. Christie S, Thibault-Halman G, Casha S. Acute pharmacological DVT prophylaxis after spinal cord injury. J Neurotrauma. 2011;28(8):1509–1514.
- Coleman JR, Kay AB, Moore EE, et al. 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 Surg. 2019;218(6):1065–1073.
- Sumislawski JJ, Kornblith LZ, Conroy AS, Callcut RA, Cohen MJ. Dynamic coagulability after injury: is delaying venous thromboembolism chemoprophylaxis worth the wait? J Trauma Acute Care Surg. 2018;85(5):907–914.
- 42. Schellenberg M, Inaba K, Biswas S, et al. 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.

- Horlocker TT, Vandermeuelen 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(3):263–309.
- 44. Gogarten W, Vandermeulen E, Van Aken H, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol. 2010;27(12):999–1015.
- 45. Stone AB, Grant MC, Lau BD, et al. Thoracic epidural anesthesia and prophylactic three times daily unfractionated heparin within an enhanced recovery after surgery pathway for colorectal surgery. Reg Anesth Pain Med. 2017;42(2):197–203.
- 46. Vella MA, Dumas RP, Chreiman K, et al. Epidural catheters are associated with an increased risk of venous thromboembolism in trauma. J Thromb Thrombolysis. 2020;49:420–425.
- 47. Zaw AA, Murry J, Hoang D, et al. Epidural analgesia after rib fractures. Am Surg. 2015;81(10):950–954.
- 48. Gage A, Rivara F, Wang J, Jurkovich GJ, Arbabi S. The effect of epidural placement in patients after blunt thoracic trauma. J Trauma Acute Care Surg. 2014;76(1):39–45; discussion 45-6.
- 49. Duhl AJ, Paidas MJ, Ural SH, et al; Pregnancy and Thrombosis Working Group. Antithrombotic therapy and pregnancy: consensus report and recommendations for prevention and treatment of venous thromboembolism and adverse pregnancy outcomes. Am J Obstet Gynecol. 2007;197(5):457.e1–457.e21.
- 50. Eubanks AA, Deering SH, Thiel LM. Risk assessment and treatment guide for obstetric thromboprophylaxis: comprehensive review of current guidelines. Am J Perinatol. 2019;36(2):130–135.
- 51. Lamont MC, McDermott C, Thomson AJ, et al. United Kingdom recommendations for obstetric venous thromboembolism prophylaxis: evidence and rationale. Semin Perinatol. 2019;43(4):222–228.
- 52. Allen CJ, Murray CR, Meizoso JP, Ginzburg E, Schulman CI, Lineen EB, Namias N, Proctor KG. Surveillance and early management of deep vein thrombosis decreases rate of pulmonary embolism in high-risk trauma patients. J Am Coll Surg. 2016;222(1):65–72.
- 53. Rostas JW, Manley J, Gonzalez RP, et al. The safety of low molecular weight heparin after blunt liver and spleen injuries. Am J Surg 2015 Jul;210(1):31-34.
- 54. Joseph B, Pandit V, Harrison C, et al. 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.

# ADDITIONAL REFERENCES

- 1. Caruso JD, Elster EA, Rodriguez CJ. Epidural placement does not result in an increased incidence of venous thromboembolism in combat-wounded patients. J Trauma 2014;77(1):61-66.
- 2. Cherry RA, Nichols PA, Snavely TM, et al. Prophylactic inferior vena cava filters: do they make a difference in trauma patients? J Trauma 2008;65(3):544-548.
- 3. Kalva SP, Athanasoulis CA, Chieh-Min F, et al. Recovery vena cava filter: experience in 96 patients. Cardiovasc Intervent Radiol 2006;29:559-564.
- 4. Miyahara T, Miyata T, Shigematsu K, et al. Clinical outcome and complications of temporary inferior vena cava filter placement. J Vasc Surg 2006;44:620-624.
- 5. Arsch MR. Initial experience in humans with a new retrievable inferior vena cava filter. Radiology 2002;225(3):835-844.
- 6. White RH, Zhou H, Kim J, et al. A population-based study of the effectiveness of inferior vena cava filter use among patients with venous thromboembolism. Arch Int Med 2000;160(13):2033-2041.

- 7. PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. Circulation 2005;112(3):416–422.
- 8. Baglin TP, Brush J, Streiff M. Guidelines on use of vena cava filters. Br J Haematol 2006;134(6):590-595.
- 9. Binkert CA, Sasadeusz K, Stavropoulos SW. Retrievability of the Recovery vena cava filter after dwell times longer than 180 days. J Vasc Interv Radiol 2006;17:299-302.
- 10. Kim HS, Young MJ, Narayan AK, et al. A comparison of clinical outcomes with retrievable and permanent inferior vena cava filters. J Vasc Interv Radiol 2007:19(3):393-399.
- 11. Grande WJ, Trerotola SO, Reilly PM, et al. Experience with the recovery filter as a retrievable inferior vena cava filter. J Vasc Interv Radiol 2005;16(9):1189-1193.
- 12. Hoff WS, Hoey BA, Wainwright GA, et al. Early experience with retrievable inferior vena cava filters in high risk trauma patients. J Am Coll Cardiol 2004;199(6):869-874.
- 13. Karmy-Jones R, Jurkovich GJ, Velmahos GC, et al. Practice patterns and outcomes of retrievable vena cava filters in trauma patients: an AAST multicenter study. J Trauma 2007;62(1):17-24.
- 14. Johnson ON, Gillespie DL, Aidinian G, et al. The use of retrievable inferior vena cava filters in severely injured military trauma patients. J Vasc Surg 2009;49:410-416.
- 15. Morris CS, Rogers FB, Najarian KE, et al. Current trends in vena caval filtration with the introduction of a retrievable filter at a level I trauma center. J Trauma 2004;57(1)32-36.
- 16. Lucas DJ, Dunne JR, Rodriguez CJ, et al. Dedicated tracking of patients with retrievable inferior vena cava filters improves retrieval rates. Am Surg 2012;78(8):870-874.

#### CPG ID: 36

# APPENDIX A: VENOUS THROMBOEMBOLISM PREVENTION GUIDELINES

RISK GROUP	PROPHYLACTIC MEASURES	
TRAUMA PATIENTS		
<ul> <li>Emergency trauma surgical procedures in patients with prohibitive risk of bleeding, or ongoing coagulopathy</li> <li>Emergency trauma surgical procedures in all patients, except patient with prohibitive risk of bleeding (once coagulopathy not present)</li> <li>Isolated major orthopedic surgery of extremities, spine, and pelvis</li> </ul>	<ul> <li>SCD (sequential compression device) until able to be anticoagulated (ideally start Enoxaparin within 12 hours of cessation of coagulopathy); see IVC filter and Duplex screening sections below.</li> <li>SCD (unless contraindicated by injury) + Enoxaparin 30 mg SC BID. If poor creatinine clearance, then Heparin 5000 U SC q 8 hours.</li> <li>SCD (unless contraindicated by injury) + Enoxaparin 30 mg SC BID and no evidence of TBI/SCI and normal creatinine clearance.</li> </ul>	
IVC FILTER PLACEMENT		
<ul> <li>Patients with:</li> <li>1. Recurrent PE despite full anticoagulation</li> <li>2. Proximal DVT and contraindications for full anticoagulation</li> <li>3. Proximal DVT and major bleeding while on full anticoagulation</li> <li>4. Progression of iliofemoral clot despite anticoagulation</li> <li>Patients with established DVT or PE and:</li> <li>1. Large free-floating thrombus in the iliac vein or IVC</li> <li>2. Following massive PE in which recurrent emboli may prove fatal</li> <li>3. During/after surgical embolectomy</li> <li>Very High-Risk Patients: those who cannot receive anticoagulation because of increased bleeding risk and:</li> <li>1. Severe closed head injury (GCS&lt;8)</li> <li>2. Incomplete spinal cord injury with paraplegia or quadriplegia</li> <li>3. Complex pelvic fractures with associated long-bone fractures</li> <li>4. Multiple long-bone fractures</li> </ul>	<ol> <li>Placement of retrievable IVC filter (RIVCF)</li> <li>Document if the IVCF is retrievable or not, manufacturer, brand, magnetic resonance imaging (MRI) compatibility, serial number, lot number and exact location in record and TMDS; PE may still occur despite IVC filter</li> <li>"Extended" indications for placement of IVC filter for patients with established DVT or PE</li> <li>Consideration of placement of prophylactic placement of IVC filter.</li> </ol>	
ROLE OF DUPLEX SCREENING		
<ul> <li>Asymptomatic patients</li> </ul>	<ul> <li>Serial duplex ultrasound imaging considered for patients with gaps in VTE prophylaxis and periods of prolonged immobility.</li> </ul>	

RISK GROUP	PROPHYLACTIC MEASURES	
<ul> <li>Symptomatic patients</li> </ul>	<ul> <li>Duplex ultrasound may be used without confirmatory venography.</li> </ul>	
GENERAL, VASCULAR, UROLOGIC SURGERY		
LOW RISK:		
Minor procedure in patients < 40 years, no risk factors	Early mobilization	
MODERATE RISK:		
<ul> <li>Minor procedure with additional risk factors for thrombosis</li> </ul>	<ul> <li>SCD + Unfractionated Heparin 5000 units SC q 8 hours or Enoxaparin 30 mg SC BID</li> </ul>	
<ul> <li>Non major surgery in patients 40-60 years, with no additional risk factors</li> </ul>	<ul> <li>Chemical VTE prophylaxis is withheld in patients with high risk of bleeding.</li> </ul>	
<ul> <li>Major surgery in patients &lt; 40 years with no additional risk factors)</li> </ul>		
HIGH RISK:		
<ul> <li>Non major surgery in patients &gt; 60 years or have additional risk factors</li> </ul>	<ul> <li>SCD + Unfractionated Heparin 5000 units SC q 8 hours or Enoxaparin 30 mg SC BID</li> </ul>	
<ul> <li>Major surgery in patients &gt; 40 years or have additional risk factors</li> </ul>	<ul> <li>Chemical VTE prophylaxis is withheld in patients with high risk of bleeding.</li> </ul>	
NEUROSURGERY		
<ul> <li>Intracranial neurosurgical procedures</li> </ul>	• SCD	
<ul> <li>High Risk neurosurgery patients</li> </ul>	<ul> <li>Chemical VTE prophylaxis following stable CT scan in consultation with neurosurgeon</li> </ul>	

# APPENDIX B: IVCF RECOMMENDATIONS

- 1. All IVCFs placed in the combat theater should be retrievable.
- Documentation detailing the ICVF brand, model, MRI compatibility, and exact location of placement should be documented in Armed Forces Health Longitudinal Technology Application – T or TC2 (Theater Medical Information Program -Joint Composite Health Care System – Cache)
- 3. All RIVCFs placed in the combat theater should be removed as soon as contraindications to chemical prophylaxis of VTE disease no longer exist or there is no longer a need for VTE prophylaxis. Exceptions include those that were placed for secondary prophylaxis in a patient who demonstrated new VTE disease while on therapeutic anticoagulation or in patients who are still deemed to be high risk.
- 4. All RIVCFs should be removed within three months unless a long-term indication for their continued use is present.
- 5. The decision to remove an RIVCF placed in the combat theater (versus leaving it in place permanently) should be made at the first CONUS MTF the patient transitions through while returning from deployment. When possible, the removal should take place at this same facility prior to transition to the next level of care. This approach decreases the chance that a decision will be deferred until removal becomes technically prohibitive.
- 6. The presence of a RIVCF in a patient should be made known to the receiving CONUS MTF. Typically, retrieval of the RIVCF will be accomplished at the CONUS MTF.
- 7. Any patient with a known DVT and without a current contraindication to therapeutic anticoagulation who has an IVCF in place should receive full dose anticoagulation. This is preferably accomplished with Coumadin to target an international normalize ratio (INR) of 2.0-3.0. If further surgical procedures are planned, consideration may also be given to the use of low molecular weight heparin dosed at 1 mg/kg bid or an unfractionated heparin drip until such time as the use of Coumadin is felt to be appropriate.
- 8. The presence of an IVCF, brand, model, MRI compatibility, whether or not it is retrievable, its exact location and the date of insertion should be clearly annotated in the medical record when the patient has returned to the United States.
- 9. Efforts should be made in the future to standardize the type of RIVCF used at all combat theater locations.

# APPENDIX C: TELEMEDICINE / TELECONSULTATION



Illustration by Raymond Samonte

GTP: https://GTP.health.mil

# APPENDIX D: INFORMATION REGARDING OFF-LABEL USES IN CPGS

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

#### BACKGROUND

Unapproved (i.e. "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

#### ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

#### ADDITIONAL PROCEDURES

#### **Balanced Discussion**

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

#### **Quality Assurance Monitoring**

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

#### Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.