

# Management of Deep Vein Thrombosis (DVT) Prophylaxis in Trauma Patients

# Shahram Paydar<sup>1</sup>, Golnar Sabetian<sup>2</sup>, Hosseinali Khalili<sup>3</sup>, Javad Fallahi<sup>4</sup>, Mohammad Tahami<sup>5</sup>, Bizhan Ziaian<sup>6</sup>, Hamid Reza Abbasi<sup>1</sup>, Shahram Bolandparvaz<sup>1</sup>, Fariborz Ghaffarpasand<sup>3</sup>, Zahra Ghahramani<sup>1\*</sup>

<sup>1</sup>Trauma Research Center, Shahid Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran <sup>2</sup>Department of Intensive Care Medicine, Trauma Research Center, Shahid Rajaee (Emtiaz) Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>3</sup>Neuroscience Research Center, Department of Neurosurgery, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Department of Internal Medicine, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>5</sup>Department of Orthopedics Surgery, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>6</sup>Department of Thoracic Surgery, Shiraz University of Medical Sciences, Shiraz, Iran

\*Corresponding author: Zahra Ghahramani Address: Trauma Research Center, Shahid Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Tel: +98-71-36360697; Fax: +98-71-36254206 e-mail: ghahreman2@yahoo.co.nz Received: July 7, 2015 Revised: September 10, 2015 Accepted: November 15, 2015

# **ABSTRACT**

Deep vein thrombosis (DVT) and pulmonary embolism (PTE) are known as venous thromboembolism (VTE). DVT occurs when a thrombus (a blood clot) forms in deep veins of the body, usually in the lower extremities. It can cause swelling or leg pain, but sometimes may occur with no symptoms. Awareness of DVT is the best way to prevent the VTE. Patients with trauma are at increased risk of DVT and subsequent PE because of coagulopathy in patients with multiple trauma, DVT prophylaxis is essential but the VTE prophylaxis strategy is controversial for the trauma patients. The risk factors for VTE includes pelvic and lower extremity fractures, and head injury.

Keywords: Management; Deep vein thrombosis; DVT; Prophylaxis; Trauma; Patients.

*Please cite this paper as:* 

Paydar S, Sabetian G, Khalili HA, Fallahi J, Tahami M, Ziaian B, Abbasi HR, Bolandparvaz S, Ghaffarpasand F, Ghahramani Z. Management of Deep Vein Thrombosis (DVT) Prophylaxis in Trauma Patients. *Bull Emerg Trauma*. 2016;4(1):1-7.

#### Introduction

Trauma is one of the main causes of hospitalization, mortality and morbidity in Iran and the world [1,2]. Trauma patients are at high risk for deep vein thrombosis (DVT) and subsequent pulmonary embolism (PE) which are collectively referred to venous thromboembolism (VTE) [3-5]. VTE is associated with high mortality and morbidity and increased hospitalization duration and costs [6,7]. The incidence of DVT in patients with traumatic injuries is as high as 5-63% [8]. The prophylaxis of DVT is trauma practice in order to prevent the subsequent VTE [8,9]. Previous reports have shown that the incidence of VTE is up to 15% in trauma patients in prophylaxis [10]. Currently, the optimal VTE prophylaxis strategy for trauma patients is unknown. According to current lines of evidence it

is believed that long bone fractures, pelvic fractures, traumatic brain injury and prolonged hospitalization are risk factors of VTE in patients with trauma. However the definition of high-risk group for VTE prophylaxis is yet to be defined. The prophylaxis options for VTE consist of mechanical prophylaxis, pharmacological anticoagulation and placing inferior vena cava (IVC).

Modalities available for trauma patient thromboprophylaxis are classified into pharmacologic anticoagulation, mechanical prophylaxis, and inferior vena cava (IVC) filters. Mechanical prophylaxis includes graduated compression stockings (GCSs), pneumatic compression devices (PCDs), and A-V foot pumps. Administration of prophylactic dosages of lowdose heparin (LDH), low molecular weight heparin (LMWH), and factor Xa inhibitors is considered the pharmacologic anticoagulation. Both the Eastern Association for the Surgery of Trauma (EAST) and American College of Clinical Pharmacy (ACCP) guidelines recommend primary use of LMWHs in trauma patients; however there are still controversies regarding the definitive VTE prophylaxis in trauma patients. Large randomized prospective clinical studies would be required to provide level I evidence to define the optimal VTE prophylaxis in trauma patients. An autopsy study found 20% death of PE [9,10] and 65% of fatally injured patients by DVT [7,8].

The cost of economic burden of PE and DVT is high, due not only to the initial hospitalization [11]. Therefore, it will increase the likelihood of progression to death, which preventable and it shows the need for prophylaxis [12-14].

The conditions of traumatic injuries management are more different and harder than prescription of prophylaxis DVT and other medical groups. Because it will make the active and potential bleeding of these victims, such as intracranial hemorrhage, spinal fractures, pelvic fractures associated with hematoma, bleeding internal organs caused by trauma, and prescription of drugs that can aggravate bleeding.

### **Process Methods**

This is a narrative review being performed by searching the main databases including PubMed (National Library of Medicine) and Scopus with keywords of DVT, PE, VTE prophylaxis and trauma from 1975 through 2015. Out of 1109 articles recognized, prospective studies were selected and reviewed. Data collected and a consensus was received for the opinion of recommendations.

### **Risk Factors and Pathophysiology**

Many factors can increase the risk of developing DVT. Several studies showed the risk of DVT after trauma [9]. The risk factors for DVT includes age over 40 years, cancer, inflammatory bowel disease, Cancer History, Rheumatic Diseases, Obesity, Heart failure, Injury or surgery such as Hip Fracture, Femoral or Double leg fracture, Spinal Cord Injury, TBI, and GCS<8. Lower extremity fracture, head injury and pelvic fracture have been considered risk factors for VTE [15]. Acute spinal cord injury patients are at a considerable risk for developing DVT [16-18]. Spinella *et al.*, [19] found that in trauma patients who transfused by 5 or more unit of RBC, DVT was increased with the transfusion of old RBC's. Despite these numerous risk factors associated with DVT, the high risk group is unclear [20].

## Mechanical Thromboprophylaxis

Mechanical method reduce the pooling of blood in the deep venous system that is increases the blood flow of venous and return the venous to the heart. The method also prevents microvascular damage of the veins caused by stretching during venous pooling. This method includes Intermittent pneumatic compression (IPC) sleeves and Antiembolism stockings (AES). The advantage of the method is the absence of the effect on coagulation. Therefore, there is no increased risk of bleeding. The disadvantages include poor compliance, cost, exacerbation of arterial insufficiency in patients with peripheral arterial disease and lower efficacy than pharmacological method.

## Pharmacologic Thromboprophylaxis

This method depends on producing a low level of anticoagulation. Pharmacological method includes Low dose unfractionated heparin (UFH), Low dose low molecular weight heparin (LMWH) and Oral direct thrombin or Xa inhibitors. The advantages of this method are efficacy and compliance that based on the dose given to the patients. The disadvantages are bleeding due to the effect of coagulation and drug reactions. Drug reactions with heparin are rare but includes of allergy to heparin, skin necrosis and Heparin Induced Thrombocytopenia and Thrombosis (HITT). Drug reactions are less common by oral direct thrombin and Xa inhibitors. To prevent the thrombin in hospitalized patients, warfarin should not be used.

# How is Mechanical and Pharmacologic Prophylaxis Used in Prevention?

The risk of VTE can be reduced at the time of surgery with administration of appropriate prophylaxis regimen. Mechanical methods are usually used in combination with other methods. The types of mechanical prophylaxis include Stockings which are more effective in preventing DVT in the calf than in legs; of lower extremities such as elevating the foot, active and passive ankle motion that increasing blood flow through the femoral vein. External pneumatic devices are other mechanical prophylaxis of DVT which could be used in combination with other methods. In high risk patients pneumatic compression devices are the most effective route of DVT prophylaxis. These devices are expensive and not available in all the centers. Inferior vena cava (IVC) filters are among the mechanical prophylaxis of VTE devices which are used in those with extensive DVT and high risk of PE and have also contraindication of anticoagulation therapy. Application of pharmacological prophylaxis is associated with increased risk of bleeding. The most common anticoagulant is aspirin and warfarin.

Aspirin: it is easy to prescribe and use, costs little, has few complications of bleeding, and there is no need to monitoring. Therefore, it is not been proven to be more effective than other methods and may not be advisable for all patients.

Warfarin: Also called Coumadin and is most commonly used for the hip and knee of patient's replacement. It will interfere with vitamin K metabolism in liver to clot formation of DVT. 4 to 5 days need to gain maximum effectiveness because it takes at least 36 hours to start working. Warfarin normally use at low doses because higher doses can cause bleeding. Also, it can cause fatal damage.

# Comparative Effectiveness of Mechanical and Pharmaceutical Prophylaxis

There are two non-invasive mechanical methods of DVT prophylaxis that includes Intermittent Pneumatic Compression (IPC) and Anti-embolic stockings (AES). These two methods are both proven and effective when used alone or used in combination with pharmacologic prophylaxis for higher risk patients. Mechanical methods have an advantage and are not with the risk of bleeding. Both IPC and AES work to derogate the risk factor associated with VTE, unlike pharmacologic prophylaxis. These mechanical methods of VTE prophylaxis has no risk of bleeding when used as a monotherapy and can be used as an adjunct to pharmacological prophylaxis to increase the effectiveness in high risk patients.

### **Internal Bleeding**

DVT is a blood clot which develops in the deep veins in one or both legs. It can be dangerous because the clot may become large and deep and go through blood vessels and lodge in the lungs. Anticoagulants such as heparin, Low Molecular Weight Heparin (LMWH), or coumadin have been the main treatment for DVT. IV thromboembolic is no longer recommended for treating DVT because it will increase the chance of bleeding. Study of Joseph *et al.*, [21] showed no significant correlation between early anticoagulation and development of bleeding complications. It says using of early enoxaparin anticoagulation maybe a safe option in trauma patients.

#### **Spinal Injuries**

Patients with spinal cord injury are at the high risk of VTE. Using mechanical prophylaxis recommended when anticoagulant prophylaxis is contraindicated but no evidence exist to support the use of mechanical prophylaxis as a single prophylaxis method [22,23]. The risk of VTE in spinal cord patients will increase during their rehabilitation phase and should continue the thromboembolic prophylaxis [24].

Patients with spinal cord injuries are at a high risk of gastrointestinal hemorrhage or bleeding even during periods of rehabilitation [25,26]. All acute spinal cord injured patients and patients with rehabilitations may benefit from receiving chemical prophylaxis for ulceration [27]. Prevention could be the basis in the management of this problem.

## **Pelvis Fractures**

In a trauma patients who have sustained pelvic or acetabular fractures, proximal vein thrombosis frequently occurs. For these patients, LMWH is recommended as a mean of thromboembolic prophylaxis after hemostasis [28]. When LMWH is contraindicated, mechanical thromboembolic prophylaxis is recommended [22,23,29]

## **Hip Fractures**

The complications of thromboembolic events remain an important cause of mortality and morbidity associated with hip fractures.

Patients with hip fractures are at very high risk of VTE. In a study of Marsland *et al.*, [30] aspirin is reduces the risk of VTE but does not provide protection compared with other pharmacological prophylaxis. Therefore, it is not recommended. Warfarin, LMWH, and Fondaparinx reduce the risk of DVT. The study showed that chemical VTE prophylaxis should be used for all patients with hip fractures.

Studies showed that without prophylaxis the rate of DVT in patients with hip fracture ranges from 46%-75% [31-34]. Therefore, all patients with hip fracture need prophylaxis against VTE. Another studies showed that the risk of VTE in hip fracture patients starts at the time of surgery [35,36]. The study of Niikura et al., [37] evaluates the rate of VTE after complex lower limb fracture surgery without pharmacological prophylaxis. The study showed that VTE was high in patients undergoing this surgery. Also, study of Chu et al., [38] showed that major trauma patients have an approximate six fold increased risk of developing VTE during admission compared with minor trauma patients. This study supports the use of prophylaxis to treat minor trauma patients.

### **Traumatic Brain Injury**

TBI are at increased risk of DVT [39] and it is because of hypercoagulability which is happen in TBI patients from a variety of mechanisms such as tissue factor [40]. All TBI patients should receive Intermittent Pneumatic Compression Devises (IPC) at the time of admission to hospital [41]. Also a head CT should be obtained to find about the lack of progression of further bleeding. The CT scan should be performed at 24 hours of intervals. Chemical thromboprophylaxis should be started in 24-48 hours after head CT and found about progression of bleeding [42-44].

#### **Prevention of Venous Thromboembolism**

Although mechanical methods have been shown to reduce the risk of DVT, they have been studied less than pharmacological treatment methods [45]. Mechanical methods of prophylaxis include IPC and AES and Venous foot pump. Mechanical prophylaxis should be used in patients who are in high risk of bleeding or as an adjunct with pharmacological methods.

Comparison stocking have been shown to reduce DVT, but their use is associated with an increase in skin complications [46].

The DVT management includes PE prevention. Study of Clark-pearson suggests that IPC is as an option for VTE prophylaxis in patients undergoing gynecologic surgery. Clinicians who are treating women with more than one risk factor should use pharmacologic rather than mechanical methods to prevent VTE [47].

DVT and PE are clinically important complications of strock. The study of Mazzone *et al.*, [48] showed that mechanical prophylaxis appears safe in patients with strock.

#### **Current Status**

Existing guidelines of trauma usually cannot speak in detail about the harsh conditions of traumatic injuries because of trauma conditions elaboration and there is no evidence of levels I and II in the field and there are no other evidences. In a guideline of American College of Chest physician (ACCP) recommends the use of LMWH for major trauma patients. [49] An acceptable recommendation is using LMWH and the optimal use of the mechanical prophylaxis. ACCP also recommends thromboprophylaxis for major trauma patients with impaired mobility until they discharged [49]. Using of Kaprini disk should also be reviewed for the trauma victims [39].

The Eastern Association for the Surgery of Trauma (EAST) guideline also shows several important points about patient's management with bleeding and cerebral hemorrhage [50]. EAST guideline has no level I recommendation for LMWH. According to Level II, LMWH can use for the pelvic fractures, lower extremity fractures and spinal cord injury. According to level III, patients with ISS> 9 should receive LMWH [51].

At the start of DVT prophylaxis for patients with brain problems levels of cc reflects to start the DVT prophylaxis treatment. The onset and rate of treatment is only the evidence of level III that indicating the safety of starting mechanical prophylaxis from the beginning of hospitalization and pharmacological prophylaxis starting from 24-48 hours after the stability of brain injury.

#### Recommendations

All patients should receive mechanical prophylaxis



Fig. 1. Algorithm 1: Decision for Starting DVT Prophylaxis in Trauma Patients



Fig. 2. Algorithm 2: Starting DVT prophylaxis in patients with damage to internal organs or internal bleeding and pelvic fractures

Conclusion

### or pharmacologic prophylaxis

Risk of bleeding and thromboembolism should be assessed in all patients at admission.

For the majority of inpatients who do not have contraindications, pharmacologic prophylaxis has been the default mode of prophylaxis [52,53].

Internal bleeding means any damage to internal organs with the risk of bleeding such as solid organs, lung, gut or pelvic fracture. Algorithm 1-3 shows the decision for starting DVT prophylaxis in trauma patients (Figure 1, 2 and 3).

### References

- Gosselin RA, Spiegel DA, Coughlin R, Zirkle LG. Injuries: the neglected burden in developing countries. *Bull World Health Organ*. 2009;87(4):246-a.
- 2. Modarres SR, Shokrollahi MH, Yaserian M, Rahimi M, Amani N, Manouchehri AA. Epidemiological Characteristics of Fatal Traumatic Accidents in Babol, Iran: A Hospital-Based Survey. *Bull Emerg Trauma*.

2014;**2**(4):146-150.

- 3. In: U.S. Department of Health and Human Services. The surgeon general's call to action to prevent deep vein thrombosis and pulmonary embolism. 2008. Available from: http://www.ncbi.nlm.nih.gov/books/ NBK44178/pdf/TOC.pdf
- 4. Prevention of venous thrombosis and pulmonary embolism. NIH Consensus Development. JAMA.

1986;256(6):744-9.

The detection of both PE and DVT are difficult.

Therefore, it is good to concentrate on preventing

their development by using mechanical or

pharmacological methods. Combining vascular compression stockings with low-dose heparin is an

effective strategy for patients at high or very high

risk of venous thromboembolism [54].

Conflict of Interest: None declared.

- Shackford SR, Moser KM. Deep venous thrombosis and pulmonary embolism in trauma patients. *Journal of Intensive Care Medicine*. 1988;3(2):87-98.
- 6. Sevitt S. Fatal road accidents. Injuries, complications, and causes of death in 250 subjects. *Br J Surg.* 1968;**55**(7):481-505.
- 7. Spyropoulos AC, Lin J. Direct medical



Fig. 3. Algorithm 3: Starting prophylaxis in trauma patients with cerebral hemorrhage

costs of venous thromboembolism and subsequent hospital readmission rates: an administrative claims analysis from 30 managed care organizations. *J Manag Care Pharm.* 2007;**13**(6):475-86.

- Piotrowski JJ, Alexander JJ, Brandt CP, McHenry CR, Yuhas JP, Jacobs D. Is deep vein thrombosis surveillance warranted in highrisk trauma patients? *Am J Surg.* 1996;172(2):210-3.
- 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):1601-6.
- **10.** Hill SL, Berry RE, Ruiz AJ. Deep venous thrombosis in the trauma patient. *Am Surg.* 1994;**60**(6):405-8.
- Sevitt S, Gallagher N. Venous thrombosis and pulmonary embolism. A clinico-pathological study in injured and burned patients. *Br J Surg.* 1961;48:475-89.
- 12. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, et al. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis: American College of

Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2012;**141**(2\_suppl):e227S-e77S.

- Laporte S, Mismetti P, Decousus H, Uresandi F, Otero R, Lobo JL, et al. Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. *Circulation*. 2008;117(13):1711-6.
- Pasquale M, Fabian TC. Practice management guidelines for trauma from the Eastern Association for the Surgery of Trauma. *J Trauma*. 1998;44(6):941-56.
- **15.** Fakhry S, Michetti C. Bleeding and coagulation complications. Trauma. 2004:1251-70.
- Fujii Y, Mammen EF, Farag A, Muz J, Salciccioli GG, Weingarden ST. Thrombosis in spinal cord injury. *Thromb Res.* 1992;68(4):357-68.
- 17. Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. Prevention of venous thromboembolism after injury: an evidence-based report-part II: analysis of risk factors and evaluation of the role of vena caval filters. *J Trauma*. 2000;**49**(1):140-4.

- 18. Myllynen P, Kammonen M, Rokkanen P, Bostman O, Lalla M, Laasonen E. Deep venous thrombosis and pulmonary embolism in patients with acute spinal cord injury: a comparison with nonparalyzed patients immobilized due to spinal fractures. J Trauma, 1985;25(6):541-3.
- 19. Spinella PC, Carroll CL, Staff I, Gross R, Mc Quay J, Keibel L, et al. Duration of red blood cell storage is associated with increased incidence of deep vein thrombosis and in hospital mortality in patients with traumatic injuries. *Crit Care*. 2009;13(5):R151.
- Gearhart MM, Luchette FA, Proctor MC, Lutomski DM, Witsken C, James L, et al. The risk assessment profile score identifies trauma patients at risk for deep vein thrombosis. *Surgery*. 2000;128(4):631-40.
- 21. Joseph B, Pandit V, Harrison C, Lubin D, Kulvatunyou N, Zangbar B, 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):194-8.
- 22. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous

thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004;**126**(3 Suppl):338S-400S.

- **23.** Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. *J Trauma*. 2002;**53**(1):142-64.
- 24. Prevention of venous thromboembolism in the acute treatment phase after spinal cord injury: a randomized, multicenter trial comparing low-dose heparin plus intermittent pneumatic compression with enoxaparin. J Trauma. 2003;54(6):1116-24; discussion 25-6.
- **25.** Charney KJ, Juler GL, Comarr AE. General surgery problems in patients with spinal cord injuries. *Arch Surg.* 1975;**110**(9):1083-8.
- Tanaka M, Uchiyama M, Kitano M. Gastroduodenal disease in chronic spinal cord injuries. An endoscopic study. *Arch Surg.* 1979;114(2):185-7.
- Anwar F, Al-Khayer A, El-Mahrouki H, Purcell M. Gastrointestinal bleeding in spinal injuries patient: Is prophylaxis essential? *Alcohol.* 2013;5:26.3.
- 28. Ginzburg E, Cohn SM, Lopez J, Jackowski J, Brown M, Hameed SM. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *Br J Surg.* 2003;90(11):1338-44.
- **29.** Eastman AB. Venous thromboembolism prophylaxis in trauma patients. *Techniques in Orthopaedics*. 2004;**19**(4):293-9.
- **30.** Marsland D, Mears SC, Kates SL. Venous thromboembolic prophylaxis for hip fractures. *Osteoporos Int.* 2010;**21**(Suppl 4):S593-604.
- **31.** Agnelli G, Cosmi B, Di Filippo P, Ranucci V, Veschi F, Longetti M, et al. A randomised, double-blind, placebo-controlled trial of dermatan sulphate for prevention of deep vein thrombosis in hip fracture. *Thromb Haemost.* 1992;**67**(2):203-8.
- **32.** Lowe GD, Campbell AF, Meek DR, Forbes CD, Prentice CR. Subcutaneous ancrod in prevention of deep-vein thrombosis after operation for fractured neck of femur. *Lancet.* 1978;**2**(8092 Pt 1):698-700.
- **33.** Powers PJ, Gent M, Jay RM, Julian DH, Turpie AG, Levine M, et al. A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery

for fractured hip. *Arch Intern Med.* 1989;**149**(4):771-4.

- **34.** Rogers PH, Walsh PN, Marder VJ, Bosak GC, Lachman JW, Ritchie WG, et al. Controlled trial of lowdose heparin and sulfinpyrazone to prevent venous thromboembolism after operation on the hip. *J Bone Joint Surg Am.* 1978;**60**(6):758-62.
- **35.** Hefley FG, Jr., Nelson CL, Puskarich-May CL. Effect of delayed admission to the hospital on the preoperative prevalence of deep-vein thrombosis associated with fractures about the hip. *J Bone Joint Surg Am.* 1996;**78**(4):581-3.
- **36.** Zahn HR, Skinner JA, Porteous MJ. The preoperative prevalence of deep vein thrombosis in patients with femoral neck fractures and delayed operation. *Injury*. 1999;**30**(9):605-7.
- **37.** Niikura T, Sakai Y, Lee SY, Iwakura T, Kuroda R, Kurosaka M. Rate of venous thromboembolism after complex lower-limb fracture surgery without pharmacological prophylaxis. *J Orthop Surg (Hong Kong).* 2015;**23**(1):37-40.
- **38.** Chu CC, Haga H. Venous thromboembolism associated with lower limb fractures after trauma: dilemma and management. *J Orthop Sci.* 2015;**20**(2):364-72.
- **39.** Praeger AJ, Westbrook AJ, Nichol AD, Wijemunige R, Davies AR, Lyon SM, et al. Deep vein thrombosis and pulmonary embolus in patients with traumatic brain injury: a prospective observational study. *Crit Care Resusc.* 2012;**14**(1):10-3 3.
- **40.** Laroche M, Kutcher ME, Huang MC, Cohen MJ, Manley GT. Coagulopathy after traumatic brain injury. *Neurosurgery*. 2012;**70**(6):1334-45.
- **41.** DeMuro JP, Hanna AF. Prophylaxis of Deep Venous Thrombosis in Trauma Patients: A Review. *J Blood Disorders Transf.* 2013;**4**(151):2.
- 42. Phelan HA, Wolf SE, Norwood SH, Aldy K, Brakenridge SC, Eastman AL, et al. A randomized, doubleblinded, placebo-controlled pilot trial of anticoagulation in low-risk traumatic brain injury: The Delayed Versus Early Enoxaparin Prophylaxis I (DEEP I) study. J Trauma Acute Care Surg. 2012;73(6):1434-41.
- **43.** Saadeh Y, Gohil K, Bill C, Smith C, Morrison C, Mosher B, et al. Chemical venous thromboembolic prophylaxis is safe and effective for patients with traumatic brain injury when started 24 hours after the absence of hemorrhage progression on head CT. *J Trauma Acute Care Surg.* 2012;73(2):426-30.
- 44. Kim J, Gearhart MM, Zurick A, Zuccarello M, James L, Luchette FA.

Preliminary report on the safety of heparin for deep venous thrombosis prophylaxis after severe head injury. *J Trauma*. 2002;**53**(1):38-42; discussion 3.

- **45.** Christie S, Thibault-Halman G, Casha S. Acute pharmacological DVT prophylaxis after spinal cord injury. *J Neurotrauma*. 2011;**28**(8):1509-14.
- 46. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, et al. 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-325S.
- **47.** Clarke-Pearson DL, Dodge RK, Synan I, McClelland RC, Maxwell GL. Venous thromboembolism prophylaxis: patients at high risk to fail intermittent pneumatic compression. *Obstet Gynecol.* 2003;**101**(1):157-63.
- **48.** Mazzone C, Chiodo GF, Sandercock P, Miccio M, Salvi R. Physical methods for preventing deep vein thrombosis in stroke. *Cochrane Database Syst Rev.* 2004;(4):CD001922.
- **49.** Hirsh J, Guyatt G, Lewis SZ. Reflecting on eight editions of the American College of Chest Physicians antithrombotic guidelines. *Chest.* 2008;**133**(6):1293-5.
- **50.** Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. *J Trauma*. 2002;**53**(1):142-64.
- 51. Cushman JG, Agarwal N, Fabian TC, Garcia V, Nagy KK, Pasquale MD, et al. Practice management guidelines for the management of mild traumatic brain injury: the EAST practice management guidelines work group. *J Trauma*. 2001;51(5):1016-26.
- **52.** Kakkar AK, Cimminiello C, Goldhaber SZ, Parakh R, Wang C, Bergmann JF. Low-molecular-weight heparin and mortality in acutely ill medical patients. *N Engl J Med.* 2011;**365**(26):2463-72.
- **53.** Lederle FA, Zylla D, MacDonald R, Wilt TJ. Venous thromboembolism prophylaxis in hospitalized medical patients and those with stroke: a background review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med.* 2011;**155**(9):602-15.
- **54.** Goldhaber SZ, Fanikos J. Prevention of deep vein thrombosis and pulmonary embolism. *Circulation*. 2004;**110**(16):e445-e7.