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## Article 1

# Anticoagulation in orthopaedic practice

## Abstract

Venous thromboembolism is a known complication following fractures and surgery. The incidence in orthopaedic surgeries is higher than in other specialities. Proper post procedural anticoagulation will help prevent most thromboembolic events. Several guidelines have been published directing the use of anticoagulation, most optimal agent to use and duration. The decision to anticoagulate must be based on a case-by-case basis considering patient factors as well. The following review article attempts to address these issues regarding anticoagulation in orthopaedic practice.

## Introduction

Deep vein thrombosis (DVT) with or without ensuing pulmonary embolism is a complication of any surgery. The risk for venous thromboembolism increases with orthopaedic surgery than with other surgical procedures with the incidence of DVT ranging up to 40% to 60% in major orthopaedic surgery. [1]

This increase can be attributed to the factors that contribute towards the pathophysiology of hypercoagulability that are seen in orthopaedic procedures. These include use of tourniquet, immobilization and bed rest leading to blood stasis, surgical manipulations of the limb that cause endothelial vascular injuries, increase in prothrombotic factors such as fibrinogen, factor V111 associated with multiple trauma, use of polymethylmethacrylate (PMMA) bone cement that increases hypercoagulability etc.

Other patient related factors that increase the risk of venous

thromboembolism (VTE) include age, obesity, varicose veins, family history of VTE, thrombophilia's, combined oral contraceptives, hormone replacement therapy, pregnancy and puerperium and underlying malignancies. These patients are at increased risk for thromboembolic events.

Randomized clinical trials have concluded that the rates of venographic documented DVT and proximal DVT, 7 to 14 days after major orthopaedic surgery in patients who did not receive any VTE prophylaxis are approximately 40% to 60% and 10% to 30%, respectively. [1]

Hypercoagulability can persist for six weeks after a hip fracture, while venous function remains significantly impaired for up to 42 days following hip fracture surgery. [2,3] VTE can occur up to three months after total knee and hip arthroplasty. [4] With routine VTE prophylaxis in orthopaedic patients symptomatic VTE within three months has been reduced to 1.3% to 10%. [4]

All this points to the very important aspect of offering postoperative thromboprophylaxis to patients with orthopaedic procedures.

## Thromboprophylaxis

Thromboprophylaxis can be two folds, mechanical and pharmacological.

Mechanical thromboprophylaxis includes early mobilization, graduated compression stockings (GCS), intermittent pneumatic compression device (IPCD) and venous foot pumps (VFP). Although they play a contributory role in helping to reduce thrombotic events there is no strong evidence that mechanical prophylaxis alone is adequate to prevent VTE.

Pharmacological agents used in thromboprophylaxis include Aspirin, Unfractionated Heparin,

Low Molecular Weight Heparin (LMWH) (enoxaparin, dalteparin, nadroparin, tinzaparin) Fondaparinux, Newer oral anticoagulants – (Rivaroxaban, Dabigatran, Apixaban) and Vitamin K antagonists such as Warfarin.

## Guidelines

Many guidelines [ACCP guideline of 2012, American Association of Orthopaedic Surgery (AAOS) guidelines (2007), SIGN guidelines (2010, updated in 2015) and NICE guidelines (2018)] have addressed thromboprophylaxis in orthopaedic surgeries and agree on most aspects of treatment options. [5,6,7,8]

### Aspirin

Although Aspirin is recommended and has been used in VTE thromboprophylaxis, all guidelines suggest that in the presence of other effective agent, mostly LMW Heparins, use of Aspirin is to be discouraged.

### Warfarin

Warfarin is an age-old anticoagulant which has been in use since 1954. It inhibits the gamma

carboxylation of Vitamin K dependent clotting factors II, VII, IX and X. Since the factors that are already formed are in the circulation of the patient and need to decay it takes about 72 hours after the initiation or change in dose of warfarin for the maximum effect to be seen. Thus a patient who is started on warfarin will have the full expected effect in 72 hours (3 days). Warfarin therapy is monitored with INR and a dose that achieves a target range of INR 2- 3 is suggested as adequate dose. The initial period up to adequate anticoagulation needs to be covered with LMWH.

### Unfractionated and Low Molecular Weight Heparins

Unfractionated Heparin can be administered subcutaneously or intravenously. The subcutaneous administration requires higher doses as it is less bioavailable. UFH is recommended by the latest ACCP guidelines for VTE prophylaxis in patients undergoing THR, TKR or hip fracture surgery. [9] The therapeutic effect is monitored by APTT and the Heparin dose is titrated according to the APTT value.

Due to the necessity of monitoring by laboratory tests, both warfarin and UFH are less convenient than LMWH.

LMW Heparins are derived by enzymatic or mechanical breakdown of the UFH molecules and have the most action against anti Xa. There is no need for monitoring of treatment except in a few rare instances (renal failure, very obese, pregnancy). Monitoring is by measuring anti- Xa levels. All the guidelines and many studies have concluded that LMWH is the best drug to be used in VTE thromboprophylaxis. Renal function tests and a Full Blood Count must be done prior to commencement. Dose adjustments can be made in renal impairment while severe renal failure is a contraindication for administration. The prophylaxis dose varies for each preparation. For example a daily SC 40 mg of Enoxaparin is adequate as thromboprophylaxis.

When LMWH is used for VTE prophylaxis in patients undergoing total hip replacement, it is recommended to start either 12 hours or more

pre-operatively or 12 hours or more post-operatively. [10] Suggested duration of anticoagulant treatment by ACCP is for minimum 10 to 14 days and up to 35 days. [5]

During hospitalization, the use of dual prophylaxis with an IPCD device for at least 18 hours daily along with an antithrombotic agent is recommended. Doppler ultrasonography (DUS) screening before hospital discharge is not recommended for asymptomatic patients. [5]

NICE guidelines suggest LMWH for 10 days and then aspirin for another 28 days or LMWH for 28 days in combination with anti-embolism stockings until discharge for patients undergoing elective THR. [11] For patients undergoing elective TKR, they suggest aspirin (75 mg or 150 mg) for 14 days, or LMWH for 14 days in combination with anti-embolism stockings until discharge. [11]

### **Fondaparinux**

Fondaparinux is a synthetic pentasaccharide which also has anti-Xa activity which is higher than LMWH. It is given as a subcutaneous injection at a dose of 2.5 mg daily. The latest ACCP guidelines recommend fondaparinux as a method of VTE prophylaxis for patients undergoing THR, TKR or hip fracture surgery.

### **Other oral anticoagulants**

Rivaroxaban is an orally administered direct inhibitor of activated factor X (Xa). It was found to be more effective than enoxaparin in preventing VTE after THR or TKR in phase III clinical trials. Rivaroxaban is administered in a fixed daily oral dose of 10 mg for VTE prophylaxis after elective THR and TKR. [12] The latest ACCP guidelines recommend rivaroxaban as a method of VTE prophylaxis in patients undergoing THR and TKR.

It is not recommended for hip fracture surgery as it has not been evaluated in this scenario.

Dabigatran is an orally administered antithrombin inhibitor. It is recommended for VTE prophylaxis after THR and TKR at a dose of 150 mg and 220 mg daily, starting with a half dose given soon after surgery. As with Rivaroxaban it has not been evaluated in hip fracture surgery and therefore not recommended in this event.

Apixaban is also a direct factor Xa inhibitor used in VTE prophylaxis following THR and TKR. Given at a daily dose of 2.5 mg twice daily starting 12 to 24 hours after surgery, it can be continued for 35 days for THR and 12 days for TKR. [13] Apixaban is also not recommended after hip fracture surgery.

### **Anticoagulation non THR/TKR patients**

Current ACCP guidelines suggest no VTE prophylaxis rather than prophylaxis for patients undergoing knee arthroscopy. However, in the presence of other risk factors for DVT such as a history of VTE, malignancy etc. thromboprophylaxis may be initiated.

The incidence of DVT with short leg cast immobilization is in the range of 4% to > 16%. [14,15] Therefore, current ACCP guidelines suggest no VTE prophylaxis in patients with isolated lower-leg injuries requiring leg immobilization.

For patients undergoing spine surgery who do not have additional VTE risk factors, thromboprophylaxis is not necessary. However, on a patient-to-patient basis if additional risk factors are present thromboprophylaxis with UFH or LMWH can be offered.

In spinal cord injury, if acute bleeding is suspected mechanical thromboprophylaxis is the option. With time if no bleeding or haematoma is ascertained by MRI thromboprophylaxis can be initiated.

Upper limb surgeries do not require thromboprophylaxis unless prolonged local anaesthesia has been used.

## Conclusion

The risk of bleeding is present with all anticoagulants specially when over anticoagulated. It is imperative that proper doses be administered. Monitoring must be done with laboratory tests (for UFH, Warfarin ) with proper titration of doses .

Renal function tests, liver function tests, FBC and coagulation screen must be done prior to initiation of treatment.

VTE associated with orthopaedic procedures is preventable and all measures need to be taken to prevent it in the at risk patient.

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