

TELE-REHABILITATION GUIDELINE**Deep Vein Thrombosis Guidelines in Spinal Cord Injury.**

Drafted:

Peer Review:

Finalized:

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), 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 (81%) of 26 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. 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. a loss of sympathetic input to vasoconstrict blood vessels.
- c. an 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,
- 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, factor VIII, vWF, platelet aggregation (returns to normal in later stages of injury), fibrinogen, euglobulin clot lysis time, plasma alpha-1 antitrypsin activity, and antigen concentration. ^{4,6}
 - b. The following are decreased:
 - i. plasma alpha-2 antiplasmin antigen concentration and 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}
- v. 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)
 - i. m) Protein C and Protein S deficiency (hypercoagulability)
 - ii. n) Antithrombin III deficiency (hypercoagulability)
- vi. Risk factors that are additive to SCI risks⁹
 1. Advanced age
 2. Male gender
 3. Level of injury (paraplegia vs tetraplegia)
 4. Completeness of injury (motor complete vs motor incomplete)
 5. History of thrombosis
 6. Lower extremity fracture
 7. Dehydration
 8. Flaccid paralysis
 9. Obesity
 10. Delayed thromboprophylaxis
 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

- 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 treatment:

- a. There is level 4 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 rivaroxaban (Xarelto), dabigatran (Pradaxa), and apixaban (Eliquis) all appear to be effective and safe, but data in older and sicker patients are limited.¹³

ii. 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
- c. Warfarin

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 should be withheld 48 to 72 hours until appropriate medical therapy is implemented.¹⁶
- iii. Heparin Induced Thrombocytopenia 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
- iv. 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.
- v. Hyper-coagulable condition associated with a 5% per day risk of thrombosis. Thrombosis in up to 60% of patients and can precede thrombocytopenia.
- vi. 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. 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%
- ii. 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

- a. Compression hose or pneumatic devices should be applied to the legs of all SCI patients for the first 2 weeks:
 - i. Knee or thigh length.
 - ii. Single or sequential chamber compression
 - iii. Effectiveness enhanced in combination with other antithrombotic agents
- b. In patients whose thrombo-prophylaxis has been delayed > 72 hours, testing to exclude DVT should be performed prior to applying compression devices.
- c. Active and Passive ROM
- d. Elevation of legs
- e. Gradient elastic stockings (TED)
- f. Electrical Stimulation
- 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 adjusted dose unfractionated heparin within 72 hours after SCI, if no active bleeding, evidence of TBI, or coagulopathy. Continue until discharge with incomplete injury, for 8 weeks in uncomplicated complete SCI, and for 12 weeks with complete SCI with other risk factors.
- j. DVT prophylaxis should be instituted within 72 h post injury. (Single study but large difference; therefore suggest strong recommendation with weak data.)
- k. LMWH should be held on the morning of surgery and resumed within 24 h following surgery. (Balance of risks and benefits; strong recommendation, weak data.) ¹⁹
- l. Reinstitution of DVT Prophylaxis:
 - i. Chronic SCI if they are immobilized with bed rest for a prolonged period of time.
 - ii. Readmitted for medical illness or altered medical condition.

- iii. Undergoing surgical procedures.
- m. 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.

Selected References

1. Furlan JC, Fehlings MG: Role of screening tests for deep venous thrombosis in asymptomatic adults with acute spinal cord injury: an evidence-based analysis. *Spine* 32:1908–1916, 2007.
2. Geerts WH, Code KI, Jay RM, et al: A prospective study of venous thromboembolism after major trauma. *N Engl J Med* 331:1601–1606, 1994
3. Brandstater ME, Roth EJ, Siebens HC. Venous thromboembolism in stroke: literature review and implications for clinical practice. *Arch Phys Med Rehabil.* 1992;73(suppl 5): S379–S391.
4. Bravo G, Guizar-Sahagun G, Ibarra A, Centurion D, Villalon CM. Cardiovascular alterations after spinal cord injury: an overview. *Curr Med Chem Cardiovasc Hematol Agents.* 2004; 2:133–148.
5. Merli GJ, Crabbe S, Doyle L, Ditunno JF, Herbison GJ. Mechanical plus pharmacological prophylaxis for deep vein thrombosis in acute spinal cord injury. *Paraplegia.* 1992;30: 558–562.
6. Miranda AR, Hassouna HI. Mechanisms of thrombosis in spinal cord injury. *Hematol Oncol Clin North Am.* 2000;14: 401–416.
7. Yelnik A, Dizien O, Bussel B, et al. Systematic lower limb phlebography in acute spinal cord injury in 147 patients. *Paraplegia.* 1991;29:253–260.
8. Lim AC, Roth EJ, Green D. Lower limb paralysis: its effect on the recanalization of deep-vein thrombosis. *Arch Phys Med Rehabil.* 1992;73:331–333.
9. Worley, S; Short, S; Dalteparin Vs Low-Dose Unfractionated Heparin for Prophylaxis Against Clinically Evident Venous Thromboembolism in Acute Traumatic Spinal Cord Injury: A Retrospective Cohort Study. *J Spinal Cord Med.* 2008;31:379–387
10. Furlan, JC Fehlings, MG. Role of Screening Tests for Deep Venous Thrombosis in Asymptomatic Adults With Acute Spinal Cord Injury An Evidence-Based Analysis. *Spine* 2007;32:1908–1916

11. Goodacre S, Sampson F, Stevenson M, et al: Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis. *Health Technol Assess* 10:1168, 2006
12. Teasell RW, Hsieh JT, Aubut JL, Eng JJ, Krassioukov A, Tu L, for the Spinal Cord Injury Rehabilitation Evidence Review Research Team. Venous thromboembolism after spinal cord injury. *Arch Phys Med Rehabil* 2009;90: 232-45.
13. The Medical Letter, January 6, 2014;56(1433):3-4.
14. Castelucci LA, et al. Clinical and Safety Outcomes Associated with Treatment of Acute Venous Thromboembolism: A systematic review and Meta –analysis. *JAMA* 2014;312(11): 1122-1135.
15. Chatterjee S, et al Thrombolysis for Pulmonary Embolism and Risk of All-cause Mortality, Major Bleeding and Intracranial Hemorrhage: a Meta-analysis. *JAMA* 2014; 311(23): 2414-2421.
16. Prevention of Thromboembolism in Spinal Cord Injury. Second Edition. Consortium for Spinal Cord Medicine Clinical Practice Guidelines September 1999.
17. McGown, KE, et Al. Reducing the hospital burden of heparin-induced thrombocytopenia: impact of an avoid-heparin program. 2016 Jan 27. pii: blood-2015-07-660001. [Epub ahead of print]
18. Decosus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patient with proximal deep-vein thrombosis. *NEJM* 338(1998): 409-415.
19. Christie S, Thiabult-Halman G, Casha S. Acute Pharmacological DVT Prophylaxis after Spinal Cord Injury. *JOURNAL OF NEUROTRAUMA* 28:1509–1514 (August 2011)