

# The duration of deep vein thrombosis prophylaxis after major abdominal or pelvic surgery

David Bergqvist

Department of Surgical Sciences, Section of Vascular Surgery, Uppsala University Hospital, Uppsala, Sweden

When prophylaxis against postoperative deep vein thrombosis (DVT) started on a widespread basis, the duration for pharmacological prophylaxis was around 1 week, which was often equal to the duration of hospital stay. This was considered practical. The optimal duration, however, was never studied, but the effect of this regimen was very good although not 100% effective. There were 2 observations, which stimulated the question how long should indeed the prophylaxis continue and was 1 week really enough? The first observation, based on a large autopsy study, was that some patients died in pulmonary embolism rather late after the surgical procedure, also after more than 30 days,<sup>1</sup> indicating that some patients perhaps developed their thrombosis late in the postoperative course. The observation was supported in a clinical study, again showing that pulmonary embolism could occur late postoperatively.<sup>2</sup> The second observation was, that high risk patients after major abdominal surgery and without phlebographic thrombosis at discharge, in fact in around ¼ developed thrombosis after discharge while being in their home.<sup>3</sup> These observations indicated a risk period longer than during hospitalization, at least in some patients.

With this background the authors of this article suggested performing randomized studies to analyze whether or not prolongation or extension of prophylaxis could in some cases be of benefit and therefore indicated.<sup>4</sup> We chose first to study elective hip replacement as it is a high risk group for venous thromboembolism (VTE) and a relatively standardized surgical trauma. It was clearly shown that 1 month of prophylaxis significantly reduced the frequency of venographically proven of postoperative thrombosis compared to giving prophylaxis for the conventional 1 week.<sup>5</sup> This observation was then verified in several studies and the results have been summarized in at least

2 meta-analyses.<sup>6,7</sup> The activation of the coagulation system as well as venous emptying are still pathological after around 1 month. This has led the recent American College of Chest Physicians (ACCP) guidelines to recommend prolonged prophylaxis in patients undergoing hip surgery.<sup>8</sup>

The next group of patients that was of both practical and theoretical interest were those operated on for malignant disorders. With a similar design as in the hip arthroplasty studies we were able to show the same effect, that is a reduction of venographically proven DVT from around 12 to 5% in prolonging prophylaxis from 1 to 4 weeks in patients operated on for abdominal or pelvic malignancies.<sup>9</sup> The patients were followed for 3 months as there has been a discussion if the thrombotic process is just delayed by the extended prophylaxis and a rebound effect to be awaited. A few DVT developed after the first month, but at 3 months there was the same difference between the groups (14 and 6% respectively). There are 3 more studies on extended prophylaxis in non-orthopedic surgery, and they are now summarized and meta-analyzed in a Cochrane review.<sup>10</sup> Together they comprise around 1000 patients, and the evidence is quite clear with convincing statistical power that extending prophylaxis significantly reduces all VTE, all DVT, proximal DVT and symptomatic VTE without increasing the risk of hemorrhagic complications or mortality (TABLE).

Unfortunately 2 of the studies were stopped prematurely because lack of funding, both analyzing the effect of tinzaparin.<sup>11,12</sup> The other 2 used other low-molecular-weight heparins (LMWHs), enoxaparin<sup>9</sup> and dalteparin.<sup>13</sup> Although every LMWH should be judged as a unique pharmacological substance, there is no reason to believe that they should differ in this prophylactic respect and in fact the size and the direction of the effect

**Correspondence to:**

Prof. David Bergqvist MD, PhD, FRCS,  
Department of Surgical Sciences,  
Section of Vascular Surgery, Uppsala  
University Hospital, Akademiska  
street, 751 85 Uppsala, Sweden,  
phone: +46-18-611 46 33,  
fax: +46-18-611 46 32, e-mail:  
david.bergqvist@surgsci.uu.se

Received: March 3, 2009.

Accepted: March 4, 2009.

Conflict of interest: none declared.

Pol Arch Med Wewn. 2009;

119 (4): 192-193

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**TABLE** The effect of extending prophylaxis with low-molecular-weight heparin in patients undergoing abdominal or pelvic surgery (from Rasmussen et al.)<sup>10</sup>

Outcome	Effect size (OR and 95% CI)
all VTE	0.41 (0.26; 0.63)
all DVT	0.43 (0.27; 0.66)
proximal DVT	0.27 (0.13; 0.57)
symptomatic VTE	0.22 (0.06; 0.80)
bleeding complications	1.11 (0.62; 1.97)
mortality	1.12 (0.65; 1.93)

Abbreviations: DVT – deep vein thrombosis, OR – odds ratio, VTE – venous thromboembolism

are rather similar between the 4 studies. Only our study<sup>9</sup> included only patients with malignant diseases but also in the others such patients dominated. Unfortunately it is stated in the Cochrane review that our study evaluated patients operated on for benign and malignant disease, although it is obvious already in the title of the paper that the study deals with cancer surgery.<sup>9</sup> So the conclusion on the benefit of extended prophylaxis is clear for patients operated on for cancer in the abdomen or pelvis, it is less clear for benign disorders. There we need more studies. When analyzing pharmacological effects, using double-blind methodology is highly recommended if not mandatory. Two of the studies were open,<sup>11,13</sup> but the authors clearly state that the venographic evaluation was performed by blinded assessors. One concern is that the open study by Rasmussen has been analyzed and reported intermistically a couple of times.<sup>14</sup> Whether these analyzes led to an up-calculation of the sample size is not clear. Intermistic analyzes should ideally be planned beforehand and documented in the study protocol and this is even more important in open studies.

It may be of interest to see how the problem of extended or prolonged prophylaxis in non-orthopedic surgery is handled by the recent guidelines from the ACCP.<sup>8</sup> There is a grade 2A recommendation: “For selected high-risk general surgery patients, including some of those who have undergone major cancer surgery or have previously had VTE, we suggest that continuing thromboprophylaxis after hospital discharge with LMWH for up to 28 days be considered”.

In Sweden prolonged prophylaxis after cancer surgery in the abdominal and/or pelvic cavity is increasingly used, although not routinely in all hospitals yet. In guidelines from the National Board of Health and Welfare it is stated that “prolonged prophylaxis with LMWH in 3 further weeks may be indicated after abdominal cancer surgery, especially if there are other risk factors”. The basic recommendation is 5–10 days postoperatively so the prolonged would be 26–31 days. Those guidelines are from 2004 and in guidelines on colorectal disease (2007) the recommendation is “the prolonged thromboprophylaxis for around one month, will probably reduce the thromboembolic risk further (that is compared to one week) (good scientific evidence)”.

**CONCLUSION** In patients operated on for malignant diseases within the abdominal and pelvic cavities, extension of thromboprophylaxis to around 1 month must be strongly considered and not extending prophylaxis must be motivated and documented.

The conclusion is less clear in patients operated on for benign diseases but in the presence of additional risk factors (i.e. inherited thrombophilia, previous VTE) prolongation of prophylaxis should be considered.

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