*Orthopaedic Surgery* (2010), Volume 2, No. 2, 81–85

GUIDELINE

# Prevention of venous thromboembolism after major orthopaedic surgery

Chinese Orthopaedic Association

Because of its high incidence, venous thromboembolism (VTE) after major orthopaedic surgery is one of the main causes of death of patients in the perioperative period, and also an important cause of unexpected hospital deaths. In patients undergoing major orthopaedic surgery, taking effective preventive measures can not only reduce the risk of occurrence of VTE and relieve the suffering of patients, but also has been confirmed by a large number of pharmaceutical economic studies to decrease the overall expense[1,2]. In order to improve prevention of orthopaedic-related VTE and to standardize preventive methods, this 'Chinese Guideline for Prevention of Venous Thromboembolism after Major Orthopaedic Surgery' has been specially formulated. In this guideline, 'major orthopaedic surgery' refers specifically to total hip replacement (THR), total knee replacement (TKR), and hip fracture surgery (HFS). This guideline provides only academic guidance, and implementation of its recommendations in the hospital setting must be tailored to each patient's specific medical condition.

## Overview

VTE: this term refers to abnormal coagulation of venous blood, resulting in complete or incomplete vascular obstruction; thus it is a type of venous return disorder[3]. It includes two different clinical manifestations which occur at different stages and in different parts of the body: deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE).

DVT: although this can occur in veins in various parts of the body, it most often affects the deep veins of the lower limbs, and commonly occurs after major orthopaedic surgery. Because proximal DVT of the lower limbs (popliteal vein or its proximal parts) is the main source of PTE, prevention of DVT can reduce the risk of occurrence of PTE.

**Address for correspondence** Gui-xing Qiu, MD, Department of Orthopaedic Surgery, Peking Union Medical College Hospital, 1 Shuaifuyuan Hutong, Beijing, China 100730 Tel and Fax: 0086-10-65296081; Email: zhaosk1981@yahoo.cn

Received: 31 July 2009; accepted 3 September 2009
DOI: 10.1111/j.1757-7861.2010.00068.x

PTE: this refers to disorders of pulmonary circulation and respiratory function caused by thrombi from the venous system or right heart obstructing the pulmonary artery or its branches[4,5], and is one of the important causes of orthopaedic perioperative death.

Epidemiology of VTE after major orthopaedic surgery: a survey of the incidence of DVT after THR, TKR, and HFS from 19 orthopaedic centers in seven Asian countries by phlebography showed the incidence of DVT to be 43.2% (120/278) [6]. In China, the results of a multi-center study by Qiu *et al*. showed that the incidence of DVT after THR and TKR was 30.8% (16/52) in a group in which no preventive measures were instituted, and 11.8% (8/68) in a group in which they were[7]. Yu *et al*. reported an incidence of DVT of 20.6% (83/402) after THR and 58.2% (109/187) after TKR[8]. Lv *et al*. reported that the incidence of DVT after THR and TKR was 47.1% (24/51)[9]. Lu *et al*. reported that the incidence of DVT after was 30.6%femoral shaft fracture surgery and 15.7% after HFS[10].

## Risk factors for VTE

Any factors resulting in venous injury, intravenous blood stagnation and hypercoagulability of the blood are risk factors for VTE, major orthopaedic surgery being one of the very high-risk factors[11,12]. Other common secondary risk factors include old age, trauma, a previous history of VTE, obesity, paralysis, lying in bed, tourniquet application during surgery, general anesthesia, malignant tumor, central venous cannulation, and chronic venous valvular insufficiency. Rare primary risk factors are antithrombin deficiency and others. The more risk factors that are present, the greater is the occurrence risk of VTE. Therefore when major orthopaedic surgery is accompanied by other risk factors, the overall risk escalates. The classification of risk of VTE after orthopaedic surgery is shown in Table 1[13,14].

## Measures for prevention of VTE after major orthopaedic surgery

For patients undergoing major orthopaedic surgery, conventional methods for prevention of venous

**Table 1** Risk of VTE for patients after orthopaedic surgery

| Risk grade | Risk factors |
|---|---|
| Low risk | Operating time < 30 min, no other risk factors, <40 years old |
| Moderate risk | Operating time < 30 min, no risk factors, 40–60 years old<br>or operating time < 30 min, and one or more risk factors<br>or operating time > 30 min, no risk factors, <40 years old |
| High risk | Operating time < 30 rain, and one or more risk factors, >60 years old<br>or operating time > 30 min, and one or more risk factors, 40–60 years old |
| Extremely high risk | Major orthopaedic surgery, severe trauma, and spinal cord injuries<br>or operating time > 30 min, and some risk factors, >40 years old |

thrombosis are needed. These methods include primary prevention, physical prevention and drug prevention.

### *Primary preventive measures*[15,16]

(i) the surgical technique should be as delicate and subtle as possible to avoid venous intimal injury; (ii) the use of a tourniquet should be standardized; (iii) the injured limb should be elevated after surgery to assist venous return; (iv) conventional education concerning venous thrombosis should be given, and the patients should be encouraged to turn over frequently, do early functional exercise, get out of bed and be active, take deep breaths and cough; (v) appropriate amounts of supplementary fluids should be administered during the intraoperative and postoperative periods, and the patients should be encouraged to drink more water to avoid dehydration; and (vi) the patients should be advised to improve their lifestyles in regard to stopping smoking, quitting drinking alcohol, and controlling blood glucose and lipids.

### *Physical preventive measures*

Plantar venous pumps, intermittent pneumatic compression devices and gradient compression elastic stockings can accelerate the venous blood flow of the lower limbs, reduce blood retention, and reduce the incidence of postoperative DVT through applying simple mechanical principles. In addition, drug prevention is also recommended. The application of physical prevention alone is not enough even for patients with coagulation disorders and a high risk of bleeding. Once the risk of bleeding has been reduced, drug prevention is still recommended. For patients whose injured limb is unavailable or not capable of undertaking physical prevention measures, these measures should be used on the healthy limb. Routine screening for contraindications should be performed before application.

Physical prevention measures are not appropriate for the following situations: (i) congestive cardiac failure, pulmonary edema or severe edema of the lower limbs; (ii) DVT of the lower limbs, thrombotic phlebitis or PTE; and (iii) intermittent pneumatic compression devices and gradient compression elastic stockings are not suitable for such local abnormalities of the lower limbs as dermatitis, gangrene, recent skin transplantation surgery, severe vascular atherosclerosis or other ischemic vascular diseases of the lower limbs, or severe malformations of the lower limbs.

### *Drug preventive measures*

For patients with a risk of bleeding, the relative merits of prevention of DVT of the lower limbs versus the dangers of increasing the risk of bleeding should be assessed.

#### *Unfractionated heparin*

Unfractionated heparin can reduce the risk of DVT of the lower limbs, but it has a narrow therapeutic window. When it is used, great importance should be attached to the following factors: (i) routine monitoring of the activated partial prothrombin time to adjust the dosage appropriately; (ii) monitoring of the platelet count to prevent hemorrhage caused by heparin-induced thrombocytopenia; and (iii) long-term use of heparin may lead to osteoporosis.

#### *Low molecular weight heparin*

Characteristics of low molecular weight heparin: (i) the dosage is based on body weight (ii) it is easy to administer subcutaneously; (iii) there are few severe bleeding complications; and (iv) there is no need for conventional hematological monitoring.

#### *Factor Xa inhibitors*

These have a wide therapeutic window and fixed dose, there is no need for conventional hematological monitoring and the complication of heparin-induced thrombocytopenia is avoided.

(i) Indirect Xa factor inhibitors for subcutaneous injection are effective in reducing the incidence of DVT of the lower limbs after major orthopaedic surgery, fondaparinux sodium being more effective than enoxaparin. The safety of fondaparinux is similar to that of enoxaparin.

(ii) Direct Xa factor inhibitors (e.g. rivaroxaban) are easy to use, being administered orally once a day, and have fewer interactions with drugs and food. Compared with low molecular weight heparin, they can significantly reduce the occurrence of VTE without increasing the risk of bleeding.

*Vitamin K antagonists*

At present, vitamin K antagonists (e.g. warfarin) are used in the clinic most frequently. Because of their low price, they can be used for the long-term prevention of DVT of the lower limbs. Their main disadvantages are: (i) a narrow therapeutic dose range; (ii) large differences between individuals in the dosage required, necessitating conventional monitoring and dosage adjustments to keep the international normalized ratio (INR) within the range of 2.0–2.5 (the risk of bleeding is increased if the INR > 3.0); and (iii) vulnerable to the influence of drugs and food.

*Precautions required during drug prevention*

1. Each drug has its own instructions for use, precautions and side effects. As a result of differences in the mechanisms, molecular weights, units, and dosages, as well as in their anti-Xa and anti-II factor activity, only one drug can be used for prevention of DVT, drug substitution is not recommended.
2. Pay particular attention to the dosage for patients with renal and hepatic dysfunction. Low molecular weight heparin and fondaparinux sodium are not suitable for patients with severe renal dysfunction.
3. Intraspinal hematoma is rare, but has serious consequences. Therefore, the use of anticoagulant drugs should be briefly avoided before and after intraspinal operations (such as surgery and lumbar puncture).
4. For patients undergoing regional block anesthesia or analgesia (lumbar plexus, etc.), attention should be paid to drug use, drug withdrawal, and extubation time. Clopidogrel should be withdrawn 7 days before nerve block; aspirin should be withdrawn 5 days before surgery; where low molecular weight heparin is being used, extubation should be performed no sooner than 18 h after the last dose; where heparin is being used, extubation should be performed no sooner than 8–12 h after the last dose, and the next dose should be administered only 2–4 h after extubation; where warfarin is being used, epidural anesthesia is not recommended and extubation must be performed no sooner than 48 h after the last dose; and fondaparinux sodium, because of its long half-life, is not recommended for use before epidural anesthesia or analgesia.

*Contraindications to drug prevention*

(i) Absolute contraindications include: recent active bleeding and coagulation disorder; osteofascial compartment syndrome; serious head trauma or acute spinal cord injury; platelet count $< 20 \times 10^9$ /L; heparin-induced thrombocytopenia (where this is present, heparin and low molecular heparin are absolutely contraindicated; and in pregnant women, warfarin is absolutely contraindicated.

(ii) Relative contraindications include: previous intracranial hemorrhage; previous gastrointestinal bleeding; acute intracranial injury or tumor; platelet count decreased to $20–100 \times 10^9$/L; and patients with rheumatoid retinopathy.

## Specific guidelines for prevention of DVT after major orthopaedic surgery[17]

### *THR and TKR*

Please refer to the relevant content in the section entitled "Measures for prevention of VTE after major orthopaedic surgery" for primary and physical prevention measures.

Some specific guidelines for drug prevention are as follows:

1. Do not use low molecular heparin within the 12 h prior to surgery. Inject the standard dose of low molecular weight heparin subcutaneously 12–24 h after surgery (2–4 h after removal of an epidural catheter), or inject half of the standard dose 4–6 h after surgery and return to the full standard dose the following day.
2. Administer 2.5 mg of fondaparinux sodium subcutaneously, starting 6–24 h after surgery (2–4 h after removal of an epidural catheter).
3. Administer 10 mg of rivaroxaban subcutaneously, starting 6–10 h after surgery (6–10 h after removal of an epidural catheter).
4. In the case of vitamin K antagonists (e.g. warfarin), starting the night after surgery, administer the dose already established by monitoring, to maintain the INR within 2.0–2.5, definitely no greater than 3.0.
5. Low doses of unfractionated heparin, aspirin, and dextran are not recommended for use on their own, nor is the routine preventive placement of an inferior vena caval filter to prevent PTE.
6. For THR or TKR patients with a high risk of bleeding, plantar venous pumps or intermittent pneumatic compression devices are recommended for physical prevention. Once the high risk of bleeding has decreased, prevention with drugs can also be adopted.

### *HFS*

Please refer to the relevant content in the section entitled "Measures for prevention of VTE after major orthopaedic surgery" for primary and physical prevention measures.

Some specific guidelines for drug prevention are as follows:

1. For patients undergoing surgery within 12 h of injury, administer a standard dose of low molecular weight heparin subcutaneously 12–24 h after surgery (2–4 h after removal of an epidural catheter); or inject half the standard dose 4–6 h after surgery, and return to the full standard dose the following day.

   Another option is to administer 2.5 mg of fondaparinux sodium subcutaneously, starting 6–24 h after surgery.

   A third option is to use vitamin K antagonists (e.g. warfarin), in which case, starting before surgery or the night after surgery, administer the dose already established by monitoring, to maintain the INR within 2.0–2.5, definitely no greater than 3.0.
2. For delayed surgery comprehensive prevention should be started from the day of hospital admission. Low molecular weight heparin should be withdrawn 12 h before surgery. Because fondaparinux sodium has a long half-life, it is not recommended for use before surgery. Where anticoagulation drugs have been used prior to surgery, epidural anesthesia is contraindicated. Postoperative preventive medication is the same as for patients undergoing surgery within 12 h of injury.
3. Rivaroxaban: no indications are available.
4. For HFS patients with a high risk of bleeding, plantar venous pumps or intermittent pneumatic compression devices are recommended for physical prevention. Once the high risk of bleeding has decreased, prevention with drugs can also be adopted.

### *Time of initiation and duration of DVT prevention*

Because the first 24 postoperative hours are the high risk period for perioperative DVT after major orthopaedic surgery, prevention should be instituted as soon as possible. However, the sooner drug prevention is introduced after surgery, the higher the risk of bleeding will be. Therefore, the time to initiate DVT drug prevention should be determined by weighing up the risk and benefits.

After major orthopaedic surgery, the increased coagulability of blood may persist for up to 4 weeks, while the increased risk of postoperative DVT may last for 3 months. The duration for which anticoagulation prevention is required is longer in the case of THR than it is for TKR[18–20]. For the patients subjected to THR, TKR, and HFS, it is recommended that the duration of drug prevention be at least 10 days, and extendable to 11–35 days.

## Several notes on this guideline

1. Please read the product instructions provided by pharmaceutical and medical device manufacturers before taking any preventive measures.
2. Use a comprehensive combination of primary prevention, physical prevention, and drug prevention measures in patients with a high risk of VTE. Use the drug prevention measures carefully for patients with a high risk of bleeding.
3. The use of aspirin alone is not recommended for prevention of VTE.
4. Closely observe the side effects when using anticoagulant drugs. According to the specific circumstances, institute the relevant laboratory examinations or invite the appropriate departments for consultation to undertake prompt treatment if a severe bleeding tendency appears.
5. Because the use of drugs in combination may increase the possibility of bleeding complications, combinations are not recommended.

Even when the above recommendations have been followed, DVT and PTE may still occur. In this event, the relevant departments should immediately be invited for consultation in order to make a prompt diagnosis and institute appropriate treatment.

## Disclosure

A Chinese version of this guideline has been published in the Chinese Journal of Orthopaedics, 2007, 27: 790–792.

## References

1. Ollendorf DA, Vera-Llonch M, Oster G. Cost of venous thromboembolism following major orthopedic surgery in hospitalized patients. Am J Health Syst Pharm, 2002, 59: 1750–1754.
2. Geerts WH, Pineo GF, Heit JA, *et al*. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest, 2004, 126 (3 Suppl.): S338–S400.
3. Mosby. Mosby's Dictionary of Medicine, Nursing & Health Professions, 7th ed. St. Louis: Mosby, 2006; 115–116.
4. Wang C. Pulmonary Embolism. Beijing: People's Medical Publishing House, 2003; 125–429.
5. Lu WX, Wang C. Pulmonary Circulation Disease. Beijing: People's Medical Publishing House, 2007; 463–490.

**6.** Piovella F, Wang CJ, Lu H, *et al*. Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography. J Thromb Haemost, 2005, 3: 2664–2670.

**7.** Qiu GX, Yang QM, Yu NS, *et al*. A multi-center study on deep vein thrombosis prevention of low limbs after hip and knee surgery with low molecular heparin. Zhonghua Gu Ke Za Zhi (Chin), 2006, 26: 819–822.

**8.** Yu NS, Chen DF. Several issues concerning venous thromboembolism after joint replacement. Zhonghua Gu Ke Za Zhi (Chin), 2005, 25: 44–48.

**9.** Lu HS, Xu B. Deep vein thrombosis of lower limbs after joint replacement. Zhonghua Gu Ke Za Zhi (Chin), 1999, 19: 155–156.

**10.** Lu Y, Ma BT, Guo RL, *et al*. Deep vein thrombosis risk in traumatic orthopaedic patients. Zhonghua Gu Ke Za Zhi (Chin), 2007, 27: 693–698.

**11.** Heit JA, O'Fallon WM, Petterson TM, *et al*. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. Arch Intern Med, 2002, 162: 1245–1248.

**12.** Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation, 2003, 107 (23 Suppl. 1): S9–S16.

**13.** Caprini JA. Thrombosis risk assessment as a guide to quality patient care. Dis Mon, 2005, 51: 70–78.

**14.** Geerts WH, Heit JA, Clagett GP, *et al*. Prevention of venous thromboembolism. Chest, 2001, 119 (1 Suppl.): S132–S175.

**15.** Snow V, Qaseem A, Barry P, *et al*. Management of venous thromboembolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med, 2007, 146: 204–210.

**16.** Segal JB, Streiff MB, Hofmann LV, *et al*. Management of venous thromboembolism: a systematic review for a practice guideline. Ann Intern Med, 2007, 146: 211–222.

**17.** Geerts WH, Bergqvist D, Pineo GF, *et al*. Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical practice guidelines (8th Edition). Chest, 2008, 133 (6 Suppl.): S381–S453.

**18.** Dahl OE. Continuing out-of-hospital prophylaxis following major orthopaedic surgery: what now? Haemostasis, 2000, 30 (Suppl. 2): S101–S105.

**19.** Agnelli G, Mancini GB, Biagini D. The rationale for long-term prophylaxis of venous thromboembolism. Orthopedics, 2000, 23 (6 Suppl.): S643–S646.

**20.** Agnelli G, Taliani MR, Verso M. Building effective prophylaxis of deep vein thrombosis in the outpatient setting. Blood Coagul Fibrinolysis, 1999, 10 (Suppl. 2): S29–S35.