ORIGINAL ARTICLE

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An Outpatient Program To Treat Deep Venous Thrombosis with Low-Molecular-Weight Heparin

CONTEXT. Although recent trials have demonstrated the safety and efficacy of low-molecular-weight (LMW) heparin, clinicians may need help incorporating this drug into routine practice.

OBJECTIVE. To describe the development, implementation, and early results of an outpatient LMW heparin program for acute deep venous thrombosis (DVT).

DESIGN. Before–after study.

SETTING. Eight health centers of Harvard Vanguard Medical Associates, a multispecialty group practice in Boston.

PATIENTS. Patients with confirmed acute, lower-extremity DVT before (40 patients given a diagnosis from January to August 1996) and after (67 patients given a diagnosis from September 1996 to April 1997) implementation of the LMW heparin program.

INTERVENTION. A centrally coordinated outpatient LMW heparin program.

DATA SOURCES. Hospital and HMO financial databases; electronic patient medical records.

OUTCOME MEASURES. Costs of care for 2-week episodes and short-term clinical outcomes.

RESULTS. The proportion of patients with DVT treated in the hospital decreased from 90% to 46% after the introduction of the LMW heparin program. The mean cost of treatment for all patients with DVT decreased from $5465 to $3719 per patient. For the subset of patients actually treated in the outpatient program, the average cost was $1402 per patient. There were no deaths, no clinically recognized pulmonary emboli, and no cases of significant bleeding among patients treated in the program, although 3 patients were subsequently hospitalized for worsening leg pain.

CONCLUSIONS. The cost of caring for patients with DVT decreased after introduction of the outpatient LMW heparin program. Given explicit selection criteria, short-term clinical outcomes after outpatient management have been excellent. This program may serve as a model for physicians and health plans interested in establishing a program for treating acute DVT in the outpatient setting.

"Low-molecular-weight heparin can be used safely and effectively to treat patients with proximal deep-vein thrombosis at home." This conclusion, supported by compelling results from a large randomized trial performed in Europe, was published in the March 14, 1996, issue of *The New England Journal of Medicine*.[1] A second study and an accompanying editorial echoed the theme: Low-molecular-weight (LMW) heparin should be introduced into routine care for patients with deep venous thrombosis (DVT).[2, 3]

The abstract of this paper is available at ecp.acponline.org.

See related editorial on pages 240–243.

Edited by Lisa Schwartz, MD, MS

In the United States, the long-established standard of care for proximal DVT has been immediate hospitalization and administration of intravenous unfractionated heparin for at least 5 days.[4–6] However, treatment with LMW heparin was shown in randomized trials to produce equal to superior clinical outcomes, no greater risk for complications, superior quality of life with treatment at home, the promise of reduced hospital utilization, and lower costs.[1,2] Low-molecular-weight heparin seemed to offer great potential for better care at a substantially lower cost.

Nevertheless, introducing outpatient LMW heparin treatment into clinical practice in the United States is not straightforward. Primary care physicians have not used this drug before, and its formal approval for treatment of DVT is still pending before the U.S. Food and Drug Administration. This lack of experience compounds the difficulty of duplicating the success of clinical trials in the more challenging domain of real-world practice, where an infrastructure for patient evaluation, treatment, and monitoring has to be reproduced without the financial and logistical support of a clinical trial.

More than 3 years after the publication of the successful LMW heparin clinical trials, no subsequent published studies have evaluated attempts to translate this new knowledge into improved clinical practice in the United States. This paper describes the rapid development and implementation of an outpatient LMW heparin program covering an HMO population of more than 140,000 adult members. We present the short-term clinical outcomes of the first 36 patients treated in our outpatient program and compare the cost of care for patients with DVT before and after the introduction of the program.

Methods

Setting

This study was conducted in the patient population of Harvard Vanguard Medical Associates (HVMA), a multispecialty physician group in Boston whose patients belong to Harvard Pilgrim Health Care, the largest HMO in New England. At the time of this study, approximately 140,000 of HVMA's adult members received care at one of eight centrally located health centers, all of which sent most patients with suspected DVT for diagnostic testing to Brigham and Women's Hospital. Patients who were found to have acute DVT by ultrasonography or venography were traditionally sent immediately to the hospital's emergency department for initiation of intravenous heparin therapy and subsequent admission.

Outpatient Low-Molecular-Weight Heparin Program

Because the treatment of DVT at home represented a radical departure from previous practice, the program was anchored to a central coordinating group of physicians and nurses in the urgent care (walk-in) department of the largest HVMA health center. This department is staffed with primary care physicians and nurses 7 days a week from 7:30 a.m. through 11:00 p.m. It is less than a mile from Brigham and Women's Hospital, making transportation between the two sites relatively easy. Key features of the program are shown in **Figure 1**.

Patient Referral

The determination of patient eligibility for the program and initiation of treatment is outlined in **Figure 2**. Patients with suspected DVT are first screened in a physician's office for eligibility for outpatient treatment before being sent for diagnostic testing. Eligibility criteria for the program were adopted from the same clinical and social criteria described in the published clinical trials.[1,2] Eligible patients are informed that they may be referred to the urgent care department for initiation of outpatient treatment if their ultrasonogram is positive for acute DVT.

Positive ultrasonography results are relayed to the referring primary care clinician by the ultrasonographer at Brigham and Women's Hospital. If the patient is deemed eligible for outpatient treatment and if the thrombus is not large or unstable (e.g., iliofemoral) enough to represent an acute threat, the primary care physician directs the ultrasonographer to send the patient to the urgent care department.

The primary care physician referring the patient to the outpatient heparin program verbally relays the clinical history to a nurse in the urgent care department so that the department is ready to care for the patient on arrival. The name of the primary care physician who will assume responsibility for the patient at the completion of the program is confirmed at this time.

Centrally Coordinated Care

In the urgent care department, the patient's eligibility for the program is reviewed and confirmed by an examining physician, and baseline complete blood count, electrocardiography, room-air oxygen saturation testing, and stool testing for occult blood are performed. Patients are counseled about the entire program, advised about activity at home while under treatment for DVT, and given an educational handout to take home. Once all questions have been answered, the nurse administers the first injection of enoxaparin, 1 mg/kg of body weight. Patients who are interested in self-injection at

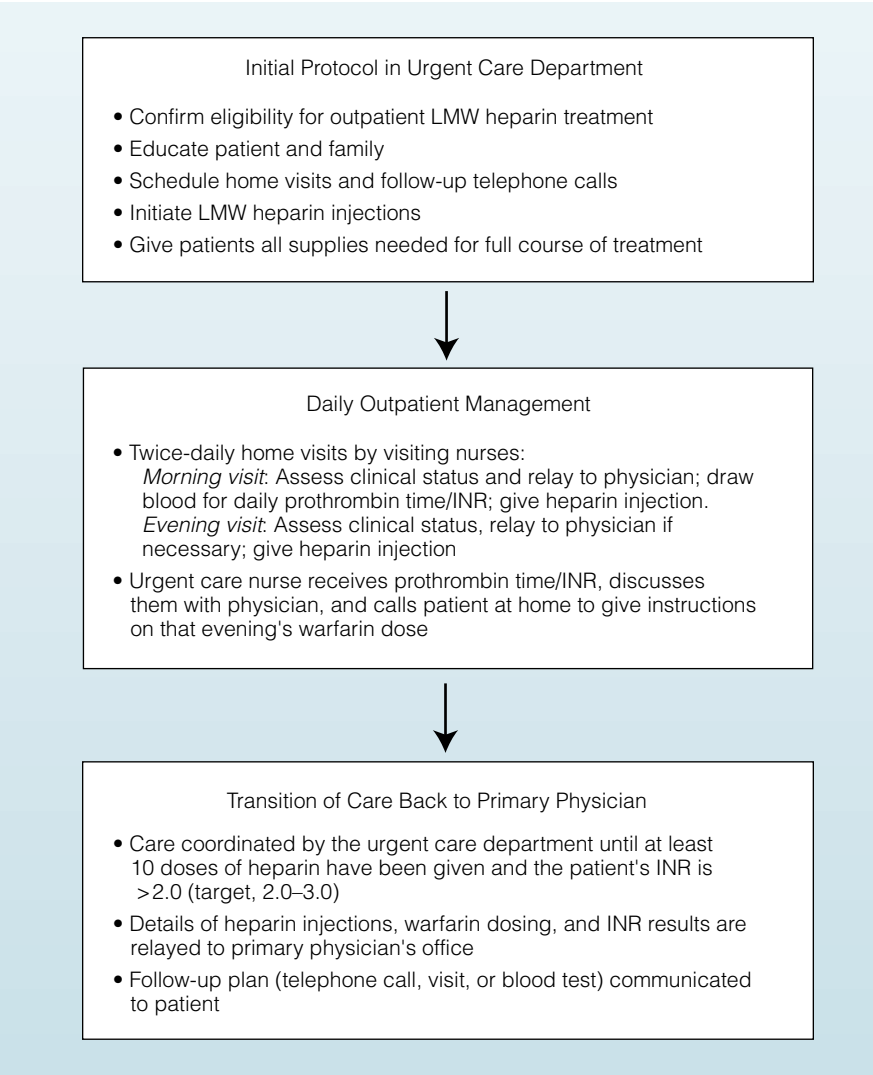

FIGURE 1. Key features of the outpatient low-molecular-weight heparin treatment program.

home receive initial education in proper technique and syringe disposal. The health center pharmacy prepares syringes filled with enoxaparin (with the dose determined according to patient weight) for a 5-day course of twice-daily injections, and these syringes are sent home with the patient along with a supply of warfarin (100 tablets of 2.5 mg).

When the patient first arrives in the urgent care department, the case management department is contacted to arrange home nursing visits for the patient. Few patients opt for self-injection and therefore are seen twice daily by the visiting nurse. All patients receive at least one home visit from the nurse each morning to be evaluated for any signs of worsening DVT or complications of treatment. The nurse also draws a blood sample for a daily check of the prothrombin time and the international normalized ratio (INR). After the morning home visit, the visiting nurse calls the urgent care department and speaks with a physician to discuss the patient's condition and confirm that outpatient treatment is progressing satisfactorily. Each afternoon, the prothrombin time and INR results are reviewed by an urgent care physician, who then determines the appropriate evening dose of warfarin and communicates this information to the patient at home. Therapy with warfarin (usually an initial dose of 10 mg) is begun on the first evening after initiation of LMW heparin treatment. Daily notes in the medical record and a flow sheet kept in the urgent care department for each patient assure continuity and coordination of care.

When the patient has reached an INR greater than 2.0 and has received at least 10 injections of enoxaparin (5 days), the patient's care is transferred back to the designated primary care physician through a call to the physician's office. The most recent warfarin doses, prothrombin time, and INR are relayed, and the primary care physician's office contacts the patient to establish a follow-up appointment within 1 to 5 days.

Before–After Study Design

To evaluate the financial implications of the outpatient LMW heparin program, we compared the 40 patients

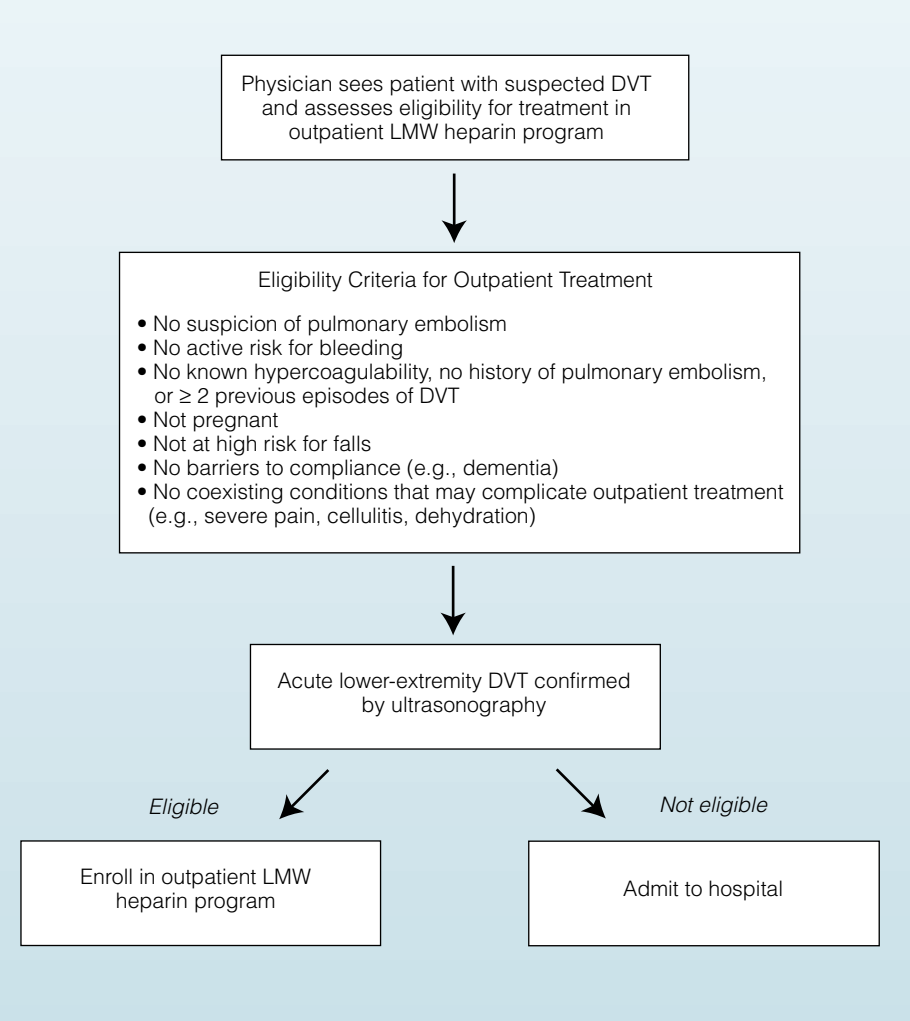

FIGURE 2. Physician determination of patient eligibility for treatment in the outpatient heparin program.

with DVT diagnosed in the 7 months before the program started (January through July 1996) with the 67 patients with DVT diagnosed in the 7 months after implementation (September 1996 through March 1997).

Patient Identification

To identify all HMO patients given a diagnosis of DVT from January 1, 1996, through April 1, 1997, we searched the computerized outpatient medical record of HVMA and the Brigham and Women's Hospital discharge database. We looked for all patients with diagnostic codes consistent with DVT (International Classification of Diseases, ninth revision, codes 451.1x, 451.2, 453.8, and 453.9). The medical records of all potentially eligible patients were then reviewed manually and were included in further analyses if the following conditions were met: 1) A new, acute episode of lower-extremity DVT was confirmed by diagnostic ultrasonography or venography, and 2) the patient was not admitted to the hospital for suspected pulmonary embolism or stroke.

During the month preceding the formal launch of the outpatient program, some patients were treated in the program after having been referred by physicians who had already heard of its existence. In order not to bias the analyses done for this study, all patients with DVT during this month of mixed treatment patterns were excluded from analysis.

Outcome Measures

Clinical: For all patients with DVT treated in the outpatient program, we manually reviewed medical charts to determine the clinical outcomes of death, recurrent thrombosis, clinically appreciated pulmonary embolism, and bleeding. We also checked the medical records and hospital database for hospital admissions or readmissions within 2 weeks of the diagnosis of DVT.

Cost: The HVMA financial database provided direct cost data on hospital stays, pharmacy costs for enoxaparin, and visiting nurse costs. At the time of this study, the cost to the HVMA in-house pharmacy for each 30-mg vial of enoxaparin was $12.43.

TABLE 1
Identification of Study Patients*

VARIABLE	BEFORE LMW HEPARIN PROGRAM	AFTER LMW HEPARIN PROGRAM
Patients meeting ICD-9 criteria for deep venous thrombosis, *n*	82	103
Exclusion criteria:		
Acute thrombosis not confirmed by ultrasonography or venography, *n*	36	29
Hospitalization for suspicion of pulmonary embolism or stroke, *n*	6	7
Final sample, *n*	40	67

**ICD-9 = International Classification of Diseases, ninth revision; LMW = low-molecular-weight.*

The cost of a nurse home visit was $55. On the basis of internal cost accounting, the cost of face-to-face patient visits to the urgent care department was estimated at $199 for the initial comprehensive visit and at $49 for subsequent visits. Any other outpatient physician visits for DVT care were estimated at $110 per visit. No costs were assumed for telephone calls to or from patients. No full-time equivalents or other fixed costs were added to the outpatient LMW heparin program.

All costs of treatment were summed for a 2-week period after the diagnosis of DVT to estimate a cost for the entire episode of care.

Analyses

The chi-square and the Student *t*-test were used to compare categorical and continuous data, respectively, between patients treated before and those treated after implementation of the outpatient heparin program.

Results

In the 7 months before institution of the LMW heparin program, 40 patients who had uncomplicated acute DVT were identified (**Table 1**). The outpatient heparin program was formally implemented in September 1996. During the first 7 months of the outpatient program, 67 patients had acute lower-extremity DVT. No significant differences were seen in the age and sex of patients in whom DVT was diagnosed between the baseline and postintervention periods (**Table 2**).

Patients and Treatment Patterns

In contrast to "traditional" care, for which 90% of patients were hospitalized for treatment, 54% of 67 patients with DVT were treated as outpatients after implementation of the outpatient heparin program. One of these patients was initially hospitalized for pain control but was discharged within 24 hours and completed LMW heparin treatment at home without further incident. Patients treated in the outpatient program were more likely to have isolated calf-vein DVT (58% vs. 33%; $P = 0.03$) and were younger on average (52.6 years vs. 60.7 years; $P = 0.04$) than patients who were deemed ineligible for the program. The most common reasons given for ineligibility were an increased risk for bleeding (8 patients), pain or other difficulties ambulating (6 patients), and an acute thrombus that was judged too large or unstable (5 patients). As expected, patients who were deemed ineligible for outpatient treatment had a more complicated course, and they had longer average lengths of stay and higher mean hospital costs than did the average patient in the baseline period (**Table 2**).

Patients in the outpatient program were treated for an average of 6.5 days (minimum, 3; maximum, 17) before prothrombin times and INRs reached therapeutic levels and heparin treatment could be stopped. The urgent care physicians caring for patients in the program reported that many patients required surprisingly high and prolonged doses of warfarin before therapeutic prothrombin times and INRs could be reached.

TABLE 2
Patient Characteristics and Treatment Patterns*

VARIABLE	BEFORE LMW HEPARIN PROGRAM (*n* = 40)	AFTER LMW HEPARIN PROGRAM (*n* = 67)
Mean age ± SD, *yr*	56.7 ± 13	56.4 ± 15
Women	58%	57%
Outpatient treatment	10%	54%
Inpatient treatment	90%	46%
Utilization and cost among inpatients only		
Patients, *n*	36	31
Mean inpatient days	4.2	5.8
Mean hospital cost	$6048	$7529

**LMW = low-molecular-weight.*

TABLE 3
Average Utilization and Cost of Care*

VARIABLE	BEFORE LMW HEPARIN PROGRAM (*n* = 40)	AFTER LMW HEPARIN PROGRAM (*n* = 67)
Utilization		
Inpatient length of stay, *d*	3.9	2.5
Outpatient visits within 2 weeks of diagnosis, *n*	1.1	2.4
Visiting nurse home visits, *n*	0.0	2.4
Costs†		
Hospitalization	$5328	$3113
Outpatient visit	137	280
Home visit	0	132
LMW heparin	0	194
Mean cost per patient	$5465	$3719

**LMW = low-molecular-weight.*
†All values represent mean per-patient costs for the entire group of patients with deep venous thrombosis in each period.

Costs of Treatment

To evaluate the impact of the outpatient heparin program, we compared the mean costs for all patients with DVT diagnosed in the 7-month intervals before and after the initiation of the outpatient program (**Table 3**). Even though only 54% of patients in the postintervention period were actually treated in the outpatient program, the total mean cost per patient decreased from $5465 to $3719 ($P < 0.01$), for an average savings of $1746 per patient. This lower cost was achieved through substantially lower hospitalization costs (offset only minimally by higher costs of outpatient care, home visits, and LMW heparin). Among the 36 patients who were treated in the outpatient program, the mean cost of all treatment was $1402. This figure factors in the costs of hospitalization for the few patients who were hospitalized during the course of outpatient treatment.

Table 4 breaks down the costs of care for patients in the outpatient program. Outpatient visits and pharmacy costs accounted for the largest portion of average costs. Patients in the outpatient program averaged 4.2 outpatient visits in the 2 weeks after the diagnosis of DVT. This average is strongly influenced by several patients who opted to return daily or even twice daily to the urgent care department to receive their heparin injections rather than have visiting nurses come to their homes.

Clinical Outcomes in the Outpatient Program

Among the 36 patients treated in the outpatient LMW heparin program, 3 (8% [95% CI, 1% to 19%]) were subsequently admitted to the hospital for worsening leg pain after beginning outpatient treatment. Only 1 of these patients had proven extension of the original clot. Two of the patients were treated with unfractionated heparin, and 1 was maintained on LMW heparin during a brief hospitalization. None of these patients required a hospital stay longer than 3 days. No patients treated in the LMW heparin program died within 4 weeks of diagnosis. Within this same time frame, no patient had clinically recognized pulmonary embolism, and no cases of bleeding secondary to LMW heparin or warfarin treatment were noted in the medical record. Thus, the observed rate of adverse clinical outcomes was 0% (CI, 0% to 8%).

Discussion

The medical literature contains many examples of interventions with proven efficacy that have been incompletely incorporated into clinical practice.[7–10] Even when physicians know the "right" thing to do, ample evidence demonstrates that other barriers, often linked to inadequate systems of care, prevent delivery of the highest-quality medical care.[11]

Our results demonstrate a rapid and successful translation of new clinical knowledge into a cost-effective treatment program for an entire population. However, considerable planning was required to create the infrastructure necessary to support the outpatient LMW heparin program. We consulted with the study investigators of the clinical trials to discuss their exclusion criteria, consulted with clinicians at other institutions who had experience with LMW heparin, and then met with clinical leaders of the hospital departments

TABLE 4
Average Cost of Care for the 36 Patients Treated in the Outpatient Program

ITEM	COST
Visiting nurse home visits	$246
Low-molecular-weight heparin	361
Urgent care and other physician visits	470
Hospital costs*	325
Mean cost per patient	$1402

**Four patients had brief hospitalizations during the course of treatment.*

responsible for the diagnosis and treatment of thromboembolism. These discussions laid the groundwork for identifying the communication issues central to a new paradigm in which patients with a positive result on a test for DVT would be "re-routed" from the ultrasonography site back to the outpatient setting.

Discussions were also held in our HMO to coordinate the significant roles of the pharmacy and the case management department in the program. Nurses in the urgent care department took the lead in developing a patient education handout to explain the program. They also created an internal tracking system to ensure that responsibility for patient management would flow smoothly from day to day without risk for losing track of key communications, laboratory results, and actions that needed to be done on a daily basis.

Centralization of the program was a key philosophical and logistic decision. The efficiency and quality of patient education and monitoring were greatly enhanced through centralization. In addition, with approximately 70 new cases each year predicted in our population of 140,000 members, it was clear that individual primary care physicians were unlikely to gain significant experience and comfort with LMW heparin treatment within a short period. We found it useful for the three physicians in our group who had the most knowledge and experience with LMW heparin treatment to be on-call at all times for questions about patient eligibility and treatment. Providing this kind of clinical backup to physicians who have never treated patients with LMW heparin was an important part of gaining support for use of the program.

With a conservatively estimated incidence of 70 new cases of lower-extremity DVT in our HMO population each year, our estimated savings of $1746 per patient would save $122,220 per year. As our experience and comfort with treating patients in the outpatient heparin program increase, it is likely that a higher percentage of patients with DVT will be considered eligible for outpatient treatment. However, increasing the pool of eligible patients for the program may also increase the risk that treatment will fail or that complications will occur.

Our study is limited by its before–after design and its reliance on data from a single group practice. The data are preliminary because we do not yet know the longer-term outcomes of our patients. We are also reporting on a relatively small number of patients. Previous larger series have found recurrent thromboembolism in approximately 5% to 9% of patients treated with LMW heparin for acute DVT, and although the risk for serious bleeding is low, it is not zero.[1, 2, 12] Clinical failures and complications are inevitable in any treatment program for DVT, and patients and their families should be clearly advised about these risks. Close communication and follow-up for patients treated at home must be rigorously maintained to minimize the inevitable adverse outcomes.

The centralization of elements of the program in the urgent care department seeks to guarantee the highest degree of reliability in evaluating prospective patients, documenting their eligibility for the program, and ensuring that necessary follow-up and day-to-day management of these patients are handled seamlessly. The central components of this program could be duplicated easily, however, in smaller physician groups. In all settings, physicians will need to continue to follow the evolving data on the use of LMW heparin to keep patient selection criteria and dosing algorithms consistent with the most recent evidence. Although further research is clearly needed to monitor the outcomes from programs such as ours, we hope that this report will encourage others to make LMW heparin treatment available to their patients as part of a safe and effective program that is likely to provide superior outcomes, enhance patient satisfaction, and contain costs.

Take-Home Points

- **Recent clinical trials have shown that outpatient treatment of acute lower-extremity DVT with LMW heparin is safe and efficacious.**
- **Because of the monitoring involved and lack of familiarity with the drug, clinicians may need help incorporating LMW heparin into routine practice.**
- **We established a centrally coordinated outpatient program to provide monitoring and support and found that about half of our patients with DVT could be managed as outpatients.**
- **The average cost savings have been more than $1500 per patient with DVT, and the short-term clinical outcomes for patients treated in the program have been excellent.**
- **With proper attention to patient selection, patient education, and systematic follow-up, treatment of acute lower-extremity DVT can safely be shifted from the inpatient to the outpatient setting.**

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