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Uptake of new treatment strategies for deep vein thrombosis: an international audit

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Abstract

Objective. Study of the uptake of new medical technologies provides useful information on the transfer of published evidence into usual practice. We conducted an audit of selected hospitals in three countries (Canada, France, and Switzerland) to identify clinical predictors of low-molecular-weight (LMW) heparin use and outpatient treatment, and to compare the pace of uptake of these new therapeutic approaches across hospitals.

Design. Historical review of medical records.

Setting and participants. We reviewed the medical records of 3043 patients diagnosed with deep vein thrombosis (DVT) in five Canadian, two French, and two Swiss teaching hospitals from 1994 to 1998.

Measures. We explored independent clinical variables associated with LMW heparin use and outpatient treatment, and determined crude and adjusted rates of LMW heparin use and outpatient treatment across hospitals.

Results. For the years studied, the overall rates of LMW heparin use and outpatient treatment in the study sample were 34.1 and 15.8%, respectively, with higher rates of use in later years. Many comorbidities were negatively associated with outpatient treatment, and risk-adjusted rates of use of these new approaches varied significantly across hospitals.

Conclusion. There has been a relatively rapid uptake of LMW heparins and outpatient treatment for DVT in their early years of availability, but the pace of uptake has varied considerably across hospitals and countries.

Keywords: anticoagulation, deep vein thrombosis, low-molecular-weight heparins, practice variation, process of care

Treatment of acute deep vein thrombosis (DVT) has undergone major change during the last decade. While initial in-hospital treatment with intravenous unfractionated heparin used to be the traditional treatment, there is strong published evidence that subcutaneous low-molecular-weight (LMW) heparins in one or two daily doses are at least as safe, effective, and more cost-effective than intravenous unfractionated heparin [1,2]. Further, between 12 and 53% of patients with DVT can be safely and effectively treated at home with subcutaneous LMW heparins [3–5]. Outpatient treatment for DVT has been shown to be highly cost-effective and likely to be preferred by patients in comparison to in-hospital intravenous heparin therapy [5,6].

New evidence is often adopted into practice with a significant delay [7] and may show considerable geographic variation. This variation in practice across countries, hospitals, or health care providers is a common finding that has been a frequent focus for health care researchers interested in studying quality of care [8,9]. The interest in studying practice variation arises from the justifiable concern that variable processes of care are an indicator of variable quality across providers. Similarly, low rates of use of established therapies suggest suboptimal care [10,11]. Such findings are valuable because they provide information on where educational and quality interventions are most needed and likely to improve care.

Given the new available approaches to DVT care and the lack of studies documenting usual care practices for DVT treatment, we conducted a multicenter study to: (i) identify clinical predictors of LMW heparin use and outpatient treatment in the management of DVT; (ii) compare use of these

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new treatment approaches across years; and (iii) use the resulting information on clinical predictors to derive risk-adjusted rates of LMW heparin use and outpatient treatment in nine hospitals located in three countries.

Methods

Identification of cases

Based on established collaborative ties between investigators, this multicenter study was conducted in nine teaching hospitals, of which five are situated in Alberta, Canada, two in France, and two in Switzerland. DVT cases from 1994 to 1998 were identified from emergency room records by screening for emergency room contacts with any of the following ICD-9-CM diagnosis codes: 451.11, 451.19, 451.2, 451.81, 451.83, 451.84, 451.89, 451.9, 453.2, 453.8, 453.9, 671.3x, 671.4x, or 671.9x. For each hospital, a random sample of 75 DVT case records was selected from each of the years 1994 through 1998. For some hospitals, all cases of DVT were reviewed because <75 cases were available. A total of 3226 patient records were reviewed in the nine hospitals.

Chart review

This sampling approach led to the identification of 3226 DVT cases. A careful review of the emergency room records for these cases (and ensuing in-patient charts if patients were admitted) was conducted to determine: (i) specific diagnosis and whether or not there was a concomitant diagnosis or suspicion of pulmonary embolism, or a history of prior venous thromboembolism; (ii) patient sociodemographic variables (age, sex, year of admission); (iii) existence of any of the 17 comorbidity variables that constitute the Charlson index [12]; (iv) alcohol or street drug abuse; (v) indicators of instability (i.e. any subjective indication in the chart that the patient appears 'unstable', or explicit documentation of hypotension or hypoxemia); (vi) history of bleeding (prior/current gastrointestinal bleeding) or condition associated with bleeding risk (cerebral aneurysm/arteriovenous malformation, current oral anticoagulation, history of stroke); and (vii) pregnancy. All of these variables were collected because they were considered a priori to be potential determinants of LMW heparin use and/or outpatient therapy.

As a measure of overall LMW heparin use in the treatment of DVT, we recorded for each patient whether or not a LMW heparin was used at any given time in the management of the patient (i.e. either initially, during hospitalization, or at discharge). We also documented whether patients with DVT were treated as outpatients or admitted for in-patient treatment.

Data analysis

We performed univariate comparisons between patients who received LMW heparins as in-patients and those who were treated in an outpatient setting. We compared continuous variables using a two-sample Wilcoxon rank-sum test, and categorical variables by using Fisher's exact test. Two-sided P values <0.05 were considered statistically significant.

In order to identify those clinical variables that are independently associated with the use of LMW heparins, we constructed logistic regression models with LMW heparin use as the dependent variable. This analysis was repeated to explore independent clinical predictors of outpatient treatment. We avoided variable selection criteria based on univariate statistical significance because our objective in these analyses was simply to explore multivariable associations with LMW heparin use and outpatient treatment.

From the logistic regression model, we calculated the expected rate (E) of LMW heparin use for each of the nine study hospitals. The observed rate of LMW heparin use (O) was then divided by E to generate an O/E ratio for each hospital by averaging individual patients' model-predicted probability of use within hospitals. To calculate the adjusted rate of LMW heparin use for each hospital, we multiplied the O/E ratio by the overall rate of use. This analysis was repeated to calculate the expected rate, O/E ratio, and adjusted rate for outpatient treatment. All analyses were performed using STATA version 7.0 (Stata Corporation, College Station, TX).

Results

Patient characteristics

We excluded 183 of the 3226 initially screened patients for the following reasons: (i) no leg DVT on closer review of the hospital records; (ii) admission before 1994 or after 1998; and (iii) missing information about the method of treatment. As a result, 3043 patients with objectively confirmed DVT were included in our study analyses. Table 1 describes the characteristics and comorbidities of the 3043 patients. The mean age was 61.4 years and 49.7% of the study population were women. Arterial hypertension (25.1%), any malignancy (20%), and chronic lung disease (10%) were the most frequent comorbidities. Twenty-nine percent of the study patients had a previous history of venous thromboembolism. In 22.8% of all cases, a concomitant pulmonary embolism was either clinically suspected or objectively confirmed. Nearly 8% of patients were considered 'unstable' or had hypoxemia, but the prevalence of hypotension was low (1%).

Predictors of LMW heparin use

For 25.7% of all patients in our study sample, a LMW heparin was the first anticoagulant used, while 1038 (34.1%) patients were treated using it at some time. Of these, 62.6% received traditional in-patient care whereas 37.4% were treated as outpatients. In-patients who received LMW heparins were older (64 versus 56 years; $P < 0.001$) and had significantly more comorbid diseases than those who were treated with LMW heparin as outpatients. Specifically, patients who received LMW heparin as in-patients were more likely to have peripheral vascular disease, arterial hypertension, malignancy,

Table 1 Characteristics of 3043 patients with deep vein thrombosis in nine hospitals between 1994 and 1998

Mean age ± SD (years)	61.4 ± 18.6
Females, *n* (%)	1513 (49.7)
Prior history of venous thromboembolism, *n* (%)	880 (28.9)
Prior history of stroke, *n* (%)	127 (4.2)
Prior/current gastrointestinal bleeding, *n* (%)	107 (3.5)
Brain aneurysm/arteriovenous malformation, *n* (%)	23 (0.8)
Current oral anticoagulation, *n* (%)	334 (11)
Peripheral vascular disease, *n* (%)	147 (4.8)
Unstable or stable angina, *n* (%)	226 (7.4)
Myocardial infarction, *n* (%)	124 (4.1)
Congestive heart failure, *n* (%)	213 (7)
Cerebrovascular disease, *n* (%)	159 (5.2)
Arterial hypertension, *n* (%)	763 (25.1)
Chronic lung disease, *n* (%)	304 (10)
Peptic ulcer disease, *n* (%)	156 (5.1)
Mild liver disease, *n* (%)	50 (1.6)
Moderate/severe liver disease, *n* (%)	23 (0.8)
Chronic renal disease, *n* (%)	109 (3.6)
Diabetes mellitus, *n* (%)	219 (7.2)
Diabetes with complications, *n* (%)	28 (0.9)
Any malignancy, *n* (%)	608 (20)
Metastatic solid tumor, *n* (%)	300 (9.9)
Human immunodeficiency virus disease, *n* (%)	21 (0.7)
Rheumatological disease, *n* (%)	172 (5.7)
Dementia, *n* (%)	137 (4.5)
Hemi-/paraplegia, *n* (%)	112 (3.7)
Alcohol abuse, *n* (%)	198 (6.5)
Street drug abuse, *n* (%)	27 (0.9)
Suspected or confirmed pulmonary embolism, *n* (%)	695 (22.8)
'Unstable-looking patient'[1], *n* (%)	227 (7.5)
Arterial hypotension[2], *n* (%)	29 (1)
Hypoxemia[3], *n* (%)	232 (7.6)
Pregnancy, *n* (%)	24 (0.8)

SD = standard deviation.
[1]Designates subjective measures of instability (e.g. 'looks unwell', 'diaphoretic') rather than traditional vital parameters.
[2]Systolic blood pressure <90 mmHg.
[3]paO_2 <60 mmHg or O_2 saturation <90%.

rheumatological diseases, suspected or confirmed pulmonary embolism, and hypoxemia, and were more often considered unstable than patients treated with LMW heparins as outpatients ($P < 0.001$ for each pairwise comparison).

Multivariate associations between the use of LMW heparins and the patient characteristics are shown in Table 2. The strongest independent positive association with LMW heparin use was the year of hospitalization. The odds ratios (ORs) for patients being treated with LMW heparins rose steadily from 1.00 in 1994 (the reference year) to 11.36 [95% confidence interval (CI) 8.33–15.49] in 1998, reflecting the rapid shift over time toward the use of LMW heparins in the treatment of DVT. The evolution in use of LMW heparins over time is also shown for all hospitals combined (Figure 1) and by hospital (Figure 2).

Other variables independently associated with LMW heparin use include the presence of rheumatological disease (OR 2.04; 95% CI 1.44–2.90), human immunodeficiency virus (OR 3.01; 95% CI 1.13–8.03), any malignancy (OR 1.33; 95% CI 1.02–1.74), and an 'unstable' medical condition (OR 1.66; 95% CI 1.18–2.33). Significant negative associations with LMW heparin use were generally more frequent than positive ones. Current oral anticoagulation (OR 0.74; 95% CI 0.55–0.98), cerebrovascular disease (OR 0.62; 95% CI 0.38–0.99), chronic lung disease (OR 0.69; 95% CI 0.51–0.94), peptic ulcer disease (OR 0.48; 95% CI 0.31–0.76), diabetes with complications (OR 0.31; 95% CI 0.11–0.88), metastatic solid tumor (OR 0.43; 95% CI 0.30–0.63), street drug abuse (OR 0.34; 95% CI 0.12–0.99), and hypoxemia (OR 0.44; 95% CI 0.30–0.66) were all independently associated with less LMW heparin use.

Predictors of outpatient treatment

Outpatient treatment was used for 15.8% of patients. Multivariate associations between outpatient treatment and the patient characteristics are shown in Table 2. The only significant positive independent association with outpatient treatment was the year of hospitalization, with ORs rising steadily from 1.00 in 1994 to 11.67 (95% CI 7.49–18.17) in 1998. The evolution in use of outpatient treatment over time is also shown for all hospitals (Figure 1) and by hospital (Figure 3).

Independent patient factors negatively associated with outpatient treatment were current oral anticoagulation (OR 0.54; 95% CI 0.33–0.87), unstable or stable angina (OR 0.17; 95% CI 0.07–0.44), arterial hypertension (OR 0.60; 95% CI 0.44–0.82), peptic ulcer disease (OR 0.33; 95% CI 0.15–0.75), metastatic solid tumor (OR 0.46; 95% CI 0.24–0.87), rheumatological disease (OR 0.43; 95% CI 0.21–0.86), suspected or confirmed pulmonary embolism (OR 0.08; 95% CI 0.04–0.14), 'unstable' medical condition (OR 0.23; 95% CI 0.09–0.59), hypoxemia (OR 0.08; 95% CI 0.01–0.55), and pregnancy (OR 0.16; 95% CI 0.04–0.74). The last four negative associations were particularly strong. Older age nearly achieved statistical significance (OR 0.94 for 10-year increments; 95% CI 0.88–1.00; $P = 0.05$). The patient characteristics moderate/severe liver disease, diabetes with complications and street drug abuse could not be included in the multivariate analysis for predictors of outpatient treatment, as none of these patients were treated as outpatients.

Inter-hospital comparison

Table 3 shows the crude and adjusted rates of LMW heparin use and outpatient treatment (i.e. proportions of DVT patients treated with LMW heparins and as outpatients) in the

Table 2 Clinical characteristics associated with low-molecular-weight (LMW) heparin use and outpatient treatment

Characteristic	Multivariate odds ratio (95% CI)	
	LMW heparin use[1]	Outpatient treatment[2]
Age (10-year increments)	0.99 (0.94–1.04)	0.94 (0.88–1.00)
Female sex	1.16 (0.98–1.38)	1.10 (0.87–1.37)
Year of hospitalization		
1994	1.00 (reference)	1.00 (reference)
1995	2.17 (1.57–3.00)	1.24 (0.73–2.11)
1996	3.77 (2.76–5.15)	4.03 (2.54–6.40)
1997	6.51 (4.81–8.83)	6.74 (4.31–10.52)
1998	11.36 (8.33–15.49)	11.67 (7.49–18.17)
Prior history of VTE	1.04 (0.86–1.26)	0.81 (0.62–1.05)
Prior history of stroke	1.33 (0.80–2.23)	0.34 (0.11–1.01)
Prior history of GI bleeding	0.89 (0.54–1.46)	0.52 (0.22–1.22)
Brain aneurysm/AV malformation	0.61 (0.23–1.60)	0.20 (0.02–1.62)
Current oral anticoagulation	0.74 (0.55–0.98)	0.54 (0.33–0.87)
Peripheral vascular disease	1.43 (0.97–2.13)	0.79 (0.39–1.64)
Unstable or stable angina	0.97 (0.69–1.36)	0.17 (0.07–0.44)
Myocardial infarction	1.13 (0.73–1.74)	1.22 (0.64–2.35)
Congestive heart failure	0.97 (0.68–1.38)	1.08 (0.61–1.93)
Cerebrovascular disease	0.62 (0.38–0.99)	1.16 (0.51–2.61)
Arterial hypertension	0.98 (0.80–1.20)	0.60 (0.44–0.82)
Chronic lung disease	0.69 (0.51–0.94)	0.81 (0.52–1.25)
Peptic ulcer disease	0.48 (0.31–0.76)	0.33 (0.15–0.75)
Mild liver disease	1.07 (0.55–2.09)	1.30 (0.47–3.57)
Moderate/severe liver disease	2.14 (0.81–5.65)	NA
Chronic renal disease	0.84 (0.53–1.35)	0.92 (0.45–1.91)
Diabetes mellitus	0.90 (0.65–1.24)	0.76 (0.46–1.25)
Diabetes with complications	0.31 (0.11–0.88)	NA
Any malignancy	1.33 (1.02–1.74)	0.74 (0.50–1.09)
Metastatic solid tumor	0.43 (0.30–0.63)	0.46 (0.24–0.87)
AIDS/HIV disease	3.01 (1.13–8.03)	0.70 (0.14–3.56)
Rheumatological disease	2.04 (1.44– 2.90)	0.43 (0.21–0.86)
Dementia	1.42 (0.96–2.11)	0.43 (0.21–0.86)
Hemi-/paraplegia	1.03 (0.64–1.66)	0.41 (0.17–1.02)
Alcohol abuse	0.91 (0.63–1.32)	0.63 (0.36–1.11)
Street drug abuse	0.34 (0.12–0.99)	NA
Suspected/confirmed PE	0.83 (0.67–1.02)	0.08 (0.04–0.14)
'Unstable looking patient'	1.66 (1.18–2.33)	0.23 (0.09–0.59)
Arterial hypotension	0.42 (0.16–1.16)	0.25 (0.03–2.20)
Hypoxemia	0.44 (0.30–0.66)	0.08 (0.01–0.55)
Pregnancy	0.61 (0.24–1.58)	0.16 (0.04–0.74)

CI, confidence interval; VTE, venous thromboembolism; GI, gastrointestinal; AV, arteriovenous; AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; PE, pulmonary embolism.
[1]Logistic regression model with LMW heparin as a dependent variable and the clinical characteristics listed in this table as independent variables had an area under the receiver operating characteristic (ROC) curve of 0.74.
[2]Logistic regression model with outpatient treatment as a dependent variable and the clinical characteristics listed in this table as independent variables had an area under the ROC curve of 0.84.

nine study hospitals. Expected rates of LMW heparin use and outpatient treatment are also shown. The observed rate of LMW heparin use and outpatient treatment varied markedly from 9.0 to 80.5% and 0 to 46.4%, respectively. The expected rate of LMW heparin use and outpatient treatment calculated from the multivariate models shown in Table 3 also varied somewhat, from 27.1 to 41.5% and 6.0 to 24.1%, respectively. These differences in model-predicted rates of use reflect the

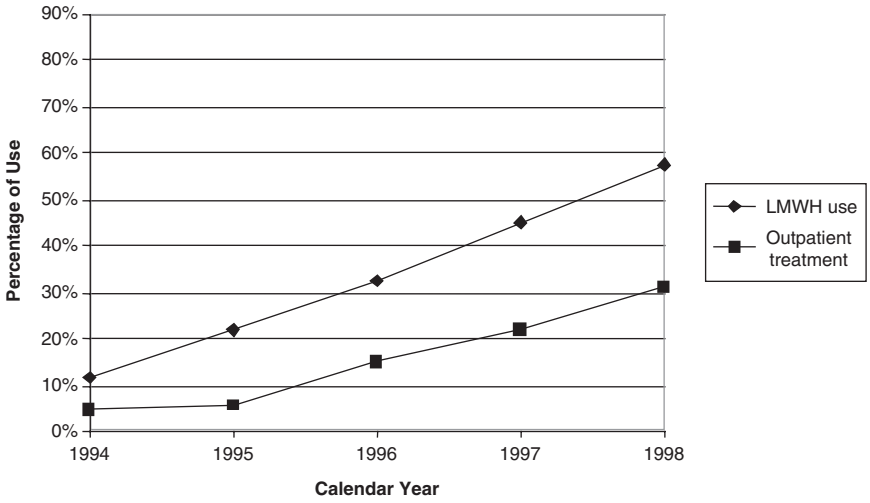

Figure 1 Overall low-molecular-weight heparin use and outpatient treatment for all nine hospitals. LMWH, low-molecular-weight heparin.

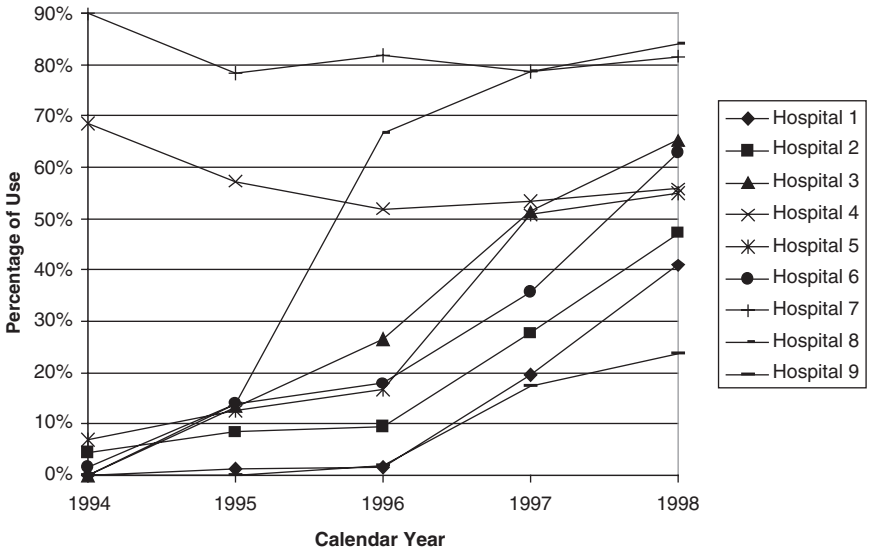

Figure 2 Low-molecular-weight heparin use in the nine hospitals studied, by hospital.

differing average severity of illness across hospitals. The ratios of O/E treatment use are also shown in Table 3. Values >1.0 indicate greater-than-average use, while values <1.0 indicate lower than average use. The O/E ratios are then used to calculate the risk-adjusted rates of LMW heparin use and outpatient therapy use, shown in Table 3 (adjusted rate = O/E × average rate). The differences between the observed and adjusted rates were generally quite small, although adjustment did occasionally change rates notably.

Between-country comparisons

While we fully recognize that the selected hospitals are not necessarily representative of the countries in which they reside, we nevertheless compared treatment strategies across the three countries. The adjusted rates of LMW heparin use were 26.2% for Canada, 63.0% for France, and 25.0% for Switzerland. For outpatient treatment, the adjusted rates were 17.2% for Canada, 1.8% for France, and 20.3% for Switzerland.

Discussion

Our results show that a number of clinical variables were positively and negatively associated with LMW heparin use and outpatient treatment. As most outpatients are treated with LMW heparins, many of the observed associations are common to both analysis endpoints. The strongest positive predictor for both LMW heparin use and outpatient treatment turned out to be the year of hospitalization, with later years being associated with greater use of the new treatment methods. The steady rise in the uptake of LMW heparins and

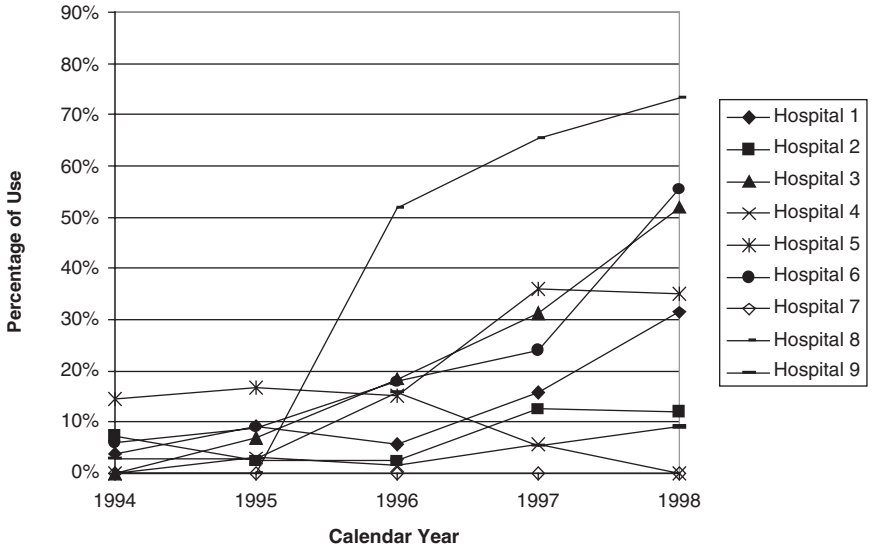

Figure 3 Outpatient treatment in the nine hospitals studied, by hospital.

Table 3 Observed and adjusted rates of low-molecular-weight (LMW) heparin use and outpatient treatment according to hospital site between 1994 and 1998

Hospital	Number of cases	LMW heparin use				Outpatient treatment			
		Expected rate (%)	Observed rate (%)	O/E ratio[1]	Adjusted rate[2] (%)	Expected rate (%)	Observed rate (%)	O/E ratio[3]	Adjusted rate[2] (%)
1	347	34.0	13.5	0.40	13.5	17.6	13.8	0.78	12.4
2	376	27.1	17.0	0.63	21.4	9.0	7.5	0.84	13.2
3	375	34.0	31.2	0.92	31.3	17.5	21.6	1.24	19.6
4	335	33.1	57.6	1.74	59.3	6.0	2.1	0.35	5.6
5	340	32.7	27.1	0.83	28.3	14.4	22.9	1.59	25.2
6	319	33.1	26.3	0.79	27.1	19.7	22.6	1.15	18.1
7	287	41.5	80.5	1.94	66.1	14.7	0.0	0	0.0
8	308	39.3	57.8	1.47	50.2	24.1	46.4	1.92	30.4
9	356	34.6	9.0	0.26	8.9	20.6	6.7	0.32	5.1

[1]The ratio between the observed and expected rate of LMW heparin use.
[2]Rate is adjusted for all of the clinical variables listed in Table 2.
[3]The ratio between the observed and expected rate of outpatient treatment.

outpatient treatment over time reflects a relatively rapid response to new evidence as compared, for example, with the historical example of sluggish uptake of thrombolysis for acute myocardial infarction [7]. Based on these data, it is conceivable that some of the hospitals studied will have succeeded in treating almost all eligible patients with these new treatments by 2004. The proportion of patients who are eligible for outpatient treatment will vary somewhat across hospitals, but may be 75–80%, or even higher.

There were a number of patient factors negatively associated with outpatient treatment that seem to reflect highly appropriate clinical decisions. Indeed, patients with multiple comorbidities and complex medical issues may not be ideal candidates for outpatient treatment with LMW heparins. We also found that variables indicative of bleeding risk (oral anticoagulation, peptic ulcer disease) were associated with lower use of LMW heparins, perhaps reflecting a reluctance among providers—which may or may not be appropriate—to use LMW heparins in the face of bleeding risk. Interestingly, although LMW heparin use is negatively associated with pulmonary embolism, this association is not significant. A possible explanation is that ~30% of patients with concomitant proven or suspected pulmonary embolism were treated with LMW heparins. Furthermore, there is growing evidence in the medical literature that this approach is safe and effective, at least in patients with submassive pulmonary embolism 13–15. While LMW heparin use is positively associated with the presence of any malignancy, its use has a negative association with

metastatic solid tumor. A possible explanation for this discrepancy could be that many patients with metastasis (some of them with brain metastasis) present an elevated bleeding risk or are so ill that anticoagulation with LMW heparins is perceived by treating physicians not to be a desirable option.

The results of the inter-hospital comparison show that observed rates of LMW heparin use and outpatient treatment are highly variable, even after adjustment for all of the patient factors listed in Table 1. Such adjustment creates a 'level playing field' for inter-hospital and between-country comparisons. With adjustment, LMW heparin use across hospitals varied from 8.9 to 66.1%, and outpatient treatment varied from 0 to 30.4%. Somewhat surprisingly, however, the two hospitals (4 and 7) with the highest rates of LMW heparin use had the lowest rates of outpatient treatment. These findings add to the results of a previous study which found considerable variation in the prophylactic use of LMW heparins among British hospitals [16].

Similar to the inter-hospital comparison, the between-country comparison of patient-factor-adjusted LMW heparin use and outpatient treatment exhibited large variability. The adjusted rates of LMW heparin use varied between 26.2 and 62.9%, while those for outpatient treatment ranged from 1.8 to 20.3% of the study patients. As there are only few clinical situations where unfractionated heparin may be superior to LMW heparins (e.g. renal insufficiency), these findings suggest that LMW heparin therapy was generally underused in our study population. Although the rates of outpatient treatment in our study are consistent with the variability in rates of use reported in the literature (12–53% [4–6]), four out of nine hospitals had observed outpatient treatment rates of <10%, clearly indicating under-use. An important caveat to this interpretation, however, is that we only studied the early years of availability of LMW heparins.

There are several possible reasons for the marked variation between hospitals and countries in the extent to which LMW heparins and outpatient treatment are used. There may exist differences across hospitals and/or countries in the timing of licensing of new medications, formulary changes (at hospital level), health insurance coverage, local bed pressures, and varying degrees of physician comfort with new drugs. In addition, the development of infrastructure necessary to support outpatient care may vary across regions and countries. We cannot rule out the possibility that the small percentage of patients treated as outpatients in some centres could relate to unique local practice patterns that channel outpatient DVT patients toward outpatient treatment centres, bypassing hospitals entirely (case sampling for this study was hospital-based).

Notable strengths of this study are the collection of detailed clinical data on usual care practices for DVT, and the compilation of data on >3000 patients treated in nine hospitals and three countries. Further, the collection of data from a 5-year time period provides a longitudinal perspective on the uptake of new therapeutic approaches to DVT. This study is thus useful in documenting the early years of the transition from purely in-patient therapy for DVT with unfractionated heparin to increasing use of LMW heparins and outpatient therapy.

An acknowledged limitation of our study is the non-random selection of hospital centers in three countries. However, we anticipate that similar variation would also probably have been seen with a random hospital sample. Further, as the review of >3000 charts in nine hospitals has been a time-consuming task, our study documents only the early years (1994–1998) of the practice change. A review of more recent years in future work, for which this study provides baseline information, may reveal a further increase in the uptake of LMW heparins and outpatient treatment.

Finally, our study focused on clinical factors as predictors of utilization of LMW heparins and outpatient treatment. There are also notably a number of physician and system structure factors that could influence the utilization of LMW heparins and outpatient treatment in patients with DVT [17]. Examples of such factors include the presence or absence of hospital guidelines for DVT care, the timing of the addition of LMW heparins to hospital formularies, and the availability of outpatient clinics for close follow-up of outpatients. A statistically meaningful exploration of such factors would have necessitated the systematic collection of structural data, and the inclusion of a much larger number of study sites, an undertaking that was clearly beyond the scope of this project.

These limitations notwithstanding, our study is useful in documenting a steady and relatively rapid uptake of LMW heparins and outpatient treatment in nine hospitals. A number of clinical variables appear to be appropriately guiding clinical decisions around these new therapies. The marked variation in practice between hospitals and countries indicates, however, that providers in some hospitals have been more sluggish than others in their adoption of a new standard for the treatment of DVT. Educational and quality interventions may be needed in some centers to accelerate the uptake of novel and efficacious approaches to managing DVT. Further research should focus on potential associations between structural factors and processes of care in the management of DVT.

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