



# The use of low molecular weight heparins for the prevention of postoperative venous thromboembolism in general surgery

## A survey of practice in the United States

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**Background.** Even though low molecular weight heparins (LMWHs) have become the standard for venous thromboembolism (VTE) prophylaxis in most European countries and Canada, it was not until recently that LMWHs were approved for use in the United States. The main objective of this study was to assess the current preferences and attitudes of United States surgeons toward the prevention of VTE with particular reference to LMWH.

**Methods.** A survey with questions relative to VTE awareness, risk factors, and prevention practices was mailed to 10,000 Fellows of the American College of Surgeons.

**Results.** A total of 1,145 (11.45%) usable questionnaires were returned. The vast majority (96%) of respondents use prophylaxis against VTE. Although LMWHs were rated first regarding efficacy and second regarding simplicity of use, conventional unfractionated heparin at fixed doses remains the preferred pharmacological agent for VTE prevention (74%), followed by 2 LMWHs: enoxaparin (34%) and dalteparin (16%). Overall, 52% of surgeons preferred physical methods over pharmacological methods when used separately and 26% of surgeons utilize combined physical-pharmacological modalities.

**Conclusions.** North American general surgeons have substantially modified their approach to VTE prevention in the last 4 years. Physical methods and unfractionated heparin remain the preferred prophylactic modalities, but LMWHs have gained rapid acceptance since their approval for use for VTE prevention in North America. Even though the results of this survey must be interpreted with caution because of the limited response rate and possible sampling bias, they

still reflect the current preferences and attitudes of North American surgeons toward prophylaxis.

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Although recent consensus conferences have provided specific recommendations regarding the use of prophylactic modalities,<sup>1-5</sup> venous thromboembolism (VTE) prophylaxis remains underutilized in the United States.<sup>6</sup> Reasons for the disparity between current clinical practice and consensus guidelines may be related to physicians' concerns about the cost and complications derived from the use of anticoagulants in surgical patients, and a possible lack of awareness of VTE as a major medical problem.<sup>7-9</sup>

Several surveys have shown evidence of wide practice variations regarding the use of VTE prophylaxis among general surgeons in different countries.<sup>10-17</sup> For example, after several meta-analyses revealed that LMWHs are at least as effective and safe as unfractionated heparin,<sup>18-22</sup> most European countries adopted them as the standard for VTE prophylaxis in general surgical patients.

The authors of this study conducted a previous survey assessing the attitudes of North American surgeons toward prophylaxis in 1993, before LMWHs were approved for use in the United States.<sup>18</sup> The objective of this study was

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to assess, by means of a nationwide survey, the current preferences and attitudes of general surgeons regarding VTE prophylaxis, with particular attention to both the development and change of practice during the last 5 years and the effects of the recent introduction of LMWH in the United States.

### Materials and methods

A multi-phase survey was sent to 10,000 Fellows of the American College of Surgeons in the United States. Phase I involved the mailing of a VTE questionnaire that assessed demographics, awareness of the condition, knowledge of risk factors, timing of prophylaxis, modalities implemented, specific prophylactic recommendations to given clinical scenarios and preferred methods of diagnosing deep vein thrombosis (DVT).

Phase II involved re-sending the questionnaire to those surgeons who did not respond to the first mailing. A third and final phase involved a repeat mailing to all non-respondents once again. Each mailing included a pre-stamped return envelope. The first phase of the mailing was completed on September 8, 1998. The second phase was completed on October 13, 1998, and the third and final phase on November 14, 1998. Statistical analysis of the results consisted of using the  $\chi^2$  test for comparing proportions of responses to each question with the level of significance, set at a p-value of less than 0.05.

### Results

The overall response rate to the questionnaire was 11% (1,145/10,000). Most surgeons (80%) indicated that they see less than 1 patient with VTE per month. However, more than 60% consider the condition to be a moderate to very serious problem among general surgical patients. A vast majority (96%) of respondents reported that they utilize some sort of prophylactic measure to prevent post-operative VTE. Of those who did not utilize prophylactic methods (4%), the main reasons for such an attitude were: considering the inci-

TABLE I.—Time of utilization of physical methods.

Methods	Preop. (%)	Intraop. (%)	Postop. (%)	Post-discharge (%)
Early ambulation	—	—	97	49
Elastic stockings	51	75	86	31
Short-leg compression	25	92	90	3
Long-leg compression	30	91	89	3
Foot compression	30	76	88	8

TABLE II.—Awareness and current use of pharmacological agents used for the prophylaxis of VTE in general surgery.

Agents	Awareness (%)	Current use (%)
Fixed doses of low-dose heparin	70	74
Enoxaparin (Lovenox®)	46	34
Aspirin	27	20
Dalteparin (Fragmin®)	25	16
Adjusted doses of low-dose heparin	11	11

TABLE III.—Time of utilization of pharmacological agents.

Agents	Preop. (%)	Intraop. (%)	Postop. (%)	Post-discharge (%)
Fixed low-dose heparin	78	39	93	10
Adjusted low-dose heparin	72	55	94	12
Lovenox	64	36	95	11
Fragmin	81	40	92	11
Aspirin	49	18	78	61

dence of VTE to be low in their own experience (4%), the risk of complications secondary to the use of anticoagulants (1%) and the high cost of currently available modalities (1%). Less than one-third of the respondents followed their patients beyond 3 months postoperatively and 34% for only 1 to 2 months postoperatively.

Those surgeons responding to the survey estimated that approximately 52% of their patients received only physical prophylaxis, 8% of patients received only pharmacological prophylaxis and 26% received a combination of both. Apart from early ambulation, recommended by 92% of surgeons, the preferred physical methods were short-leg pneumatic compression (53%), followed by elastic compression stockings (48%), long-leg pneumatic compression (43%) and foot pneumatic compression (10%). Most of these physical methods were implemented intra-

operatively and continued postoperatively (Table I). Among pharmacological agents, fixed-dose unfractionated heparin was the dominant method, selected by 75% of surgeons, followed by enoxaparin (Lovenox®), (34%), aspirin (20%), and dalteparin (Fragmin®), (16%). The degree of awareness and implementation of various pharmacological agents is shown in Table II and the timing of implementation in Table III. Surgeons who practice vascular surgery more frequently (42.5%) use enoxaparin for VTE prophylaxis than do their colleagues who perform general abdominal surgery (33%), ( $p < 0.05$ ).

Regarding familiarity with current consensus guidelines for VTE prevention, 47% of the surgeons were somewhat or very familiar with the 1986 NIH Consensus Conference,<sup>1</sup> and 31% with the American College of Chest Physicians Guidelines.<sup>5</sup> Ninety percent of the respondents were not familiar with the THRIFT Conference<sup>2</sup> or the European Consensus Conference Guidelines.<sup>3</sup>

Approximately 25% of the surgeons reported that they practice in a setting that has VTE prophylaxis protocols for surgical patients. Most of them practiced in larger hospitals and 91% followed their given protocol most of the time or always. Surgeons were requested to identify the party responsible for the "decision-making" regarding the physical methods or pharmacological agents used in their practice. Most frequently the purchasing department (44%), followed by the attending physician (33%), hospital committee (33%), pharmacy (10%), and chairman of department (2%) made the decision.

Most surgeons (58%) agreed with the statement, "low molecular weight heparins reduce the risk of heparin-induced thrombocytopenia compared to unfractionated heparin". It is interesting to note that the surgeons who disagreed with the statement appeared to be the ones who frequently performed vascular surgery.

Surgeons were asked to rate physical and pharmacological methods according to safety, efficacy, simplicity, and cost-effectiveness on a scale of 1 to 5. Tables IV, V, VI, and VII reflect the resulting hierarchy within each characteristic. Leg pneumatic devices were rated the highest in terms of safety, LMWHs were rated the highest with respect to efficacy, elastic

TABLE IV.—Score given by respondents regarding safety.

Respondents	Average	Significance
1. Leg pneumatic compression devices	4.77	1>2-7*
2. Foot pump	4.67	2>4-7
3. Elastic stockings	4.63	3>4-7
4. Fragmin	4.01	4>6-7
5. Lovenox	3.97	5>6-7
6. Low-dose heparin (unfractionated)	3.75	6>7
7. Coumadin	2.34	7<1-6

\*Means that item #1 achieved statistically higher assessment ( $p < 0.05$ ) than did all other. (2-7) methods. Scale from 1 to 5.

TABLE V.—Score given by respondents regarding efficacy.\*

Respondents	Average	Significance
1. Lovenox	4.14	1>3-7
2. Fragmin	4.13	2>3-7
3. Low-dose heparin (unfractionated)	3.93	3> 4-7
4. Coumadin	3.82	4> 6-7
5. Leg pneumatic compression devices	3.79	5>6-7
6. Foot pump	3.13	6>7
7. Elastic stockings	2.42	7<1-6

\*Scale from 1 to 5.

TABLE VI.—Score given by respondents regarding simplicity.\*

Respondents	Average	Significance
1. Elastic stockings	4.46	1>2-7
2. Fragmin	4.07	2>5-7
3. Lovenox	4.05	3>5-7
4. Leg pneumatic compression devices	3.99	4>7
5. Low-dose heparin (unfractionated)	3.91	5>7
6. Foot pump	3.91	6>7
7. Coumadin	2.26	7<1-6

\*Scale from 1 to 5.

TABLE VII.—Score given by respondents on cost-effectiveness.

Respondents	Average	Significance
1. Low-dose heparin (unfractionated)	3.93	1>2-7
2. Leg pneumatic compression devices	3.53	2>3-7
3. Elastic stockings	3.36	3>4-7
4. Foot pump	3.20	N.S.
5. Coumadin	3.14	N.S.
6. Lovenox	3.13	N.S.
7. Fragmin	3.12	7<1-3

\*Scale from 1 to 5.

stockings the highest in regard to simplicity and low-dose unfractionated heparin the highest in regard to cost-effectiveness.

TABLE VIII.—Modification in approach to venous thromboembolism prophylaxis in the past 2 years regarding physical methods.

Methods switched to	Switching from		
	Low dose Heparin (%)	Enoxaparin (Lovenox) (%)	LMWH (other) (%)
Enoxaparin (Lovenox)	57	—	—
Dalteparin (Fragmin)	26	13	9
LMWH (unspecified)	24	4	—
Low-dose heparin	—	34	36
Base	(56)	(23)	(13)

TABLE IX.—Modification in approach to venous thromboembolism prophylaxis in the past 2 years regarding physical methods.

Methods switched to	Switching from		
	Elastic stockings (%)	Pneumatic compression devices (%)	Other (%)
Pneumatic compression devices	76	—	29
Foot pump	9	66	7
Elastic stockings	—	33	10

Forty percent of the respondents had modified their approach to VTE prophylaxis over the past 2 years. Their reasons for doing so included the availability of improved pharmacological agents (67%), increased awareness of the condition (42%), improved physical methods (32%), concerns about liability (18%) and the availability of new VTE protocols and guidelines (14%). Most of the surgeons who had modified their approach to VTE prophylaxis did so by switching pharmacological agents (75%), with 52 and 22% of the respondents switching from a prior agent to enoxaparin (Lovenox®) and dalteparin (Fragmin®), respectively. The most prevalent pharmacological modification was from unfractionated heparin to a LMWH (Table VIII). With regard to physical methods of prophylaxis, one-third of the respondents switched types of physical methods used in their practice. Leg pneumatic compression devices demonstrated the greatest increase in use, with 76% of respondents switching from elastic stockings to leg pneumatic compression devices (Table IX).

Risk factors that were considered by respondents to be important for prescribing VTE pro-

TABLE X.—Most critical risk factors influencing the decision to utilize venous thromboembolism prophylaxis.

Risk factors	%
History of previous thromboembolism	89
Blood disorder	45
Length of surgical procedure	42
Anticipated immobilization	41
Cancer	41
Obesity	26
Pelvic surgery	25
Advanced age	17

TABLE XI.—Modality of venous thromboembolism prophylaxis that would be recommended for each clinical situation indicated.

Parameters	A (%)	B (%)	C (%)	D (%)	E (%)
No prophylaxis	17	2	22	1	45
Lovenox	5	21	2.4	31	2
Fragmin	4	11	2	15	2
Low-dose heparin	17	37	11	49	6
Stockings	26	31	23	33	27
IPC	61	79	62	81	36
Physical only	58	35	74	12	44
Pharmacological	7	9	4	10	3
Pharm+physical	16	55	9	77	5

IPC: intermittent pneumatic compression.

Clinical situations:

A) 55-year-old woman undergoing elective cholecystectomy through laparotomy, no other risk factors.

B) 75-year-old man scheduled for colon resection for rectal carcinoma with history of congestive heart failure.

C) 47-year-old woman scheduled for laparoscopic cholecystectomy without additional risk factors.

D) 78-year-old woman with acute cholecystitis undergoing laparoscopic cholecystectomy. Severe varicose veins and a history of deep vein thrombosis on 2 prior occasions.

E) 60-year-old man scheduled for repair of indirect inguinal hernia under epidural anesthesia and without additional risk factors.

phylaxis are presented in Table X. Other influencing factors that were not mentioned in the questionnaire, but were considered to be important by respondents, were type of surgery (14%), laparoscopic procedures (7%) and position of the patient during surgery (5%). Some respondents (9%) reported that all of their patients received routine prophylaxis without regard to risk factors or any other criteria, while 40% replied that nothing other than risk factors influenced their decision.

The responses to the seven clinical scenarios that were presented in order to identify which prophylactic modalities would be prescribed for a given surgical patient are presented in Table XI.

Regarding methods of diagnosing a suspect-

ed DVT, 90, 6, 2, and 1% of the responding surgeons stated that they would order a duplex scan, a hand-held Doppler, outflow plethysmography, and a venogram, respectively.

The most common surgical procedures performed by respondents were general abdominal surgery (81%), laparoscopic surgery (77%), colorectal surgery (75%), hernia repair (75%) and vascular surgery (39%). Most respondents (66%) practiced in hospitals with at least 200 beds, 52% had an academic appointment, 65% had been practicing for more than 10 years and more than 40% practiced in cities with a population of over 500,000.

### Discussion and conclusions

Several modalities of VTE prophylaxis such as low dose heparin, Dextran, graduated compression stockings and intermittent pneumatic compression (IPC) are known to significantly reduce the rate of postoperative VTE in general surgical patients.<sup>23-29</sup> More recently, LMWHs have been developed with prolonged half-life and better bioavailability, making them more convenient for VTE prophylaxis.<sup>30</sup> In recent studies, LMWH appear to be at least as effective as unfractionated heparin for VTE prevention in general surgery.<sup>20, 21, 31, 32</sup> Furthermore, LMWH may be associated with fewer bleeding complications and a lower incidence of heparin-induced thrombocytopenia.<sup>31</sup> For these reasons, LMWHs have practically replaced unfractionated heparin in most European countries.

Although the vast majority of responding surgeons in this study reported seeing less than 1 patient suffering from VTE per month, it is encouraging that they still considered the condition a serious problem and, accordingly, 96% utilized specific prophylaxis compared to 86% 6 years ago ( $p < 0.001$ ).<sup>18</sup> The main reason for not using prophylaxis was reported as a perceived low incidence of VTE, followed by the risk of complications associated with the use of anticoagulant prophylaxis.

The best way to determine current clinical practice and discover the true implementation of VTE prophylaxis is through studies involving medical record reviews<sup>7, 8</sup> or by audits.<sup>33-35</sup> Unfortunately, these types of studies provide

information limited to local areas, hospitals, or clinical departments. On the other hand, surveys mailed to a large number of physicians practicing in a given country reflect an overall assessment of physicians' preferences, concerns, and attitudes regarding VTE prophylaxis and not just quantitative information regarding the percentage of patients receiving prophylaxis.

Similar to our 1993 survey, fewer than 50% of the respondents were familiar with the 2 main North American consensus guidelines for VTE prophylaxis,<sup>1, 5</sup> and fewer than 10% were familiar with the European guidelines.<sup>2, 3</sup> In addition, only one-fourth of the responding surgeons practiced in a setting with specific VTE prophylaxis protocols even though the availability of written protocols has been shown to improve prophylaxis implementation.<sup>34</sup> The most critical risk factors influencing the decision to utilize prophylaxis were a history of previous VTE, blood coagulation disorders, and the duration of the surgical procedure. This reflects the fact that U.S. surgeons are well aware of at least several risk factors that are responsible for an increased risk of developing VTE.<sup>4, 5</sup>

In the United States, safety and simplicity are apparently very important factors for influencing the use of VTE prophylaxis. This is shown by the very high implementation of physical modalities, which are considered the safest and simplest, but also the least effective modality. The preferred physical methods were short-leg intermittent pneumatic compression (IPC), (53%) and elastic stockings (48%). The relatively new foot compression devices, which are effective in some orthopedic patients,<sup>36</sup> were employed by only 10% of respondents.

Cost-effectiveness seemed to be another important factor influencing a decision to choose a prophylactic method, since the preferred pharmacological agent, low dose heparin, is also considered the most cost-effective method. LMWHs were found to be the least cost-effective prophylactic method even though they were also rated the most effective method.

In the 1993 survey, the main modification in the approach to VTE prophylaxis was related to improved physical methods, whereas the results of this survey show that the majority of the surgeons (67%) modified their approach because of the availability of improved pharmacologi-

cal agents. The preferred pharmacologic methods were fixed low dose heparin (74% in 1998 and 60% in 1993) and enoxaparin (34%) (Lovenox®). It is interesting to note that dalteparin (Fragmin®), the first LMWH product approved in the United States for use in general surgery, was used by only 16% of surgeons, behind aspirin, which was implemented by 20%. This last finding is somewhat distressing, since aspirin usage has increased since the 1993 survey (17%)<sup>18</sup> despite the fact that aspirin has been found to be ineffective in preventing VTE in general surgical patients.<sup>4, 5, 37</sup>

The real efficacy of preoperatively or postoperatively initiated VTE prophylaxis remains controversial, as direct comparisons have not been conducted in general surgery.<sup>38</sup> The results of this study showed that IPC was used intra- and postoperatively, while elastic stockings were applied before the operation and continued by one-third of surgeons beyond hospital discharge. The preoperative administration of low dose heparin significantly increased from 54% in 1993 to close to 80% in this survey. Enoxaparin was given preoperatively by 64% of respondents. This is an important finding since a recent meta-analysis comparing preoperative with postoperative initiation of prophylaxis with LMWH in patients undergoing total hip replacement has reported a significant reduction of DVT when prophylaxis was initiated preoperatively.<sup>39</sup> Two Swedish studies have demonstrated that the administration of a LMWH the evening before surgery is as effective and safe as starting unfractionated heparin 2 hours before surgery.<sup>40, 41</sup>

Another controversial issue is the real need for a prolongation of prophylaxis after hospital discharge in general surgical patients. Although there is evidence that the risk of both DVT and pulmonary embolism (PE) continues after hospital discharge in general surgical patients,<sup>42-44</sup> the results of this survey indicate that only 10% of surgeons recommend heparin or LMWH after discharging a patient from the hospital.

Analysis of the different clinical scenarios confirmed that LMWHs have become the second most preferred pharmacological agent, especially for high-risk patients (Table XI). In addition, there was a trend toward increasing

the use of combined pharmacological-physical methods in high-risk patients. Interestingly, when a single method was selected, it was usually a physical method (52%). The utilization of a pharmacological method without a physical method remains very low (8%), even for moderate or high-risk patients.

This study confirms the findings of similar surveys in which physical methods of VTE prophylaxis are more popular among North American general surgeons than among their colleagues in Europe, Australia and New Zealand.<sup>16-18</sup> A recent survey addressing current practices in the prophylaxis of venous thromboembolism among surgeons performing bariatric surgery obtained very similar results to our survey, since 50% of respondents preferred low dose unfractionated heparin, followed by intermittent pneumatic compression (33%) and LMWH (13%).<sup>45</sup> Similarly, another recent observational study carried out in Canada revealed that most patients admitted to a medical surgical intensive care unit received unfractionated heparin while no patients received LMWH.<sup>46</sup> This is interesting since the latest ACCP recommendations suggested LMWH as one of the best options for high-risk patients.<sup>47</sup> Reasons for such a persistent reluctance to use newer pharmacological agents might be a fear of bleeding complications in surgical patients as well as their higher cost. This apprehension of using LMWH in surgical patients is also reflected in a recent survey of British orthopedic surgeons, wherein half of the surgeons did not use LMWH due to concerns of potential bleeding complications.<sup>48</sup> However, LMWH represent the second most common agent used, after warfarin, among Canadian orthopedic surgeons<sup>49</sup> and are becoming more frequently used in medical patients in Europe.<sup>50, 51</sup>

This survey shows that there is a noticeable increase in the use of LMWH in the United States, which has now become the second most common pharmacological method of VTE prophylaxis in general surgical patients, despite having been available for only a short period of time compared to Europe. If this trend continues, LMWH may soon replace unfractionated heparin as the most common pharmacological method of VTE prophylaxis in general surgical patients.

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