Evaluation of Physicians' and Nurses' Compliance with a Heparin Protocol for Acute Coronary Syndromes

Chantal Pharand, Stéphanie Castonguay, and Virginie Héroux

ABSTRACT

Background: Titration protocols have been developed for anticoagulant medications, with the aim of reducing the time to therapeutic anticoagulation and increasing the time spent in the therapeutic range.

Objectives: To evaluate compliance with a heparin titration protocol in patients presenting with acute coronary syndromes. Two secondary objectives were to evaluate the time required to reach therapeutic activated partial thromboplastin time (aPTT) and the time spent in the therapeutic range.

Methods: The medical records of 170 consecutive patients with cardiac disease admitted to the coronary care unit over a 5-month period and requiring heparin therapy were reviewed. These patients received a total of 190 courses of therapy. Information about patients' baseline characteristics, along with data related to their therapy and aPTT monitoring, were extracted for analysis.

Results: Most of the 190 courses of therapy (133 or 70%) were for patients admitted with non-ST-elevation acute coronary syndromes. Therapeutic aPTT was reached in 21 ± 18 h (mean ± standard deviation), and aPTT remained in the therapeutic range for 63% of the time, on average. Of 587 interventions to adjust the rate of heparin infusion, 96 (16%) were not compliant with the protocol; 94 (49%) of the 190 courses of therapy were therefore subject to at least one noncompliant dosing adjustment. Of the 69 noncompliant modifications performed by nursing personnel, 32 (46%) involved miscalculations or misreading of the protocol and 16 (23%) involved a required dosage change that was not done. Of the 27 noncompliant adjustments performed by physicians, 12 (44%) involved reinitiation of heparin infusion at an inadequate rate.

Conclusions: In using a heparin titration protocol to guide treatment of patients with acute coronary syndromes, physicians and nursing personnel performed many noncompliant dosing adjustments. These noncompliant adjustments were for the most part related to miscalculations of doses and misreading of the protocol.

Key words: heparin, titration protocol, acute coronary syndromes

Can J Hosp Pharm 2005;58:273-8

RÉSUMÉ

Historique : On a mis au point des protocoles d'ajustement posologique des anticoagulants dans le but de réduire le délai d'obtention d'une anticoagulation thérapeutique et d'accroître le temps passé dans l'écart thérapeutique.

Objectifs : Évaluer le degré d'adhésion au protocole d'ajustement posologique de l'héparine chez les patients présentant un syndrome coronarien aigu. Deux autres objectifs secondaires étaient d'évaluer le temps nécessaire pour atteindre un temps de prothrombine partiel activé (aPTT) thérapeutique et le temps passé dans l'écart thérapeutique.

Méthodes : Les dossiers médicaux de 170 patients atteints d'une coronaropathie admis consécutivement à l'unité de soins coronariens sur une période de cinq mois et nécessitant une héparinothérapie ont été examinés. Ces patients ont reçu un total de 190 traitements à l'héparine. Les renseignements relatifs aux caractéristiques de base des patients, ainsi que les données concernant leur thérapie et le monitorage de l'aPTT ont été obtenus pour fin d'analyse.

Résultats : La plupart des traitements à l'héparine (133/190 ou 70 %) ont été administrés aux patients présentant un syndrome coronarien aigu sans élévation du segment ST. L'aPTT thérapeutique a été atteint en 21 ± 18 heures (moyenne ± écart type) et l'aPTT s'est maintenu dans l'écart thérapeutique en moyenne 63 % du temps. Des 587 interventions visant à ajuster la vitesse de perfusion de l'héparine, 96 (16 %) n'étaient pas conformes au protocole, et 94 (49 %) des 190 traitements à l'héparine ont fait l'objet d'au moins un ajustement posologique non conforme. Des 69 modifications non conformes effectuées par le personnel infirmier, 32 (46 %) étaient attribuables à de mauvais calculs ou à une mauvaise interprétation du protocole et 16 (23 %) impliquaient une modification posologique nécessaire qui n'a pas été faite. Des 27 ajustements non-conformes effectués par les médecins, 12 (44%) concernaient la réinstauration de la perfusion d'héparine à une vitesse inadéquate.

Conclusions : Dans le cadre de la prise en charge des patients présentant un syndrome coronarien aigu, les médecins et le personnel infirmier ont effectué de nombreux ajustements posologiques de l'héparine non conformes au protocole. Ces ajustements non conformes étaient la plupart du temps attribuables à de mauvais calculs ou à une mauvaise interprétation du protocole.

Mots clés : héparine, protocole d'ajustement posologique, syndrome coronarien aigu

INTRODUCTION

IV heparin is commonly administered to cardiac patients, particularly those with acute coronary syndromes. This drug has proven effective for the prevention and treatment of venous thrombosis and pulmonary embolism, for the prevention of mural thrombosis after myocardial infarction, and for the treatment of patients with unstable angina and myocardial infarction.[1]

Data from the GUSTO-I trial demonstrated that therapeutic anticoagulation was associated with lower reinfarction and mortality rates after acute myocardial infarction.[2] In addition, a higher incidence of moderate or severe bleeding and reinfarction was observed among patients with higher activated partial thromboplastin time (aPTT).

To reduce the time to therapeutic anticoagulation and to increase the time spent in the therapeutic range, many institutions have developed and used titration protocols.[3-5] The main objective of this study was to evaluate compliance by physicians and nursing personnel in applying such a protocol for patients with acute coronary syndromes. Two secondary objectives were to evaluate the time required to reach therapeutic aPTT and the time spent in the therapeutic aPTT range.

METHODS

In this study the authors analyzed all courses of heparin therapy given to all patients admitted to the coronary care unit of the Hôpital du Sacré-Cœur de Montréal over a 5-month period. The patients' medical records were reviewed to obtain data on the heparin treatments.

At the authors' centre, heparin is administered intravenously to patients with cardiac disease who are admitted to the coronary care unit according to a protocol approved by the Pharmacology and Therapeutics Committee. The protocol used at the time of this study is presented in Appendix 1. In brief, the treating physician orders the initial loading dose and specifies the infusion rate according to the protocol. Both the loading dose and the initial infusion rate can be adjusted for the patient's body weight if the physician so desires. Nurses are subsequently responsible for ordering tests of aPTT (6 h after the loading dose, 6 h after each dosage change, and daily thereafter), monitoring the results, and making the appropriate dosage adjustments on the basis of the protocol. The protocol does not account for weight in subsequent adjustments but rather dictates a percent increase or decrease in the infusion rate based on the extent of the discrepancy between actual and desired aPTT values. The goal is to achieve a target aPTT of 45–75 s or 1.5–2.5 times control. Nonetheless, physicians are allowed to make dosage changes that do not conform to the protocol if they deem it necessary.

For the purposes of this study, the times at which changes in heparin dosage were ordered and the actual dose administered were recorded, as were the times at which aPTT tests were ordered and the actual values obtained; these data were compared with the protocol to evaluate the compliance of any adjustments with the protocol. In addition, the time necessary to attain a therapeutic value of aPTT and the time spent in the therapeutic range were estimated by calculating the slope of the line between each set of 2 consecutive data points that rested on each side of 1 of the 2 therapeutic aPTT boundaries (less than 45 s or greater than 75 s) and estimating the time at which the boundary would be crossed; from this estimation, time spent in the therapeutic range was calculated for that interval. All time intervals inside or outside the therapeutic range were then summed, as needed. Finally, the impact of noncompliance with the protocol on time spent in the therapeutic range and time necessary to attain a therapeutic aPTT was evaluated and compared with that of compliant interventions.

The results are expressed as mean values ± standard deviation or number (and percentage) of patients. Differences between groups were evaluated by analysis of variance (for continuous data) or by chi-square analysis (for categorical variables). A p value of less than 0.05 was considered significant.

RESULTS

This study analyzed 190 courses of heparin treatment given to 170 consecutive patients admitted to the coronary care unit between November 18, 1996, and April 2, 1997. The baseline characteristics of the patients are presented in Table 1. Of the 190 heparin treatments given, 133 (70%) were prescribed for patients who presented with non-ST-elevation acute coronary syndromes, and 181 (95%) were administered concomitantly with acetylsalicylic acid. In 61 cases (32%), a weight-adjusted loading dose and infusion were prescribed to initiate heparin therapy; in the other cases, there was no adjustment for body weight.

Data regarding the efficiency of the protocol in achieving therapeutic aPTT values are summarized in Table 2. The duration of heparin infusion was 87 ± 62 h (median 74 h). The mean infusion rate by the time therapeutic aPTT was achieved was 917 ± 231 U/h (12.6 ± 2.8 U/kg per hour; median 960 U/h). Therapeutic values of aPTT were achieved during heparin infusion for 187 (98%) of the treatment courses. On average, 21 ± 18 h (median 17 h) elapsed from the time the

Table 1. Baseline Characteristics

Characteristic	Mean ± SD or No. (%)			*p* Value
	All Treatment Courses (n = 190)	Without Noncompliant Interventions (*n* = 96)	With Noncompliant Interventions (*n* = 94)	
Age (yr)	65 ± 13*	66 ± 14†	65 ± 12‡	0.91
Sex (no. and % of men)	115 (68)*	59 (68)†	56 (68)‡	0.96
Weight (kg)	74 ± 14*	74 ± 14†	74 ± 15‡	0.73
Diagnosis on admission				
Unstable angina	90 (47)	47 (49)	43 (46)	0.77
Non-ST-elevation MI	43 (23)	14 (15)	29 (31)	0.01
ST-elevation MI	49 (26)	29 (30)	20 (21)	0.21
Other	8 (4)	6 (6)	2 (2)	0.29
Weight-based heparin dosing	61 (32)	29 (30)	32 (34)	0.68
Starting infusion rate, U/kg per hour				
Adjusted for body weight	14.9 ± 2.5	15.0 ± 2.8	14.8 ± 2.1	0.80
Not adjusted for body weight	14.1 ± 2.7	14.3 ± 3.0	13.8 ± 2.3	0.27
Concurrent medication				
Alteplase	15 (8)	4 (4)	11 (12)	0.10
Streptokinase	21 (11)	7 (7)	14 (15)	0.15
Acetylsalicylic acid	181 (95)	91 (95)	90 (96)	0.97
Warfarin	14 (7)	6 (6)	8 (9)	0.75
Ticlopidine	35 (18)	13 (14)	22 (23)	0.12

SD = standard deviation, MI = myocardial infarction.
*Data calculated and presented on the basis of 170 patients.
†Data calculated and presented on the basis of 87 patients.
‡Data calculated and presented on the basis of 83 patients.

Table 2. Attainment of Therapeutic Values for Activated Partial Thromboplastin Time (aPTT)

Clinical Parameter	Mean ± SD or No. (%) of Treatment Courses			*p* Value
	All Treatment Courses (n = 190)	Without Noncompliant Interventions (*n* = 96)	With Noncompliant Interventions (*n* = 94)	
Heparin infusion rate (U/h)*	917 ± 231	907 ± 211	930 ± 255	0.024
Duration of heparin infusion (h)	87 ± 62	79 ± 46	96 ± 74	0.25
Therapeutic aPTT† at any time during infusion	187 (98)	95 (99)	92 (98)	0.99
Time to reach therapeutic aPTT† (h)	21 ± 18	18 ± 16	25 ± 19	0.43
Therapeutic aPTT† reached within 24 h	92 (48)	56 (58)	36 (38)	0.009
aPTT > 75 s at any time during infusion	131 (69)	65 (68)	66 (70)	0.82
% of time in aPTT zones				
<45 s (subtherapeutic)	22 ± 22	18 ± 19	26 ± 24	0.017
45–75 s (therapeutic)	63 ± 23	68 ± 21	57 ± 23	0.001
>75 s (supratherapeutic)	16 ± 17	14 ± 16	17 ± 18	0.21

SD = standard deviation.
*Rate of heparin infusion when target aPTT is reached.
†Therapeutic aPTT = 45–75 s.

infusion was initiated until aPTT values reached therapeutic levels, and only 92 (48%) of the treatment courses led to therapeutic aPTT values within 24 h. Patients spent only 63% ± 23% of the time in the therapeutic range (aPTT between 45 and 75 s). Supratherapeutic values of aPTT (above 75 s) at any time during the infusion period were observed for 131 (69%) of the treatment courses.

In total, 587 interventions were performed, 190 by physicians and 397 by nurses. Overall, half of the treatment courses (94 of 190) included heparin dosing adjustments that were not compliant with the approved protocol (Table 3), and there were a total of 96 noncompliant modifications.

Of the 190 interventions performed by physicians, 27 (14%) were noncompliant with the protocol. In close to half of these cases, heparin was reinitiated (after a period of discontinuation) at a different infusion rate than specified by the protocol.

Of the 397 interventions performed by nursing personnel, 69 (17%) were noncompliant with the protocol. Miscalculations or misreading of the protocol were the source of noncompliant adjustments in 32 (46%) of these 69 cases. In addition, 27 (39%) of the noncompliant adjustments were due to unauthorized interventions, such as lack of modification of the infusion rate as specified by the protocol or an unwarranted change in heparin dosing regimen.

Patients for whom noncompliant dosing adjustments were made spent less time in the therapeutic aPTT range than patients for whom all interventions were compliant with the protocol (57% ± 23% vs 68% ± 21%, $p = 0.001$) (median 58% vs 72%) and more time in the subtherapeutic zone (26% ± 24% vs 18% ± 19%, $p = 0.017$) (median 19% vs 11%) or the supratherapeutic zone (17% ± 18% vs 14% ± 16%, $p = 0.21$) (median 12% vs 10%). Finally, a smaller proportion of patients whose heparin infusion rate was adjusted inappropriately reached therapeutic aPTT levels within 24 h (38% vs 58%, $p = 0.009$).

DISCUSSION

In this study, half of the patients underwent at least one heparin dosing adjustment that was noncompliant with the titration protocol; such noncompliant adjustments were performed by both physicians and nurses. The most common types of noncompliant adjustment appeared to involve calculation of new infusion rates. These "out of protocol" interventions were associated with a delay in reaching therapeutic aPTT and a decrease in the time spent in the therapeutic aPTT range.

Delays in achieving therapeutic aPTT levels may be detrimental to patients. In a cohort of patients with acute myocardial infarction who were receiving recombinant tissue-type plasminogen activator, Hsia and others[6] found that early anticoagulation (therapeutic aPTT at 8 and 12 h after the start of fibrinolysis) resulted in a greater proportion of patients with patency of the infarct-related artery. Conversely, elevated aPTT levels have resulted in an increased risk of bleeding, reinfarction, stroke, and death.[2]

Several researchers have tried to find ways to improve heparin anticoagulation, in particular through rapid achievement of a desired range of anticoagulation.[3,4,7] Nomograms for weight-adjusted dosing are in most cases superior to standard-dose heparin or non-weight-based heparin nomograms in achieving rapid therapeutic anticoagulation.[5,8-19] Hochman and others[11] compared the efficacy of 2 weight-adjusted heparin regimens (70 U/kg bolus, maximum of 5000 U, followed by 15 U/kg per hour, maximum of 1000 U/h [n = 19 patients]; or 60 U/kg bolus, maximum of 4000 U, followed by 12 U/kg per hour, maximum of 900 U/h [n = 38 patients]) with that of standard heparin dosing (5000 U bolus, followed by infusion of 1000 U/h [n = 23 patients]) in patients with acute coronary syndromes. Of the patients receiving standard heparin dosing, 52% were within the therapeutic range at 24 h, whereas 79% of those with the high-dose weight-adjusted regimen and 74% of those with the low-dose weight-adjusted regimen reached the

Table 3. Physicians' and Nurses' Compliance with Heparin Protocol

	No. (%)*
No. of treatment courses with at least one noncompliant dosing adjustment (n = 190)	94 (49)
No. of interventions	587
By nurses	397 (68)
By physicians	190 (32)
Dosing adjustments noncompliant with protocol	96
By nurses	69 (72)
By physicians	27 (28)
No. of noncompliant interventions by nurses	69
No increase or decrease in infusion rate when needed	16 (23)
No change in dosing regimen despite physician's order	3 (4)
Unauthorized increase or decrease in infusion rate	8 (12)
aPTT measured too early	4 (6)
Infusion initiated late	6 (9)
Miscalculation or misreading of infusion rate	32 (46)
No. of noncompliant adjustments by physicians	27
Reinitiation of infusion at inadequate rate	12 (44)
Loading dose given with streptokinase	7 (26)
Unwarranted loading dose	1 (4)
Unwarranted lack of loading dose	6 (22)
Unwarranted change in infusion rate	1 (4)

aPTT = activated partial thromboplastin time.
*Percentages in each section of the table are calculated using the n value in the first row of the section as the denominator.

therapeutic range within 24 h. In the present study, 32% of the patients were initiated on a weight-adjusted heparin regimen, and only 53% of these patients achieved a therapeutic aPTT level within 24 h after initiation of heparin therapy.

Although use of a weight-based heparin dosing protocol improves the clinical efficacy of heparin treatment by reducing the time needed to achieve therapeutic anticoagulation or increasing the time spent in the therapeutic window, the existence of such protocols does not guarantee compliance or absence of dosing errors. In fact, a weight-based nomogram might be associated with an even greater potential for error. Sherman and others[20] assessed protocol compliance in the treatment of 20 patients with heart failure who required heparin therapy. Of 334 interventions, 12% were noncompliant, and 61% of the noncompliant adjustments were accounted for by dosing errors. The remaining noncompliant interventions were related to aPTT testing, which was either performed at an incorrect time or was not performed at all. In another study of 100 patients with deep vein thrombosis or pulmonary embolism, the noncompliance rate was 64%, and 47% of the noncompliant adjustments were dosing errors.[14]

In this study of 190 heparin treatments, the noncompliance rate among the 397 interventions performed by nursing personnel was 17%, similar to that observed by Sherman and others,[20] whose study focused on nurses. Noncompliance was associated with a significantly shorter time spent in the therapeutic range and fewer patients reaching therapeutic anticoagulation within 24 h. Most of the noncompliant interventions were related to dosing, and only 6% were associated with testing of aPTT.

A variety of approaches could be used to improve the compliance rate. The protocol used in the authors' institution is based on percentage increases or decreases in infusion rate rather than absolute increases or decreases. Given that a significant proportion of the noncompliant interventions were related to miscalculations, it appears that compliance could be improved if the protocol was modified to dictate absolute changes in the infusion rate instead of percentage changes. In addition, a computer-based heparin dosing protocol might improve compliance and reduce dosing errors. Kershaw and others[21] demonstrated that pharmacy-based, computer-assisted heparin dosing resulted in faster treatment (median time to reach therapeutic aPTT 15 h vs 7 h in historical control and computer-assisted dosing groups, respectively; $p < 0.001$) and more accurate dosing (time with aPTT in the therapeutic range 43% vs 75%, $p < 0.001$).

The current study had several limitations, including study design (a chart review). As such, interventions that were deemed noncompliant might not have been considered noncompliant in a prospective study. Another drawback was the relatively small number of patients and the fact that they were from a single centre, which limited the external validity. Several authors have already confirmed the superiority of a weight-adjusted heparin regimen over standard dosing. Therapeutic aPTT values would probably have been achieved more quickly had a weight-adjusted heparin protocol been used. However, although such a practice has been recommended by the American College of Cardiology and the American Heart Association,[22] it was not standard practice at the authors' institution at the time this study was conducted. Finally, the recommendations for heparin dosing in patients with acute coronary syndromes have changed since this study was performed,[23,24] and the results regarding the efficiency of the protocol cannot be extrapolated to current practice.

In conclusion, use of a heparin protocol for cardiac patients was associated with achievement of target aPTT in 70% of cases, but aPTT was in the therapeutic range only 63% of the time, on average. Physicians and nursing personnel made noncompliant adjustments in applying the protocol, which were associated with suboptimal anticoagulation. Development of a weight-based heparin nomogram that specifies changes in infusion rates in absolute terms, rather than percentages, may decrease the time necessary to reach the therapeutic range and reduce the number of non-compliant interventions.

References

1. Hirsh J, Anand SS, Halperin JL, Fuster V; American Heart Association. Guide to anticoagulant therapy: heparin. A statement for healthcare professionals from the American Heart Association. *Circulation* 2001;103:2994-3018.
2. Granger CB, Hirsh J, Califf RM, Col J, White HD, Betriu A, et al. Activated partial thromboplastin time and outcome after thrombolytic therapy for acute myocardial infarction: results from the GUSTO-I trial. *Circulation* 1996;93:870-8.
3. Flaker GC, Bartolozzi J, Davis V, McCabe C, Cannon CP. Use of a standardized heparin nomogram to achieve therapeutic anticoagulation after thrombolytic therapy in myocardial infarction. TIMI 4 investigators. Thrombolysis in Myocardial Infarction. *Arch Intern Med* 1994;154:1492-6.
4. Cruickshank MK, Levine MN, Hirsh J, Roberts R, Siguenza M. A standard heparin nomogram for the management of heparin therapy. *Arch Intern Med* 1991;151:333-7.
5. Gunnarsson PS, Sawyer WT, Montague D, Williams ML, Dupuis RE, Caiola SM. Appropiate use of heparin: empiric vs nomogram-based dosing. *Arch Intern Med* 1995;155:526-32.
6. Hsia J, Kleiman N, Aguirre F, Chaitman BR, Roberts R, Ross AM. Heparin-induced prolongation of partial thromboplastin time after thrombolysis: relation to coronary artery patency. HART Investigators. *J Am Coll Cardiol* 1992;20:31-5.
7. Becker RC, Ball SP, Eisenberg P, Borzak S, Held AC, Spencer F, et al. A randomized, multicenter trial of weight-adjusted intravenous heparin dose titration and point-of-care coagulation monitoring in hospitalized patients with acitve thromboembolic disease. Antithrombotic Therapy Consortium Investigators. *Am Heart J* 1999;137:59-71.

8. Mungall D, Lord M, Cason S, Treadwell P, Williams D, Tedrick D. Developing and testing a system to improve the quality of heparin anticoagulation in patients with acute cardiac syndromes. *Am J Cardiol* 1998;82:574-9.
9. Davydov L, Dietz PA, Lewis P, Twichell ML, Bertino JS Jr. Outcomes of weight-based heparin dosing based on literature guidelines and institution individualization. *Pharmacotherapy* 2000;20:1179-83.
10. Price CK, Colodny L. Partnering with nurses to manage heparin therapy with a weight-based protocol. *Am J Health Syst Pharm* 2000;57:110-6.
11. Hochman JS, Wali AU, Gavrila D, Sim MJ, Malhotra S, Palazzo AM, et al. A new regimen for heparin use in acute coronary syndromes. *Am Heart J* 1999;138:313-8.
12. Hollingsworth JA, Rowe BH, Brisebois FJ, Thompson PR, Fabris LM. The successful application of a heparin nomogram in a community hospital. *Arch Intern Med* 1995;155:2095-100.
13. Raschke RA, Gollihare B, Peirce JC. The effectiveness of implementing the weight-based heparin nomogram as a practice guideline. *Arch Intern Med* 1996;156:1645-9.
14. Shalansky KF, FitzGerald JM, Sunjerji R, Traboulay SJ, O'Malley B, McCarron BI, et al. Comparison of a weight-based heparin nomogram with traditional heparin dosing to achieve therapeutic anticoagulation. *Pharmacotherapy* 1996;16:1076-84.
15. Paradiso-Hardy FL, Cheung B, Geerts WH. Evaluation of an intravenous heparin nomogram in a coronary care unit. *Can J Cardiol* 1996;12:802-8.
16. Chamuleau SA, de Winter RJ. Activated partial thromboplastin time (aPTT) monitoring to achieve therapeutic anticoagulation before and after introducing a nomogram for adjunctive heparin treatment with thrombolytic therapy for acute myocardial infarction. *Int J Cardiol* 1998;67:241-6.
17. Zimmermann AT, Jeffries WS, McElroy H, Horowitz JD. Utility of a weight-based heparin nomogram for patients with acute coronary syndromes. *Intern Med J* 2003;33:18-25.
18. Lackie CL, Luzier AB, Donovan JA, Feras HI, Forrest A. Weight-based heparin dosing: clinical response and resource utilization. *Clin Ther* 1998;20:699-710.
19. Raschke RA, Reilly BM, Guidry JR, Fontana JR, Srinivas S. The weight-based heparin dosing nomogram compared with a "standard care" nomogram. A randomized controlled trial. *Ann Intern Med* 1993;119:874-81.
20. Sherman DS, Clarke SH, Lefkowitz JB, Valuck RJ, Lindenfeld J, Stringer KA. An institution-specific heparin titration nomogram: development, validation, and assessment of compliance. *Pharmacotherapy* 2001;21:1167-74.
21. Kershaw B, White RH, Mungall D, Van Houten J, Brettfeld S. Computer-assisted dosing of heparin. Management with a pharmacy-based anticoagulation service. *Arch Intern Med* 1994;154:1005-11.
22. Ryan TJ, Anderson JL, Antman EM, Braniff BA, Brooks NH, Califf RM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1996;28:1328-428.
23. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—2002: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). *Circulation* 2002;106:1893-900.
24. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Circulation* 2004;110:e82-e292.

Chantal Pharand, PharmD, BCPS, is an Associate Professor, Faculty of Pharmacy, Université de Montréal, and an Adjunct Researcher and Clinical Pharmacist with the Research Centre and Department of Pharmacy, Hôpital du Sacré-Coeur de Montréal, Montréal, Quebec.

Stéphanie Castonguay, BPharm, is a medical student in the Faculty of Medicine, Université de Montréal, Montréal, Quebec.

Virginie Héroux, MSc, is a pharmacist at the Centre hospitalier universitaire de Sherbrooke, Sherbrooke, Quebec.

This work was performed at the Hôpital du Sacré-Coeur de Montréal, Montréal, Quebec

Address correspondence to:
Dr Chantal Pharand
Centre de recherche
Hôpital du Sacré-Cœur de Montréal
5400, boulevard Gouin ouest
Montréal QC
H4J 1C5

e-mail: chantal.pharand@umontreal.ca

Appendix 1. Heparin protocol for patients with non-ST-elevation and ST-elevation acute coronary syndromes

The heparin regimen is to be started with a loading dose of 5000 U or 70 U/kg IV, followed by an infusion of 1000 U/h or 15 U/kg per hour IV. The choice of a standard or weight-adjusted regimen is left to the discretion of the treating physician. For patients treated with streptokinase, heparin is to be started 12 h later without a loading dose.

aPTT (s)	Heparin Dose	Timing of Repeat aPTT
< 35	Loading dose of 1000 U and increase infusion rate by 25%	6 h later
35–39.9	Increase infusion rate by 15%	6 h later
40–44.9	Increase infusion rate by 10%	6 h later
45–75	No change	Next day
75.1–85	Decrease infusion rate by 15%	6 h later
85.1–95	Decrease infusion rate by 20%	6 h later
95.1–100	Decrease infusion rate by 25%	6 h later
> 100	Stop infusion for 30 min and decrease infusion rate by 30%	6 h later

aPTT = activated partial thromboplastin time.