

THROMBOPROPHYLAXIS IN ORTHOPAEDICS

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ABSTRACT

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INTRODUCTION

Significant advances have been made in the field of orthopaedics in the recent years. Better surgical techniques, less invasive approaches and non-acceptance of joint problems as part of the ageing process has led to an increasing number of people seeking orthopaedic consults and interventions. The excellent surgical and postoperative care has obviously translated to significant positive impact on quality of life for such patients. However, apart from the immediate postoperative period, it may be said that there is a lack of importance given to complications in the later period. One of these complications is venous thromboembolism (VTE) which may remain silent initially but can be associated with high morbidity and mortality in orthopaedic patients.

Patients undergoing major orthopaedic surgery including total hip replacement (THR), total knee replacement (TKR) and surgery for hip and pelvic fractures are considered the patient group with the highest risk for VTE. In the absence of thromboprophylaxis, the incidence of proximal deep vein thrombosis (DVT) in the first one to two weeks in these patients is as high as 10–30%. But if an active search for a thrombus is made by venography, the incidence can be even higher reaching a level of upto 60%, although some of these cases may not be associated with the classical symptoms. In the current era, prevention of such VTE episodes with appropriate thromboprophylaxis may

be considered as the part of a complete care for the patient.

WHY DO ORTHOPAEDIC PATIENTS DEVELOP CLOTS?

Rudolf Virchow suggested three reasons for the development of thrombosis in any patient—stasis, hypercoagulability and endothelial damage (figure 1). If each of this is taken into consideration, it may be speculated that lower limb orthopaedic problems are at the highest risk of thrombosis compared to many other surgical or medical patients. For example, the very fact that the patient has a lower limb pathology needing surgical intervention would mean that their mobility is limited causing stasis of the blood in the legs. In addition, immobility which is the principle behind advising a plaster cast for fractures and in occasional postoperative state would increase the risk of stasis further. Postoperatively, many patients are advised not to weight-bear and walk with crutches which will similarly increase the risk. Considering hypercoagulability as a cause, although it may be uncommon for Indian population to have hereditary thrombophilia, there are several other reasons, why the blood in these individuals may be “thicker”. Levels of coagulation factors increase with age (clearly the reason why the most common cause of death is arterial or venous thromboembolism). In addition, the presence of co-morbid factors like diabetes and



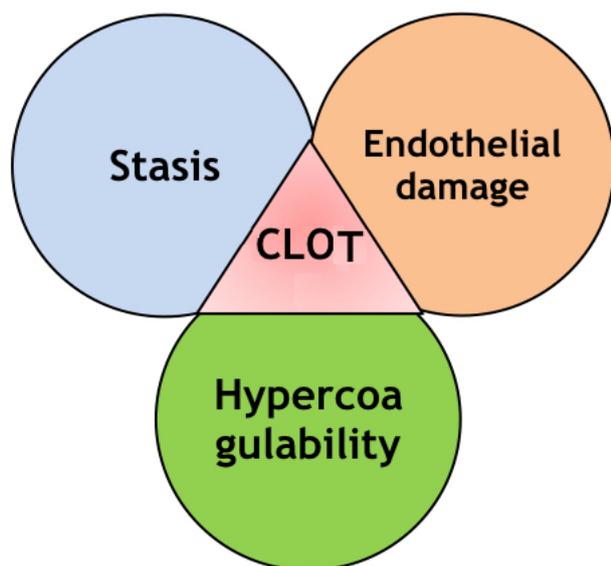


FIGURE 1

hypercholesterolemia also increases the risk several-fold. Added to this, the current epidemic of obesity will compound the problem several-fold. Different lifestyles which have crept into the Indian household predominantly blamed on the affluence and also on the office-based work-pattern and less-active entertainment opportunities (web-based rather than outdoor) also add to the problem. Endothelial damage is quite common in these patients both from the point of view of tissue injury in trauma cases and surgical interventions. A list of the common risk factors for the development of thrombosis is given in the table 1.

THE SILENT AND PROBLEM VTE

Thromboprophylaxis is routine in most of the hospitals in the United Kingdom which has translated to nearly 0% incidence fatal PE especially after THR or TKR. Despite this, there are reports of symptomatic DVT in 1-10% of patients within 3 months after surgery. Asymptomatic DVT is common and affects the majority of the patients. Even in the absence of thromboprophylaxis, many of these silent thrombi may resolve spontaneously without causing any long-term sequelae. However, there are subsets of patients who continue to form the thrombi probably due to a combination of various reasons mentioned before. The important thing to bear in mind in these situations is that the symptoms may develop several days after the surgery. Patients may attribute the leg swelling from DVT as an 'expected' symptom after a lower limb surgery. Also, if the limb is in a plaster cast, leg oedema may be overlooked as a clinical sign. Similarly pain developing in the leg after surgery may be considered 'part of the process' and may be discounted. It would

be useful to explain to the patient that any new pain which has developed in the days further away from the surgery needs assessment.

WHICH ANTICOAGULANT TO CHOOSE

There are two types of anticoagulants currently available—subcutaneous injections which are the heparins—unfractionated or low molecular weight formulations or fondaparinux; and the oral types—vitamin K antagonists like warfarin or the newer direct oral anticoagulants. The mechanisms of action of these agents are given in the figure 2.

Until very recently, it was standard to use low molecular weight heparins as standard prophylaxis in all cases (doses based on weight in table 2). Although warfarin has been around for longer period of time, the need to monitor the anticoagulation intensity with INR has dissuaded its use in many patients (and also not surgeon preference). The arrival of the newer oral anticoagulant has made the scenario much more convenient. We have agents which are as effective as low molecular weight heparins but can be taken orally which is a definite advantage. Several trials published in the last 10 years have shown this efficacy. The key references for these trials are given in the table 3 for interested readers. Also the characteristics of the currently available newer oral anticoagulants are given in table 4. It should be noted that the newer drugs are only licensed for hip and knee replacement surgeries.

TIMING OF THROMBOPROPHYLAXIS

The most effective preventive measure against VTE development in orthopaedic patients is early mobilisation, which should be encouraged regularly, if possible by the surgeon, junior doctors, nurses and also encouragement from families. When it comes to pharmacological thromboprophylaxis after surgery, guidelines do state when a patient should be commenced on. In most cases, it is 6 hours after the surgery. In the author's opinion, this decision about commencement should be undertaken by a senior surgeon after careful assessment of the patient's clinical state, review of any contraindications, the operative site and drainages and mobility status. Too early commencement can make the patient lose confidence in a pharmacological measure which is intended as prophylaxis rather than treatment. It is also useful to measure the leg circumference to be as a baseline so that any changes can be objectively documented and appropriate radiological investigations can be undertaken if necessary (very rarely, thromboprophylaxis can fail).

DURATION OF THROMBOPROPHYLAXIS

Once again, the guidelines should be followed as below

- Total knee replacement — 14 days

TABLE 1. Risk Factors for Thrombosis in Orthopaedic Patients.

<p>Patient characteristics</p> <ul style="list-style-type: none"> • Age > 60 • History of or concurrent malignancy • Oestrogen therapy or pregnancy • Obesity • Varicose veins • Comorbid conditions (arthritis, cardiovascular disease) • Hereditary thrombophilia <p>Surgical characteristics</p> <ul style="list-style-type: none"> • Complicated surgery • Duration of surgery • Delay in surgery • Surgery for malignant disease • Infection of the operative site with blood stream spread <p>Perioperative characteristics</p> <ul style="list-style-type: none"> • Hydration status of the patient • Drugs—especially chemotherapy or immunoglobulins • Longer anaesthetic time • Type of anaesthesia • Epidural catheters • Indwelling central venous catheter

TABLE 2. The Low Molecular Weight Heparins and Fondaparinux Dosing.

	<50 kg	50–100 kg	>100 kg
Enoxaparin (Clexane)	20 mg	40 mg	40 mg bd
Dalteparin (Innohep)	2500 units	5000 units	5000 units bd
Tinzaparin (Innohep)	3500 units	4500 units	4500 units bd
Fondaparinux (Arixtra)	2.5 mg	5 mg	10 mg

All the agents advised to be started 6-12 hours after the surgery.

- Total hip replacement — 28 days
 - Hip fracture — on admission if no other bleeding, but stop 12 hours before surgery. Postoperatively — 28 days
 - Prolonged surgery (>60-90mins) until mobility restored
- If there is any doubt about mobility after the stipulated periods, following a discussion with the patient, it

TABLE 3. Pivotal Trials With the Newer Oral Anticoagulants in Orthopaedics.

<p><i>Hip arthroplasty/replacement</i></p> <ul style="list-style-type: none"> • Eriksson BI, <i>et al.</i> Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double blind, non-inferiority trial. <i>Lancet</i> 2007; 370: 949–956. • Eriksson BI, <i>et al.</i> Oral dabigatran versus enoxaparin for thromboprophylaxis after primary total hip arthroplasty (RE-NOVATE II). A randomised, double blind, non-inferiority trial. <i>Thromb Haemost</i> 2011; 105: 721–729. • Kakkar AK, <i>et al.</i> Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. <i>Lancet</i> 2008; 372: 31–39. • Lassen MR, <i>et al.</i> Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. <i>N Engl J Med</i> 2010; 363: 2487–2498. <p><i>Knee arthroplasty/replacement</i></p> <ul style="list-style-type: none"> • Eriksson BI, <i>et al.</i> Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the REMODEL randomized trial. <i>Journal of thrombosis and haemostasis : J Thromb Haemost</i> 2007; 5: 2178–2185. • Lassen MR, <i>et al.</i> Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. <i>N Engl J Med</i> 2008; 358: 2776–2786. • Turpie AG, <i>et al.</i> Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. <i>Lancet</i> 2009; 373: 1673–1680. • Lassen MR, <i>et al.</i> Apixaban versus enoxaparin for thromboprophylaxis after knee replacement (ADVANCE-2): a randomised double-blind trial. <i>Lancet</i> 2010; 375: 807–815.

may be advised to continue the anticoagulation until mobility is improved considerably.

PRECAUTIONS WITH EPIDURAL CATHETER

- Catheter may be inserted after 12 hours of the last dose of low molecular weight heparin has been given
- Anticoagulants can be used in the presence of an epidural catheter
- However the catheter must only be removed over 4 hours after the last dose
- There is currently no data for newer anticoagulants in this setting.

ARE THERE ANY COMPLICATIONS WITH ANTICOAGULANT USE?

Bleeding

Of course, the most worrying complication of any anticoagulant is bleeding. Daily review whilst an inpatient is necessary to identify bleeding at the

earliest. It is unusual for bleeding to develop several days after an anticoagulant has been started so search for an additional cause should be considered. It is important to bear in mind in this situation that low molecular weight heparins and the newer anticoagulants do not have a complete reversal agent which can remove the drug from the circulation rapidly as would be possible with warfarin. This fact should be discussed with the patient. In the case of warfarin, limb or life-threatening bleed should be reversed using prothrombin complex concentrates while continued but not clinically significant bleed can be managed by withholding the drug or giving vitamin K.

Rare Complications

The use of heparins (unfractionated or low molecular weight formulations) can be rarely associated with a complication called heparin-induced thrombocytopenia where the platelet count drops 5-10 days after the commencement and predisposes the patient to thrombosis despite the continued use of the anticoagulant. Hence, it is useful to check the count

Mechanism of action of anticoagulants

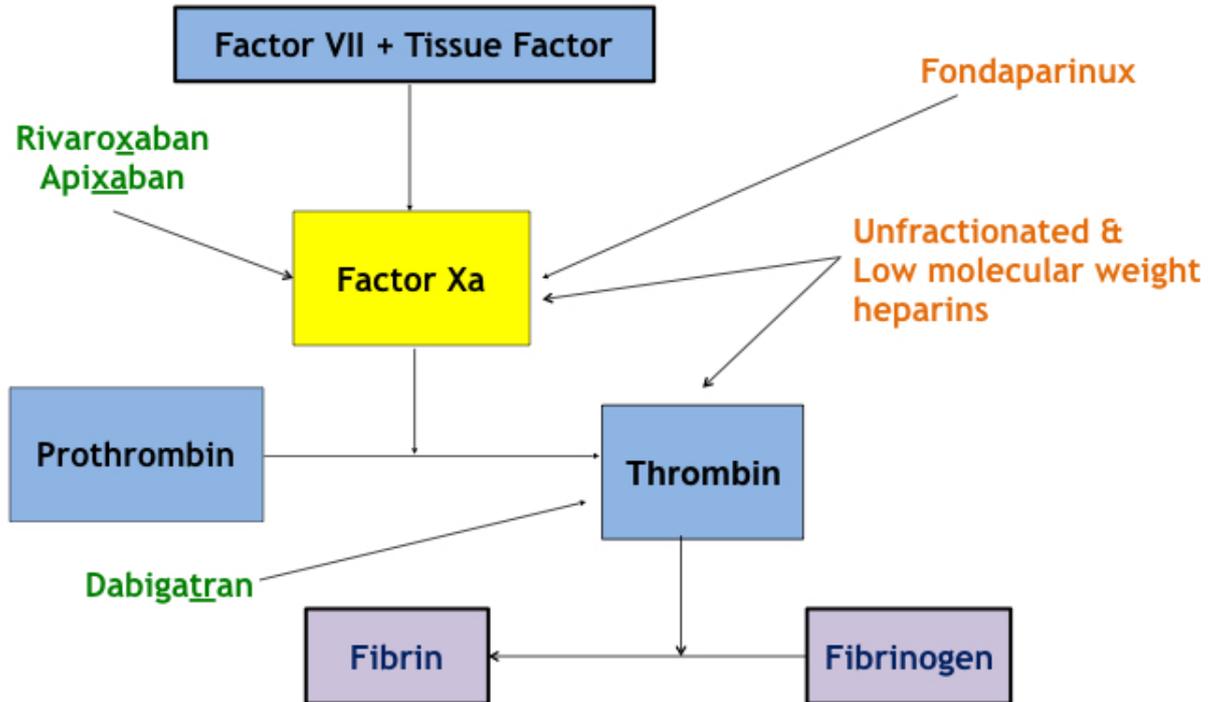


FIGURE 2

in the first 7 days after starting thromboprophylaxis with heparins. Both low molecular weight heparins and newer anticoagulants are excreted through the kidneys and hence have to be used with caution in those with moderate to severe renal impairment. It is useful to check the patient's kidney function the same time as the platelet count at the follow up visit.

Practical Issues

The need for injections in the case of low molecular weight heparin can be practically problematic in the patients who don't require staying in hospital after the initial postoperative period. Although it is routine in the western world for patients or their families to learn to inject these drugs, this practice may not be acceptable for some people. Also, antiseptic provisions are required to avoid injection-site infections and abscesses. Also disposal of the needles after use also need to be considered to avoid reuse of needles in certain areas. The correct administration of the

injection is also necessary to avoid abdominal bruising and discomfort. The patients have to be informed that heparins are made from porcine sources in case of religious preferences.

THE ROLE OF MECHANICAL THROMBOPROPHYLAXIS

The National Institute for Health and Clinical Excellence (NICE) guidelines from the UK recommend combined mechanical and pharmacological prophylaxis to reduce the risk of VTE in patients undergoing orthopaedic surgery. The various available methods are thigh-length graduated compression/anti-embolism stockings (compression provided should be approximately 18mmHg at the ankle, 14mmHg at the mid-calf point and 8mmHg at the upper thigh), intermittent foot impulse devices or pneumatic compression can be used as alternatives to stockings or in conjunction with them. They should be fitted

TABLE 4. Characteristics of Newer Oral Anticoagulants.

	Dabigatran	Rivaroxaban	Apixaban
Dose	220mg, 150 mg	10 mg daily	2.5 mg twice daily
When to start	110 mg daily 1–4 hours after surgery then 220 mg daily	6–10 hours after surgery	12–24 hours after surgery
How long to continue	TKR — 10 days THR — 28–35 days	TKR — 2 weeks THR — 5 weeks	TKR — 10 to 14 days THR — 30–35 days
Contraindications	Active bleeding Platelet count less than 50,000 Moderate to severe renal impairment Severe hepatic impairment	Active bleeding Platelet count less than 50,000 Severe renal impairment Severe hepatic impairment	Active bleeding Platelet count less than 50,000 Severe renal impairment Severe hepatic impairment

from the time of hospital admission until the stipulated duration (stockings). The mechanical methods are contraindicated in patients with peripheral vascular disease, skin grafts, gross oedema or neuropathy.

CAN ASPIRIN SUBSTITUTE FOR AN ANTICOAGULANT?

The use of aspirin as thromboprophylaxis has been a longstanding debate in the orthopaedic setting. The latest ACCP guidelines recommend the use of aspirin as thromboprophylaxis. However, there has been several arguments for and against this approach. The main proponent was the PEP trial which evaluated over 13,000 patients with hip fractures and over 4000 who underwent THR. The investigators found that the overall DVT rate was decreased by 30% and that of PE by 40% with the use of 160 mg/day of aspirin compared with placebo. The arguments against aspirin come from the fact that anticoagulants can decrease the risk of VTE by much higher levels and there were some methodological flaws with the PEP trial. Despite this, some other recent trials have suggested that the use of aspirin combined with mechanical pneumatic compression devices may be effective in some circumstances in preventing VTE. In the author's opinion, aspirin may have been a convenient choice while the only anticoagulants available were injectable forms or warfarin. With the advent of newer anticoagulants, the only place of aspirin is if cost is an issue.

OTHER PROCEDURES AND TRAUMA SCENARIOS

For knee arthroscopy, patient and surgical factors should be considered. Specific surgical factors are the duration of the procedure including the time of the use of tourniquets, whether more tissue injury may have occurred with more invasive procedures rather a diagnostic look.

In the case of soft tissue injuries (cartilage or tendon rupture) in the lower limb, it is not routine

to provide pharmacological thromboprophylaxis, but in the presence of other risk factors (not related to the current injury) and the requirement for plaster cast immobilisation, it may be advisable to prescribe it especially in the younger individuals with no contraindications.

In the case of lower limb fractures, once again, a similar policy is followed although the fact that these patients are likely to be immobile for longer and thromboprophylaxis in patients with lower-leg immobilisation can reduce clots in two-thirds, it may be considered (as suggested in the ACCP guidelines).

WHY THE RELUCTANCE TO GIVE THROMBOPROPHYLAXIS? — ADOPTING A BALANCED VIEW

Although this article detailed several reasons why an orthopaedic procedure should be followed by pharmacological thromboprophylaxis, there are several opponents to this view. Some of the reasons for this view are

- Bleeding is a visible complication which can have an impact on the postoperative outcomes in comparison with a possible risk of thrombosis
- Since coagulation is a physiological process aimed at stopping bleeding from the surgery or injury, why interfere with that process?
- Coagulation is the first step towards wound healing. Anticoagulation trials didn't always formally report the wound-healing rates in the postoperative patients
- The trials in some cases went looking for a thrombus—routine ultrasound following hip or knee surgery rather than scanning after a symptom suggestive of deep vein thrombosis had developed. Is this appropriate? Will a thrombus not develop in all patients in the lower limb after a major surgery in the vicinity?

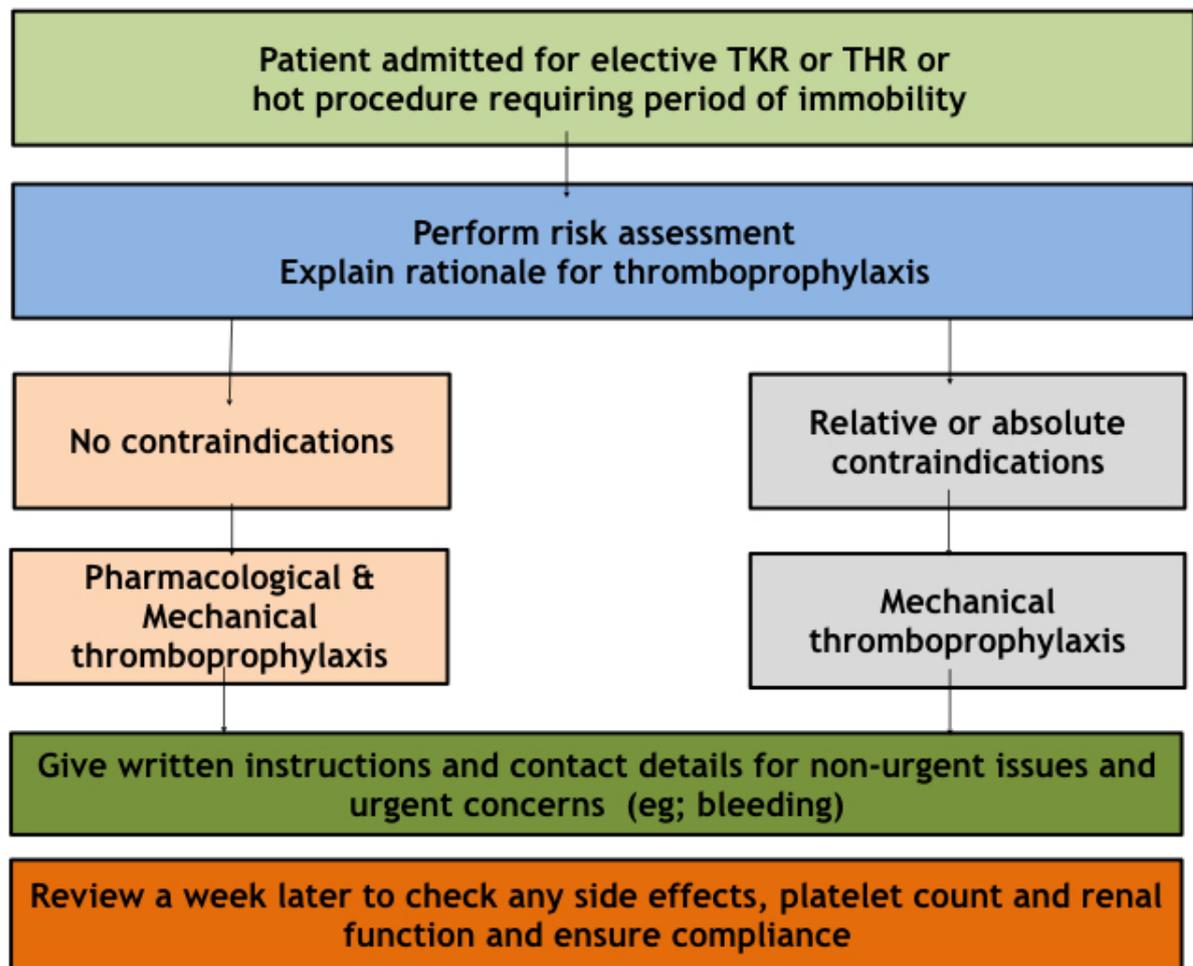


FIGURE 3

- Thromboprophylaxis guidelines are created by haematologists who may not clearly understand the several detailed aspects of the surgeries and techniques involved.

A practical approach to orthopaedic thromboprophylaxis is given in figure 3.

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