Utilization and Effectiveness of a Weight-Based Heparin Nomogram at a Large Academic Medical Center

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Abstract

Objective: **To determine the utilization rate of a weight-based heparin nomogram and to assess the performance of the nomogram outside of experimental conditions.**

Study Design: **Prospective cohort analysis.**

Patients and Methods: **A total of 747 consecutive patients treated with intravenous heparin therapy for any indication on an internal medicine service were evaluated for the utilization rate of the weight-based nomogram, the time needed to exceed heparin's therapeutic threshold (activated partial thromboplastin time [aPTT] of >1.5 times the control value), and the time needed to achieve heparin's therapeutic range (aPTT of 1.5 to 2.4 times the control value). Physicians were encouraged to use the weight-based nomogram by using conventional continuing medical education techniques and by configuring the computerized order entry system to give physicians an equally easy and voluntary choice between choosing the weight-based nomogram or ordering heparin in the traditional fashion.**

Results: **The study program had no effect in increasing the utilization rate of the nomogram; this rate remained the same as before the program was initiated (10%). Less time was needed both to exceed the therapeutic threshold and to achieve a therapeutic range with the weight-based nomogram compared with physician-guided dosing ($P < .001$ and $P = .021$, respectively). No difference was demonstrated between the weight-based and physician-guided groups in incidence of bleeding complications or in the proportion of patients with one or more supratherapeutic aPTTs.**

Conclusions: **The weight-based nomogram led to superior intermediate outcomes compared with physician-guided dosing. However, despite efforts intended to modify physician behavior, the utilization rate remained so low that it was ineffective. Further research into the reasons why physicians chose not to use the weight-based nomogram and further research into methods to translate efficacious therapies into effective patient care are indicated.**

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The central role of heparin therapy in the treatment of thromboembolic disorders has been well established.[1-4] Studies have shown that adequate heparinization results in substantially lower rates of recurrent deep venous thrombosis[3-9] and reduced rates of recurrent cardiovascular events in patients with unstable angina or non–Q-wave myocardial infarction.[2,10-12] Intravenous heparin, however, is notoriously difficult to dose appropriately,[13-16] and studies have demonstrated that many patients treated with intravenous heparin do not attain a therapeutic activated partial thromboplastin time (aPTT) by 24 hours. Physician-guided dosing

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practices often result in an inadequate heparin initial bolus or infusion rate[13-19] or a delay ordering or responding to laboratory coagulation test results.[13,14,17,19-22] Also, physicians' responses to laboratory test results are sometimes inappropriate.[13-15,22]

Physician-guided dosing practices can be improved with standardized nomograms.[5,17,19-31] Investigators have demonstrated that heparin protocols, weight-based heparin protocols in particular,[5,17,22,24-31] result in a greater percentage of patients achieving a therapeutic aPTT by 24 hours,[5,17,20-22,24-31] produce lower recurrence rates of deep vein thrombosis,[5,21] show no difference in rates of clinically significant bleeding,[5,17,21-24,26,27,29-31] and require fewer heparin dosage adjustments to remain in the therapeutic range[5,24,25] compared with physician-guided heparin dosing.

Although the efficacy of weight-based heparin protocols has been proved superior to that of physician-guided heparin dosing in clinical trials and this information has been widely disseminated,[5,17,22,24-29] only 2 studies have described how this proven efficacy translates outside of experimental conditions or whether it has changed physician behavior.[29,32] To further address this issue, we assessed the utilization rate of an available weight-based heparin protocol compared with physician-guided heparin dosing, as well as the effect of an intervention aimed at increasing the utilization of the weight-based protocol, over a 3-month period on the medical service at a single academic institution. In addition, we evaluated the effectiveness of the weight-based protocol at our institution to ensure the generalizability of the previously published studies.

··· PATIENTS AND METHODS ···

Setting

All patient care orders on the medical service at our institution, a 900-bed academic medical center in southern New England, are written by the approximately 100 members of the internal medicine house staff. All medication orders are entered via a menu-driven computerized order entry system. One year before this study, an established weight-based heparin protocol[5] was configured for the computerized order entry system so that house staff attempting to order continuous-infusion intravenous heparin therapy for any indication were given an equal and voluntary choice between ordering the weight-based protocol or ordering heparin via a physician-guided mechanism. Particular attention was given to designing the weight-based protocol screens within the computerized order entry system to ensure that the protocol was understandable, simple, and easy to use. For example, the patient's actual body weight (entered on admission by the intake nurse) was visible on the screen, and when that weight was selected by the house officer, the system automatically calculated the correct bolus and infusion rate. Heparin boluses were calculated at 80 U/kg and rounded to the nearest 100 U up to a maximum of 125 kg; thereafter, the suggested bolus dose was 80 U/kg but was left for the physician to type in. Heparin infusion rates were calculated at 18 U/kg with the same rounding, maximum weight, and suggestion for extreme obesity as for the bolus. Adjustments to therapy, based on aPTT, were as reported by Raschke et al.[5]

Internal medicine house staff were encouraged with conventional continuing medical education techniques to use the weight-based protocol. During the period July 1, 1996, through January 7, 1997, one of the authors (TJB) made multiple, formal conference presentations to the approximately 100 internal medicine house staff. This author, a former internal medicine house officer, former medical chief resident (1995-1996), and current junior faculty member at the institution, was known and recognized as a physician-leader among the house staff. The 1-hour conferences included lunch and focused on the data supporting the weight-based protocol, recommended that it be used for any patient in whom therapeutic heparinization was a goal, and presented data regarding the current utilization rate of the protocol, the local experience that therapeutic aPTT was obtained in less time with the protocol, and our findings of a low complication rate. During this same period, this author also attended morning report on a regular basis and had extensive contact with the medical house staff on the patient care units, during which time the house staff were again reminded of the superiority of the weight-based protocol.

Measurements

All patients admitted to the medical service and treated with intravenous heparin for any indication between October 18, 1996, and January 7, 1997, were identified through a daily query of the computerized order entry system. Patients receiving warfarin before initiation of intravenous heparin therapy were excluded. Because we were primarily interested in examining the impact of the weight-based heparin nomogram on initial heparinization, only patients receiving intravenous heparin who had

at least one aPTT determination 6 or more hours later were included. Data available and collected for each patient via the computerized order entry system included patient age, gender, total body weight, time of heparin order, initial heparin infusion rate, total heparin dose in 24 hours, type of heparin therapy ordered (weight based vs physician guided), and name of ordering physician. Laboratory records for each patient were checked for the following:

- baseline hemoglobin
- interval between heparin order and first aPTT determination
- number of aPTT determinations in the initial 48 hours of heparin therapy
- presence or absence of a drop in hemoglobin of greater than 2 g/dL in the 7 days after initiation of heparin therapy, and
- time from heparin order until first achievement of the therapeutic threshold (first aPTT value exceeding the therapeutic threshold of 55 seconds or 1.5 times the control aPTT value) and the therapeutic range (first aPTT value within the therapeutic range of 55-85 seconds or 1.5-2.4 times the control aPTT value).

Concomitantly, the hospital's cost accounting database was checked for each patient's discharge diagnoses as coded by International Classification of Diseases, 9th revision (ICD-9), and ethnicity. Patients were assessed as having had a bleeding complication if they had a primary or any one of 9 secondary discharge codes noting a retroperitoneal, intracranial, gastrointestinal, intra-articular, or other site of bleeding (ICD-9s: 459.00, 432, 431.00, 430.00, 578.10, 786.30).

All blood specimens were collected in siliconized Vacutainer tubes (Becton-Dickinson Company; Rutherford, NJ) that contained buffered citrate for aPTT determinations and calcium EDTA for complete blood count determinations. The laboratory used Dade FSL actin thromboplastin (Baxter Healthcare Corporation, Dade Division; Miami, FL) and an automated coagulation system (MLA Electra 1000c, Medical Laboratory Automation Inc; Pleasantville, NY) to determine aPTT values. At our hospital, the normal range for aPTT in patients without known coagulopathy and not receiving anticoagulants was 25-36 seconds. We used the upper limit of this normal range (36 seconds) as our control aPTT value, and an aPTT of 55-85 seconds (1.5 to 2.4 times the control aPTT value) correlated with heparin levels of 0.35-0.61 IU/mL by anti–factor X activity. The therapeutic threshold therefore was established as 55 seconds, and the therapeutic range was established as 55-85 seconds. Any aPTT values greater than 85 seconds were considered supratherapeutic.

Six weeks after the initiation of the study, we performed a survey of house officers regarding their experience with and opinion of the protocol. The simple, 2-question survey asked each physician if he or she preferred the weight-based protocol or empiric therapy, and then asked the reason(s) for his or her preference.

Statistical Methods

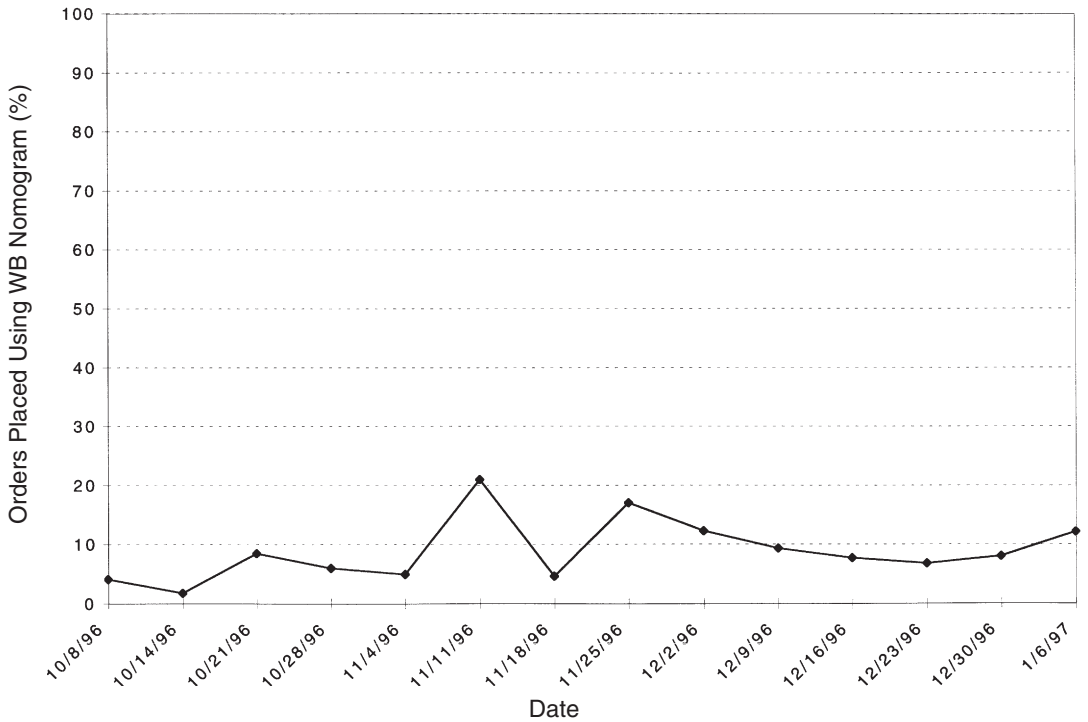
The Statistical Analysis System (SAS version 6.12, SAS Institute; Cary, NC) was used for all calculations and statistical analyses. Continuous variables were compared using the Student *t* test, and discrete variables were compared using the Fisher exact or chi-square test, as appropriate. The time to therapeutic threshold and time to therapeutic range were determined by using time-to-event analysis, and the 2 patient groups (weight-based and physician-guided heparin dosing) were compared by means of the log-rank test.

Multivariable analysis by means of the Cox proportional hazards model was performed to assess differences between the weight-based and physician-guided groups in the time to therapeutic threshold and the time to therapeutic range, after adjusting for age, gender, and primary discharge diagnosis. Data were censored at 72 hours if the outcomes (therapeutic threshold and therapeutic range) were not achieved by 72 hours.

··· RESULTS ···

A total of 747 consecutive patients admitted to the internal medicine service were treated with continuous-infusion intravenous heparin therapy during the study period. Sixty-seven (9%) patients received heparin via the weight-based protocol, and 680 (91%) patients received heparin via physician-guided mechanisms. Utilization of the available weight-based protocol was approximately constant at 10% throughout the study period and did not vary in response to the educational interventions (Figure 1). There was no difference in mean postgraduate training year between the physicians using the weight-based protocol and those using the physician-guided mechanisms. A small proportion of physicians (29/138 or 21%) accounted for all weight-based orders, and no physician placed 100% of his or her

Figure 1. Utilization Rate of the Weight-Based (WB) Heparin Nomogram



The utilization rate remained at 20% or less throughout the study period despite interventions intended to increase the use of the weight-based nomogram (n = 747).

Table 1. Patient Characteristics

Characteristic	Weight-Based Group	Physician-Guided Group	*P*
No. of patients	67 (9%)	680 (91%)	
Mean age, y (SD)	65.9 (13.1)	62.9 (14.9)	.123
No. of women	31 (46%)	262 (39%)	.219
Mean initial hemoglobin, g (SD)	12.8 (2.2)	13.1 (1.8)	.253
Mean weight, kg (SD)	81.6 (25.0)	82.8 (20.4)	.753
No. of nonwhite patients	13 (20%)	109 (16%)	.448

heparin orders using the weight-based protocol.

Thirty-six residents completed the survey administered at 6 weeks; 13 (36%) reported they favored the weight-based protocol and 23 (64%) reported they preferred determining the heparin bolus and infusion rate without the protocol. Examining these latter residents' reasons for their choice revealed that 5 (22%) reported they had difficulty obtaining patient weights, 10 (43%) reported they did not believe that the protocol could attain a therapeutic aPTT as quickly as physician-determined dosing, and 5 (22%) reported they found the protocol too difficult to understand.

Patient characteristics were similar in the weight-based and physician-guided groups (Table 1). There were significant differences between groups in the proportion of patients with discharge diagnoses

of myocardial infarction, cardiac arrhythmia, acute coronary syndrome, and malignancy (Table 2).

The average initial heparin infusion rate and the total dose of heparin in 24 hours were significantly greater in the weight-based group compared with the physician-guided group (Table 3). No difference was noted between groups in mean time elapsed from heparin order until first aPTT determination or in the mean number of aPTT determinations in the first 48 hours after heparin determination.

The success of the protocols was compared using time-to-event analysis (Figures 2 and 3). The weight-based protocol achieved both primary outcomes, aPTT exceeding the therapeutic threshold and aPTT within the therapeutic range, more rapidly than physician-guided heparin dosing ($P < .001$ and $P = .021$, respectively, by the log-rank test). The proportion of patients exceeding the therapeutic threshold by 24 hours was 79% in the weight-based group and 56% in the physician-guided group ($P < .001$); by 48 hours, the proportions increased to 88% and 66%, respectively ($P < .001$). Forty-seven percent of patients in the weight-based group and 39% in the physician-guided group ($P = .270$) attained an aPTT in the therapeutic range by 24 hours; by 48 hours, the proportions increased to 69% and 52%, respectively ($P = .019$).

After adjusting for differences in age, gender, and primary discharge diagnosis, the time to therapeutic threshold remained significantly shorter ($P < .001$) in the weight-based group than in the physician-guided group. The difference between groups in time to therapeutic range was close to statistical significance ($P = .078$).

No difference was noted between the 2 groups in the incidence of complications (Table 4). There were 8 bleeding complications among the physician-guided patients; 4 were melena, 2 were hemoptysis, 1 was "hemorrhage not otherwise specified," and 1 was an intracerebral hemorrhage. The only patient in the weight-based group with a complication was noted to have melena. The proportion of patients with at least one supratherapeutic aPTT within 72 hours of initiation of heparin therapy was similar in both groups, as was the proportion of patients with a drop in hemoglobin con-

Table 2. Primary Discharge Diagnoses

Diagnosis	No. (%) of Patients: Weight-Based Group (n = 67)	No. (%) of Patients: Physician-Guided Group (n = 680)	*P*
Acute coronary syndrome	17 (25)	273 (40)	.018
Cardiac arrhythmia	14 (21)	54 (8)	.001
Congestive heart failure	6 (9)	51 (8)	.669
Deep vein thrombosis/pulmonary embolism	1 (2)	20 (3)	.990
Malignancy	4 (6)	12 (2)	.047
Myocardial infarction	10 (15)	184 (27)	.031
Pneumonia	5 (7.4)	30 (4)	.231
Stroke/transient ischemic attack	2 (3)	5 (1)	.124
Other	8 (12)	51 (8)	.199

Table 3. Heparin Doses and aPTT Determinations

Process	Weight-Based Group	Physician-Guided Group	*P*
Mean initial heparin infusion rate, U/h (SD)	1321 (297)	1074 (311)	<.001
Mean total heparin dose in 24 h, U (SD)	31,328 (6883)	25,784 (8240)	<.001
Mean time from heparin dose until first aPTT determination, h (SD)	7.71 (3.5)	6.94 (4.9)	.103
Mean number of aPTT determinations in first 48 h after initiation of heparin therapy (SD)	2.94 (1.1)	3.00 (1.5)	.725

aPTT = activated partial thromboplastin time.

centration of more than 2 g/dL in the 7 days after initiating heparin therapy (Table 4).

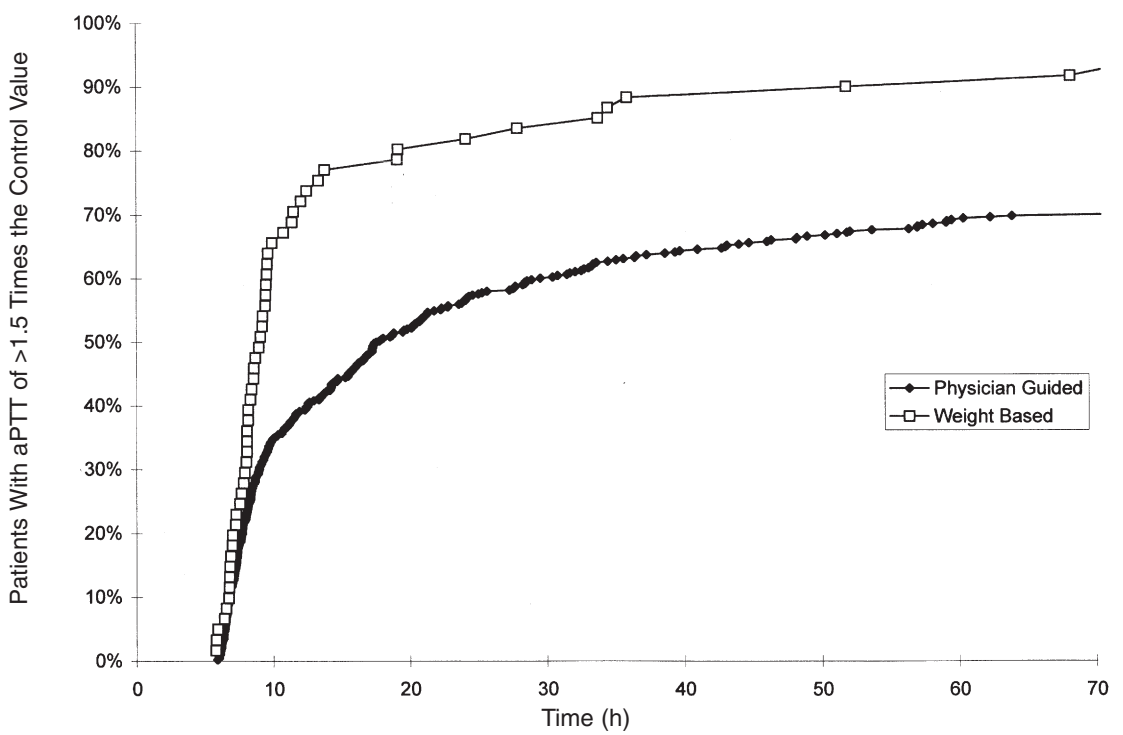
··· DISCUSSION ···

Fewer than 10% of the patients who received intravenous heparin therapy at our institution had their dosage determined via an available, efficacious, and easy-to-use weight-based nomogram. Furthermore, only 21% of physicians placed even a single heparin order using the weight-based nomogram. This low rate of utilization occurred despite wide dissemination in the literature of the superior efficacy of weight-based heparin protocols,[5,17,22,24-29] easy accessibility of the protocol via the computerized order entry system, and use of a combination of methods demonstrated to modify physician behavior, including education, concurrent feedback, and participation by a physician-leader.[33,34]

In this study we also confirmed what had been established in previous studies: the superiority of the weight-based nomogram over physician-guided dosage determination.[5,29] Our patients receiving heparin via the weight-based protocol during the study period were significantly more likely to exceed the therapeutic threshold and significantly more likely to attain an aPTT within the therapeutic range than were patients receiving physician-guided heparin; furthermore, no difference was demonstrated in the proportion of patients with one or more supratherapeutic aPTTs within 72 hours of initiating heparin therapy, in the incidence of coded complications, or in the incidence of a fall in hemoglobin.

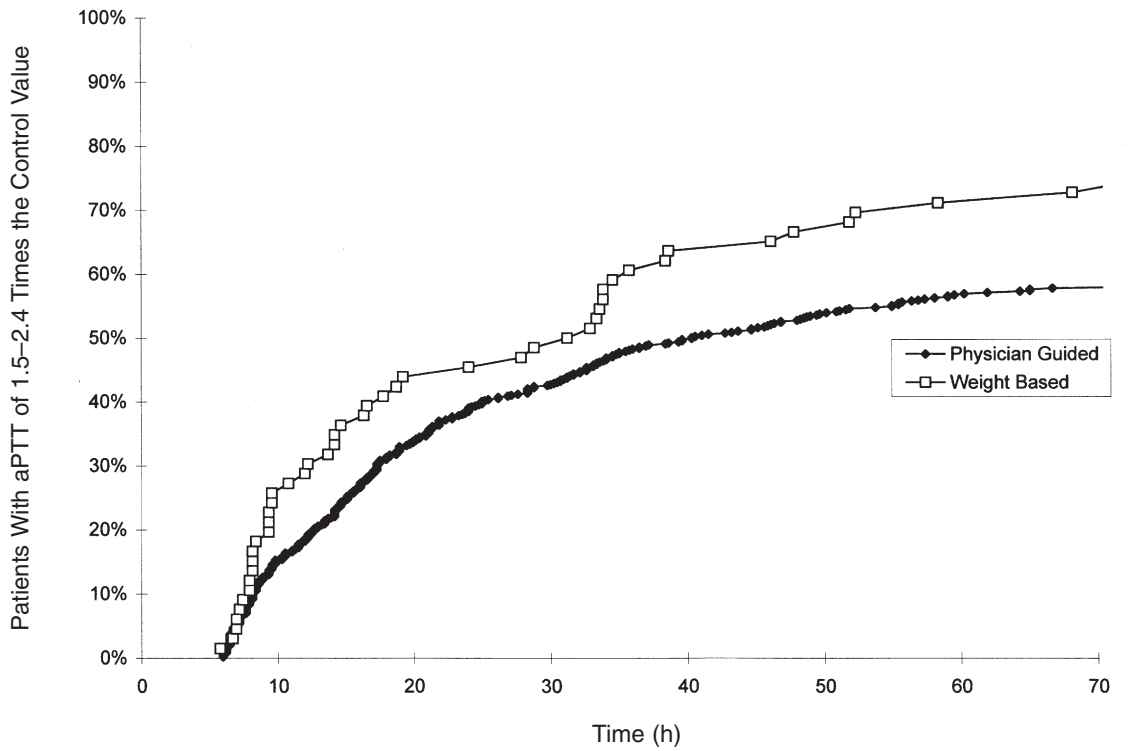
These results highlight a gap between efficacy and effectiveness and provide an outstanding opportunity and challenge to improve the care of our patients. Although we confirmed the superior efficacy of weight-based heparin,[5,29] at the same time we

Figure 2. Kaplan-Meier Curve for the Heparin Therapeutic Threshold



The weight-based nomogram achieved an activated partial thromboplastin time (aPTT) above the therapeutic threshold more rapidly than physician-guided heparin dosing ($P < .001$).

Figure 3. Kaplan-Meier Curve for the Heparin Therapeutic Range



The weight-based nomogram achieved an activated partial thromboplastin time (aPTT) within the therapeutic range more rapidly than physician-guided heparin dosing ($P = .021$).

demonstrated that the protocol was ineffective because of a very low utilization rate. Our findings of nonadherence to the weight-based protocol occurred in the face of strong evidence favoring it, wide dissemination of this evidence in the literature, multiple presentations and informal feedback to the ordering physicians by a physician champion, and a simple ordering mechanism via a computerized order entry system. This combination of interventions failed to induce the ordering physicians to change their behavior.

Few reports have detailed failures in translating efficacy into effectiveness and instead have focused mostly on the success-

Table 4. Complications of Heparin Therapy

Complication	No. of Patients (%)		*P*
	Weight-Based Nomogram	Physician-Guided Dosing	
Drop in hemoglobin of >2 g/dL	1 (1)	24 (4)	.718
Coded complication	1 (1)	8 (1)	.572
Patients with one or more supratherapeutic aPTTs within 72 h of initiating heparin therapy	27 (40)	286 (42)	.242

aPTT = activated partial thromboplastin time.

es.[33,35-39] To ensure that efficacious therapies, protocols, and pathways are effectively translated into improved patient care, there is an ongoing need for study and dissemination of the results of efforts to influence physician behavior. Although one report comparing physician-guided with weight-based heparin dosing noted a low utilization rate, the authors concluded that the reluctance to use the nomogram was due to a lack of familiarity with the nomogram rather than a lack of confidence in its efficacy.[26] Furthermore, they speculated that a "nomogram preprinted on physician order forms" could result in more "widespread usage." Indeed, a preprinted nomogram combined with physician education and a system-level commitment to quality improvement yielded excellent utilization of a weight-based nomogram.[32] In this report, however, we relate our findings that a preprinted nomogram in the form of a computerized order entry screen, combined with educational interventions and encouragement to use the nomogram, failed to increase the utilization rate of an efficacious weight-based heparin nomogram to the level where it could be considered effective. Our study, however, differed from others that demonstrated successful implementation[29,32] in that it relied on a computerized interface for order entry. We speculate that a preprinted "special" paper order sheet (as used in both previous studies[29,32]) may be more effective in implementing a new program than simple modification of an existing computerized order entry screen to contain another option.

Our study has several limitations. Our reliance on computerized records—which makes determination of lab values, time to achieve therapeutic range or threshold, utilization rate, and so forth extremely reliable—also makes determination of other clinical characteristics difficult. For example, our 2 primary outcomes, time to exceed the therapeutic threshold and time to achieve the therapeutic range, are surrogates for clinical outcomes that, in the case of deep venous thrombosis, are well established as predictors of disease recurrence.[4-8] Although this surrogate is not equally well established in the treatment of arterial thrombotic disorders, the importance of attaining a therapeutic range is established,[10-12] and it seems reasonable that this range should be reached within 24 hours of initiating therapy. Although the number of patients with deep vein thrombosis or pulmonary embolism was small, the protocol utilization rate among this group (5%) was no greater than that among patients with acute coronary syndromes (6%) or cardiac arrhythmias (21%). Subgroup analysis revealed no differences in time to exceed the therapeutic threshold or time to achieve the therapeutic range, nor in the complication rate when stratified by discharge diagnosis; the protocol did not perform any less well with one diagnosis compared with the others. Because we only required a single aPTT value for a patient to attain a therapeutic threshold or range, we may have overestimated the proportion of patients attaining these goals compared with studies where 2 or more such values were required. On the other hand, we may have underestimated the proportion because of those patients in whom heparin therapy was discontinued after at least 6 hours but before 24 hours. Nevertheless, we have no evidence that either of these 2 issues would affect 1 group of patients more than another.

Our reliance on ICD-9 codes for comparison of groups with regard to discharge diagnosis and complication rate (coded complication) is also a limitation. Although the difficulties encountered in using claims data are known,[40,41] any error is equally likely to occur in either the weight-based or the physician-guided group and is not a likely source of systematic bias. Furthermore, although our 2 groups differed with respect to discharge diagnoses, our Cox proportional hazards model demonstrated that the time needed to achieve the therapeutic threshold, after adjustment for these differences, remained significantly shorter in the weight-based group.

Our survey provided only limited data about the reasons why physicians chose overwhelmingly not to use the weight-based protocol. In addition to the survey, however, we also presented our data at our institution's medical grand rounds and solicited comments from our audience regarding reasons for nonadherence to the protocol. Reasons voiced by our audience paralleled those reasons found in our survey; namely, physicians were often unsure of the patient's actual weight, they did not believe that the protocol could attain a therapeutic aPTT as fast as physician-guided dosing, and they did not understand or believe in the value of attaining a therapeutic aPTT by 24 hours—even in treating deep vein thrombosis or pulmonary embolism.

At our institution, however, clinical experts have attested to the value of attaining a therapeutic aPTT by 24 hours in patients with venous and arterial thromboembolism, and we have focused on improving the utilization rate of the heparin protocol among all patients (regardless of indication for heparin use) in whom a therapeutic aPTT is the goal. Until this point our academic institution has

not restricted or confined physicians with respect to ordering heparin; they have had an equal and voluntary choice to order heparin in the manner they see fit. However, in addition to improving access to the patients' weights (increasing the availability on the computer screens, for example) and increasing educational interventions by including the floor pharmacists in addition to physician champions, we have instituted a change in our order entry system. This change does not restrict access to non–weight-based heparin, but it does increase the difficulty in completing the order. We hope that this combination of enhanced feedback, increased difficulty in ordering non–weight-based heparin via the order entry system, and improved access to patient's weights will improve utilization of this efficacious protocol.

Our study provides evidence that the weight-based heparin nomogram is efficacious, safe, and easy to use, yet is difficult to incorporate into practice on a large medical service at an academic medical center. These difficulties occurred in the face of efforts to encourage its use, and they suggest that further, concentrated efforts need to be directed at improving utilization. The low rate of utilization of weight-based heparin at our institution is an example of the immense opportunity to improve the care of our patients by improving our ability to implement efficacious therapies and translate them into effective patient care. Further study into methods to accomplish such translations is indicated.

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