Cost-effectiveness of low-molecular-weight heparin and unfractionated heparin in treatment of deep vein thrombosis

Evidence

Études

Marc Rodger,* MD; Christopher Bredeson,* MD, MSc; Philip S. Wells,* MD, MSc; Julie Beck,† BSc, CCHRA(C); Brenda Kearns,† CCHRA(C); Lothar B. Huebsch,* MD

From the *Department of Medicine, University of Ottawa, and the †Clinical Trials and Research Unit, Division of Hematology, Ottawa Hospital, Ottawa, Ont.

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Abstract

Background: Acute deep vein thrombosis has traditionally been treated with unfractionated heparin (UFH), administered intravenously, but low-molecular-weight heparins (LMWH), administered subcutaneously, have recently become available. The authors sought to determine which therapy was more cost-effective for inpatient and outpatient treatment of deep vein thrombosis.

Methods: An incremental cost-effectiveness analysis based on a decision tree was performed for 4 treatment strategies for deep vein thrombosis. Rate of major hemorrhage while receiving heparin, rate of recurrence of venous thromboembolism 3 months after treatment and mortality rate 3 months after treatment were determined by meta-analysis. Costs for the UFH therapy were prospectively collected by a case-costing accounting system for 105 patients with deep vein thrombosis treated in fiscal year 1995/96. The costs for LMWH therapy were modelled, and cost-effectiveness was determined by decision analysis.

Results: Meta-analysis revealed a mean difference in risk of hemorrhage of –1.1% (95% confidence interval [CI] –2.4% to 0.3%), a mean difference in risk of recurrence of venous thromboembolism of –2.6% (95% CI –4.5% to –0.7%) and a mean difference in risk of death of –1.9% (95% CI –3.6% to –0.4%), all in favour of subcutaneous unmonitored administration of LMWH. The cost to treat one inpatient was $2993 for LMWH and $3048 for UFH. Even more would be saved if LMWH was delivered on an outpatient basis (cost of $1641 per patient). The cost-effectiveness analysis showed that LMWH in any treatment setting is more cost effective than UFH. A sensitivity analysis demonstrated the robustness of this conclusion.

Interpretation: Treatment of deep vein thrombosis with LMWH is more cost effective than treatment with UFH in both inpatient and outpatient settings.

Résumé

Contexte : La thrombose veineuse profonde aiguë a toujours été traitée au moyen d'héparine non fractionnée (HNF) administrée par voie intraveineuse, mais des héparines de faible poids moléculaire (HFPM), administrées par voie sous-cutanée, sont disponibles depuis peu. Les auteurs ont cherché à déterminer la thérapie la plus rentable pour traiter les patients hospitalisés et en service externe victimes d'une thrombose veineuse profonde.

Méthodes : On a réalisé une analyse de rentabilité différentielle fondée sur un arbre de décision dans le cas de quatre stratégies de traitement de la thrombose veineuse profonde. On a déterminé par méta-analyse le taux d'hémorragie majeure chez les sujets qui prenaient de l'héparine, le taux de récidive de la thrombo-embolie veineuse 3 mois après le traitement et le taux de mortalité 3 mois après le traitement. Les coûts de la thérapie à l'HNF ont été recueillis de façon prospective au moyen d'un système de comptabilisation du coût des cas

pour 105 patients victimes d'une thrombose veineuse profonde et traités au cours de l'exercice 1995/1996. On a modélisé les coûts de la thérapie aux HFPM et déterminé la rentabilité par analyse de décision.

Résultat : La méta-analyse a révélé une différence moyenne du risque d'hémorragie de –1,1 % (intérvalle de confiance [IC] à 95 %, –2,4 % à 0,3 %), une différence moyenne du risque de récidive de la thrombo-embolie veineuse de –2,6 % (IC à 95 %, –4,5 % à –0,7 %) et une différence moyenne du risque de décès de –1,9 % (IC à 95 %, –3,6 % à –0,4 %). Toutes ces différences jouent en faveur de l'administration sans surveillance de HFPM par voie sous-cutanée. Le coût du traitement d'un patient hospitalisé s'est établi à 2993 $ dans le cas des HFPM et à 3048 $ dans celui de l'HNF. On économiserait encore davantage si les HFPM étaient administrées en service externe (coût de 1641 $ par patient). L'analyse de rentabilité a montré que dans n'importe quel contexte de traitement, les HFPM sont plus rentables que l'HNF. Une analyse de sensibilité a démontré la solidité de cette conclusion.

Interprétation : Le traitement de la thrombose veineuse profonde au moyen des HFPM est plus rentable que le traitement à l'HNF en contexte tant externe qu'interne.

Deep vein thrombosis has an estimated annual incidence rate of 48 cases per 100 000 population.[1] The traditional treatment for above-knee deep vein thrombosis has been admission to hospital for continuous intravenous administration of unfractionated heparin (UFH), regularly monitored with coagulation assays, but recently, low-molecular-weight heparins (LMWH) have become available. These compounds appear to be at least as safe and effective as UFH in the treatment of deep vein thrombosis.[2-4] They have excellent bioavailability, predictable dose responses and longer half-lives than UFH, which allows subcutaneous, once-daily, unmonitored administration.[5] In 1996, 2 studies[6,7] suggested that outpatient LMWH therapy for deep vein thrombosis is as safe and effective as inpatient UFH therapy.

The economic evaluations published to date[8,9] comparing the costs of LMWH and UFH therapy have had several limitations. No meta-analyses were performed to take into account previous research on the treatment of deep vein thrombosis with LMWH; both studies used effectiveness and safety data from single clinical trials. A meta-analysis would allow the effectiveness and safety of LMWH to be estimated with narrow confidence intervals. Neither study used a method to accurately estimate the cost of resources used. Both assigned costs using generic per diem amounts — the least precise method of costing, according to the Canadian Coordinating Office for Health Technology Assessment,[10] because it is not sensitive to small differences in resource use (e.g., nursing workload). Our goal was to compare the cost-effectiveness of LMWH and UFH by means of a meta-analysis of appropriate trials and patient-specific case-costing data.

Methods

Overview

We conducted an incremental cost-effectiveness analysis based on a decision tree using mean cost per patient and mean efficacy and safety data for 4 treatment strategies: inpatient UFH therapy; inpatient LMWH therapy; outpatient LMWH therapy for patients eligible for outpatient care and inpatient LMWH therapy for patients not eligible for outpatient care; and outpatient LMWH therapy for patients eligible for outpatient care and inpatient UFH therapy for patients not eligible for outpatient care. We also conducted a meta-analysis of randomized trials comparing subcutaneous unmonitored administration of LMWH and inpatient intravenous administration of UFH to obtain efficacy and safety data. The UFH cost data were derived from actual patient case-costing, and modelled costs were used for LMWH treatment (details of the model are available at **www.hematology.ogh.on.ca**). Our analysis was conducted from a third-party payer perspective, and the analytic horizon was 3 months.

Meta-analysis and pooled analysis of efficacy and safety

We conducted a MEDLINE search for studies published between January 1984 and April 1996 using the following terms: LMWH and deep vein thrombosis, LMWH and thromboembolic disease, LMWH and clinical trials, and LMWH and treatment. Articles that evaluated randomized controlled trials of LMWH and UFH were retrieved. Each article was reviewed by 2 of the authors (M.R. and P.S.W.), and disagreements were resolved by consen-

sus. To be included in our analyses, the studies had to meet 3 criteria: intravenous monitored administration of UFH had to have been compared with weight-adjusted (per kilogram) subcutaneous unmonitored adminis-tration of LMWH; patients had to have been evaluated for major hemorrhage while receiving heparin, for recurrence of venous thromboembolism (for a minimum of 3 months) and for death (for a minimum of 3 months); and a blinded objective outcome assessment had to have been performed. Detailed summaries of the relative risk, risk reduction and significance tests were calculated using a random-effects model. The Mantel–Haenszel test was used to estimate common relative risk. Study heterogeneity was tested using the *Q*-statistic for overall heterogeneity. A p value of less than 0.05 for the test indicated statistically significant heterogeneity.

Data from eligible studies were pooled to determine the probability of major hemorrhage causing death. The number of deaths from major hemorrhage were divided by the number of major hemorrhages to yield the probability of death from this cause. The probability of death from a recurrence of venous thromboembolism was determined from a similar calculation.

Costs of treatment and complications

Cost data for the decision-tree-based cost-effectiveness analysis were derived from a review of case-costing data for patients treated for deep vein thrombosis in fiscal year 1995/96 at the Ottawa General Hospital, a tertiary-care teaching centre in a catchment area with a population of about 1 million. The case-costing data were obtained from an online resource-utilization-based patient-specific cost accounting system (TI 1985; Transition System Inc., Boston, Mass.). This system measures the resources used by each patient and assigns a fully allocated cost to those resources (e.g., a nursing-workload tool measures the amount of time a nurse spends with a patient, and the cost of nursing time units includes direct costs [e.g., salaries] and indirect costs [e.g., hotel costs]).

A chart review identified 105 patients with a primary or secondary discharge diagnosis of deep vein thrombosis treated in fiscal year 1995/96. Only patients with deep vein thrombosis confirmed by contrast venography or duplex ultrasonography who had been treated as inpatients with intravenously administered UFH were included in the analysis.

The patient records were then divided into 2 subgroups: outpatient-eligible inpatients, who would have been eligible for outpatient therapy but who had been treated as inpatients; and outpatient-ineligible inpatients, who would have been ineligible for outpatient therapy and who had been treated as inpatients. The outpatient eligibility criteria were those used in the 2 outpatient LMWH treatment studies published at the time of our analysis.[6,7] The age and sex distribution of the outpatient-eligible patients was similar to that of the patients in the published studies.

Approval from the review board at our institution was not sought because the board does not review investigations that do not involve direct patient contact. Confidentiality of patient records was maintained throughout the chart review.

We used a variety of information to determine the costs of treatment for our analysis. For inpatient UFH treatment, we used the actual costs for patients treated this way.

For inpatient treatment with LMWH, we modelled what the costs would have been had all 105 patients received this treatment. We modelled the savings in nursing time (based on data from time and motion studies conducted as part of this analysis, details of which are available at **www.hematology.ogh.on.ca**), laboratory-monitoring costs and additional drug costs (based on our pharmacy's acquisition and preparation costs for LMWH). Details of the methods used to model these costs are available at **www.hematology.ogh.on.ca**.

For outpatient treatment with LMWH, we used the actual cost of treating outpatients in our medical day care unit and assumed that all outpatient-eligible patients had been treated with LMWH on an outpatient basis. In such a scenario, patients would have presented to our medical day care unit for daily injections of LMWH, nursing assessment and monitoring of warfarin therapy; all antithrombotic drug costs would have been paid for by the hospital. A detailed breakdown of the costs is available at **www.hematology.ogh.on.ca**.

The actual costs of treating a major hemorrhage were used for our analysis. The costs of treating recurrence of venous thromboembolism were assumed to be the same as those for treating a first venous thromboembolic event with UFH.

Cost-effectiveness analysis based on a decision tree

The decision-tree-based incremental cost-effectiveness analysis was performed with Decision Tree Software (Tree Age 3.0.2, 1988; Simware, Williamstown, Mass.). The events examined in the decision tree were major hemorrhage while receiving heparin therapy, recurrence of venous thromboembolism within 3 months of treatment and death within 3 months of treatment (Fig. 1). The probabilities used in the decision tree were determined from the meta-analysis and from the pooled analysis of efficacy and

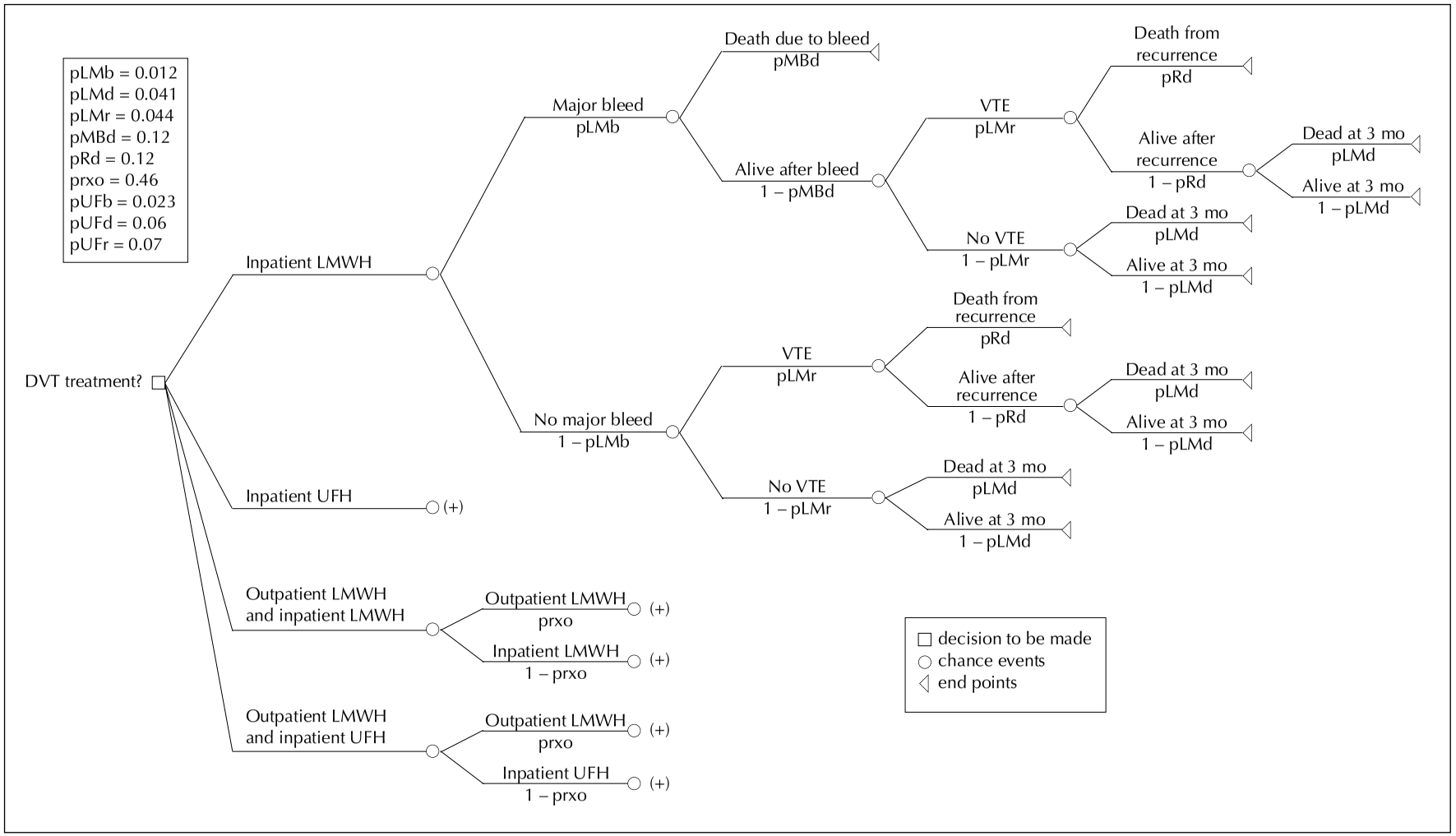

Fig. 1: Decision tree for incremental cost-effectiveness analysis of 4 treatment strategies for deep vein thrombosis (DVT): inpatient unfractionated heparin (UFH) therapy; inpatient low-molecular-weight heparin (LMWH) therapy; outpatient LMWH therapy for patients eligible for outpatient care and inpatient LMWH therapy for patients not eligible for outpatient care; and outpatient LMWH therapy for patients eligible for outpatient care and inpatient UFH therapy for patients not eligible for outpatient care. For each treatment strategy, the events modelled were major hemorrhage (bleed) while receiving heparin and recurrence of venous thromboembolism (VTE) or death within 3 months of treatment. pLMb = probability of a major bleed while receiving LMWH; pLMd = probability of death within 3 months of initial LMWH treatment; pLMr = probability of recurrence of venous thromboembolism within 3 months of initial LMWH treatment; pMBd = probability of a major bleed leading to death; pRd = probability of recurrence of venous thromboembolism leading to death; prxo = probability of being eligible for outpatient treatment; pUFb = probability of a major bleed while receiving UFH; pUFd = probability of death within 3 months of initial UFH treatment; pUFr = probability of recurrence of venous thromboembolism within 3 months of initial UFH treatment. The + symbol indicates points where the decision branching shown for inpatient LMWH treatment would be repeated for the other treatment strategies. The complete decision tree can be seen at www.hematology.ogh.on.ca.

safety. The costs used in the decision tree were those determined in our analysis of the cost of treatment and complications. We were interested in 2 variables: patient outcome at 3 months and cost of treatment (in 1995 dollars). Incremental cost-effectiveness estimates were calculated by comparing the hypothetical strategies with inpatient UFH treatment. The full decision tree, with 129 probability nodes, is available at **www.hematology.ogh.on.ca**.

We performed a worst-case sensitivity analysis for UFH treatment. A best-case analysis and one-way sensitivity analyses were also performed but are not presented here because they did not change the conclusions of the overall analysis. In the worst-case analysis, all cost, efficacy and safety data were simultaneously varied to favour UFH as the most cost-effective method. For this analysis, we assumed that only 20% of the patients would have been eligible for outpatient care. We used the upper 95% confidence limits, favouring UFH, of the meta-analysis and the pooled analysis of efficacy and safety (Table 1). We used the lower limits of savings in nursing time and in laboratory-monitoring costs with LMWH treatment, and we used the costs of the most expensive LMWH on the Canadian market.

Table 1: Probabilities used for cost-effectiveness decision tree

Event	Situation; probability, %	
	Base-case analysis	Worst-case sensitivity analysis*
Major hemorrhage		
While receiving LMWH	1.2†	2.6†‡
While receiving UFH	2.3†	2.3†‡
Leading to death	13.0§	40.0‡§
Recurrence of venous thromboembolism within 3 mo		
After LMWH treatment	4.4†	6.3†
After UFH treatment	7.0†	7.0†
Leading to death	12.0§	5.0§
Death within 3 mo		
After LMWH treatment	4.1†	5.6†
After UFH treatment	6.0†	6.0†

Note: LMWH = low-molecular-weight heparin, UFH = unfractionated heparin.
*Biased in favour of UFH analysis.
†Based on our meta-analysis. Mean difference in risk of hemorrhage –1.1% (95% confidence interval [CI] –2.4% to 0.3%), in risk of recurrence of venous thromboembolism –2.6% (95% CI –4.5% to –0.7%) and in risk of death –1.9% (95% CI –3.6% to –0.4%), all in favour of LMWH.
‡Given that in the worst-case analysis there are more major hemorrhages with LMWH, the upper limit of the probability of a major hemorrhage leading to death was used for this analysis to bias it in favour of UFH.
§Based on our pooled analysis.

Results

Meta-analysis and pooled analysis of efficacy and safety

The meta-analysis and pooled analysis indicated that LMWH treatment results in fewer major hemorrhages, fewer recurrences of venous thromboembolism and fewer deaths (Table 1).

Costs of treatment and complications

In fiscal year 1995/96, 105 patients had objectively confirmed deep vein thrombosis and were treated with intravenous UFH as inpatients. Fifty-six of the 105 patients would have been ineligible for outpatient therapy, 34 because they required inpatient care for a concurrent medical illness. The patients who would have been eligible for outpatient therapy were younger (median age 56 years) than those who would have been ineligible for such care (median age 69 years) by a statistically significant margin (p = 0.005). The sex distribution was similar in the 2 groups.

The mean case cost for inpatient UFH treatment for the 49 patients who would have been eligible for outpa-

Table 2: Resource use, unit costs and total costs for various strategies for treating deep vein thrombosis*

Treatment strategy	Costs of heparin			Costs of anticoagulation monitoring			Mean nursing cost per stay, $	Total case costs,† $
	Mean length of therapy, d	Daily cost, $	Mean cost per stay, $	Mean no. of PTT or INR per admission	INR or PTT cost, $	Total PTT or INR cost per stay, $		
Inpatient UFH (*n = 105*)	5.8	10.37	60.15	10.6	7.02	74.41	2097	3048
Outpatient-eligible inpatient UFH (*n = 49*)	5.9	10.37	61.18	11.0	7.02	77.22	1600	2553
Inpatient LMWH (*n = 105*)	5.8	37.30	216.34	5.9	7.02	41.42	1920	2993
Outpatient LMWH (*n = 49*)	5.9	37.30	220.07	5.9	7.02	41.42	603	1641

Note: INR = international normalized ratio, PTT = partial thromboplastin time.
*Costs for UFH are actual costs; those for LMWH are modelled on the basis of estimates from time and motion studies, estimates of drug costs and estimates of anticoagulation monitoring.
†Other costs (not shown) include other drug costs, investigations for concomitant illness and investigations for deep vein thrombosis. By design, these costs are assumed to be the same for the different strategies, except that with outpatient LMWH therapy, patients incur the costs of any other medications they are taking (mean cost of $41.00 over 5.9 days).

tient treatment was $2553 (Table 2). The mean case cost for all 105 patients (eligible or ineligible for outpatient treatment) was $3048. The difference was $495 per patient (Table 2).

To determine potential savings associated with inpatient LMWH treatment, we used data from our time and motion studies. For the base-case inpatient model, 36.5 minutes of nursing time would have been saved on the first day of treatment had LMWH been used instead of UFH. Similarly, for each subsequent day of therapy, 14.5 minutes would have been saved with LMWH. Given a mean duration of 5.8 days of heparin therapy and the mean hourly nursing cost (direct and indirect) of $100, the mean savings per patient if inpatient LMWH therapy had been used would have been $177. On average, 4.7 partial thromboplastin time tests would have been avoided for each patient, to yield an additional mean saving of $33 per patient in lab monitoring costs. Our pharmacy's current drug acquisition and preparation cost for LMWH is about $27/day more than for UFH, so the total mean cost of inpatient LMWH treatment (for 5.8 days) would have been about $155 more than for UFH. The net result would have been a saving of $55 per patient (Table 2).

Data on outpatient LMWH treatment from our medical day care unit indicated that the mean nursing costs for the first day of treatment were $110 and for each subsequent day were $100. Given that the mean length of heparin therapy for outpatients is 5.93 days, the mean nursing cost per patient is just under $604. For each outpatient, the cost of LMWH is $37.30/day, and the mean number of international normalized ratio determinations is 5.9. Therefore the cost of treating a patient with LMWH on an outpatient basis would be $912 less than the cost to treat such a patient with UFH on an inpatient basis (Table 2).

Table 3: Costs used for cost-effectiveness decision tree*

Treatment strategy or complication	Cost, $	
	Base-case analysis	Worst-case sensitivity analysis†
Inpatient UFH (all patients)	3048	3048
Inpatient UFH for outpatient-eligible patients	2553	2553
Inpatient LMWH (all patients)	2993	3120
Outpatient LMWH for outpatient-eligible patients	1641	2256
Recurrence of venous thromboembolism	2553	2553
Major hemorrhage	3774	8000

*Anticoagulation costs beyond initial anticoagulation are not included because they would be the same for UFH and LMWH. All costs are in 1995 dollars. LMWH costs were modelled using estimates from time and motion studies, estimates of drug costs and estimates of savings in anticoagulation monitoring; all other costs are actual costs.
†Biased in favour of UFH.

Major hemorrhages occurred in 4 of the 105 patients. The mean cost of treating these hemorrhages ($3774) was used in the base-case analysis (Table 3).

Cost-effectiveness analysis based on a decision tree

Whether delivered on an inpatient basis, an outpatient basis or a combination of the two, LMWH therapy is less expensive and results in fewer deaths up to 3 months after therapy than inpatient UFH therapy (Table 4). For the base-case analysis, the most cost-effective model was treatment with LMWH in both inpatient and outpatient settings.

In the worst-case sensitivity analysis for inpatient treatment (i.e., biased in favour of UFH), the saving in nursing time was modelled at only 15 minutes, the cost of nursing time was valued at $90/hour, and pharmacy drug acquisition and preparation costs for LMWH were set at $45/day (for the most expensive formulation available). On the basis of this model, it would have cost $72 more to treat inpatients with LMWH than UFH. In the worst-case sensitivity analysis for outpatient treatment, nursing costs were valued at $110/day, LMWH cost was set at $45/day and the cost of complications was the actual cost to treat the most expensive major hemorrhage ($8000). We also added transportation costs of $50/day and other drug costs of $14/day, but treating deep vein thrombosis with LMWH on an outpatient basis would still have been $297 cheaper than treating an inpatient with UFH.

When we used all of the 95% confidence limits of our efficacy and safety data favouring UFH therapy in the same model, the decision analysis still favoured LMWH therapy given on an outpatient basis. In our worst-case sensitivity analysis, LMWH given on an inpatient basis was more costly than UFH given on an inpatient basis. The incremental cost effectiveness of inpatient LMWH

Table 4: Base-case analysis of the cost-effectiveness of 4 strategies for treating deep vein thrombosis*

Treatment strategy	Cost per patient for 3 mo of care, $	Mortality rate within 3 mo of treatment, %
Inpatient UFH	3313	7.0
Inpatient LMWH	3150	4.7
Outpatient LMWH with inpatient UFH†	2634	6.0
Outpatient and inpatient LMWH	2546	4.7

*As determined by decision analysis incorporating costs of initial deep vein thrombosis therapy, costs of major hemorrhage and costs of recurrence of venous thromboembolism over 3 months. Decision-tree-based analysis modelled the probability of death from major hemorrhage, recurrence of venous thromboembolism and other-cause mortality within 3 months of treatment.
†For patients ineligible for outpatient treatment.

therapy relative to inpatient UFH therapy was $25 667 per life saved at 3 months, on the basis of the worst-case analysis (Table 5).

Interpretation

The outpatient treatment of deep vein thrombosis is not only feasible, safe and effective,[6,7] it is also cost-effective, which is particularly important as hospitals are restructured and the focus shifts from inpatient to outpatient care. Our cost-of-treatment analysis demonstrates that outpatient LMWH therapy is substantially less expensive than inpatient UFH therapy. Our analysis also reveals that in the inpatient setting, LMWH therapy is less expensive than UFH therapy: the significant reductions in nursing time required and laboratory costs offset the higher cost of LMWH itself. Only when all of our assumptions were simultaneously varied to favour UFH therapy were these savings eliminated. Even under those assumptions, the incremental cost-effectiveness of inpatient LMWH therapy over inpatient UFH therapy was still reasonable ($25 667 per life saved at 3 months).

Two economic analyses have been published, both of which were based on single LMWH treatment trials.[8,9] Neither analysis used case-costing data. The treatment trial conducted by Hull and colleagues[11] suggested that LMWH and UFH were equivalent in terms of recurrence of venous thromboembolism; however, LMWH therapy resulted in fewer major hemorrhages, and 3 months after treatment, the mortality rate was lower. LMWH treatment trials by Koopman and associates[7] and Levine and collaborators[6] suggested that LMWH and UFH were equally effective and equally safe. The findings of our meta-analysis are consistent with those of other recently published meta-analyses.[2–4] LMWHs appear to be associated with fewer major hemorrhages, fewer recurrences of venous thromboembolism up to 3 months after treatment and fewer deaths up to 3 months after treatment. It is possible that LMWH preparations are not equally effective. Ideally, the effectiveness of each preparation should be compared in large treatment trials, but until that is done meta-analyses combining the results for different preparations can provide estimates of effectiveness with narrow confidence intervals. If equivalent efficacy and safety are assumed for LMWH and UFH, as was recently demonstrated,[12] our study becomes a cost-minimization analysis. Given that LMWH is cheaper to deliver than UFH in any treatment setting, the cost-effectiveness conclusions of our study remain unchanged.

Table 5: Worst-case sensitivity analysis (biased in favour of UFH) of the cost-effectiveness of 4 strategies for treating deep vein thrombosis*

Treatment strategy	Cost per patient for 3 mo of care, $	Mortality rate within 3 mo of treatment, %
Inpatient UFH	3409	7.2
Inpatient LMWH	3486	6.9
Outpatient LMWH with inpatient UFH†	3252	7.1
Outpatient and inpatient LMWH	3314	6.9

*As determined by decision analysis incorporating costs of initial deep vein thrombosis therapy, costs of major hemorrhage and costs of recurrence of venous thromboembolism over 3 months. Decision-tree-based analysis modelled the probability of death from major hemorrhage, recurrence of venous thromboembolism and other-cause mortality within 3 months of treatment.
†For patients ineligible for outpatient treatment.

The strengths of our analysis include the precise costing data obtained through case-costing (the Canadian Coordinating Office for Health Technology Assessment considers only microcosting more precise than case-costing[10]), the determination of efficacy and safety by meta-analysis of level I studies, and the demonstration of the robustness of our conclusions by a sensitivity analysis, in which all variables were simultaneously changed to favour UFH therapy. Furthermore, our analysis was independent of any pharmaceutical or other funding agency. One weakness of the analysis is the absence of quality-of-life measures. Our experience and published data[7] reveal that patients treated with LMWH enjoy a better quality of life than patients treated with UFH. Our analysis did not include societal costs such as time off work; however, our experience is that patients treated with LMWH as outpatients quickly return to their work and family life. Hence, including the value of time off work would have further favoured LMWH therapy. We reduced cost-shifting in our analysis by assuming that the third-party payer would pay for the LMWH. For our worst-case sensitivity analysis, we further assumed that the third-party payer would pay for other "shifted" costs (e.g., patient transportation and other drug costs). Despite this, LMWH remained cost-effective. Another criticism of our study might be the retrospective nature of our determinations of patient eligibility for outpatient care. We used very conservative outpatient eligibility criteria. In our current practice well over 80% of patients are eligible for outpatient treatment. Hence, even more of the study patients would probably have been eligible for outpatient treatment, which would have further favoured LMWH therapy. In addition, in the worst-case sensitivity analysis only 20% of patients were deemed eligible for outpatient care, yet our conclusions were unchanged.

In conclusion, treatment of deep vein thrombosis with LMWH therapy, in both inpatient and outpatient settings, is more cost effective than treatment with UFH in the inpatient setting.

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Reprint requests to: *Dr. Marc A. Rodger, Ottawa General Hospital, Suite 7209, 501 Smyth Rd., Ottawa ON K1H 8L6; fax 613 737-8861*