

Deep Vein Thrombosis Guidelines in Spinal Cord Injury.

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I. Definition, Assessment, Diagnosis

a. Definition.

- i. A Deep Vein Thrombosis (DVT) is a blood clot located in one or more of the deep veins of an extremity. It is one of the major complications in the acute phase of a spinal cord injury (SCI) that can lead to a pulmonary embolism (PE), sudden death or chronic thrombophlebitis and swelling.
- ii. The frequency of DVT and PE without prophylaxis based on clinical diagnosis alone is in the 12-64% range.¹ In a prospective study conducted within 3 weeks of admission to the hospital with serial plethsmography or contrast venography 21 of 26 (81%) patients with acute SCI, who did not get prophylaxis, had a DVT.²
- iii. Despite the recent advancements in managing the risk of DVT, SCI patients treated with appropriate prophylaxis in the acute phase of a traumatic injury have a mortality rate of 9.7% due to a PE during the first year after a SCI.¹
- iv. A thrombi can progress proximally in 20% of cases²⁰ and may embolize in up to 50%²¹. Venous thromboembolism (VTE) should be considered a continuum from small, asymptomatic thrombi to massive, fatal PE. For these reasons, it is essential that aggressive thromboprophylaxis be provided to SCI patients.
- v. DVT is very uncommon in children who acquire a SCI between birth and twelve years of age, but was identified in 8% of those injured between thirteen and fifteen years of age and 9% of those injured between sixteen and twenty-one years of age.²⁷
- vi. The cause of DVT in a SCI is multifactorial, but are associated with Virchow's triad: Venous Stasis, endothelial Integrity and hypercoagulability.

1. Venous Stasis

- a. Immobility - a 10-fold increase in the DVT risk of a paretic leg in stroke compared with the nonparetic leg. ³
- b. Loss of sympathetic input to vasoconstrict blood vessels.
- c. Increase in venous flow resistance. ⁴
- d. Anticoagulation alone may not be enough and multiple mechanical methods of VTE prophylaxis are advocated. ⁵

2. Endothelial Integrity

- a. Decreased fibrinolytic reactivity (which is closely related to endothelial integrity),
- b. Increased D-dimer level,
- c. Impaired rhythmical circadian variations in fibrinolytic parameters possibly secondary to a deregulated autonomic nervous system. ^{4,6}
- d. Decrease in fibrinolysis may explain the increased proximal migration of DVTs ⁶, persistence and recurrence of VTEs despite adequate anticoagulation ⁷ and low rates of venous recanalization in the SCI population. ⁸

3. Hypercoagulability

- a. Documented changes to coagulation include an increase in:
 - i. Platelets and platelet aggregation (returns to normal in later stages of injury)
 - ii. factor VIII,
 - iii. vWF,
 - iv. fibrinogen,
 - v. euglobulin clot lysis time,
 - vi. plasma alpha-1 antitrypsin activity, and antigen concentration. ^{4,6}
- b. The following are decreased:
 - i. plasma alpha-2 antiplasmin antigen concentration and
 - ii. total antiplasmin activity.

- c. The pathophysiology has not been fully determined, but many of them are felt to be related to neurohormonal factors induced by the SCI. ^{4,6}
- vii. Risk factors:
1. Bed rest (venous stasis)
 2. Tobacco smoking (hypercoagulability)
 3. COPD during acute Exacerbation (venous stasis, hypercoagulability)
 4. Surgery (esp. TKA (2.4%) and THA (3.4%))
 5. Trauma (vessel injury)
 6. Cancer (hypercoagulability)
 7. Pregnancy (venous stasis)
 8. Obesity (venous stasis)
 9. Estrogen treatment (hypercoagulability)
 10. Hx of DVT (all 3)
 11. Anticardiolypin antibodies (hypercoagulability)
 12. Factor V Leiden Mutation (hypercoagulability)
 13. **Protein C and Protein S deficiency (hypercoagulability)**
 14. Antithrombin III deficiency (hypercoagulability)

- viii. Risk factors that are additive to SCI risks ⁹
 - 1. Advanced age
 - 2. Male gender
 - 3. Level of injury (paraplegia (6.3%) > tetraplegia(3.4%)²²)
 - 4. Completeness of injury (motor complete (AIS A) > motor incomplete (AIS B, C, D)²³)
 - 5. History of thrombosis prior to SCI – Six fold higher risk ²⁴
 - 6. Lower extremity fracture
 - 7. Dehydration
 - 8. Flaccid paralysis
 - 9. Obesity
 - 10. Delayed thromboprophylaxis: start of thromboprophylaxis within two weeks after injury was strongly associated with reduced risk of VTE in SCI compared with a delayed start- Odds Ratio 0.2. ¹⁶
 - 11. Estrogen therapy
 - 12. Pregnancy
 - 13. Heterotopic ossification
 - 14. Various comorbidities: cancer, congestive heart failure, chronic obstructive pulmonary disease, and diabetes mellitus
- b. Assessment
 - i. Signs and Symptoms:
 - 1. Unexplained Fever
 - 2. Unilateral leg pain or erythema
 - 3. Sudden onset of hypotension, tachycardia, chest pain, arrhythmia or hypotension

4. Unilateral leg swelling, 2 cm circumference difference
 - ii. Rule out other causes of symptoms
 - a. Vascular System
 - i. Hematoma
 - b. Infectious
 - i. Cellulitis
 - ii. Osteomyelitis
 - c. Oncologic
 - i. Osteosarcoma
 - ii. Osteochondroma
 - d. Orthopedic
 - i. Heterotopic ossification
 - ii. Fracture
 - c. Diagnosis
 - i. Diagnosis of DVT:
 - a. Clinical diagnostic signs are: leg swelling difference of 2-3 cm in diameter; + Homan's sign – pain with dorsiflexion of the foot (SCI sensation impaired)
 - b. Elevated d-dimer, sensitive but not specific and elevated with acute inflammation due to surgery, trauma and UTI
 - c. Venous duplex Doppler ultrasound is clinical choice but relatively low sensitivity for proximal imaging (29%) and for both proximal and distal imaging (18.2%) in patients in the acute stage after SCI is a concern.
 - d. Contrast venography of the lower limbs is considered the gold standard for diagnosis of DVT, but its invasive nature, potential complications, technical issues, and costs preclude its routine use.
 - e. CT or MR venography could overcome the limitations of the ultrasonographic diagnosis of DVT, but technical refinement is required prior to their use in clinical practice.
 - f. Impedance plethysmography can be used to diagnose DVT by detecting increased venous outflow resistance in the deep veins of the lower limbs, but its use has been discontinued in many centers due to its relatively low sensitivity for detecting proximal-vein DVT (66%).

- g. Nuclear medicine techniques such as ¹¹¹In-labeled platelet scintigraphy, ^{99m}Tc-labeled platelet glycoprotein IIb/IIIa receptor antagonist, and ¹²⁵I-labeled fibrinogen are not currently used in clinical practice because they are costly and are not advantageous in terms of accuracy in comparison with other diagnostic tests.¹⁰
- h. In a systematic review, Goodacre and colleagues¹¹ studied the diagnostic role of noninvasive tests for proximal DVT and isolated calf DVT in patients with clinically suspected DVT and in high-risk asymptomatic patients (i.e. SCI). The authors concluded the most cost-effective diagnostic strategies were:
 - i. Wells prediction score,
 - ii. D-dimer test, and
 - iii. Ultrasonography

ii. Diagnosis of PE:

- a. Most common symptoms: Dyspnea, Pleurisy, Cough, hemoptysis
- b. Simplified Wells Score
 - i. Clinical signs of DVT
 - ii. Heart rate > 100 beats/min
 - iii. Recent surgery or immobilization
 - iv. Previous PE or DVT
 - v. Hemoptysis
 - vi. Cancer
 - vii. Alternative diagnosis less likely than PE
- c. Computed Tomography pulmonary angiography
- d. Ventilation/perfusion (V/Q) scanning

II. Management and Treatment Recommendations

a. Management/treatment recommendations

i. DVT Prophylaxis¹⁶

- a. Avoid use of oral vitamin K antagonists (warfarin) acutely due to bleeding risk, need for procedures and difficult adjusting dose

- b. Start LMWH as soon feasible and safe and if delayed for bleeding risk, assess risk daily and start once risk vs benefit is in acceptable range, It is safe at 24 hours and should be started by 72 hours if possible. ^{28,29,30}
- c. Consider use of direct oral anticoagulants (DOAC) during the rehabilitation phase of recovery.
- d. Use Mechanical prophylaxis in children with SCI of all ages and anticoagulant prophylaxis in adolescents with SCI.
- e. Do not screen asymptomatic patients for DVT with Doppler Ultrasound (DUS), routinely.
 - i. DUS in asymptomatic patients is neither as specific or as sensitive as it is with symptomatic patients.
 - ii. Clinical significance is uncertain as there does not appear to be increased risk of PE or symptomatic DVT in these patients and there is increased risk of treatment side effects and costs of treatment.
 - iii. Cost of DUS is not insignificant.
 - iv. May be considered if associated with high risk factors, such as older age and more severe SCI. ³²
- f. Do not use of prophylactic IVC filters in SCI patients:
 - i. Evidence supporting filter benefit (reduction in PE or mortality) is absent,
 - ii. Complication rates associated with filter use exceed the rates of the disease that filters are designed to prevent,
 - iii. Current filters are not safe when left in place for the long term, and there are enormous, unjustified costs associated with these devices.

ii. DVT treatment:

- a. There is good evidence that enoxaparin, administered subcutaneously, is safe, cost-effective, and less labor-intensive than intravenous heparin for acute DVTs post-SCI.¹²
- b. New oral anticoagulants (DOACs) rivaroxaban (Xarelto), dabigatran (Pradaxa), and apixaban (Eliquis) all are effective and safe, but data in older and sicker patients are limited.¹³
- c. Oral vitamin K antagonists (warfarin)

iii. PE Treatment:

- a. Thrombolytic therapy if PE with severe cardiopulmonary compromise¹⁵
 - i. Lower rate of all cause mortality (OR 0.53)
 - ii. Greater risks of major bleeding (OR 2.73) and ICH (OR 4.63)
 - iii. Bleeding risk less if patient ≤ 65 (OR 1.25)
- b. Low-molecular weight heparin (LMWH)
- c. Oral vitamin K antagonists (warfarin)
- d. New oral anticoagulants (DOACs) rivaroxaban (Xarelto), dabigatran (Pradaxa), and apixaban (Eliquis) all are effective and safe.

b. Restrictions:

- i. Early mobilization and passive exercise should be initiated ASAP once the patient is medically and surgically stable.
- ii. If documented DVT, mobilization and exercise of the lower extremities can cause migration of the DVT proximally, but there are no good studies to provide guidance. Therefore, mobilization and exercise should resume when the clinical team feels it is safe.
- iii. Heparin Induced Thrombocytopenia (HIT) is an immune-mediated reaction to UFH and LMWH. Incidence 5% of post-surgical patients and 0.6% of non-surgical patients exposed to heparin. Decreased risk with LMWH noted in one hospital study¹⁷
 1. Drop in platelet count of 30-50% within 5-10 days of heparin exposure or in 1-2 days after re-exposure. ~10% can be above 150K.

2. Hyper-coagulable condition associated with a 5% per day risk of thrombosis. Thrombosis in up to 60% of patients and can precede thrombocytopenia.
 3. Stop Heparin, start argatroban (IV) or possibly fondaparinux(sq). 30 days of anticoagulation if no thrombosis or 3 months if associated with thrombosis.
- c. Major outcomes:
- i. Use of LMWH started within 24 hours of a SCI in acute care appears to be safe and effective. ²⁸
 - ii. Risk of recurrent venous thromboembolism was higher with UFH-Vitamin K antagonist combination compared to LMWH –Vitamin K antagonist combination 1.42 Hazard Ratio ¹⁴
 - a. UFH –Vitamin K antagonist combination 1.84%
 - b. LMWH – Vitamin K antagonist combination 1.30%
 - iii. Major bleeding events during 3 months of anticoagulation
 - a. LMHW – Vitamin K antagonist combination 0.89%
 - b. Rivaroxaban (direct Factor Xa inhibitor) 0.49%
 - c. Apixaban (direct Factor Xa inhibitor) 0.28%

III. Prevention and Education ¹⁶

- a. Compression hose or pneumatic devices should be applied to the legs of all SCI patients as soon as feasible if not contraindicated by leg injury:
 - i. Knee or thigh length.
 - ii. Single or sequential chamber compression
 - iii. Effectiveness enhanced in combination with other antithrombotic agents
- b. Thrombo-prophylaxis with LMWH should be started in acute care as soon as there is no signs of active bleeding.
- c. Active and Passive ROM reduce venous stasis but questionable benefit.
- d. Elevation of legs in bed or wheelchair can increase blood flow
- e. Gradient elastic stockings (TED) can be helpful but need to be worn continuously to be effective.
- f. Electrical Stimulation of calf muscles enhances venous flow and velocity but limited utility in SCI due to sensation in incomplete SCI and need for continuous use.
- g. External Pneumatic compression devices
 - i. Thigh and calf
 - ii. Calf
 - iii. Foot only
- h. IVC filter indicated for the following reasons: (note: not a substitute for thromboprophylaxis) ¹⁶
 - i. Failed anticoagulant prophylaxis
 - ii. Contraindication to anticoagulation (active or potential bleeding sites)
 - iii. Complete motor paralysis due to lesions in the high cervical cord (C2, C3) with poor cardiopulmonary reserve, or with thrombus in IVC despite adequate anticoagulation.
 - iv. Shown to decrease the risk of PE acutely (1.1% vs 4.8%) but increase the risk of recurrent DVT at two years (20.8% vs 11.6%) No difference in Mortality rate (2.5%). ¹⁸
- i. Use either LMWH or Direct over unfractionated heparin if no active bleeding as there is a fortyfold greater risk of heparin-induced thrombocytopenia (HIT) with unfractionated heparin ²⁵.
- j. Continue thromboprophylaxis for 8 weeks in SCI with limited mobility, majority of new episodes of VTE are found during the first two weeks after injury, with a substantial decrease after eight weeks after injury ^{24,26}.
- k. The specific duration should be individualized, taking into consideration the level and completeness of the SCI, concomitant injuries and medical conditions,

bleeding risk, functional status, and feasibility. Factors suggesting longer duration are motor complete injuries, lower-extremity fractures, older age, previous VTE, cancer, and obesity. Some Guidelines recommend 12 weeks.³¹

- l. DVT prophylaxis should be instituted as soon as feasible and bleeding risk is low.
- m. LMWH should be held on the morning of surgery and resumed within 24 h following surgery.¹⁹
- n. Reinstitution of DVT Prophylaxis:
 - i. Chronic SCI if they are immobilized with bed rest for a prolonged period.
 - ii. Readmitted for medical illness or altered medical condition.
 - iii. Undergoing surgical procedures.
- o. Education: Patients, family members and significant others should be educated to take prevent measures and to recognize DVTs.

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

Guideline Developers

Guideline developed by Thomas S. Kiser, MD, in collaboration with the TRIUMPH team led by Thomas S. Kiser, MD, and Rani H Lindberg, MD.

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