Thromboprophylaxis in orthopaedic surgery
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General introduction and outline of the thesis
GENERAL INTRODUCTION AND OUTLINE OF THE THESIS

Thromboprophylaxis after major orthopaedic surgery is common practice nowadays, as the risk of venous thromboembolism after total hip and knee arthroplasty is well recognized. This thesis describes the use of thromboprophylaxis modalities by the Dutch orthopaedic departments over a period of ten years. Several uncertainties in orthopaedic thromboprophylaxis still remain regarding smaller procedures, immobilization and upper extremity surgery.

In this thesis a few of these topics are addressed: the incidence of venous thromboembolism after arthroscopic cruciate ligament reconstruction, lower extremity amputation, plaster cast immobilization and shoulder arthroplasty.

History of thromboprophylaxis

The relationship between surgery and venous thromboembolism (VTE) has been described as early as 1937. Heparin was initially used to prevent post-operative thrombosis in surgical patients. In the beginning of the nineteen-eighties low molecular weight heparin (LMWH) was found to be superior to unfractionated heparin.

Vitamin K antagonists (VKA) were used as therapeutic agents for venous thromboembolism from 1954 onward. Three meta-analyses have shown LMWH to be more effective than Vitamin K antagonists. Currently, LMWH is still the preferred thromboprophylactic agent according to the leading ACCP (American College of Chest Physicians) guidelines.

The synthetic pentasaccharide fondaparinux, a selective factor Xa inhibitor, was introduced in 2002 in Europe. A pooled analysis of the ACCP, based on moderate-quality evidence, revealed that 12 fewer symptomatic VTE per 1,000 would be expected with the use of fondaparinux compared to placebo. However, fondaparinux comes with an increase of 12 major bleeds per 1,000 compared to placebo. Fondaparinux shows a substantial reduction in asymptomatic deep venous thrombosis (DVT) compared to LMWH, but no difference was observed in the incidence of symptomatic DVT and pulmonary embolism (PE). There was a substantial increase in bleeding requiring reoperation associated with the use of fondaparinux (RR 1.85; 95 % CI, 1.1-3.11), but the results failed to demonstrate a difference in nonfatal major bleeding (RR 1.35; 95 % CI, 0.89-2.05).

Currently, three new oral antithrombotic agents (NOACs) are also available for the prevention of venous thrombo-embolism after hip and knee arthroplasty. Rivaroxaban and apixaban are factor Xa inhibitors, dabigatran is a direct inhibitor of thrombin. They were introduced on the Dutch market in 2008 (dabigatran and rivaroxaban) and 2011 (apixaban). To compare these agents in an indirect way, a few network meta-analyses and systematic reviews with pooled effects have been carried out. Rivaroxaban and apixaban were more effective than dabigatran regarding the prevention of VTE. One meta
analysis did not show any difference in the risk of bleeding, while another meta analysis showed more bleeding events in the rivaroxaban group and less bleeding events in the apixaban group in comparison to the LMWH enoxaparin.

**Thromboprophylaxis and blood management in the Netherlands**

To assess changing patterns in Dutch Orthopaedic thromboprophylaxis practices, three surveys were conducted. The first survey, performed in 2002, showed that evidence-based national guidelines were not properly adhered to.\(^{11,12}\) During the following years, more attention was given to thromboprophylaxis and new pharmacological modalities, such as oral anticoagulants, were introduced. The results of the second (2007) and third (2012) survey are described in chapter 2 and 3 respectively.

When using pharmacological thromboprophylaxis after orthopaedic surgery, a major concern is the possibility of an increase in bleeding complications. Blood transfusions are frequently required after hip and knee arthroplasties. It is important to reduce the need for allogeneic blood transfusions, to minimize the adverse events associated with blood transfusions. This can be achieved by increasing the patient's haemoglobin level preoperatively, by reducing blood loss and by auto-transfusion. In chapter 4, the use of blood saving modalities in Dutch orthopaedic departments during a 10-year follow-up period is described.

**International guidelines regarding thromboprophylaxis**

Because many VTE's occur after discharge, orthopaedic surgeons may have a falsely low perception of the thrombosis rate in their practice. Why do surgeons have different views on the use of aspirin, heparin and Vitamin K antagonists when considering the same body of evidence? Chapter 5 aims to compare eleven (inter)national guidelines on thromboprophylaxis from different countries, and to interpret their differences.

**Arthroscopic cruciate ligament reconstruction**

Arthroscopically assisted cruciate ligament (ACL) reconstruction is common practice these days and is performed during day-care or short-stay surgery. After routine arthroscopy without ligament reconstruction the risk of symptomatic VTE appears to be rather low (1.5 - 2%).\(^{1,13}\) The risk on asymptomatic DVT ranges from 5-18% depending on the screening method and population studied.\(^{13-17}\) Arthroscopically assisted arthroscopic anterior cruciate ligament reconstruction is considered less traumatic to an extremity than joint arthroplasty, but more traumatic than uncomplicated arthroscopic procedures such as meniscectomy, where no osseous drilling is required. There is a possibility that the incidence of thromboembolic events may actually be increased following knee ligament surgery vs. routine arthroscopy. Moreover, ACL reconstruction can be associated with haemarthrosis and postoperative leg swelling and therefore
complicate the accurate clinical diagnosis of deep venous thrombosis. There is, however, surprisingly little data on the incidence of venous thromboembolism after arthroscopic cruciate ligament reconstruction. Therefore, we conducted a study to determine the incidence of deep venous thrombosis after ACL reconstruction, as detected by compression ultrasound. The results are presented in chapter 6.

**Lower extremity amputation**

Lower extremity amputations are mostly performed in (diabetic) patients with end-stage vascular disease\(^{18}\), with very high mortality rates up to 53% in the first year following surgery.\(^{18-23}\) Uncertainty exists, however, about the incidence of DVT in the amputated leg, causing subsequent pulmonary embolism and death. Since most of these patients present with acute vascular occlusion prior to amputation, a state of hypercoagulability is very likely. Also, increased incidences of venous thrombosis prior to amputation have been reported (7.3-8.3%).\(^{24-25}\) In the study, described in chapter 7, we prospectively determined the presence of deep venous thrombosis and pulmonary embolism both pre- and postoperatively by means of duplex-ultrasonography and ventilation-perfusion lung scintigraphy.

**Plaster cast immobilisation**

Generally, immobilisation is considered a major risk factor for VTE. A meta-analysis regarding six studies concerning leg plaster cast immobilisation, showed a highly significant and clinically relevant reduction in asymptomatic events with LMWH prophylaxis compared to placebo or untreated controls (RR 0.58, CI 0.39-0.86, \(p= 0.006\)).\(^{26}\) In chapter 8, a case of pulmonary embolism during trial hip plaster cast immobilisation to simulate lumbosacral fusion and a review of literature are presented.

**Shoulder arthroplasty**

There is no consensus regarding the need for perioperative thromboprophylaxis following shoulder arthroplasty\(^{1}\). To establish whether thromboprophylaxis is warranted, first the incidence of thrombosis and pulmonary embolism after shoulder arthroplasty needs to be investigated. In chapter 9 a systematic review of literature regarding symptomatic thrombosis after shoulder arthroplasty is described. Currently there are two studies regarding the incidence of symptomatic DVT following shoulder arthroplasty. In both studies, thromboprophylaxis by means of aspirin and intermittent pneumatic compression was used.\(^{27-28}\) The aim of our study, described in chapter 10, is to establish the incidence of asymptomatic venous thrombo-embolic complications as detected by bilateral complete compression ultrasonography of both legs and the operated arm after shoulder arthroplasty without thromboprophylaxis.
REFERENCES