



# Prophylaxis of Venous Thromboembolism in Orthopedic Trauma Patients: A Review

Karim Pisoudeh,<sup>1</sup> SM Javad Mortazavi,<sup>2</sup> Reza Shahriar Kamrani,<sup>2</sup> Seyyed Hamidreza Seyyedhosseinzadeh,<sup>3</sup> and Mansour Abolghasemian<sup>1,\*</sup>

<sup>1</sup>Shafa Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Joint Reconstruction Research Center, Imam Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Akhtar Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\*Corresponding author: Mansour Abolghasemian, MD, Assistant Professor of Orthopedic Surgery, Shafa Hospital, Iran University of Medical Sciences, Tehran, Iran. E-mail: mabolghasemian@gmail.com

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## Abstract

Orthopedic trauma is an area of significant controversy regarding indications and type of thromboprophylaxis. In 2014, the Iranian Orthopedic Association (IOA) organized a committee to review the available data to extract a national guideline to assist the orthopedic surgeons in decision making regarding the need and type of thromboprophylaxis for patients with orthopedic trauma. We found almost 12500 articles in regards to DVT and thromboembolism from PubMed and orthopedic journals from January 2004 to January 2017. We included only the articles related to orthopedic trauma patients (684 articles); then, we selected case control cohort and prospective studies (73 articles). Herein, we present a summary of the review.

**Keywords:** Trauma, Deep Vein Thrombosis, Guideline, Anticoagulation

## 1. Context

Venous thromboembolism (VTE) is a major cause of mortality and morbidity in orthopedic trauma patients (1-5). The rate of VTE in major trauma patients is reportedly as high as 21.8% (4, 6-11). Traumatic events can cause a hypercoagulable state due to the release of inflammatory agents where along with the often reduced venous flow (due to restricted ambulation), it can facilitate the formation of a thrombus nidus at a site of venous endothelial injury (12, 13). The role of VTE prophylaxis has been confirmed in some clinical situations (9, 14-17). Total hip and knee arthroplasty, major hip fractures and some spine surgeries are clear indications for VTE prophylaxis (18-20). American college of chest physicians (ACCP) guideline has recommended a course of 10 to 35 days for all patients with one of the above-mentioned surgeries using pharmacologic  $\pm$  mechanical prophylaxis, except when the patient is at increased risk of bleeding (21). American academy of orthopedic surgeons (AAOS) clinical practice guideline on VTE prophylaxis has only covered patients undergoing elective hip and knee arthroplasty (22-26). While somehow different from the ACCP counterpart in details of prophylactic regimens, it is very similar to the latter in recommending VTE prophylaxis, pharmacologic, and mechanical for

hip and knee arthroplasty patients. The National Institute for Clinical Excellence (NICE) guideline has a more comprehensive range of recommendations covering most orthopedic conditions (21). The current literature is less conclusive regarding the necessity of pharmacologic VTE prophylaxis for orthopedic trauma patients other than a hip fracture. This is an important defect as trauma cases comprise the largest bulk of orthopedic patients in developing countries. VTE is one of the leading causes of mortality and medical morbidity in this population (27). Iranian Orthopedic Association (IOA) conducted a literature review for collecting available data on VTE prophylaxis in orthopedic patients, including trauma cases, for providing a nationalized guideline. Hereby, we present the findings as a review. The risk of formation, propagation, and embolization of a deep vein thrombosis (DVT) is determined by interaction of numerous factors. The importance of each individual risk factor has not been determined in orthopedic patients; however, none of the stratification systems have been validated yet. Therefore, the judgment of the treating physician is crucial for deciding whether pharmacologic VTE prophylaxis is appropriate for an individual patient and if so, what would be the optimal intensity and duration of the prophylaxis.

## 2. Methods

We used the orthopedic and internal medicine journals from PubMed and Medline/Ovid (includes EMBase). We could find about 12500 articles with their updates to 2017. Then, orthopedic trauma studies were included (684 articles). Finally, high quality studies including prospective randomized and quasi-randomized studies were selected for this review.

## 3. Results

First we mention the risk factors for VTE and bleeding.

### 3.1. VTE/bleeding Risk Factors (ACCP & AAOS)

#### 1. Patient - related VTE risk factors:

History of VTE events, personal or 1st degree relatives, Thrombophilia (hereditary or acquired), Elderly age (> 60), Pregnancy and postpartum period (6 weeks), Use of exogenous estrogen hormones (including contraceptive pills), Varicose veins with phlebitis, Obesity (BMI > 30 kg/m<sup>2</sup>), Prolonged immobility (> 3 days), Nephrotic syndrome, Active malignancy, Inflammatory bowel disease (IBD), Heart failure.

#### 2. Surgery - related VTE risk factors:

Surgery site (lower limb > upper limb), Longer duration of the surgery, Anesthesia type (general > regional).

#### 3. Bleeding risk factors:

Active bleeding at any site, Hereditary bleeding diatheses (i.e. hemophilia), Acquired bleeding diatheses (i.e. hepatic, renal failure), Anticoagulation therapy (i.e. Clopidogrel), Thrombocytopenia < 75000/mm<sup>3</sup>, Presence of any pathology at risk of major bleeding (i.e. hemorrhagic cerebrovascular accident, hemorrhagic brain injury, injuries or surgeries around spinal cord).

There have been numerous attempts to stratify the risk of VTE or hemorrhagic events for individual patients based on the known risk factors. None of them have been validated yet for application to orthopedic patients. Therefore, the committee decided to delegate risk estimation to the treating surgeon.

### 3.2. Anticoagulation Modalities

There are two main anticoagulation measures with documented efficacy against VTE events, pharmacological and mechanical. Available pharmacological agents in Iran with a potential role in VTE prophylaxis include low molecular weight heparin (LMWH), low dose unfractionated heparin (LDUH), Warfarin, ASA, and Dabigatran. Mechanical prophylaxis basically includes all measures to decrease venous stasis in the limb such as intermittent pneumatic compression devices (IPCD), anti - embolism stockings (AES), and early ambulation.

### 3.2.1. General Recommendations for VTE Prophylaxis in Orthopedic Trauma Patients

Routine Doppler - ultrasonography investigation of asymptomatic patients with orthopedic trauma in order to detect DVT is not recommended (28).

1- For patients undergoing major orthopedic surgeries (i.e. hip fracture fixation) and receiving LMWH, a minimum gap of 12 hours between surgery and injection is recommended both before and after surgery (29).

2- For patients with high risk of bleeding, using mechanical VTE prophylaxis (IPCD or AES) is recommended. In addition, early ambulation and frequent ankle pump exercises are recommended. Pharmacological agents are not recommended in this group of patients (30).

3- Patients on estrogen hormonal therapy are at a high risk for VTE events for at least 4 weeks after cessation of the drug (31).

4- Regional anesthesia is recommended for major surgeries of the lower extremity, whenever clinically justified (32).

5- Early ambulation, preferably within 24 hours, is recommended for all patients with orthopedic trauma. The exact time depends on the clinical situation (33).

6- In asymptomatic patients with a major orthopedic surgery that do not receive pharmacologic VTE prophylaxis due to high bleeding risk, the routine use of inferior vena cava filtering is not recommended (34-36).

7- For pregnant patients, the use of LMWH is preferred over LDUH or warfarin, both for prophylaxis and treatment purposes (37). Low dose ASA could be continued before major orthopedic surgeries (38). No strong high - quality evidence is available in support of superiority of one anticoagulant agent over others (39). For patients at high risk of compartment syndrome, the use of pharmacological VTE prophylaxis is based on the surgeon's clinical judgment.

### 3.2.2. Injury - Specific Recommendations for VTE Prophylaxis in Orthopedic Trauma Patients

#### 3.2.2.1. Upper Extremity Trauma

Trauma of the upper extremity is known for its low propensity for VTE (21, 40-44). This has been attributed to the low incidence of stasis due to the venous circulation being located at the same level as the heart. Therefore, only about 4% of the VTE events originate from the upper limb (21, 45). This has led to a fairly conservative approach to VTE prophylaxis recommended by most authors. However, there are numerous reports of DVT formation or symptomatic PE events likely to originate from the upper extremity (46). Although it was not possible to have evidence - based conclusions for all patients with upper limb trauma, some suggestions were made by the committee

based on the available literature. Early ambulation (preferably during the first 24 hours postoperatively) is recommended whenever possible. This should include significant weight-bearing if clinically judicious. For isolated upper extremity fractures distal to elbow, we suggest no pharmacologic VTE prophylaxis.

1- For patients with surgery or significant injury of the upper limb proximal to elbow and a history of previous VTE, we recommend pharmacologic VTE prophylaxis.

2- For patients with surgically treated complex proximal humeral fractures, we suggest considering pharmacologic prophylaxis based on the severity of injury and the patient's factors.

3- Minimum duration of anticoagulation is 7 days and could be extended based on the surgeon's judgment and patient's preference. Furthermore, any patient with an upper limb injury and significant limitation in ambulation, due to any reason, for more than 3 days, should receive pharmacologic thromboprophylaxis.

### 3.2.2.2. Spine Injury

Most spine injuries are associated with a relatively low risk of VTE and routine pharmacologic thromboprophylaxis is not warranted (47-49). The following recommendations are based on the current review:

Early ambulation is strongly recommended whenever possible.

1- Mechanical thromboprophylaxis (preferably with IPCD) is recommended for all patients with spine surgery or significant spine injury.

2- Patients with a spinal injury not associated with cord injury that need surgical treatment through a single anterior or posterior approach, only mechanical prophylaxis, is recommended (49).

3- For patients with a spinal injury not associated with cord injury that need surgical treatment through combined anterior and posterior approaches, pharmacologic thromboprophylaxis in addition to mechanical prophylaxis is recommended (50-52).

4- For patients with a spinal injury associated with significant cord injury and motor deficiency, or those with malignant disease of the spine pharmacologic thromboprophylaxis, in addition to mechanical prophylaxis is recommended (48, 49, 53).

5- Options for chemoprophylaxis are LMWH, LDUH, Warfarin, ASA, and Dabigatran. Anticoagulation starts when sufficient hemostasis has been achieved and the risk of surgical site bleeding and/or cord hemorrhage are deemed to be minor based on the surgeon's judgment.

### 3.2.2.3. Lower Extremity Trauma

Patients with lower extremity trauma include a wide range of injuries with a large variety in their propensity to VTE complications. While hip fractures have a high risk of VTE without thromboprophylaxis, other anatomical portions of the lower limb are less prone to this complication. Current literature has paucity of high-quality evidence for most lower - limb injuries. The following recommendations were made based on the available literature.

### 3.3. Hip Fractures (Femoral Neck-, Per - Trochanteric Fractures)

1- In the case of hip fractures early ambulation is strongly recommended whenever possible.

2- Combined pharmacological and mechanical thromboprophylaxis (preferably with IPCD) are recommended for all patients with hip fractures.

3- Pharmacological thromboprophylaxis should be started after admission and continued until surgery.

4- Warfarin and ASA are not considered appropriate for VTE prophylaxis before surgery due to their long anticoagulation effects that limits the surgeon's freedom in selecting the time of surgery.

5- LMWH should be held 12 to 24 hours before surgery.

6- LDUH should be held 6 to 12 hours before surgery.

7- Pharmacological thromboprophylaxis should be started after surgery. Options for chemoprophylaxis in these patients includes LMWH, LDUH, Warfarin, ASA, and Dabigatran, which can be different from the agent used before surgery. LMWH and warfarin are preferred options for patients with a history of previous VTE (54). In other patients, there is no definitive evidence of inferiority of ASA comparing with other options. Time of commencement of pharmacological VTE prophylaxis after surgery is based on the surgeon's judgment and according to the following rules:

1- LMWH and ASA can be started 12 to 24 hours after surgery (54).

2- LDUH can be started 6 to 12 hours after surgery (54).

3- Warfarin could be started the night before surgery (54).

4- Dabigatran can be started 1 to 4 hours after surgery (54, 55).

Minimum duration of pharmacological VTE prophylaxis is 14 days, however, it is preferred to extend for 6 weeks, based on the surgeon's judgment (54).

### 3.3.1. Mechanical VTE Prophylaxis

Intermittent pneumatic compression device (IPCD) is the mechanical method of choice and is recommended for preoperative period as well as 3 days postoperatively. Portable type is preferred if available. Above - knee Anti -

embolism stockings (AES) are recommended after removal of IPCD until the patient regains the ability of full ambulation and weight bearing. They should be removed on a daily basis for inspection of patient's skin (56, 57).

### 3.3.2. Foot/Ankle Injuries

Most foot/ankle injuries are associated with a relatively low risk of VTE (2, 58, 59) and routine pharmacologic thromboprophylaxis is not warranted. Early ambulation and ankle pumping exercise are recommended whenever possible. Mechanical VTE prophylaxis (preferably with IPCD) is recommended for patients with foot/ankle injury if clinically feasible. Patients with a foot/ankle injury without previous history of VTE, routine use of pharmacological VTE prophylaxis is not recommended. Achilles tendon tear is an exception and considering pharmacological VTE prophylaxis is suggested (59-61). Patients with a foot/ankle injury and high risk of VTE (as when the patient remains in bed for more than 3 days peri - operatively or in multiple trauma patients) the use of pharmacological VTE prophylaxis is recommended. Options include LMWH, LDUH, Warfarin, ASA, Dabigatran, and LMWH and LDUF are preferred agents preoperatively (59).

### 3.3.3. Lower Extremity Orthopedic Trauma Not Involving Hip and Foot/Ankle

There is a paucity of evidence on the rate of VTE events and the role of anticoagulation after injuries of other parts of the lower limb (between hip and ankle). This is partly due to the fact that these patients are very non - homogeneous and often suffer from other injuries. More proximal injuries appear to be more prone to VTE events; femoral shaft/condyles and tibia plateau fractures have a higher risk in comparison to tibia shaft and Pilon fractures (62-64). Lower limb fractures are commonly splinted or casted, thus increasing the chances to develop VTE. Even minor surgeries involving the leg can have these effects if the patient is immobilized or not actively using that limb (65-67). Most VTE prophylaxis guidelines have not stated clear recommendations for this group of injuries. We are only able to make the following general recommendations based on literature review:

1- Early ambulation with maximum possible weight bearing is recommended for all patients with lower extremity trauma. Ankle pumping exercises are also encouraged as soon as clinically feasible (68).

2- Patients with a high risk of VTE (as when the patient remains in bed for more than 3 days peri - operatively or in multiple trauma patients) the use of pharmacological VTE prophylaxis is recommended (68).

3- LMWH, LDUH, Warfarin, ASA, and Dabigatran can be used. For patients at simultaneous high risk of bleeding

and VTE events, the use of mechanical VTE prophylaxis is recommended over pharmacological VTE prophylaxis (65-67).

### 3.3.4. Lower Extremity Orthopedic Trauma Treated with Limb Immobilization (Splinting, Casting)

Early ambulation with maximum possible weight bearing is recommended for all patients with lower extremity trauma. Ankle pumping exercises are also encouraged as soon as clinically feasible. Pharmacological VTE prophylaxis is not recommended for patients with isolated lower limb injury treated with immobilization (cast or splint), however it is recommended for patients with lower limb injury treated with immobilization (cast or splint) and previous history of VTE (68). Pharmacological VTE prophylaxis is recommended for patients with lower limb injury treated with immobilization (cast or splint) and prolonged (> 3d) delay in ambulation and/or weight bearing (67, 69). LMWH, LDUH, Warfarin, ASA, and Dabigatran can be used and prophylaxis must be continued for the whole duration of immobilization.

## 4. Discussion

The recommendations provided in this review are based on the available literature. Given the lack of high quality evidence in many clinical situations, the surgeons' judgment has still a crucial role in translating the recommendations to clinically appropriate actions.

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