—Review—

Venous Thromboembolism in Major Orthopedic Surgery

Tokifumi Majima and Yasushi Oshima

Department of Orthopaedic Surgery, Nippon Medical School, Tokyo, Japan

Venous thromboembolism (VTE) is one of the most important complications in orthopedic surgery. Deep-vein thrombosis occurs frequently after surgery but has few clinical symptoms. The emboli formed may cause pulmonary thromboembolism, which is associated with a high mortality rate. The cost of medical care is doubled when VTE develops after surgery. Thus, it is imperative to focus on preventing VTE after major orthopedic surgery. The prevention method should be selected after considering the balance between VTE risk and bleeding risk attributable to drug prophylaxis. Physical prophylaxis, drug prophylaxis, or both should be selected. When performing VTE prophylaxis, the risks and merits of prophylaxis must be made clear to patients. (J Nippon Med Sch 2021; 88: 268–272)

Key words: venous thromboembolism, deep-vein thrombosis, pulmonary thromboembolism, major orthopedic surgery

Introduction

Venous thromboembolism (VTE) is one of the most important complications in orthopedic surgery. Deep-vein thrombosis (DVT) occurs frequently after surgery. It is generally thought that DVT formed in a deep vein produces thrombi that are released from the blood vessel wall. These can potentially occlude the pulmonary artery and may cause pulmonary thromboembolism (PTE), which sometimes leads to sudden death. VTE has few clinical symptoms, which complicates early diagnosis. PTE has a high mortality rate; however, prevention of PTE is cost effective. Therefore, we need to focus on VTE prevention.

The Venous Thromboembolism Prevention Guidelines published by the Japanese Orthopedic Association (JOA) in 2008 cover all VTE types, including asymptomatic VTE. With subsequent accumulation of evidence on VTE and development of new prophylaxis methods, it was recognized that the important outcomes for patients are not those for asymptomatic VTE but rather those for symptomatic VTE, lethal PTE, and bleeding complications of prophylaxis with anticoagulant drugs. The need to improve understanding of these conditions led to publication of the Symptomatic Venous Thromboembolism Prevention Guidelines by the JOA in 2017, which changed the target to symptomatic VTE.

The article reviews VTE in major orthopedic surgery, including total hip arthroplasty (THA), total knee arthroplasty (TKA), and hip fracture.

Is the Prevalence of VTE Increasing?

In the past, particularly before 2000, the incidence rate of VTE was lower in Japan than in Europe and the United States. The incidence of VTE after hip and knee arthroplasty or hip fracture surgery was lower in Asian than in white populations[1,2]. According to an epidemiological survey by Sakuma et al., the incidence of DVT in Japan was 1.16/10,000 in 2006, which was approximately twice the rate for PTE[3].

PTE was reported in 30% to 64% of consecutive autopsy cases in Europe and the United States[4–6]. The rates reported in Japan are similar. Kumasaka et al. estimated that the rate of PTE cases in Japan in 1996 was 0.28/10,000[7]. Sakuma et al. reported that the rate of PTE cases in 2006 was 0.62/10,000. This rate is more than double the rate published for the 10-year period from 1996 to 2006. They also reported that the number of PTEs diagnosed as the cause of death before autopsy increased from 13.7% in 1987 to 22.1% in 1998[8]. These reports indicate that VTE is increasing in Japan.

Correspondence to Tokifumi Majima, MD, PhD, Department of Orthopaedic Surgery, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: t-majima@nms.ac.jp
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Why is VTE Prevention Necessary?

It is generally thought that a DVT in a deep vein can be released from the blood vessel wall and may potentially occlude the pulmonary artery and cause PTE. VTE, DVT, and PTE, are considered pathological conditions. The incidence rates of VTE in THA, TKA, and hip fracture without prophylaxis are 42% to 57%, 41% to 85%, and 50%, respectively. The incidence rates of lethal PTE in THA, TKA, and hip fracture without prophylaxis are 0.1% to 0.4%, 0.2% to 0.7%, and 2.5% to 7.5%, respectively[9,10].

Ota et al.[11] reported that 52% of patients with acute PTE had symptoms of shock. Of these, 56% die. Furthermore, sudden death within 1 h of onset accounted for 43% of all deaths[11]. These findings highlight the importance of preventing lower-limb DVT, the source of embolism, in the effort to prevent onset of symptomatic PTE.

In a matched case-control, economic health study of 4,717 patients with TKA, THA, and hip fracture, we found that the cost of medical care is doubled when VTE develops[12].

These facts regarding the incidence of VTE without prophylaxis, clinical course of PTE, and medical costs indicate that we must focus on preventing VTEs in major orthopedic surgery.

Trends in Overseas Guidelines

The clinical guidelines of the American Academy of Orthopedic Surgeons (AAOS) on the prevention of symptomatic PTE in patients who underwent THA and TKA in 2007 focused on preventing VTE and avoiding bleeding complications by using anticoagulant drugs[13]. These guidelines are more cautious than the American College of Chest Physician (ACCP) guidelines with respect to administration of anticoagulant therapy. In 2011, new AAOS guidelines for prevention of symptomatic VTE were published and called for elimination of bias regarding the conflict of interest (COI). In these guidelines, the term VTE disease advocated that is severe to require readmission related to VTE[14]. Additionally, routine postoperative screening with venous ultrasonography (US) of the lower leg is not recommended. This was based on the evidence that there was no significant difference in the incidence of symptomatic PTE between groups who were and were not screened with US.

Up to 2008, ACCP guidelines targeted all types of VTEs, including asymptomatic VTEs, for prevention. After the 2008 ACCP Guidelines, numerous reports were published that documented increased bleeding complications. It is unknown whether PTE incidence can be suppressed. Thus, the ACCP 2008 guidelines have been criticized[15]. The 9th edition of the ACCP Guidelines limited the prevention target to symptomatic VTE in 2012. This change was attributed to efforts to eliminate the COI and prioritize benefits to patients who received preventive care. It is believed that the important outcomes for patients are not those for asymptomatic VTE but those for symptomatic and lethal PTE with bleeding complications. As a result, the latest ACCP Guidelines (9th Edition) are more cautious about the use of anticoagulant drugs[16]. Thus, internal medicine and orthopedic guidelines agree in many instances. Both guidelines recommended anticoagulant drugs for preventing bleeding complications.

New JOA Guidelines

Guidelines for preventing PTE/VTE in Japan were published in February 2004 by a joint committee composed of representatives from related academic societies. At the time of publication of the 2004 Joint Guidelines, warfarin and unfractionated heparin were the only anticoagulants covered by insurance for VTE prophylaxis. After clinical trials in Japan for prevention of VTE in orthopedic surgery (suppression of onset), fondaparinux was released in 2007 and enoxaparin (low-molecular-weight heparin) was released in 2008. These prophylactic treatments were covered by insurance. In 2007, the AAOS published guidelines[13] on preventing symptomatic PTE after joint replacement. These guidelines were cautious regarding anticoagulant therapy. Therefore, it became necessary to convey new information to JOA members. In July 2007, the JOA PTE/DVT Prevention Guideline Revision Committee started work. In November 2008, the JOA published the VTE Prevention Guideline. Contrary to the original intention of the 2008 JOA guidelines, these were used as the basis for the dispute; as a result, the guidelines themselves were the subject of criticism. In response to trends in guidelines published in the United States, and based on the current status of prevention of symptomatic VTE in orthopedic practice in Japan, new guidelines were published by the JOA in 2017. In these revised guidelines, the target of prevention was changed to symptomatic VTE. The JOA guidelines were prepared after considering the ACCP 2012 and AAOS 2011 guidelines. Aspirin, an antiplatelet drug, was adopted as a recommended drug in the ACCP and AAOS guidelines. However, because aspirin is not approved as a VTE prophylaxis drug in Japan, the new Japanese guidelines do not recommend it.

Practice of VTE Prevention in Major Orthopedic Surgery

The aim of symptomatic VTE prevention is the reduction of the three Virchow factors. To reduce stagnation of blood flow, several measures have been recommended, including shortening the period of preoperative bed rest, selecting a suitable method of anesthesia, reducing anesthetic dose and operation time, avoiding tourniquet use, using mechanical prevention methods (wearing elastic stockings and intermittent pneumatic compression device [IPCD]), starting lower-limb active exercise early, and early walking. To suppress increased blood coagulation ability, anticoagulants are used and intramedullary pressurization during surgery is avoided. To reduce damage to vascular endothelium, it is possible to control intraoperative and limb positions and avoid intramedullary pressurization and use of tourniquets. Conversely, none of these prophylaxis measures have been shown to be effective or safe for symptomatic VTE.

Inexpensive and relatively low-risk basic preventive measures, such as shortening the preoperative bed rest period, early lower-limb active exercise, and early walking should be performed as aggressively as possible after surgery. In practice, we need to consider the balance between VTE risk and the risk of bleeding with anticoagulant drugs in individual patients and choose physical or drug prophylaxis, or both.

For prevention, risk factors of symptomatic VTE need to be evaluated. A history of symptomatic VTE is a strong risk factor of symptomatic VTE[14,17]. The incidence of perioperative symptomatic PTE in patients older than 86 years was almost 2.5 times that of younger patients. Obesity is a risk factor for VTE, owing to decreased fibrinolytic activity. Women with a body mass index (BMI) of 29 or higher had a higher incidence of PTE (odds ratio: 2.9) than did women with a BMI of less than 21[18]. Bed rest reduces active motion of the lower leg muscles, thus causing stagnation of venous blood flow and VTE. Bed rest for 1 week or longer is associated with a higher incidence of VTE than is bed rest shorter than 1 week[19]. Surgery for hip fracture more than 48 h after injury was associated with a significantly higher incidence of DVT than surgery within 48 h after injury[20]. Congenital deficiencies of antithrombin, protein C, protein S, and antiphospholipid syndrome are risks for VTE. VTE incidence in patients with malignant tumors was 5.4% to 7.8%[21,22]. The incidence of VTE in patients after chemotherapy for malignant tumors was 12.6%[23].

THA and TKA

In THA or TKA, the incidence of asymptomatic DVT with use of low-molecular-weight heparin (LMWH) is halved (RR, 0.50; 95% CI, 0.43-0.59), as compared with no prophylaxis. The incidence rate of symptomatic VTE was reported to be 1.3% with the use of LMWH. However, there was no evidence that incidence of symptomatic PTE was significantly reduced (RR, 0.58; 95% CI, 0.22-1.47). There was also no significant increase in the incidence of major bleeding with the use of LMWH (RR, 0.81; 95% CI, 0.38-1.72)[16].

An IPCD for VTE prophylaxis should be routinely applied in all patients who undergo THA and TKA. Mechanical VTE prophylaxis is the most appropriate VTE prevention in patients for whom pharmacological prophylaxis is contraindicated. However, patients with acute thrombophlebitis, congestive heart failure, pulmonary edema, or limb ischemia caused by peripheral vascular disease should not receive mechanical VTE prophylaxis. Many studies have reported that mechanical devices are effective for VTE prophylaxis[24–27].

The AAOS guidelines (revised in 2011) propose a combination of drug prophylaxis and physiotherapy, but the recommended drug was not specified[14]. Each prophylaxis usage and selection of the type of anticoagulant modalities should be decided in consultation with the patient. Both drug and physical prophylaxis are recommended for patients with a history of VTE. The balance between VTE and bleeding risks of anticoagulant drugs should be considered when selecting the optimal prophylaxis.

The following are suggested in the Japanese guidelines. THA and TKA are surgical procedures with a high risk of symptomatic VTE. Physical prophylaxis or pharmacological prophylaxis should be performed or used in combination. For patients with a history of VTE, it is advisable to use a combination of physical and drug prophylaxis.

Surgeons should carefully consider indications for pharmacological prophylaxis in patients with a high risk of bleeding. The preventive method should be selected after considering the balance between VTE risk and bleeding risk associated with drug prophylaxis.

Hip Fracture

Symptomatic and lethal VTEs occur frequently in hip fracture. In prospective clinical trials conducted from 1980 to 2002, the postoperative asymptomatic DVT and PTE incidences were 40% to 60% in patients without thrombosis prevention or in the placebo group, 23% to

30% in proximal DVT, and 0.3% to 7.5% in lethal PTE[28–30]. The incidence of symptomatic VTE during the 3 months after surgery in patients with hip fractures who received anticoagulant therapy was 1.3% to 8.2%[31–33].

In Japan, there were a few reports on the frequency of VTE in hip fractures. The incidence of DVT-positive findings on venography was 61.3%[34]. In the case of hip fracture, there was a risk of developing VTE immediately after injury. It is thus necessary to prevent VTE before surgery.

The following are consensus statements of the Japanese guideline committee: immediately after injury, patients must wear elastic stockings and undergo active ankle exercise, unless contraindicated. When IPCD is used, start as soon as possible after injury. It is desirable to perform surgery as early as possible after injury and start weight-bearing walking as early as possible to prevent symptomatic VTE. It is recommended to use edoxaban, enoxaparin (LMWH), fondaparinux, low-dose unfractionated heparin, and warfarin (dose adjustment, PT-INR, 1.5-2.5) for prophylactic anticoagulant therapy.

Surgeons should consider preoperative use of unfractionated heparin if the waiting period is longer. In patients with low body weight and decreased renal function, reduce the dose of VTE prophylaxis drugs or refrain from administration. Surgeons should consider refraining from drug prophylaxis if the risk of bleeding is high. The ACCP Guidelines (9th Edition) specify the duration of prophylactic anticoagulant administration recommended for long-term prevention up to 35 days[16]. In Japan, no clinical trials have investigated administration of edoxaban, enoxaparin, or fondaparinux for 15 days or longer, and the efficacy and safety of administration for 9 days or less or 15 days or longer have not been investigated.

Surgeons should consider indications for IPCD prophylaxis in patients with a high risk of bleeding. Regarding IPCD, the ACCP Guidelines (9th Edition)[16] recommend that a portable, battery-powered IPCD with a usage time recorder be used daily for 18 h or longer. There is no evidence in Japan for the usage time of IPCD. The consensus statements of the Japanese guideline committee for IPCD recommended it to be installed and used continually, and as much as possible. The ACCP Guidelines (9th Edition)[16] recommend a combination of anticoagulant therapy and IPCD during hospitalization. Although there is no evidence in Japan, anticoagulant combination therapy is recommended if it can be safely performed along with IPCD.

Importance of Informed Consent

For symptomatic VTE prophylaxis, the following five points must be explained to patients: a) the definition of VTE, b) the purpose of prevention, c) the consequences of prevention and risks associated with it, d) the existence of other preventive measures, and e) the possible consequences of lack of prevention. After gaining understanding, the medical staff and patient should agree on whether to implement the prevention method. For example, if anticoagulant therapy is recommended for prophylaxis, prophylaxis may reduce (but not eliminate) the risk of developing symptomatic VTE but may cause bleeding complications. There is a risk of bleeding as well as surgery. There are mechanical preventive measures other than anticoagulant therapy, such as IPCD. If prevention is not performed, the risk of developing VTE may increase. We must make these points clear to patients. Although informed consent requires considerable labor and time, it is an important clinical duty of surgeons.

Conclusion

Patients with DVT have few clinical symptoms and the condition is therefore difficult to diagnose early. PTE from DVT is associated with high mortality, but prevention is cost effective. As a result, we need to focus on VTE prevention.

For each patient, we need to consider the balance between VTE risk and bleeding risk attributable to anticoagulant prophylaxis. Physical prophylaxis, drug prophylaxis, or both, are recommended.

Conflict of Interest: None.

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