A Simple Warfarin Dosing Nomogram for Orthopedic Prophylaxis

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INTRODUCTION

Total hip replacement procedures are considered high-risk surgery, for which the prevalence of deep vein thrombosis is 45% to 57%, of pumonary embolism 6.7% to 30%, and of fatal pulmonary embolism 3.4% to 6%.[1,2] General recommendations for prophylaxis of deep vein thrombosis in patients who have undergone this type of surgery include early mobilization, intermittent pneumatic compression, elastic stockings, and early detection of subclinical venous thrombosis by duplex ultrasonography or venography.[1] The pharmacological options for preventing deep vein thrombosis include low-molecular-weight heparin, low-intensity warfarin, and adjusted-dose subcutaneous heparin.[1,2] Because low-molecular-weight heparin was not a formulary drug at the time this study was initiated (in November 1995) and subcutaneous administration of adjusted-dose heparin is labour intensive, warfarin has been used as the prophylactic agent at our institution.

Our pharmacy department was asked by the Division of Orthopedics to provide a warfarin dosing service for prophylaxis of deep vein thrombosis in patients requiring hip arthroplasty. Before this request was made, the pharmacy department had been involved in creating and implementing a weight-based heparin dosing nomogram.[3] This nomogram, which was run by the nursing staff, was found to be superior to traditional heparin dosing for rapidly and safely achieving therapeutic anticoagulation. Because of the success of this program, it was felt that a warfarin dosing service based on a nomogram could provide a similar success rate and also improve patient care. Pharmacists were chosen to run this service because of the complex pharmacokinetics of warfarin and the numerous factors affecting the anticoagulant response that must be considered before deciding on dosage adjustments. At the time of this request, orthopedic residents were responsible for prescribing warfarin. The residents were often unavailable because of prolonged surgeries or inadequate weekend coverage, which resulted in late administration of warfarin and frustration on the part of the nursing staff.

PROGRAM DEVELOPMENT

A warfarin nomogram was created with the objective of facilitating a structured approach to warfarin prescribing and delivery (Appendix 1). The general recommendations for international normalized ratio (INR) for prophylaxis of deep vein thrombosis after hip arthroplasty are 2.0 to 3.0.[1,2,4] However, the practice in our orthopedic unit was to aim for an INR of 1.5 to 2.0. A literature search revealed 2 articles supporting similar ranges: 1.6 to 2.5 in the report by Rivey and colleagues[5] and 1.8 to 2.5 in the report by the RD Heparin Arthroplasty Group.[6] After discussions with the Divisions of Hematology and Orthopedics, an INR range of 1.6 to 2.3 was adopted. Rivey and colleagues[5] published a warfarin nomogram for orthopedic prophylaxis (INR 1.6 to 2.5); the warfarin dose varied daily depending on the INR result and the postoperative day. Because of the complexity of this nomogram, we designed a simpler approach to simulate a protocol based on INR values alone (personal communication, Dr G. Pineo, University of Calgary, Calgary, Alberta, September 27, 1995). The nomogram was modified to allow flexibility of warfarin dosing according to the patient's sensitivity to the drug. For example, if the patient was elderly (> 70 years of age) and frail (< 50 kg), a lower warfarin dosage could be recommended within each INR category. The nomogram was incorporated into preprinted orders designed to give pharmacists the authority to prescribe warfarin. The nomogram was approved by the Drugs and Therapeutics Committee in

September 1995 and by the Medical Advisory Committee in October 1995.

PROGRAM IMPLEMENTATION

Before the nomogram was implemented, several in-service training sessions were conducted for nurses and physicians. Information was distributed in our pharmacy newsletter and preprinted orders were created. A target date of November 15, 1995, was set for initiation of the service. The service was provided by pharmacists 7 days per week. Patients were admitted to the hospital through the preadmission clinic on the evening before or the day of surgery. The physician prescribed the initial preoperative warfarin dose and then initiated the service by signing the preprinted order sheet (Appendix 1). Each weekday, the pharmacist reviewed each patient's chart for drug interactions, bleeding or thrombotic complications, hemoglobin level, platelet count, and INR values. The pharmacist then wrote the following statement in the chart: "Today's INR = X, give warfarin Y mg po today". Because prescriptive authority was limited to instructions given in the nomogram, physician approval was required for warfarin doses deviating from the nomogram. As well, because of the increased risk of bleeding in this postoperative population, INR values greater than 4.0 and significant reductions in hemoglobin (by > 20 g/L) after postoperative day 1 were reported to the physician to assess whether bleeding was occurring and for possible decision to reverse anticoagulation. It was recommended that all intramuscular medications be changed to the oral, intravenous, or subcutaneous route as indicated. Whenever possible, interacting drugs were changed to noninteracting ones. Warfarin therapy was terminated at discharge, and all patients with a discharge INR of greater than 1.8 were instructed to observe bleeding precautions for 1 week. On weekends, the pharmacist performed similar steps, with the exclusion of chart review because of time constraints.

PROGRAM EVALUATION

To evaluate the nomogram, the study group was compared with a control group drawn from orthopedic patients admitted to the hospital within the 3 years preceding implementation of the nomogram. Patients' charts were randomly selected by the Medical Records Department and the charts of patients who had received warfarin for prophylaxis of deep vein thrombosis were reviewed consecutively as they became available. The nomogram was evaluated by descriptive statistics compiled for weeks 1 to 4 and weeks 5 to 12 after implementation. Data collected included age, sex, and weight of the patient, baseline INR, duration of warfarin therapy, preoperative warfarin dose, time to exceed the threshold INR, and proportion of INR values within, above, and below the target range. The latter 3 values were assessed once the initial INR had exceeded the therapeutic threshold. For the analysis, we used a target INR range of 1.5 to 2.3 for all groups instead of our established range of 1.6 to 2.3 to enable a fair comparison with the control group. The narrower INR range of 1.5 to 2.0 used by physicians for patients in the control group was not formally established in print and adherence to this range could not be reliably assessed. We felt that the broader range chosen for comparative purposes was reasonable and would more likely bias the results in favour of the control arm.

Thromboembolic rates and bleeding complications were recorded for the duration of the hospital stay. Major bleeding was defined as overt bleeding with one or more of the following signs and symptoms: a decrease in hemoglobin of greater than 20 g/L, transfusion of 2 or more units of blood, or hemorrhage into the retroperitoneum, cranium, or prosthetic joint.[7] Because of the potential for intraoperative blood loss, the postoperative hemoglobin level was used as the baseline to assess for bleeding secondary to anticoagulation.

Table 1 illustrates patient characteristics and baseline data. The evaluations for weeks 1 to 4 and weeks 5 to 12 present data for different sets of patients. Three patients in the control group received warfarin prophylaxis after knee arthroplasty, whereas the other patients in the control group and all of the patients in the study groups underwent hip arthroplasty. As current guidelines recommend low-molecular-weight heparin for prophylaxis of deep vein thrombosis after knee replacement,[1,2] patients undergoing this type of surgery no longer receive warfarin prophylaxis for this indication. Baseline INRs were obtained for only 42% of the patients during weeks 1 to 4 after implementation of the nomogram. After consultation with the preadmission clinic, baseline INR tests were added to the preprinted admission orders for all orthopedic patients. As a result, the proportion of patients for whom baseline INR data were available increased to 70% during weeks 5 to 12; it is now close to 100%.

The results of the evaluation of the warfarin nomogram are shown in Table 2. Overall, the proportion of INRs within, below, and above the target range and the time to exceed the threshold INR were similar for all 3 groups. There was one pulmonary embolism in the

Table 1. Characteristics of Patients Undergoing Arthroplasty Before and After Implementation of a Warfarin Dosing Regimen

Characteristic	Before implementation*	After implementation†	
		Weeks 1 to 4	Weeks 5 to 12
No. of patients	22	31	69
Age (mean and range), years	61.4 (19 to 90)	60.2 (16 to 79)	62.0 (18 to 89)
Indication			
Knee arthroplasty	3	0	0
Hip arthroplasty	19	31	69
Baseline INR (mean and SD)	1.08 (0.18)	0.92 (0.09)	0.88 (0.06)
No. (and %) of patients with baseline INR	14 (64)	13 (42)	48 (70)

INR = international normalized ratio, SD = standard deviation.
* March 1993 to October 1995.
† Weeks 1 to 4 = November 15 to December 15, 1995; weeks 5 to 12 = December 16, 1995, to February 9, 1996.

Table 2. Evaluation of Warfarin Nomogram Performance

Variable	Before implementation*	After implementation†	
		Weeks 1 to 4	Weeks 5 to 12
Preoperative warfarin dose (% of patients)			
10 mg	41	78	66
7.5 mg	0	3	7
5 mg	9	3	7
None	50	16	20
Days on warfarin (mean and range)	10.82 (5 to 22)	7.06 (3 to 17)	7.45 (1 to 22)
INR data			
Days to INR ≥1.5 (mean and range)	2.4 (0 to 7)	2.2 (1 to 6)	2.1 (1 to 10)
Days with INR in range 1.5–2.3 (%)‡	53.6	52.4	55.4
Days with INR > 2.3 (%)‡	17.6	10.5	12.1
Days with INR < 1.5 (%)‡	19.4	18.7	17.8
Patient outcomes			
% of patients receiving transfusions (and mean units PRBC)	27.3 (3)	25.8 (1.9)	10.1 (2.4)
No. of patients with DVT or PE	1 with PE	0	0
No. of patients with major bleeding event	2	1	0

INR = international normalized ratio, PRBC = packed red blood cells, DVT = deep vein thrombosis, PE = pulmonary embolism.
* March 1993 to October 1995.
† Weeks 1 to 4 = November 15 to December 15, 1995; weeks 5 to 12 = December 16, 1995, to February 9, 1996.
‡ Percentages of days with INR within, above, and below the therapeutic range do not sum to 100% because the numerator was calculated after the INR exceeded the therapeutic threshold, whereas the denominator represents the total duration of warfarin therapy.

control group and no thromboembolic events in the study groups. As well, there were 2 major bleeding events in the control group and 1 major bleeding event in the study groups. Only 50% of control patients but at least 80% of those in the study groups received warfarin preoperatively. However, the lower proportion of patients in the control group receiving warfarin preoperatively did not appear to affect either the time to exceed the therapeutic threshold INR or the proportion of days for which INR was within the therapeutic range. The ultimate goal is for all patients to receive a preoperative warfarin dose, as recommended in the literature,[1] and our results showed substantial progress toward this goal. Warfarin therapy was terminated for all patients at discharge. The mean duration of warfarin therapy was 11 days for the control group and about 7 days for the study groups.

A recent study evaluated the costs of a pharmacist-run warfarin dosing service for orthopedic prophylaxis (hip replacement surgery) and compared them with the costs of using a low-molecular-weight heparin, enoxaparin.[8] The total costs were very sensitive to pharmacists' labour and favoured the warfarin service if pharmacists spent less than 22 min per patient.

Our pharmacists estimated it took 2 h per day to follow a caseload of approximately 12 patients. This included 15 min to work up each new patient and 5 min per patient for follow-up. On weekends, the pharmacist spent approximately 1 h checking INR results and writing warfarin orders. Thus, our warfarin service falls within the cost-effectiveness estimates reported in the literature.[8] The pharmacists were able to run the service within the time constraints of their regular clinical workload by restructuring their activities in other low-yield clinical practice units.

In conclusion, the pharmacy-based warfarin dosing service provided the following advantages: (i) timely dose administration at 5:00 PM daily; (ii) structured guidelines that removed guesswork and eliminated random prescribing; and (iii) involvement of pharmacists in direct patient care activities including prescribing, monitoring, and counselling. Previously, because pharmacists were not directly involved with warfarin management on the orthopedic service, orthopedic patients received warfarin counselling only upon request. The warfarin service was initially confined to 1 of 2 orthopedic wards where the bulk of patients who had undergone hip arthroplasty resided. The service now continues on this ward and has been expanded to include the second orthopedic ward. Furthermore, upon request from the vascular surgery department, we now provide a pharmacy-based warfarin service for the treatment of thromboembolic disorders for patients in that department. The warfarin nomogram for vascular surgery is designed for a target INR of 2.0 to 3.0 and is currently under evaluation.

References

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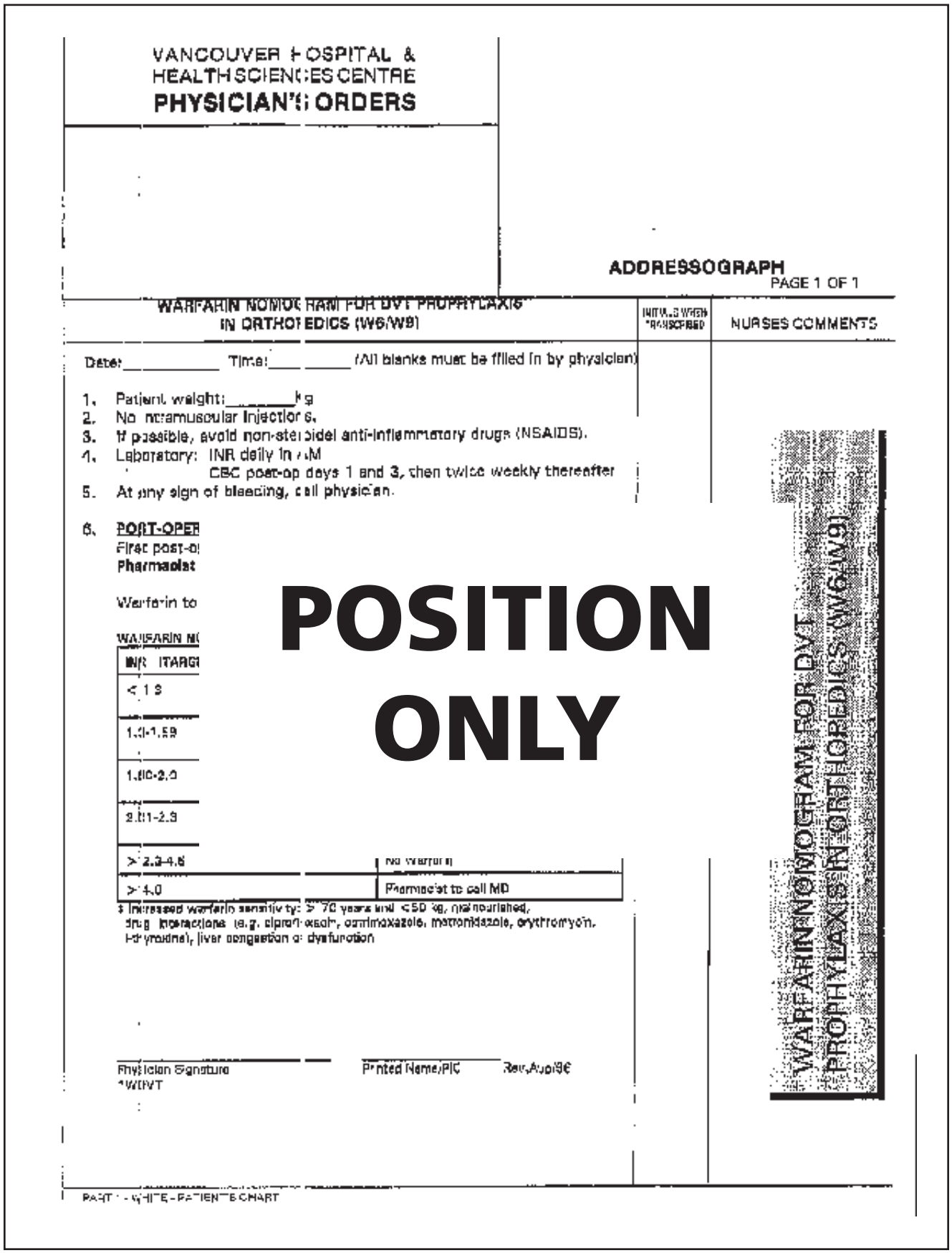
See **Appendix 1. Warfarin nomogram for prophylaxis of deep vein thrombosis in orthopedic patients** on page 44.

Appendix 1. Warfarin nomogram for prophylaxis of deep vein thrombosis in orthopedic patients



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ADDRESSOGRAPH

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WARFARIN NOMOGRAM FOR DVT PROPHYLAXIS IN ORTHOPEDICS (W6/W9)

INITIAL WHEN TRANSCRIBED | NURSES COMMENTS

Date:_____ Time:_____ (All blanks must be filled in by physician)

1. Patient weight:_____kg
2. No intramuscular injections.
3. If possible, avoid non-steroidal anti-inflammatory drugs (NSAIDS).
4. Laboratory: INR daily in AM
   CBC post-op days 1 and 3, then twice weekly thereafter
5. At any sign of bleeding, call physician.
6. POST-OPER
   First post-o
   Pharmacist

Warfarin to

WARFARIN N

INR ITARG	
< 1.9	
1.9-1.99	
1.90-2.0	
2.01-2.9	
> 2.9-4.0	No Warfarin
> 4.0	Pharmacist to call MD

* Increased warfarin sensitivity: > 70 years and <50 kg, malnourished, drug interactions (e.g. ciprofloxacin, cotrimoxazole, metronidazole, erythromycin, thyroxine), liver congestion or dysfunction

Physician Signature
WDVT

Printed Name/PIC

Rev.Aug/96

PART 1 - WHITE - PATIENT'S CHART

WARFARIN NOMOGRAM FOR DVT PROPHYLAXIS IN ORTHOPEDICS (W6/W9)

POSITION ONLY