

# A Model for Perioperative Outpatient Management of Anticoagulation in High-Risk Patients: An Evaluation of Effectiveness and Safety

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## ABSTRACT

**Objective:** To assess the effectiveness and safety of a hospital-based perioperative outpatient program for patients at risk for thromboembolic complications who require temporary interruption of oral anticoagulants for dental, surgical, or diagnostic procedures.

**Methods:** A prospective cohort study was performed with consecutive high-risk patients receiving long-term oral anticoagulant therapy who required surgical procedures during a 12-month study period. High-risk patients were defined as those with recent or recurrent venous thromboembolism, atrial fibrillation and a major risk factor, one or more mechanical heart valves, or congestive heart failure with left ventricular ejection fraction less than 30%. Warfarin was discontinued 5 days before the procedure, and 1 of 3 dalteparin regimens was started: 5000 units SC od, 200 units/kg SC od, or 120 units/kg SC bid. Dalteparin therapy was continued until 24 h before the surgery and then restarted 12 h after the procedure, along with warfarin. Dalteparin was continued until the international normalized ratio was within the therapeutic range. Rates of thromboembolic and hemorrhagic complications were recorded, and the number of hospital days avoided was estimated.

**Results:** The 47 participants underwent the following procedures: removal of colonic polyp (9 patients); cardiac catheterization (8); orthopedic surgery (7); colonoscopy, endoscopy, or bronchoscopy (7); dental surgery (6); ocular surgery (2); surgical biopsy (2); and nephrectomy, splenectomy, prostatectomy, oophorectomy, vasectomy, and endarterectomy (1 each). Two patients (4%, 95% confidence interval [CI] 1% to 14%) experienced a thromboembolic event, 2 patients (4%, 95% CI 1% to 14%) had minor hemorrhage, and no patients had major hemorrhage in the perioperative period.

**Conclusion:** Patients undergoing long-term anticoagulation who are at high risk for thromboembolic complications can be safely and effectively treated with low-molecular-weight heparin on an outpatient basis according to a hospital-based perioperative treatment model of care.

## RÉSUMÉ

**Objectif :** Évaluer l'efficacité et l'innocuité d'un programme périopératoire ambulatoire à l'hôpital pour les patients à risque de complications thromboemboliques chez qui l'on doit interrompre temporairement leur anticoagulothérapie orale en préparation d'une chirurgie dentaire, d'une opération ou d'une intervention diagnostique.

**Méthodes :** Une étude prospective de cohortes a été menée auprès d'une série consécutive de patients à haut risque qui prenaient des anticoagulants oraux à long terme et qui devaient subir une intervention chirurgicale au cours de la période d'étude de 12 mois. Les patients à haut risque étaient ceux qui présentaient l'un ou l'autre des états suivants : thromboembolie veineuse récente ou récidivante; fibrillation auriculaire avec un facteur de risque grave; une ou deux valves cardiaques artificielles; ou insuffisance cardiaque avec fraction d'éjection ventriculaire gauche de moins de 30 %. Leur traitement à la warfarine a été interrompu cinq jours avant l'intervention et on a amorcé leur traitement à la daltéparine selon l'un des trois schémas posologiques suivants : 5000 unités SC od; 200 unités/kg SC od; 120 unités/kg SC bid. Le traitement à la daltéparine a été interrompu 24 heures avant l'intervention, puis repris 12 heures après, avec le traitement à la warfarine. Le traitement à la daltéparine a été administré jusqu'à ce que le rapport international normalisé soit dans la marge thérapeutique. On a compilé les taux de complications thrombotiques et hémorragiques et évalué le nombre de jours d'hospitalisation épargnés.

**Résultats :** Les 47 participants ont subi les interventions suivantes : ablation de polypes du colon (9 patients); cathétérisme cardiaque (8); chirurgie orthopédique (7); coloscopie, endoscopie ou bronchoscopie (7); chirurgie dentaire (6); chirurgie oculaire (2); biopsie chirurgicale (2); néphrectomie, splénectomie, prostatectomie, ovariectomie, vasectomie et endartériectomie (une de chaque). Deux patients (4 %, intervalle de confiance [IC] à 95 % : 1 % à 14 %) ont eu un accident thromboembolique, deux autres (4 %, CI à 95 % : 1 % à 14 %) ont eu une hémorragie légère, mais aucun n'a eu d'hémorragie grave au cours de la période périopératoire.

**Key words:** surgery, low-molecular-weight heparin, dalteparin, heparin, warfarin, anticoagulation

**Conclusion :** Les patients qui sont sous anticoagulothérapie au long cours et qui présentent un risque élevé de complications thrombotiques peuvent recevoir en clinique externe un traitement sûr et efficace à l'héparine de faible poids moléculaire, dans le cadre d'un programme de soins périopératoires à l'hôpital.

**Mots clés :** chirurgie, héparine de faible poids moléculaire, daltéparine, héparine, warfarine, anticoagulation

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## INTRODUCTION

Patients receiving long-term oral anticoagulant therapy and at risk for thromboembolic complications present a challenge to clinicians when they require surgical or invasive procedures.<sup>1-14</sup> Interruption of warfarin therapy exposes patients to additional thromboembolic risks, which could lead to permanent disability or death.<sup>14</sup> After warfarin is discontinued, it takes several days for its antithrombotic effect to decline, and once it is restarted a similar period is required to re-establish therapeutic anticoagulation.<sup>1,2,5</sup> Conversely, maintaining anticoagulation throughout surgery can be associated with significant bleeding complications.<sup>1-6</sup>

Currently, there is little consensus on appropriate perioperative management of anticoagulation for patients on warfarin therapy. Several approaches have been used, based on the indication for anticoagulation, the number of risk factors for thromboembolic complications, and the risk of bleeding or thromboembolic complications associated with the surgery or procedure itself.<sup>1,2</sup> Such approaches have ranged from withholding warfarin for 4 or 5 days before surgery and restarting the drug after the procedure to replacing warfarin before and after surgery with full-dose unfractionated heparin or low-molecular-weight heparin (i.e., while the international normalized ratio [INR] is subtherapeutic).<sup>1,2,5</sup>

The former approach usually achieves satisfactory reversal of anticoagulation preoperatively with a low risk of postoperative bleeding.<sup>1,2</sup> This approach is generally used for patients at low risk for thromboembolic complications, such as patients with nonvalvular atrial fibrillation without prior systemic embolism.<sup>1,2</sup> The latter approach is usually reserved for patients with the highest risk for thromboembolic complications, including those with mechanical heart valves, recent arterial embolism, or recent or recurrent venous thromboembolism.<sup>1,2,5</sup>

Two recent national physician surveys regarding perioperative anticoagulation strategies demonstrated that physician preference varied widely for patients at

high risk for stroke but were more uniform for patients at low risk for stroke and those with mechanical heart valves.<sup>15,16</sup> For patients with mechanical heart valves, two-thirds of physicians preferred using IV unfractionated heparin preoperatively and postoperatively.<sup>15,16</sup> These findings raise several important issues regarding optimal perioperative anticoagulation, in particular the following: Are all high-risk patients receiving adequate perioperative anticoagulation with minimal bleeding risk? and Are there more cost-effective options for managing these patients in the perioperative period?

At the authors' centre, a hospital-based outpatient program has been developed for perioperative management of anticoagulation in patients at high risk for thromboembolic complications. The purpose of this study was to evaluate the effectiveness and safety of the program, which uses low-molecular-weight heparin.

## METHODS

### Patients

High-risk patients receiving anticoagulation and requiring surgical or invasive procedures between June 1, 1999, and June 30, 2000, who were referred to the anticoagulation clinic at the Queen Elizabeth II Health Sciences Centre in Halifax, Nova Scotia, were considered eligible for outpatient treatment with low-molecular-weight heparin. Patients at high risk for arterial or venous thrombotic disorders were defined as those with recent (within the past 3 months) deep vein thrombosis or pulmonary embolism or recurrent venous thromboembolism, atrial fibrillation and a major risk factor (i.e., previous embolism, hypertension, diabetes, age greater than 75 years, or moderate or severe left ventricular dysfunction), one or more mechanical heart valves, or congestive heart failure with left ventricular ejection fraction less than 30%. Patients with the following characteristics were excluded: renal insufficiency (serum creatinine greater than 200 µmol/L), platelet count less than  $75 \times 10^9/L$ , scheduled for spinal surgery or neurosurgery, age less than 18 years, evidence of active bleeding before surgery or procedure, or recent major bleeding episode.



## Perioperative Treatment Program

Potentially eligible patients were evaluated by a physician (D.R.A.) at least 1 week before the procedure, and those eligible were enrolled in the perioperative outpatient anticoagulation program. Standardized physician orders were developed by a physician (D.R.A.) and a pharmacist (S.J.W.) (Figure 1) and were to be completed for all patients in the program. The protocol was based upon clinical judgement and knowledge of the pharmacokinetics of low-molecular-weight heparin.<sup>17</sup> The overall care plan was discussed with the patient by a physician (D.R.A.), a pharmacist, (S.J.W.), and a nurse (L.G. or V.N.).

For patients in the study, warfarin was discontinued 5 days before the procedure, and 1 of 3 low-molecular-weight heparin regimens was started (the same day): dalteparin 5000 units SC od if the patient had had venous thromboembolic disease more than 3 months previously, dalteparin 200 units/kg SC od if the patient had atrial fibrillation and a major risk factor, recent or recurrent venous thromboembolism, or congestive heart failure; or dalteparin 120 units/kg SC bid if the patient had one or more mechanical heart valves.<sup>17</sup> These regimens were selected on the basis of clinical judgement and dalteparin's approved treatment and prophylactic dosage. For patients with mechanical heart valves, the dosage was based on the recommended dose for unstable angina and non-Q-wave myocardial infarction.<sup>17</sup>

Each morning for the first 4 days after discontinuation of warfarin, each patient received the designated dalteparin regimen; on the fifth day (i.e., 24 h before surgery), the patient received 5000 units SC. The patients were instructed to go to the outpatient clinic facility (the medical day unit), where a nurse administered the low-molecular-weight heparin by injection and samples were taken for blood work. Patients who were not mobile or lived too far away to commute were taught self-injection, or home care was arranged so that a nurse could go to the patient's home and administer the low-molecular-weight heparin.

All patients underwent baseline blood testing 5 days before surgery; the testing included a complete blood count and determination of serum creatinine level and INR. For patients with a serum creatinine level greater than 150  $\mu\text{mol/L}$ , anti-Xa level was determined daily from a sample drawn immediately before the injection of low-molecular-weight heparin, beginning on day 4 before surgery. The complete blood count and the INR determination were repeated on days 3 and 1 before surgery. If the INR was greater than 1.5 on day 3 before surgery, the patient was given vitamin K<sub>1</sub> 1 mg PO or SC.

If the INR was greater than 1.5 on day 1 before surgery, INR determination was repeated on the day of surgery. If the INR remained greater than 1.5 on the day of surgery, the surgeon was contacted.

Depending on the nature of the surgery, the patients were either admitted to hospital (e.g., total knee replacement) or were discharged the same day (e.g., colonoscopy). Starting in the evening of the day of the procedure, patients resumed their previous therapeutic dosage of warfarin or warfarin 10 mg, provided there was no active surgical bleeding and they were able to take oral medication. In addition, 12 h after the procedure, patients restarted their previous dose and frequency of dalteparin, provided hemostasis had been achieved. Dalteparin injections were continued until the INR was about 2.0 for patients with atrial fibrillation, deep vein thrombosis, or pulmonary embolism or about 2.5 for patients with mechanical heart valves. Complete blood count and INR determinations were performed on days 2 and 4 after surgery, and warfarin doses were adjusted accordingly. Patients were then referred back to the care of the pharmacist in the anticoagulation clinic (S.J.W.) for further stabilization of their oral anticoagulant therapy.

All patients were instructed to go to the local emergency department in the event of any bleeding complications or suspected thromboembolic events. In an effort to minimize cost to both the hospital and the patient, the dalteparin injections were charged to the patient's third-party insurer when possible. For patients without third-party insurance, a social worker evaluated the patient's situation for payment alternatives. For patients without social assistance options, the hospital covered the cost of the dalteparin therapy.

## Analysis

The effectiveness and safety of the perioperative program were assessed in terms of rates of thromboembolic complications, major or minor bleeding events occurring during the perioperative period, and rates of thromboembolic events during a 3-month follow-up period (with associated 95% confidence intervals [CIs]). Thromboembolic complications included cerebral emboli, coronary artery emboli, peripheral emboli, valve thrombosis, vascular death, or transient ischemic attacks. Bleeding was defined as major if it was overt and associated with either a decrease in the hemoglobin level of at least 20 g/L or a need for the transfusion of 2 or more units of blood.<sup>18</sup> Bleeding was defined as minor if it was overt but did not meet the other criteria for major bleeding.<sup>18</sup> The number of





Queen Elizabeth II  
Health Sciences Centre  
Physician Standing Order  
Department of Medicine/Medical Day Unit

## Outpatient Management of Anticoagulation Before and After Elective Surgery (Page 1 of 2)

Patient: \_\_\_\_\_

Allergies: \_\_\_\_\_

Date (YYYYMMDD) \_\_\_\_\_ Time (24hr:min) \_\_\_\_\_

1. The following orders may be used in any patient care area.
2. The following orders will be carried out by a nurse **ONLY** on the **AUTHORITY OF A PHYSICIAN**.
3. All orders to be carried out must be obtained/checked as appropriate.
4. Choose indication for Warfarin:
  - Atrial fibrillation and major risk factor (i.e. previous systemic embolism, high blood pressure, diabetes, age >75, moderate/severe left ventricular dysfunction)
  - Deep vein thrombosis or pulmonary embolism
  - Mechanical heart valve
  - Other \_\_\_\_\_
5. Vital Signs: Temperature, Pulse, Resp Rate, BP, once a day, prior to administration of Dalteparin injection.
6. Pre-Op Drug Therapy and Bloodwork:

(YYYYMMDD) DAY - 3	
• Discontinue Warfarin	
• Baseline BUN, CBC, EUN, creatinine	
• Choose <u>mg</u> only: Dalteparin	<input type="checkbox"/> 250 u/kg _____ u (total dose) SC QD <input type="checkbox"/> 120 u/kg _____ u (total dose) SC BID for mechanical valves <input type="checkbox"/> 5,000 u SC QD
(YYYYMMDD) DAY - 4	
• Daily anti-Xa level to be drawn prior to Dalteparin injection for patients weighing > 120 kg or creatinine > 150 umol/L	
• Choose <u>mg</u> only: Dalteparin	<input type="checkbox"/> 200 u/kg _____ u (total dose) SC QD <input type="checkbox"/> 120 u/kg _____ u (total dose) SC BID for mechanical valves <input type="checkbox"/> 5,000 u SC QD
(YYYYMMDD) DAY - 3	
• BUN and CBC. Notify physician if platelet count is less than 100x10 <sup>9</sup> /L.	
• Vitamin K 1 mg SC or PO if INR > 1.5	
• Choose <u>mg</u> only: Dalteparin	<input type="checkbox"/> 200 u/kg _____ u (total dose) SC QD <input type="checkbox"/> 120 u/kg _____ u (total dose) SC BID for mechanical valves <input type="checkbox"/> 5,000 u SC QD
(YYYYMMDD) DAY - 2	
• Choose <u>mg</u> only: Dalteparin	<input type="checkbox"/> 200 u/kg _____ u (total dose) SC QD <input type="checkbox"/> 120 u/kg _____ u (total dose) SC BID for mechanical valves <input type="checkbox"/> 5,000 u SC QD
(YYYYMMDD) DAY - 1	
• BUN and CBC. Notify physician if platelet count is less than 100x10 <sup>9</sup> /L.	
• Vitamin K 1 mg SC or PO if INR > 1.5 and repeat BUN the morning of the day of surgery	
• Dalteparin 5,000 u SC QD	

DATE (YYYYMMDD) \_\_\_\_\_

Physician's Signature \_\_\_\_\_

Provincial Medical Board Number \_\_\_\_\_

Physician's Name - Print \_\_\_\_\_

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Figure 1. Standing order for outpatient management of anticoagulation before and after elective surgery.



# Outpatient Management of Anticoagulation Before and After Elective Surgery

(Page 2 of 2)

## 7. Post-Op Drug Therapy and Bloodwork

+	_____ (YYYYMMDD)	<b>DAY 0</b> (Timing of surgery)
•	Choose <u>one</u> only: <b>Warfarin</b>	<input type="checkbox"/> 10 mg PO QD <input type="checkbox"/> _____ mg PO QD (previous therapeutic dosage)
•	Choose <u>one</u> only: <b>Dabigatran</b>	<input type="checkbox"/> 150 mg SC QD <input type="checkbox"/> 200 mg _____ u (total dose) SC QD <input type="checkbox"/> 120 mg _____ u (total dose) SC BID for mechanical valves
•	_____ (YYYYMMDD)	<b>DAY 1</b>
-	Warfarin _____ mg PO QD (previous therapeutic dosage)	
•	Choose <u>one</u> only: <b>Dabigatran</b>	<input type="checkbox"/> 150 mg SC QD <input type="checkbox"/> 200 mg _____ u (total dose) SC QD <input type="checkbox"/> 120 mg _____ u (total dose) SC BID for mechanical valves
+	_____ (YYYYMMDD)	<b>DAY 2</b>
•	INR and CBC. Notify physician if platelet count is less than 100,000	
•	Warfarin _____ mg PO QD (Based on Day 2 INR)	
•	Choose <u>one</u> only: <b>Dabigatran</b>	<input type="checkbox"/> 150 mg SC QD <input type="checkbox"/> 200 mg _____ u (total dose) SC QD <input type="checkbox"/> 120 mg _____ u (total dose) SC BID for mechanical valves
+	_____ (YYYYMMDD)	<b>DAY 3</b>
•	Warfarin _____ mg PO QD (Based on Day 2 INR)	
•	Choose <u>one</u> only: <b>Dabigatran</b>	<input type="checkbox"/> 150 mg SC QD <input type="checkbox"/> 200 mg _____ u (total dose) SC QD <input type="checkbox"/> 120 mg _____ u (total dose) SC BID for mechanical valves
+	_____ (YYYYMMDD)	<b>DAY 4+</b>
•	INR and CBC every 48 hours. Notify physician if platelet count is less than 100,000	
•	Warfarin _____ mg PO QD (Based on Day 4 INR)	
•	Discontinue Dabigatran on _____ (YYYYMMDD) if INR $\geq 1.5$ (prior to discharge, DVT, PE) or $\geq 1.5$ (mechanical heart valves)	

\* If able to take oral medication

† 12 hours post-procedure if there is no active surgical bleeding. If optimal analgesia is used, do not give Dabigatran within 24 hours of surgery.

DATE (YYYYMMDD)

Physician's Signature

Provincial Medical Board Number

Physician's Name - Print

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Figure 1. Continued.



hospital days potentially saved with the perioperative outpatient program was estimated (from the mean duration of outpatient dalteparin treatment and the assumption that patients would otherwise have had to be admitted for IV administration of unfractionated heparin). The number of patients who required administration of vitamin K<sub>1</sub> preoperatively and the method of payment for the dalteparin therapy were also recorded.

## RESULTS

Between June 1, 1999, and June 30, 2000, 47 patients at high risk for thromboembolic complications participated in the perioperative outpatient anticoagulation program. The characteristics of the patients, as well as the factors placing them at high risk, are presented in Table 1. Total daily dalteparin doses ranged from 5000 to 26 200 units. Nine patients who had had venous thromboembolism more than 3 months previous received dalteparin 5000 units SC od; 31 patients who had recent or recurrent venous thromboembolism, atrial fibrillation, or congestive heart failure received dalteparin 200 units/kg SC od; and 7 patients with one or more mechanical heart valves received dalteparin 120 units/kg SC bid. The mean ( $\pm$  standard deviation [SD]) duration of outpatient dalteparin treatment was  $10.5 \pm 3.01$  days.

All patients were managed preoperatively as outpatients. Nineteen patients were taught self-injection of low-molecular-weight heparin, 17 received their injections from home care nurses, and 11 received their injections in the medical day unit. Thirty patients underwent day surgery, and resumed administration of dalteparin the evening of surgery, in the same dosage as before surgery. Because of the nature of their procedures, the other 17 patients (36%) were admitted to hospital postoperatively for a median duration of 4 days (range 1 to 10). Thirteen (76%) of these 17 patients started dalteparin or unfractionated heparin the evening of the day of surgery, and 4 (24%) started unfractionated heparin 12 to 24 h after the procedure. The procedures associated with a 12- to 24-h delay in postoperative initiation of unfractionated heparin were splenectomy, prostatectomy, endarterectomy, and vasectomy. While in hospital, 8 of these patients received their full course of either dalteparin or unfractionated heparin along with warfarin until the INR was in the therapeutic range. The remaining 9 patients, once ready for discharge, resumed outpatient administration of dalteparin until they were fully anticoagulated with warfarin.

Two patients (4%, 95% CI 1% to 14%) had a thromboembolic event during the perioperative period. One patient had acute myocardial infarction 3 days after

**Table 1. Characteristics of 47 Patients at High Risk for Thromboembolic Complications Participating in a Perioperative Angicoagulation Program**

Characteristic	No. (and %) Patients*	
<b>Age (years)</b>		
Mean	61	
Range	19–81	
<b>Sex</b>		
Men	17	(36)
Women	30	(64)
<b>Factor conferring high risk</b>		
Recent or recurrent VTE	26	(55)
Atrial fibrillation with previous emboli	11	(23)
Mechanical heart valve(s)	7	(15)
Congestive heart failure (left ventricular function <30%)	3	(6)
<b>Surgical procedure</b>		
Polyp removal	9	(19)
Cardiac catheterization	8	(17)
Orthopedic procedure	7	(15)
Colonoscopy, endoscopy, or bronchoscopy	7	(15)
Dental surgery	6	(13)
Nephrectomy, splenectomy, prostatectomy, oophorectomy, vasectomy, or endarterectomy	6	(13)
Ocular procedure	2	(4)
Biopsy	2	(4)
<b>Dalteparin dose</b>		
5000 units SC od	9	(19)
200 units/kg SC od	31	(66)
120 units/kg SC bid	7	(15)

VTE = venous thromboembolism.

\*Except where indicated otherwise.

discontinuing warfarin therapy and was admitted to hospital for an additional 3 days as a result. The patient's INR was 2.0 (target 3.0 to 4.0) at the time of the event, and she had been receiving 24 000 units of dalteparin SC od (i.e., 200 anti-Xa units/kg). She was receiving oral anticoagulant therapy for antiphospholipid antibody syndrome. It was felt that the occurrence of the non-Q-wave myocardial infarction was coincidental with the switch in anticoagulant therapy. The patient's procedures were delayed for 3 months, at which time the scheduled gastroscopy and colonoscopy were performed without complications. Another patient had an ischemic stroke the evening after a total hip replacement and required an additional 10 days in hospital. The patient's INR was 1.2 at the time of the stroke, and she had been receiving oral anticoagulant therapy for recurrent venous thromboembolism.

No patients had major hemorrhage, and minor hemorrhagic episodes were experienced by 4% (95% CI 1% to 14%) of patients. One patient had bleeding from the dental sockets after a dental extraction, and another (with INR of 1.9) experienced rectal bleeding 2 days before the procedure. Neither of the minor bleeding



events delayed administration of anticoagulants or resulted in additional costs. Seven patients required doses of vitamin K<sub>1</sub> 1 mg PO or SC 3 days before surgery, and one of these patients required a second dose the day before the procedure to achieve an INR below 1.5. Need for vitamin K<sub>1</sub> did not lead to postponements of the scheduled procedures.

Twenty-six (55%) of the 47 patients had third-party insurance to cover the low-molecular-weight heparin, 12 (25%) received dalteparin therapy through social assistance, and 9 (19%) received dalteparin therapy through home care or the Victorian Order of Nurses.

## DISCUSSION

This article reports an alternative method of managing anticoagulation in patients at risk for thromboembolic complications before and after elective dental, surgical, or invasive diagnostic procedures. The results reported here demonstrate that the use of outpatient low-molecular-weight heparin therapy for high-risk patients receiving long-term oral anticoagulants can reduce unnecessary hospital stays in the perioperative period while providing safe and effective anticoagulant management. During the perioperative treatment period, 4% (95% CI 1% to 14%) of patients had thromboembolic complications, 4% (95% CI, 1% to 14%) of patients had minor bleeding, and no patients had major bleeding events. Although 2 patients experienced thromboembolic complications in the perioperative period, it is felt that these events were coincidental rather than consequent to participation in the perioperative anticoagulant program. One patient had a non-Q-wave myocardial infarction while receiving therapeutic treatment with dalteparin; her INR was 2.0 at the time of the event. The second patient had a stroke; however, she was being managed for prophylaxis of venous thromboembolism.

As a cautionary measure, patients started low-molecular-weight heparin on the same day that warfarin was discontinued preoperatively. The protocol has since been modified to start low-molecular-weight heparin on the day after warfarin is discontinued, as this time period corresponds better with the decline in warfarin's anticoagulant effect. In this study, all patients received 5 days of preoperative outpatient treatment with dalteparin, and 30 (64%) of the patients received postoperative outpatient treatment with dalteparin and warfarin. Seventeen patients required admission to hospital after the procedure as part of routine surgical care. Less than half of these patients received their full course of either dalteparin or unfractionated heparin

and warfarin while in hospital. On the basis of the mean ( $\pm$  SD) duration of outpatient dalteparin treatment of  $10.5 \pm 3.01$  days and assuming that patients would otherwise have had to be admitted for IV unfractionated heparin, approximately 352 to 635 hospital days may have been saved for the 47 patients.

One study has been published regarding outpatient administration of low-molecular-weight heparin in patients receiving long-term anticoagulation whose oral anticoagulants must be temporarily interrupted before and after surgery.<sup>19</sup> In that study, 20 patients had their warfarin discontinued 5 or 6 days before surgery and received enoxaparin 1 mg/kg SC q12h starting approximately 36 h after warfarin was stopped. Enoxaparin was withheld for 12 to 18 h before the procedure and was resumed an average of 13.5 h after the procedure. No patients experienced bleeding or thromboembolic complications during the procedure. One patient had major bleeding at the incision site 3 days after hemiorrhaphy, and 2 patients experienced minor bleeding.

Low-molecular-weight heparins have been proven safe and effective for the treatment of venous and arterial thromboembolic disorders.<sup>20-32</sup> They have several advantages over unfractionated heparin, including high bioavailability after SC administration, longer plasma half-life, and more predictable anticoagulant activity.<sup>33</sup> These properties allow these agents to be administered once or twice a day without the need for routine monitoring of anticoagulant activity. As a result, they are well suited for patients receiving long-term anticoagulation who require interruption of their warfarin in anticipation of surgery.

To date, no randomized controlled trials regarding appropriate perioperative anticoagulation have been reported. In 2 recent national surveys, physicians were generally in agreement with regard to the need for perioperative anticoagulation in high-risk patients.<sup>15,16</sup> Given the present economic environment, it is important to reduce the length of hospital stays solely for anticoagulation. The perioperative outpatient program described here is an alternative to inpatient treatment with IV unfractionated heparin. As outlined in a previous article on outpatient treatment in this journal,<sup>34</sup> there are 3 primary models for delivering low-molecular-weight heparin therapy: teaching patients self-injection of low-molecular-weight heparin, arranging for home care nurses to administer the injections, and using a hospital-based ambulatory facility, such as a medical day unit or an anticoagulation clinic.

Models based on teaching patients self-injection or arranging for home care nurses to administer injections



usually involve an initial visit. During the visit, the patient is assessed by a physician to determine appropriate perioperative anticoagulation, and the patient receives the necessary education and training (specifically the self-injection technique) to permit outpatient treatment. Videos and patient education materials available from many companies that market low-molecular-weight heparin can be provided as supplemental patient information. Follow-up involves telephone contact, either daily or every other day, to assess the patient's progress and to ensure compliance with anticoagulant therapy and blood work. The benefits of this treatment model are its convenience for patients and the low consumption of hospital resources. The benefits of administration of therapy by home care nurses are convenience for patients and minimization of potential errors in injections. Although this model of care is more costly than teaching patients self-injection, because of the cost of the nurses, it is still more cost-effective than admission to hospital.

The third treatment model involves using a hospital-based facility to deliver perioperative outpatient treatment. Medical day unit and anticoagulation clinic programs have the advantage of availability of space for patient counselling and treatment. Because patients visit the clinic daily, problems arising can be addressed immediately. Furthermore, patients who must be admitted to hospital because of the nature of their surgery and who are ready for discharge on the weekend but are not fully anticoagulated can resume their low-molecular-weight heparin immediately, as many medical day units are open 7 days a week. Despite the virtues of this treatment model, it can be both inconvenient and costly for patients in terms of commuting and parking.

Selection of a treatment model will ultimately depend on the institution's available resources and clinical expertise. For continuity of care, it is necessary to have a core group of clinicians involved in facilitating outpatient therapy. Regardless of the treatment model chosen, it is imperative to follow a clearly defined protocol that outlines all aspects of treatment, so as to minimize potential errors. Pharmacists can play an important role in the development, implementation, and management of a perioperative outpatient treatment program. To ensure a smooth treatment process for patients and caregivers, pharmacists can develop standardized physician treatment orders, arrange financial coverage for the low-molecular-weight heparin, and communicate the treatment plan to the surgeon or the anesthesiology department. Furthermore,

pharmacists can be directly involved in educating patients by providing medication counselling, monitoring for side effects, and teaching administration of low-molecular-weight heparin. Staffing resources for the program described here were drawn from current resources. The institution plans to submit this information in hopes of securing funding specifically for additional staff for this program.

Despite the low rate of complications, only 47 patients were managed perioperatively over a 1-year period. In addition, the study did not include a control group of patients admitted to hospital to receive IV heparin therapy. Therefore, no direct comparisons can be made in terms of rates of treatment complications or cost savings. Preliminary experience from this study demonstrated that high-risk patients receiving long-term oral anticoagulants can be safely and effectively managed as outpatients with low-molecular-weight heparin through a hospital-based perioperative model of care. However, controlled clinical trials are needed to confirm these results.

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