Thromboprophylaxis in orthopaedic surgery

Mulder, Marieke

Citation for published version (APA):
Ten-year follow-up on orthopedic thromboprophylaxis in the Netherlands

DATA III survey

MC Struijk-Mulder, M.D.¹, HB Ettema, M.D. PhD¹
HR Büller, Prof. M.D.², CCPM Verheyen M.D. PhD¹

¹ Department of Orthopedic Surgery and Traumatology, Isala Klinieken, Zwolle, the Netherlands
² Department of Vascular Medicine, Academic Medical Centre, Amsterdam, the Netherlands

Submitted
ABSTRACT

Introduction
Our previous surveys in the Netherlands have revealed that a wide variation exists in protocols on orthopedic thromboprophylaxis. The DATA III survey (Dutch Antithrombotic Treatment for Arthroplasties) was performed to assess the current use of thromboprophylactic modalities.

Materials and methods
All departments of orthopedic surgery in the Netherlands were sent a follow-up survey; data obtained were compared to the results of two surveys performed 5 and 10 years earlier and current national guidelines.

Results
The response rate was 92 out of 108 departments (85%). All used extended pharmacological thromboprophylaxis following total hip arthroplasty (4-6 weeks) and total knee arthroplasty (2-6 weeks). Low molecular weight heparin (LMWH) was used most frequently (79% of all departments). Ten years earlier, VKA treatment was the predominant prophylaxis (79%). For daycare surgery and arthroscopies either no prophylaxis was given (68% and 56% respectively), or a single shot of LMWH (23% and 39% respectively). After anterior cruciate ligament reconstruction, 89% of the departments used prophylaxis. Patients treated with a below knee plaster cast, received thromboprophylaxis in 88% of the departments (compared to 50% ten years ago).

Conclusions
The use of (extended) pharmacological prophylaxis after arthroplasty of the hip and knee is common practice in the Netherlands. Although currently low molecular weight heparin remains the most commonly used thromboprophylactic agent, the new oral anticoagulants are now used in 25% of departments. There is a significant increase in the use of thromboprophylaxis during plaster cast immobilization and in the use of extended thromboprophylaxis after ACL surgery.
INTRODUCTION

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are common complications after orthopedic surgery, especially after arthroplasties joint replacement and fracture surgery.[1] Dutch national guidelines [2] have not been adhered to in the past.[3] Since then more attention has been drawn to thromboprophylaxis and new pharmacological modalities have been introduced. We conducted a survey to assess the present situation. The results were also compared to two prior surveys, performed 5 and 10 years earlier [3,4] and with current national guidelines.[5] In the first study, we focused on hip and knee arthroplasties. In the second and current third study, additional questions were asked regarding daycare, short stay, fractures, and plaster cast immobilization.

MATERIALS AND METHODS

A questionnaire focussing on orthopedic departmental protocols for peri-operative thromboprophylaxis was sent to all 110 Dutch orthopedic departments in Dutch hospitals. It was tailored to fit similar ones conducted in 2002 and 2007 [3,4]. Practice profile, and current choice, initiation, and duration of thromboprophylaxis after several orthopedic procedures were assessed. Response rates in 2002 and 2007 were 79% (87 out of 110 departments) and 84% (81 out of 96 departments). The power analysis showed that, with a confidence interval of 95%, the response of at least 86 departments was required for our analysis.

In 2012, a package with the questionnaire, a cover letter, and a stamped addressed envelope was sent to all Dutch orthopedic departments. Non-respondents were sent a reminder after 4 months, and were contacted by telephone if necessary. Categorical data and dichotomous variables were summarized as percentages of the responding departments by means of SPSS 21 (New York, United States).

RESULTS

94 out of 110 departments ultimately answered the questionnaire properly. Two clinics were excluded, because they reported to perform spine surgery exclusively. The adjusted response rate therefore was 85%. All respondents stated that they had a specific departmental protocol on thromboprophylaxis.
### Table 1. In hospital and extended thromboprophylactic regimens used after arthroplasties of hip and knee in the studied orthopedic departments, N(%) 

<table>
<thead>
<tr>
<th>Arthroplasty</th>
<th>In hospital only</th>
<th>In hospital and extended thromboprophylaxis</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LMWH</td>
<td>LMWH+ VKA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Fondaparinux</td>
<td>Rivaroxaban</td>
<td>Dabigatran</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>2 (2) - -</td>
<td>14 (17) 69 (79) 63 (69) 0.11</td>
<td>65 (80) 6 (7) 0 0.01 *</td>
<td>12 (14) 6 (6) 0.07</td>
<td>18 (20) 5 (5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revision hip</td>
<td>2 (2) - -</td>
<td>13 (16) 70 (80) 75 (81) 0.05</td>
<td>66 (81) 6 (7) 1 (1) 0.02 *</td>
<td>11 (13) 6 (5) 0.07</td>
<td>10 (11) 2 (2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemi hip</td>
<td>7 (9) 3 (3) 1 (1)</td>
<td>12 (15) 68 (78) 83 (90) 0.05</td>
<td>61 (75) 8 (9) 0 0.02 *</td>
<td>9 (10) 6 (6) 0.31</td>
<td>2 (2) 1 (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total knee</td>
<td>2 (2) - -</td>
<td>16 (20) 69 (79) 63 (69) 0.17</td>
<td>62 (77) 6 (7) 1 (1) 0.002 *</td>
<td>12 (14) 6 (5) 0.06</td>
<td>18 (20) 5 (5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revision knee</td>
<td>2 (2) - -</td>
<td>15 (18) 70 (80) 75 (82) 0.51</td>
<td>64 (79) 6 (7) 1 (1) 0.002 *</td>
<td>11 (13) 6 (5) 0.07</td>
<td>10 (11) 1 (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemi knee</td>
<td>7 (9) 3 (3) -</td>
<td>6 (8) 68 (78) 75 (81) 0.51</td>
<td>66 (82) 6 (7) 1 (1) 0.002 *</td>
<td>10 (12) 3 (3) 0.05</td>
<td>13 (14) 1 (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> LMWH until adequate INR is reached.

<sup>b</sup> Significance of difference between 2007 and 2012 data are calculated

* P < 0.05: significant difference

1% of departments used aspirin after every arthroplasty in 2002

LMWH = low molecular weight heparin

VKA = Vitamin K Antagonist
Hip and knee arthroplasty

All departments used extended pharmacological thromboprophylaxis for total hip and total knee arthroplasties (Table 1). In 2007, low molecular weight heparin (LMWH) mono therapy had replaced vitamin K antagonist (VKA) as the predominant prophylactic method. Although in 2012, subcutaneous LMWH remains the most used thromboprophylactic agent, there seems to be a shift towards the newly introduced oral factor Xa and IIa inhibitors rivaroxaban and dabigatran, which are now prescribed by a quarter of the departments. If a LMWH is prescribed, nadroparin is most frequently used (Table 2). The majority of departments still give extended thromboprophylaxis for 6 weeks, although a trend towards a shorter period is observed (Table 3). Ten years ago, VKA were continued for 3 months in 65% of departments.

Table 2. Type of LMWH, N(%)  
<table>
<thead>
<tr>
<th>LMWH</th>
<th>2002</th>
<th>2007</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadroparin</td>
<td>57 (70)</td>
<td>66 (76)</td>
<td>64 (69)</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>16 (20)</td>
<td>17 (19)</td>
<td>21 (23)</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>5 (6)</td>
<td>4 (5)</td>
<td>7 (8)</td>
</tr>
<tr>
<td>Tinzaparin</td>
<td>3 (4)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3. Duration of extended thromboprophylaxis after arthroplasties of hip and knee in the studied orthopedic departments, N(%)  
<table>
<thead>
<tr>
<th></th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-3</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td></td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>10 (11)</td>
</tr>
<tr>
<td></td>
<td>70 (80)</td>
</tr>
<tr>
<td></td>
<td>7 (8)</td>
</tr>
</tbody>
</table>

THA = Total Hip Arthroplasty  
TKA = Total Knee Arthroplasty  
Hemi HA = Hemi Hip Arthroplasty

Fractures of the proximal femur and tibia

All departments used pharmacological prophylaxis after osteosynthesis or arthroplasty of the hip for proximal femur fractures, and after internal fixation of proximal tibia fractures during admission. Most departments gave extended prophylaxis after surgical treatment of these fractures, except for four departments. Nowadays 94% use LMWH for proximal femur fractures and 98% for proximal tibia fractures. LMWH is used slightly more frequently than fondaparinux and VKA compared to 2007. Although rivaroxaban and dabigatran are not registered for fracture surgery, respectively 2 and 1 percent of departments did administer these agents for hip hemi-arthroplasty. In fracture surgery
the same trend towards a shorter duration of thromboprophylaxis was observed, as with arthroplasty. Prophylaxis was continued for 4-6 weeks in 96%, whereas in 2007, 88% of departments gave 4–6 weeks and 9% gave 2–3 months of thromboprophylaxis.

**Initiation of treatment**

Thromboprophylaxis after hip and knee arthroplasty is preferably started post-operatively nowadays (70%); even more so than five years ago (Table 4). A significant difference is observed between 2007 and 2012 ($P = 0.002$). In total 48% of the departments start thromboprophylaxis during a well-defined time span postoperatively and 22% give it in the evening following surgery (regardless of the time of surgery).

| Table 4. Initiation of thromboprophylactic treatment after arthroplasties in the studied orthopedic departments, N(%) |
| 2002 | 2007 | 2012 |
| Preoperative |
| day before surgery | 74 (91) | 47 (54) | 28 (30) |
| day of surgery | 50 (62) | 27 (31) | 20 (21) |
| Postoperative |
| day of surgery | 7 (9) | 40 (46) | 64 (70) |
| evening of surgery | - | 21 (24) | 20 (22) |

**Day care, arthroscopy, and anterior cruciate ligament (ACL) reconstruction**

In daycare surgery (including arthroscopy of the knee), compared to ten and five years earlier, an increased number of departments did not use any prophylaxis in 2012 (Table 5). After ACL reconstruction, most departments prescribed LMWH. A trend towards a longer period of extended prophylaxis for ACL surgery is observed. In 2012 71% applies extended prophylaxis: 29% for 10-14 days, 21% for 3-4 weeks and 21% for 5-6 weeks. In 2007, 92% of the departments gave prophylaxis, but only 46% gave extended prophylaxis.

**Plaster cast immobilization (Table 6)**

During plaster cast immobilization, more departments use thromboprophylaxis presently. Patients treated with a below knee plaster cast, received thromboprophylaxis in 88% of the departments (compared to 50% ten years ago). Patients with a plaster cast above the knee were given thromboprophylaxis in 96% of cases. Prophylaxis was most frequently given by means of LMWH, which have replaced the VKA's that were used in 68% of departments in 2002.
Mechanical prophylaxis

Intermittent pneumatic compression was seldom applied and never routinely used. The previous surveys showed identical results. Graduated compression stockings (GCS) are not used by the majority of departments. In 2012 GCS were used by 8% after total hip arthroplasty during admission and 6% prolonged the use after discharge. After total knee arthroplasty, 9% used GCS during admission, and 8% continued them after discharge. These percentages are comparable to 2007. In 2002 more patients were given GCS: 20% after total hip arthroplasty and 11% after total knee arthroplasty.

CONCLUSIONS

We believe the results of these surveys are valid because of the repeated high response rate in all of the surveys. The present follow-up survey reveals that in ten years time the oral vitamin K antagonists have at first been largely replaced by the subcutaneous
Chapter 3

LMWH and its synthetic analogue fondaparinux, while lately the oral direct Xa and thrombin inhibitors rivaroxaban and dabigatran have gained popularity for the prevention of venous thromboembolic events (VTEs) in orthopedic surgery in the Netherlands. There is still some variation in protocols among different departments. The Dutch consensus document “Diagnosis, Prevention and Treatment of Venous Thrombo Embolism and secondary prevention of Arterial Thrombosis”[5] recommends thromboprophylaxis with fondaparinux, LMWH or VKA after major orthopedic surgery of the hip and knee. Generally to, a LMWH is prescribed after arthroplasty of the hip and knee; this shows that adherence the consensus is better than before.[3] Since the latest consensus originated in 2008, it does not include advices regarding the new oral anticoagulants such as rivaroxaban, dabigatran and apixaban. The newest ACCP guidelines (2012) do favour LMWH after arthroplasty and hip fracture surgery, whereas in 2004 fondaparinux was preferred. [6] Clearly, a considerable number of orthopedic departments have looked ahead and introduced the new oral anticoagulants before new national guidelines were published.

We found that LMWH is generally started post-operatively (after surgery or the evening after surgery) in the Netherlands. The Dutch guideline advises to start either pre- or post operatively while a peri-operative start is not mentioned. The ACCP guidelines advise to start either 12 h or more preoperatively or 12 h or more postoperatively rather than within 4 h or less preoperatively or 4 h or less postoperatively. This advice is mainly based on a systematic review, which concluded that a peri-operative start (2 h before to 4 h or less after surgery) is apparently more effective, but this is counterbalanced by a marked increase in risk of major bleeding in comparison with a preoperative or postoperative regimen.[7] It also appears that a preoperative start is no more effective than a postoperative start.[7] Data on blood loss are confirmed by another study that concluded that pre- and post operative start of prophylaxis result in the same total amount of blood loss, but there was a trend toward fewer blood transfusions with a postoperative start.[8]

Extended pharmacological thromboprophylaxis is standard after hip and knee arthroplasty and hip and knee fracture surgery. The Dutch guidelines recommend a period of 4-5 weeks postoperatively after hip arthroplasty and at least 10 days after knee arthroplasty. Most departments give similar extended thromboprophylaxis for both THA and TKA of 4-6 weeks. In the past 10 years a trend towards shorter-term prophylaxis can be observed in the Netherlands. While in 2002 most departments used prophylaxis with VKA for three months, in 2012 prophylaxis with mostly LMWH is continued for 2-6 weeks. There is a continuing discussion about the optimal duration a prophylaxis. Studies with short term prophylaxis combined with rapid mobilization protocols following joint replacement surgery show favourable results compared to more extended prophylaxis
[9,10] while recent ACCP guidelines advise towards a longer extended prophylaxis regimen of five weeks for all major orthopedic surgery patients. [1]

Although the Dutch guidelines state that intermittent pneumatic compression (IPC) can be used as an alternative to pharmacological prophylaxis after total knee surgery, the responders in our study did not use pneumatic compression devices. ACCP guidelines advice to use IPC as an addition to pharmacological prophylaxis during hospital stay, because adding a compression device to pharmacological prophylaxis reduced the incidence of asymptomatic DVT by more than 70%. Elastic stockings are used, but only as an adjuvant to a pharmacological regimen in the minority of departments.

The use of prophylaxis after smaller procedures such as arthroscopy of the knee or ACL reconstruction remains controversial. The risk after arthroscopy of the knee appears to be low. [11-13] ACCP guidelines do not recommend routine thromboprophylaxis in patients without risk factors, due to the low rate of VTE (1.5-2%, with 14 fewer symptomatic VTE per 1,000 expected with LMWH), combined with the potential risk for major bleeding (an additional three per 1,000). The studies cited are of moderate quality and multiple concomitant procedures were performed in the knee. Dutch guidelines recommend that in case of prolonged arthroscopic reconstructive surgery or complicated surgery and in patients with a high risk of VTE, thromboprophylaxis with LMWH can be considered. This uncertainty is reflected in the wide variation in regimens following these procedures in the responding departments.

The same applies to plaster cast immobilization. The national guidelines leave the choice to the clinician whether thromboprophylaxis is given and duration of thromboprophylaxis, because of lack of evidence. Furthermore, the ACPP consensus statement does not recommend routine prophylaxis with below-knee plaster cast immobilization. [1] Their analysis of literature, based on low and moderate level of evidence, did not show a benefit from LMWH. Patients with a high risk of VTE were excluded from these studies though. The incidence of VTE in the general population is expected to be higher than the mentioned risk of PE of 3:1000 and risk of DVT of 24:1000 without thromboprophylaxis. Even so, a meta-analysis of randomized controlled trials investigating thromboprophylaxis with plaster cast immobilization has shown a favourable effect of LMWH on asymptomatic endpoints.[14]

In summary, the use of pharmacological prophylaxis after arthroplasty of the hip and knee and also after fracture surgery around the hip and knee is common practice in the Netherlands. In general, national guidelines are properly adhered to. There is a significant increase in the use of thromboprophylaxis during below knee plaster cast immobilization.
immobilization and in the use of extended thromboprophylaxis after ACL surgery nowadays. Five years ago, the widely used VKA had been largely replaced with LMWH and fondaparinux. Although currently low molecular weight heparin remains the most commonly used thromboprophylactic agent, the new oral anticoagulants are now used in 25% of departments after hip and knee arthroplasty.
REFERENCES