Heparin is an anticoagulant widely used for the treatment and prevention of thromboembolic disease. Heparin therapy is generally monitored by measurement of the activated partial thromboplastin time (aPTT), with variable goals dependent on clinical setting and laboratory standards. It has been shown that in patients presenting with thromboembolic disease, achieving a therapeutic aPTT within the first 24 hours of therapy is associated with a reduction in recurrent thromboembolism [1–3].

Until recently, most patients undergoing heparinization were dosed with a 5000-U bolus followed by heparin infusion at a rate of 1000 U/hour, with infusion rates adjusted based on aPTT values [2,4]. However, with this approach as many as 60% of patients remain subtherapeutic after 24 hours [2], presumably because the dosing schedule fails to adjust for patient weight variability. Patients who fail to achieve therapeutic aPTT values within 24 hours have a 23.3% chance of recurrent venous thromboembolism versus a 4% to 6% chance in patients with early therapeutic heparinization [3]. Delays in obtaining aPPT values, inadequate responses to low aPPT values, and overly cautious responses to high aPPT values [2] may also contribute to the inadequacy of standard empiric heparin dosing.

Several studies have shown that a weight-based protocol for heparin dosing can increase the proportion of patients who achieve therapeutic anticoagulation within the first 24 hours. One study demonstrated a 90% therapeutic outcome at 24 hours for patients on a weight-based dosing protocol compared with 62% for patients on standard dosing [2], while another study demonstrated a 72.5% therapeutic outcome for patients in the weight-based arm compared with 47.1% in the standard arm [4]. A protocol used by Raschke et al resulted in therapeutic ranges at 24 hours in 97% of the patients in the weight-based dosing arm compared with 77% in the standard dosing arm [1,5].

In 1997, Providence Hospital in Washington, DC, chartered an interdisciplinary team to design and implement an institution-specific weight-based heparin protocol. Interest in implementing a weight-based protocol at the community-based, 350-bed teaching hospital originated with nursing and resident staff on the coronary care unit (CCU), who observed delays in obtaining orders to adjust heparin infusions following aPTT measurement and the absence of a consistent approach to rate adjustment among house staff. Further, it was noted that obese patients heparinized in the intensive care unit (ICU) often were not reaching therapeutic levels within 24 hours, and obese patients made up a significant percentage of the patients seen in both units. In addition, the hospital serves a large geriatric population exhibiting great variations in weight. These factors, combined with a desire to maximize the potential for positive clinical outcomes, hastened the decision of the hospital’s critical care committee to improve anticoagulation practices.

Methods
The project was initiated by the hospital’s CCU with approval of the critical care committee and chartered as an institutional continuous quality improvement activity. Team members included the medical director of the CCU, the nurse manager for cardiology, a clinical pharmacist, and an internal medicine resident. The team was charged with designing an institution-specific weight-based heparin protocol, piloting the protocol in the CCU, measuring and adjusting the protocol as needed, and implementing it throughout the institution as a patient care standard. Providence Hospital uses the quality improvement method FOCUS-PDCA (Table 1).

The dosing protocol (Table 2) used was based on the protocol described by Raschke et al [1] and called for 80 U/kg bolus as the initial dose and 18 U/kg/hour as the maintenance dose. An adjusted weight based on actual height and weight was used as the dosing weight (Table 3). The aPTT was measured every 6 hours until a value in the therapeutic

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range was achieved (between 42 and 90 seconds). The aPTT was assessed daily after the therapeutic range was reached. Adjustments to the heparin infusion rate were based on aPTT results (Table 2) and completed by a registered nurse utilizing a computerized calculation and adjustment grid. A standard concentration of 40 U/mL of heparin was used to simplify calculations and minimize errors. A work sheet was designed that allowed nurses on the pilot unit to calculate and document all doses, aPTT values, and dose adjustments. Nurses, nurse educators, and house staff received a 1-hour inservice regarding the new protocol.

To address concerns about the potential for calculation errors, a computerized calculator program was designed and incorporated into the computerized nursing reference library. The program requires the operator to enter the patient’s name, sex, height in feet and inches, and weight in pounds. If any field is left blank, the screen flashes an error message and advises aborting the calculation. If all information is entered as requested, the program displays actual weight, ideal body weight based on height, and dosing weight as calculated using the standard formula (Table 3). The program also displays a calculated initial bolus based on dosing weight and the initial maintenance infusion rate. If the program recognizes a particularly large initial bolus (> 8000 U), an alert message instructs the operator to call the prescribing physician before administering the dose. At this point, the operator is required to verify that hand and machine calculations provide the same results. As aPTT results are obtained, the program requests the aPTT value and provides the adjustment needed based on the nomogram of aPTT values and required adjustments. The operator is required to verify all adjustment suggestions provided by the computer, and may then print the recommended adjustment as a supplemental work sheet. A 24-hour summary record indicating initial bolus, infusion, and all adjustments following aPTT levels is printed nightly and remains a permanent part of the patient record (Figure 1).

Beginning in January 1997, all patients admitted to the CCU for unstable angina, acute myocardial infarction, pulmonary embolism, or rule-out myocardial infarction were placed on the protocol unless other treatment modalities were ordered by the attending physician. Obese patients (patients who weighed more than 70 kg with 20% of body weight above ideal weight calculations) treated in the ICU also were placed on the protocol, but data were not collected from this subset in the pilot phase.

**Results**

The data collected for patients treated using the protocol between January and March 1997 demonstrated that 50% of patients had a first aPTT value that exceeded 160 seconds, placing them at increased risk for bleeding. Based on these initial results, the team decided to reduce the bolus. In another study, Rainville et al [4], concerned about overanticoagulation...
in their study population, empirically reduced their bolus size to 70 U/kg while retaining an initial infusion rate of 18 U/kg/hour. Although the Providence team considered reducing the bolus to 70 U/kg, after discussion within the critical care committee it was decided to give a bolus of 75 U/kg, while retaining the initial infusion rate of 18 U/kg/hour. Education was again provided in the pilot area.

Following the protocol change, data were collected for the 210 patients admitted to the CCU between April and December 1997. Of the patients, 90.7% were African-American, 7.7% were white, 0.7% were Hispanic, and 0.07% were from other ethnic groups. Average age was 65.7 years. More than half were female (57.4%). The majority of patients (58.3%) were covered by Medicare, 26.7% had commercial insurance, 8.6% were covered by Medicaid, and 6.4% were uninsured. More than half were retired government workers residing in a residential section of the Northeast division of the District of Columbia.

The aPTT ranges at 4 consecutive measurements during the first 24 hours is shown in Figure 2. At 24 hours, 78% of patients were therapeutic, 13% were supertherapeutic.

Figure 1. Example summary record of heparin administration and therapeutic response.
The data also were used to compare the therapeutic responses of obese versus nonobese patients (Figure 3). After the 3rd aPTT measurement, 77% (65/84) of obese patients were in the therapeutic range, 5% (4/84) were subtherapeutic, and 18% (15/84) were supertherapeutic. Reported bleeding events that could be correlated with heparin use averaged 0.03% (2 events) and required temporary discontinuation of the drug.

Discussion

To maximize the potential for positive clinical outcomes in patients with thromboembolic disorders, we implemented a weight-based heparin dosing protocol in the CCU at Providence Hospital. We found the protocol to be safe and effective in providing therapeutic heparinization within 24 hours. In addition, the computerized calculator program simplified dosage calculation, reducing the potential for error and providing progressive documentation of heparin therapy.

We initially used the Raschke protocol (80 U/kg bolus followed by 18 U/kg/hour infusion) as the initial dosing regimen. The literature contains several dosing protocols, but most studies use Raschke’s as the initial dosing regimen [1,2,4,6]. In contrast to the dose, there has been much more variation among protocols with regard to the dosing weight used, which may vary among actual body weight (ABW), ideal body weight (IBW), or a calculated dosing weight based on both these measures. Yee et al [6] compared the effect of using IBW versus ABW versus a calculated dosing weight on outcomes of patients who underwent heparinization. Their results supported using ABW as the dosing weight when anticoagulating obese patients, but the authors recommended reducing the initial infusion rate to 15 U/kg/hour to avoid overdosing the morbidly obese. Due to the large population of elderly patients at Providence Hospital, the committee opted for a protocol that used a calculated dosing weight rather than ABW, with the intent of making adjustments based on the pilot results. With the volume of distribution of heparin approximating that of blood volume (40 to 60 mL/kg) [2,7], it is not surprising that we found it necessary to make adjustments to the initial protocol. Due to preliminary results that showed high rates of hypercoagulation in the study group, we modified the protocol 3 months into the study. Because we were already employing a calculated dosing weight as opposed to ABW, the logical choice was to reduce the bolus size.

There are several limitations to our study. Volume of distribution plays an important role in the impact of drug therapy, particularly for drugs that must achieve certain concentrations in the serum for maximal efficacy. Our study, because it was limited primarily to cardiology patients in the CCU, does not allow for extrapolation of the results to patients with conditions that may alter volume of distribution.

Sepsis,
hepatic failure, renal failure, and congestive heart failure are some conditions known to affect volume of distribution; we plan to observe data trends in such patients as the protocol is used in different areas of our institution.

Our study population consisted primarily of African-Americans. The medical literature has made us aware that ethnicity may play a part in drug metabolism and response rates, and our data may be slanted in a way that can only be elucidated by a comparative trial of heparinization in different ethnic groups or collective retrospective data analysis. To date, published studies strongly support the effectiveness of weight-based heparin dosing in mixed populations.

The third concern regarding our results centers around the age of the study population and the pharmacodynamics of heparin in that population compared with a younger population. Advanced age may be associated with receptor density changes, slowing of drug metabolism, and reduced drug clearance. Variability in these areas can be expected to affect the results of heparinization with regard to time to therapeutic values or actual degree of anticoagulation with a particular dose.

The protocol has been approved for use on all nursing units at Providence Hospital, and data are currently being collected to follow outcomes in all patient subgroups to note possible differences due to age or disease state. There is a special interest in the use of the protocol in diabetic patients. We intend to evaluate the impact of the protocol on length of stay and overall cost in a follow-up study. A 3-year study reported by Lechner [8] has linked the use of a weight-based heparin protocol to earlier anticoagulation and lower medical costs. With daily costs for coronary care beds exceeding $1100 to $1300 and with reimbursements by Medicare and other third-party payers based on DRG-approved patient days, there is considerable incentive to improve the clinical efficiency of heparin dosing.

References