

Treatment of venous thromboembolism: Adherence to guidelines and impact of physician knowledge, attitudes, and beliefs

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Objectives: To assess the treatment of venous thromboembolism (VTE) in hospitalized patients enrolled in a national, multicenter database.

Methods: This was a retrospective, cohort study that randomly selected VTE patients from 38 academic/teaching, community, and Veterans Administration (VA) hospitals. The study included a physician survey component. The patients selected were those treated between January 2002 and June 2003 who had an ICD-9-CM code for pulmonary embolus (PE), deep vein thrombosis (DVT), or pregnancy-related PE or DVT.

Results: The study included 939 patients: 52.7% with DVT, 28.4% with PE, and 18.8% with PE and DVT. Mean age was 59.5 years. Risk factors included obesity (body mass index >30) in 30.1%, history of VTE in 28.0%, malignancy in 27.4%, surgery in 21.1%, and immobility in 18.5%. Only 56.1% of patients were treated with low-molecular-weight heparin (LMWH). Bridging from LMWH or unfractionated heparin (UFH) to warfarin was completed during hospitalization in 486 (68.6%), but only 246 (50.6%) had an international normalized ratio (INR) ≥ 2 for 48 hours before discontinuation of the injectable anticoagulant. Length of stay in patients discharged on bridge therapy was 4.0 ± 3.7 days vs 8.1 ± 5.8 days for patients discharged on warfarin therapy ($P < .001$). Ninety-two (10.1%) patients were discharged with neither oral nor injectable anticoagulation and had a mean duration of treatment of only 10.6 ± 16.2 days. Of 245 physicians surveyed from participating hospitals, 84% and 53%, respectively, indicated that LMWH was their preferred agent for treatment of DVT and treatment of PE. With regard to warfarin, 30% did not believe it was necessary to have a therapeutic INR for ≥ 2 days before discontinuing LMWH or UFH, and 27% responded that it was necessary to keep DVT patients in the hospital until they were therapeutic.

Conclusions: In this cross-section of United States hospitals, lower than anticipated use of LMWH, insufficient bridging from UFH or LMWH to warfarin, and continuation of anticoagulation after hospitalization were all problems discovered with the treatment of VTE. Physician knowledge, attitudes, and beliefs are partially responsible for the gap between actual practice and international guidelines. These results suggest that hospitals should evaluate their adherence to international VTE treatment guidelines and develop strategies to optimize antithrombotic therapy. (*J Vasc Surg* 2005;42:726-33.)

Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), is a serious medical complication, with an annual United States

(US) incidence of approximately 200,000 cases.¹ One-year survival after VTE has been reported to be as low as 63.6%, with 1-year survival for DVT at 85.4% and 47.7% for PE with or without DVT.²

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Treatment for VTE has been widely studied, and treatment guidelines have been published and frequently updated by the American College of Chest Physicians (ACCP), American College of Emergency Physicians, Eastern Association for the Surgery of Trauma, and Institute for Clinical Systems Improvement.³ Generally, acute treatment consists of low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) for 4 to 5 days, with overlapping therapy to warfarin until an international normalized ratio (INR) of ≥ 2 for two consecutive days is achieved. Anticoagulation should be continued for at least 3 to 12 months, depending on the site of thrombosis and risk factors.^{4,5} Failure to provide adequate VTE treatment can result in patient morbidity and mortality, with a substantial economic burden.⁶

Recent data show that practitioners follow evidence-based guidelines inconsistently in a wide variety of disease

states, with an adherence rate as low as 55%.⁷ This study was performed to compare anticoagulation treatment strategies to evidence-based guidelines (ACCP 2001) over a broad cross-section of US hospitals.⁴ However, modest changes in recently published guidelines (ACCP 2004) are highlighted.⁵ In addition, physicians were surveyed to determine their knowledge, attitudes, and beliefs concerning treatment. Results were provided to participants for quality improvement and to provide a stimulus for improving antithrombotic management, where needed.

METHODS

Cohort study. This research was based on data from the National Anticoagulation Benchmark and Outcomes Report (NABOR) (EPI-Q, Inc, Oakbrook Terrace, Ill), a retrospective cohort study. NABOR was designed to evaluate anticoagulation practices among participating US hospitals and to collect quality improvement data for participating sites.

Participants were identified from referrals provided by professional societies, including the American College of Chest Physicians, the American Venous Forum, and the American Society of Health-System Pharmacists. Hospitals were recruited according to geographic location and institution type. We attempted to recruit 40 hospitals comprised of five Veterans Administration (VA) hospitals and an equal number of academic/teaching and community hospitals. To be eligible, hospitals were expected to obtain all site-mandated approvals from their respective review committee(s) and to abstract data ≤ 90 days. Seventy-five hospitals were approached for inclusion, with the first 40 responding hospitals selected. Two hospitals were not able to collect and submit data and subsequently withdrew.

The study period encompassed January 2002 through June 2003. To meet the targeted sample of 25 cases per site, one site was given a waiver to include patients before January 2002. Sites identified VTE patients discharged during the interval with the following ICD-9-CM codes: 415.11-415.19 (PE), 453.8 (DVT), 673.2-673.8 (pregnancy-related PE), and 671.00-671.9 (pregnancy-related DVT). Patients < 18 years old or those admitted from or discharged to another hospital were excluded. Each site used a random number-generated table to select the 25 VTE cases.

Trained data collection personnel performed a medical record review at each site and abstracted data by using a standard data collection form and data dictionary. Personnel entered data into NABOR software for de-identification of personal information and for partial data validation. The data collection tool included patient demographics, VTE event(s), comorbidities, acute and secondary VTE treatment, VTE risk factors, in-hospital complications, and postdischarge emergency department visits or rehospitalization ≤ 30 days of discharge. Major hemorrhage was defined as an intracranial bleed or retroperitoneal bleed. Minor hemorrhage was defined as epistaxis, ecchymosis, hematoma, or microscopic hematuria. Any missing or in-

consistent variables were resolved before transmission to the study center. Upon receipt, the study center reviewed the data for inconsistencies. Queries were resolved with each site before data analysis.

Physician Knowledge Attitudes, Beliefs, and Practices (KABP) Survey. Participating hospitals were asked to provide the study center with a physician directory from which randomly to select names of physicians involved in VTE care. Physician specialties were internal medicine, cardiology, orthopedic surgery, family practice, and emergency medicine. Physicians were contacted by e-mail, phone, or office fax and invited to participate in the survey. The survey was completed either on-line, or by return fax for physicians without Internet access. To be included in the analysis, physicians must have reported treating > 5 cases of VTE within the past 12 months. Respondents provided their specialty, gender, number years in practice, and board certification. They were asked to respond either with *agree*, *disagree*, or *uncertain* to a series of questions regarding anticoagulant selection preference, perceived effectiveness of available agents, practice regarding bridging from injectable to oral agents, risk of complications related to therapy, and attitudes regarding patient self management of therapy postdischarge.

Analysis. Descriptive analysis of the clinical cohort data was performed to examine the distribution of characteristics among VTE patients and the treatment profile of these patients across different hospitals. Univariate analyses were used on the basis of the preliminary descriptive statistics. The relationship between treatment profile and clinical outcomes was examined. Differences were assessed with either the χ^2 test or Fisher's exact test for categorical variables, and the Mann-Whitney *U* test for non-normally distributed continuous variables. Analysis of the survey results was descriptive, with frequency of responses reported for each survey item. This study was performed in 2003, before the publication of 2004 ACCP guidelines. Therefore, we examined two indicators for the discontinuation of LMWH or UFH, namely an INR ≥ 2.0 for two consecutive days and 4 days of overlapping (bridge) therapy, which is in the 2001 ACCP guidelines vs at least 5 days of concomitant LMWH or UFH, which is in the 2004 ACCP guidelines.^{4,5}

RESULTS

Cohort study. The benchmark database included 939 patient records representing 38 hospitals (21 academic/teaching hospitals, 13 community hospitals and 4 VA hospitals) from 27 states. A total of 826 patients (88.0%) were admitted for VTE, and 113 patients (12.0%) experienced the event during hospitalization.

Isolated DVT was identified in 495 patients (52.7%); isolated PE was identified in 267 (28.4%); and 177 patients (18.8%) had both PE and DVT. The average age was 59.4 ± 17.6 years and the ratio of men to women was 49.0:51.0. The most frequently identified risk factors were obesity

Table I. Venous thromboembolism risk factors

Total patients N = 939	Incidence n (%)
Obesity (BMI >30)	283 (30.1)
Previous VTE	263 (28.0)
Malignancy	257 (27.4)
Surgery ≤90 days	198 (21.1)
Immobility ≥72 hours	174 (18.5)
Congestive heart failure	100 (10.6)
Previous stroke, TIA, or systemic embolus	76 (8.1)
Trauma	54 (5.8)
Oral contraceptive/estrogen use	44 (4.7)
Varicose veins	29 (3.1)
Pregnancy	23 (2.4)
Congenital and acquired thrombophilia	88 (9.4)

BMI, Body mass index; VTE, venous thromboembolism; TIA, transient ischemic attack.

(body mass index >30) (30.1%), prior history of VTE (28.0%), malignancy (27.4%), surgery within the past 30 days (21.1%), and immobility >72 hours (18.5%) (Table I) Idiopathic VTE occurred in 37.4% of the patients. Thirty-two patients died during hospitalization, resulting in a mortality rate of 3.4%. The mortality rate in those with isolated DVT was 2.2%, isolated PE was 5.6%, and both PE and DVT was 3.4%.

Acute treatment. For acute VTE treatment, 562 patients (59.9%) received UFH, 527 patients (56.1%) received LMWH, 78 patients (8.3%) received adjusted-dose subcutaneous UFH, 6 patients (0.6%) received a direct thrombin inhibitor (Table II), and 260 patients (27.7%) received two or more of these treatment categories. Fifty-two patients were not treated with injectable therapy and only received warfarin during hospitalization.

Internists were involved in the care of 618 patients (65.8%), emergency department physicians treated 249 (26.5%), surgeons treated 101 (10.8%), cardiologists treated 148 (15.8%), oncologists treated 100 (10.6%), and family practitioners prescribed anticoagulation in 70 patients (7.5%). Other specialists, including pharmacists and nurse practitioners, prescribed anticoagulation in 234 patients (24.9%). For 389 patients (41.4%), two or more specialties were involved in the prescription of anticoagulation during their hospital stay.

Use of warfarin with or without bridge therapy. Seven hundred sixty patients (80.9%) received warfarin during hospitalization. Of those, 709 patients (93.3%) received bridge therapy (UFH or LMWH plus warfarin) before discharge, and the remaining 51 patients did not. The injectable agent, either UNF or LMWH, was discontinued in 486 patients (68.6%) during hospitalization. However, only 246 (50.6%) of these had obtained an INR value ≥2.0 for 48 hours before the injectable agent was discontinued. Of the remaining 240 patients with an INR <2 for 48 hours before injectable agent was discontinued, only 74 (30.8%) had received at least 4 days of bridge therapy. The mean duration of bridge therapy in those who achieved a therapeutic INR for 48 hours was 4.5 ± 2.8 days. The

Table II. Initial venous thromboembolism treatment*

	Total Patients N = 939 (%)	DVT N = 495 (%)	PE N = 267 (%)	PE and DVT N = 177 (%)
LMWH	527 (56.1)	286 (57.8)	147 (55.1)	94 (53.1)
UFH†‡	562 (59.8)	256 (51.7)	185 (69.3)	121 (68.4)
ADH	78 (8.3)	45 (9.1)	23 (8.6)	10 (5.6)
DTI	6 (0.6)	3 (0.6)	2 (0.7)	1 (0.6)

DVT, Deep vein thrombosis; PE, pulmonary embolism; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; ADH, adjusted-dose subcutaneous heparin; DTI, direct thrombin inhibitor.

*Total exceeds 100% because some patients received more than one treatment. Given the retrospective nature of the study, no determination was available indicating why patients were switched from one agent to another. †UFH utilized significantly more in PE vs DVT ($P < .001$).

‡UFH utilized significantly more in PE and DVT vs DVT ($P = .002$).

mean initiation and discharge daily dose of warfarin in this group was 6.9 ± 3.0 mg and 5.7 ± 3.1 mg, respectively.

Patients received warfarin for a mean of 4 ± 4.9 days before discharge, and the mean discharge INR was 2.0 ± 1.0. Of the 362 warfarin patients discharged before achieving an INR value ≥2.0 for 48 hours, only 219 (60.5%) were discharged on bridge therapy.

Discharge anticoagulation regimen and length of stay. Of the 907 VTE patients discharged, 72 (7.9%) were discharged with a prescription for an injectable anticoagulant, 241 (26.6%) with bridge therapy, and 460 (50.6%) with warfarin (Fig 1). Those discharged on bridge therapy had an average length of stay (LOS) of 4.0 ± 3.7 days vs 8.1 ± 5.8 days in those discharged on warfarin ($P < .001$) (Fig 2). An additional 134 patients (14.8%) received noncontinuous anticoagulation therapy during their hospitalization and had a mean LOS of 12.7 ± 17.8 days.

Although PE is usually a contraindication to early discharge, 66 isolated PE patients were discharged on bridge therapy and had an average LOS of 4.4 ± 3.5 days compared with 133 patients who were discharged on warfarin and recorded an average LOS of 7.9 ± 4.8 days ($P < .001$). Likewise, the average LOS for 138 isolated DVT patients discharged on bridge therapy was 3.6 ± 3.6 days, compared with 228 patients who were discharged on warfarin and recorded an average LOS of 7.4 ± 5.6 days ($P < .001$).

Ninety-two (10.1%) VTE patients were discharged without a prescription for oral or injectable anticoagulation; however, these patients only received a mean duration of treatment of 10.6 ± 16.2 days. In addition, 39 of these were diagnosed with idiopathic VTE, 33 had malignancy, and 24 had previous history of VTE. Of 139 patients discharged to a long-term care facility, 32 (22.9%) had no discharge anticoagulation orders.

The LOS in community and academic hospitals was 6.9 ± 5.8 days and 7.5 ± 9.1 days, respectively, compared with 9.7 ± 13.4 days in VA hospitals. The mean LOS in those <65 years old, 65 to 75 years old, and >75 years old was 7.6 ± 10.2 days, 7.4 ± 6.1 days, and 7.8 ± 6.8 days,

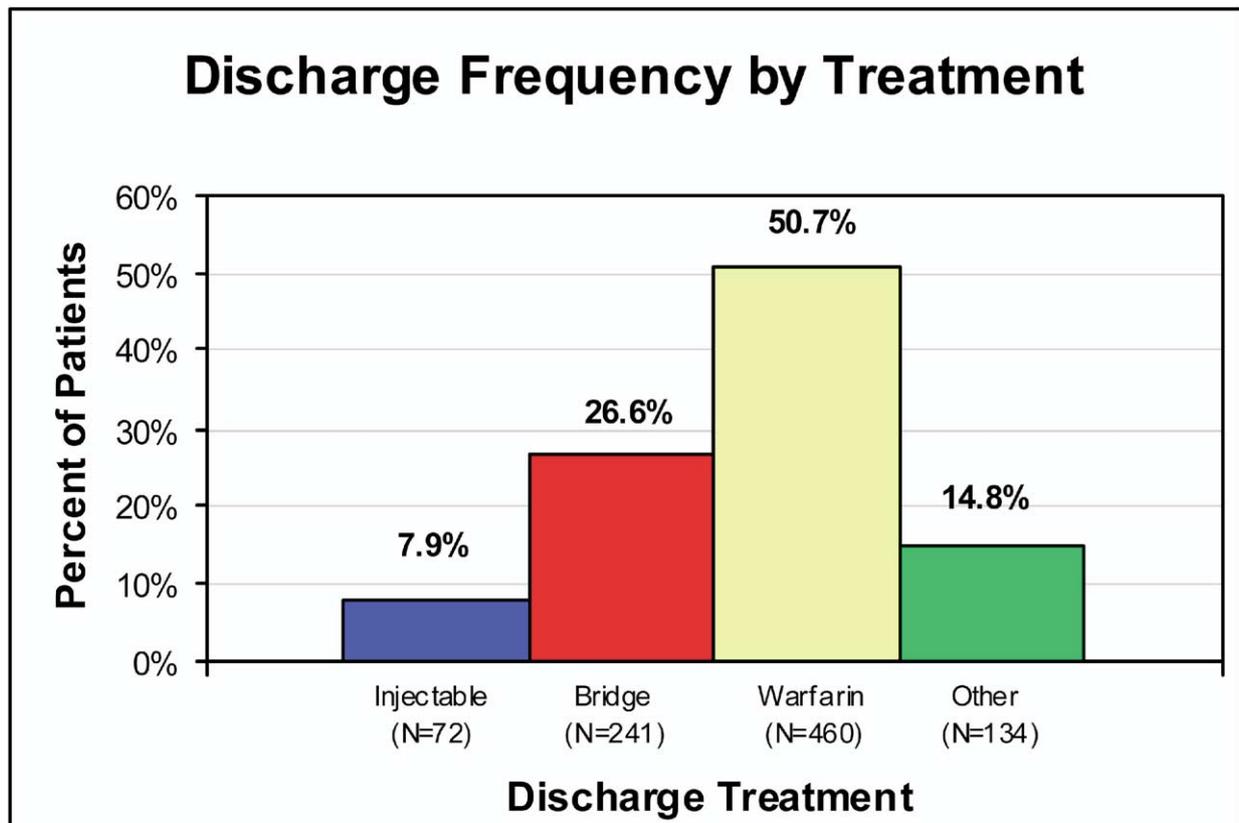


Fig 1. Discharge frequency by treatment for 907 patients with venous thromboembolism.

respectively. LOS was 6.9 ± 8.9 days for patients with isolated DVT and 7.7 ± 7.5 days and for patients with PE.

Hemorrhage and VTE recurrence. During hospitalization, 79 patients (8.4%) experienced minor hemorrhage on anticoagulation, and 20 patients (2.1%) had a major hemorrhage. Of the 760 patients who received warfarin, 68 patients (8.9%) achieved an INR >4 . Of these, three patients (4.4%) experienced a major hemorrhage compared with nine (1.3%) of those with an INR ≤ 4.0 ($P = .08$). Patients with an INR ≥ 4.0 were nearly three times more likely to experience a minor hemorrhage than patients with an INR ≤ 4.0 ($n = 12, 17.6\%$ vs $n = 46, 6.6\%$) ($P = .001$). Hospital medical records showed that 22 patients (2.4%) had a documented emergency department visit or hospitalization ≤ 30 days of discharge for recurrence of VTE or another embolic event.

Physician KABP survey. All 38 sites participated in the survey, with the exception of four VA hospitals. From the 950 physicians contacted, 315 responses were received for a 33% response rate. Of these, 246 physicians indicated treatment of at least five cases of DVT, PE, or both, within the past year. Most respondents were internists (52%), followed by emergency physicians (17%), family practitioners (13%), cardiologists (11%), and orthopedic surgeons (7%). Most were men (75%) and were board certified

(75%). Sixty percent had practiced for at least 6 years. With respect to use of evidenced-based guidelines, 32% indicated that they followed professional society guidelines, 22% followed guidelines developed by their institution, and 46% reported treatment decisions were made on a case-by-case basis (Table III).

Physician preferences for treatment. Most survey respondents (82.9%) indicated that LMWH and UFH were equally effective for managing DVT, which is consistent with ACCP guidelines (2001, 2004) that recommend treatment with either agent.^{4,5} Despite this belief, 84.1% indicated that LMWH was their preferred agent. Conversely, fewer (58.4%) indicated that LMWH and UFH were equally effective for managing PE and therefore only 52.7% indicated LMWH was their preferred treatment. ACCP guidelines (2004) state that LMWH is at least as effective and safe as intravenous UFH in the treatment of PE and that LMWH is recommended over UFH in patients with acute nonmassive PE, except in those with severe renal failure.⁵

With regard to duration of LMWH or UFH therapy, only two (65.3%) of three physicians thought that the duration should be until a therapeutic INR is reached for two consecutive days. However, 90.6% thought it was safe to send a stable DVT patient home on an injectable anti-

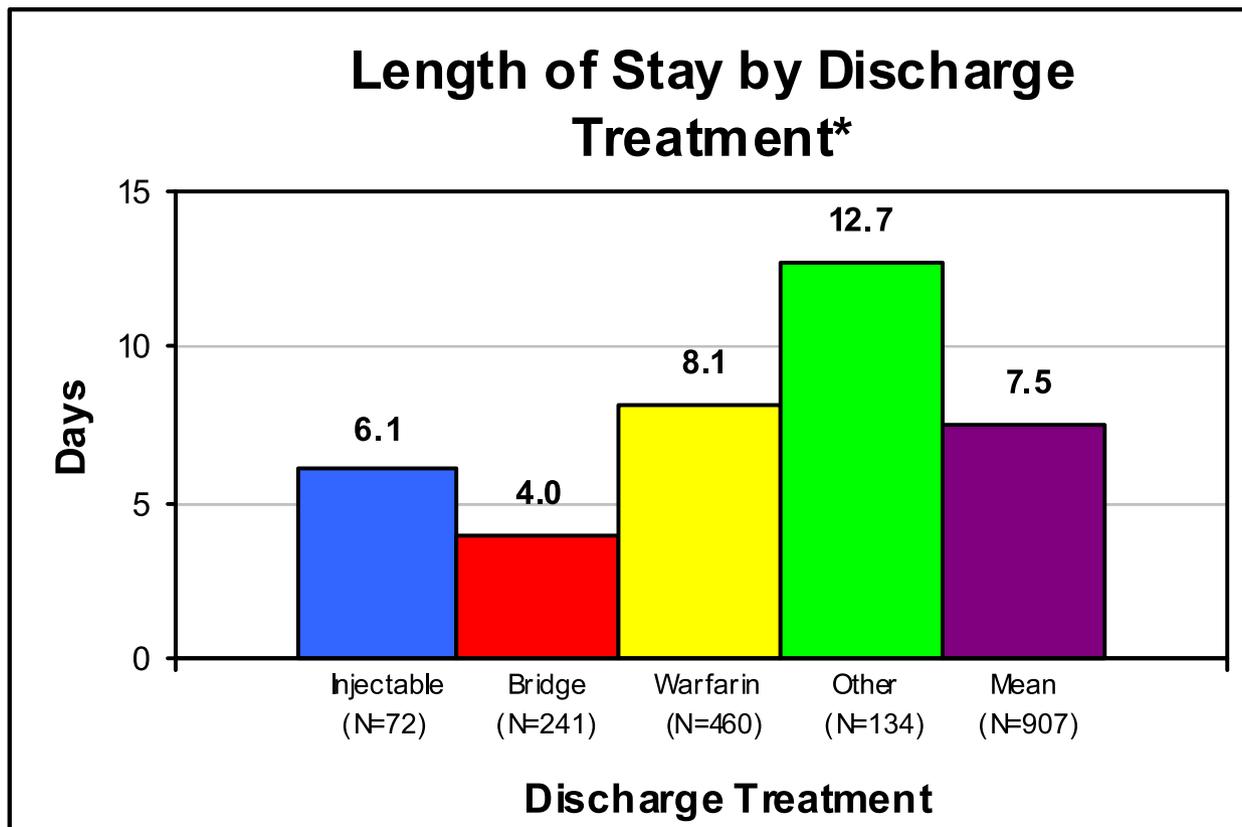


Fig 2. Length of stay by discharge treatment for 907 patients with venous thromboembolism. *Statistically significant difference in length of stay between injectable vs bridge ($P < .01$), injectable vs warfarin ($P < .01$), warfarin vs bridge ($P < .001$).

coagulant, and 63.1% thought it was safe to send a stable PE patient home on an injectable anticoagulant. ACCP guidelines (2004) recommend treatment of DVT as an outpatient, if possible, but do not make a similar recommendation for the treatment of PE.⁵

Beliefs and attitudes concerning warfarin. An INR range of 2.0 to 3.0 was believed to usually be safe care by 92.2% and effective care by 94.3% of the respondents. Conversely, a subtherapeutic INR range of 1.6 to 1.9 was believed to usually be safe care by 23.4% and effective care by only 8.6% of the respondents. Contrary to our study results, only 27% of survey respondents indicated that it was necessary to hospitalize a DVT patient until therapeutic on warfarin. An explanation for this difference between the study and the survey might be because only 59.2% of respondents expressed confidence that most patients were capable of safely taking warfarin. Further, 32.6% indicated that lack of an anticoagulation monitoring service would preclude their use of warfarin.

DISCUSSION

The key issues identified in our analysis of the treatment of VTE were the inadequate treatment overlap of LMWH

or UFH with warfarin, a tendency to delay discharge in isolated DVT patients rather than providing ambulatory overlapping (bridge) therapy, and inadequate or lack of treatment postdischarge, especially in those admitted to a long-term care facility. These are important findings considering 30-day mortality rates of approximately 6% for DVT and 12% for PE.⁸

ACCP treatment guidelines (2004) indicate that DVT patients should be treated with UFH or LMWH for at least 5 days (compared with 4 to 5 days in 2001 guidelines) and a vitamin K antagonist until the INR is stable and >2.0 (compared with therapeutic for 2 consecutive days in 2001 guidelines) before discontinuation of UFH or LMWH, that patients with acute DVT can be treated with LMWH as an outpatient; and that a first episode of DVT transient to a reversible risk factor should receive long-term treatment greater than 3 months with a vitamin K antagonist.^{4,5} The 54% self-reported physician use of institutional or professional society guidelines is likely a significant contributing factor to the issues identified.

Risk profile. The risk profile of our study population is similar to that described in other recent studies. Anderson and Spencer⁹ reviewed 1231 consecutive patients treated

Table III. Responses to Physician Knowledge, Attitude, Belief, and Practices survey

Statement	Agree n (%)	Response Disagree n (%)	Uncertain n (%)
LMWH is my preferred agent for initial DVT treatment.	206 (84.1)	36 (14.7)	3 (1.2)
LMWH is my preferred agent for initial PE treatment.	129 (52.7)	103 (42.0)	13 (5.3)
LMWH and UFH are equally effective for managing the DVT patient.	203 (82.9)	35 (14.3)	7 (2.9)
LMWH and UFH are equally effective for managing the PE patient.	143 (58.4)	67 (27.3)	35 (14.3)
It is necessary to have an INR ≥ 2.0 for two consecutive days before stopping UFH or LMWH.	160 (65.3)	74 (30.2)	11 (2.9)
It is safe to send stable DVT patients home while they are still receiving an injectable anticoagulant.	221 (90.6)	19 (7.8)	2 (1.6)
It is safe to send stable PE patients home while they are still receiving an injectable anticoagulant.	154 (63.1)	69 (28.3)	21 (8.6)

LMWH, Low-molecular-weight heparin; DVT, deep vein thrombosis; PE, pulmonary embolism; UFH, unfractionated heparin.

for VTE. Goldhaber and Tapson¹⁰ studied 5451 consecutive patients with acute DVT confirmed by ultrasound. Our population's incidence of major risk factors, including obesity, history of previous VTE, malignancy, major surgery, and immobility was 30.1%, 28%, 27.4%, 21.1%, and 18.5%, respectively, compared with Anderson and Spencer with 37.8%, 26%, 22.3%, 11.2%, and 12%, respectively, and Goldhaber and Tapson with 27%, 22%, 32%, 38%, and 34%, respectively.

Use of low-molecular-weight heparin. Our data show only a 56% usage of LMWH in our sample of US hospitals, despite survey data that indicated it was the preferred agent for 84% of physicians treating DVT and 58% of physicians treating PE. A recent European registry found that 88% of patients evaluated received VTE treatment with LMWH.¹¹ Although LMWH has all but eliminated usage of UFH in many parts of Europe,¹² our study demonstrates that US practitioners have been slower to adopt LMWH, despite evidence that it is as effective and safe as UFH,^{13,14} can decrease hospital LOS,^{15,16} and is recommended over UFH in 2001 ACCP guidelines.⁴

Bridging therapy. To our knowledge only one other study has investigated bridging from heparin to warfarin. Brandjes et al¹⁷ compared acenocoumarol alone vs heparin and acenocoumarol combined-therapy in the initial treatment of DVT. This randomized, double-blind study was terminated early because of an excess of both symptomatic (20% vs 6.7%; $P = .58$) and asymptomatic (39.6% vs 8.2%; $P < .001$) events in the group that received acenocoumarol alone.¹⁷

Our bridging data show that only one half of hospitalized patients received both heparin and warfarin until the INR was therapeutic for 48 hours. Seventy percent of those who were without a therapeutic INR for at least 48 hours failed to receive at least 4 days of combined therapy. Further, only two thirds of physicians surveyed believed it was necessary to have a therapeutic INR for two consecutive days before discontinuing LMWH or UFH. Inappropriate bridging may place patients at risk for increased morbidity and mortality.

Initially, warfarin may exert a procoagulant effect by decreasing the anticoagulant proteins C and S more rapidly

than the reduction in clotting factors. In addition, the initial effect of warfarin is to deplete factor VII, but the antithrombotic effect of warfarin, caused by depletion of factors II and X, takes 4 to 6 days to occur.¹⁸ Therefore, thrombus propagation may occur if an immediate-acting anticoagulant is not given concurrently with warfarin.

Because the induction phase of oral anticoagulation is unpredictable, we examined the duration of bridge therapy required to achieve a therapeutic INR range. In a study of 55 DVT patients receiving a warfarin initiation dose of 5 mg, Ageno et al¹⁹ found that only 54.4% of patients reached a therapeutic INR ≤ 7 days. Kovacs et al²⁰ found that only 46% of 97 VTE patients receiving warfarin at an initiation dose of 5 mg achieved a therapeutic INR ≤ 5 days. Our results indicate that approximately 50% of patients will achieve a therapeutic INR range with a mean warfarin initiation dose of approximately 7 mg and a mean duration of 4.5 days of bridge therapy. These findings, as well as those of others, indicate that at a minimum, 5 days of bridge therapy is required to achieve a therapeutic INR range. Many patients will require >5 days of combined LMWH and warfarin to achieve a therapeutic INR range.

Length of stay. LMWH has been shown to safely and effectively treat VTE on an outpatient basis, thereby decreasing hospital cost.^{15,21-24} We found a 4-day mean decrease in LOS in patients discharged on bridge therapy compared with patients discharged home on warfarin. Segal et al²¹ in an analysis 3762 patients from eight studies (three randomized trials and five cohort studies) observed a 3.8-day shorter hospitalization, a median cost savings of \$1600, and similar rates of major bleeding and recurrence in patients discharged early on LMWH vs those who received injectable therapy in the hospital. Only 27.9% of our isolated DVT population was discharged on bridge therapy, despite 91% of physicians believing it was safe to send a stable patient home on injectable heparin. This represents a significant opportunity for patients and providers.

Treatment duration. This study demonstrates that patients in a broad selection of US hospitals are not receiving the appropriate duration of anticoagulation therapy for treatment of VTE. Huisman et al²⁵ found that 51% of patients with symptomatic DVT had asymptomatic PE.

Treatment for VTE is usually 3 to 12 months (ACCP 2004)⁵; however, controversy exists for treatment of calf vein thrombosis.²⁶ We found that of 10% of patients not discharged with anticoagulation, 42% had idiopathic VTE, 36% had malignancy, and 26% had a previous VTE event. This high percentage may be partially explained by individual patient refusal of treatment or hospice status. Still, duration of VTE treatment is important because long-term sequelae can include fatal PE, post-thrombotic syndrome, and recurrence.²⁷

Limitations. A potential source of study bias, with regard to our findings being representative of all US hospitals, was the actual composition of the participating hospitals. Academic facilities comprised 55% of those enrolled. In addition, we did not record inferior vena cava filter placement or exclude patients discharged to hospice, which could influence treatment selection and duration of anticoagulation.

Given the retrospective design of our study, 30-day complication and mortality rates were limited to readmission and emergency department records reviewed from the sentinel hospital. Therefore, actual 30-day mortality and readmission rates may be understated.

We randomly selected subjects for both the study and the physician KABP survey, therefore there was not an exact correlation in the frequency of responses by specialty in our survey compared with frequency of patients cared for by specialty in our study. In addition, the survey did not include physicians from the VA hospital setting.

CONCLUSIONS

We have discovered a significant gap between actual and evidence-based practice in a cross-section of US hospitals, for which contributing factors are physician knowledge, attitudes, beliefs, and consistent use of guidelines. Our findings suggest that hospitals should evaluate their treatment of VTE and implement performance-improvement initiatives to align actual practice with evidence-based guidelines. Until more effective and less complex therapies are available, practitioners must maximize VTE treatment outcomes by appropriately using UFH, LMWH, and warfarin and treating patients for a duration that will limit recurrence and mortality.

REFERENCES

- Heit JA. Venous thromboembolism epidemiology: implications for prevention and management. *Semin Thromb Hemost* 2002;28(S2):3-13.
- Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. *Arch Intern Med* 1999;159:445-53.
- Department of Health and Human Services, USA. National Guideline Clearinghouse: Venous thromboembolism. Available at: <http://www.guideline.gov/search/searchresults.aspx?Type=3&txtSearch=Venous+thromboembolism&num=20>. Accessed June 3, 2004.
- Hyers TM, Agnelli G, Hull RD, Morris TA, Samama M, Tapson V, et al. Antithrombotic therapy for venous thromboembolic disease. *Chest* 2001;119(suppl):176s-93s.
- Büller HR, Agnelli G, Hull RD, Hyers TM, Prins MH, Raskob GE. Antithrombotic therapy for venous thromboembolic disease. *Chest* 2004;126:401S-28S.
- Caprini JA, Botteman MF, Stephens JM, Nadipelli V, Ewing MM, Brandt S, et al. Economic burden of long-term complications of deep vein thrombosis after total hip replacement surgery in the United States. *Value Health* 2003;6:59-74.
- McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, et al. The quality of health care delivered to adults in the United States. *N Engl J Med* 2003;348:2635-45.
- White RH. The epidemiology of venous thromboembolism. *Circulation* 2003;107:1-4-8.
- Anderson FA, Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003;107:1-9-16.
- Goldhaber SZ, Tapson VF. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. *Am J Cardiol* 2004;93:259-62.
- Arcelus JI, Caprini JA, Monreal M, Suarez C, Gonzalez-Fajardo J. The management and outcome of acute venous thromboembolism: a prospective registry including 4011 patients. *J Vasc Surg* 2003;38:916-22.
- Weitz JI. Low-molecular-weight heparins. *N Engl J Med* 1997;337:688-98.
- Simonneau G, Sors H, Charbonnier B, Page Y, Laaban J, Azarian R, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for acute pulmonary embolism. *N Engl J Med* 1997;337:663-9.
- The Columbus Investigators. Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. *N Engl J Med* 1997;337:657-62.
- Koopman MMW, Prandoni P, Piovella F, Ockelford PA, Brandjes DPM, Van Der Meer J, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. *N Engl J Med* 1996;334:682-7.
- Levine M, Gent M, Hirsh J, LeClerc J, Anderson D, Weitz J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. *N Engl J Med* 1996;334:677-81.
- Brandjes DP, Heijboer H, Buller HR, de Rijk M, Jagt H, ten Cate JW. Acenocoumarol and heparin compared with acenocoumarol alone in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1992;327:1485-9.
- Hirsh J, Dalen JE, Anderson DR, Poller L, Bussey H, Ansell J, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest* 2001;119:8S-21S.
- Ageno W, Steidl L, Urtori C, Dentali F, Marchesi C, Mera V, et al. The initial phase of oral anticoagulation with warfarin in outpatients with deep venous thrombosis. *Blood Coagul Fibrinolysis* 2003;14:11-14.
- Kovacs MJ, Rodger M, Anderson DR, Morrow B, Kells G, Kovacs J, et al. Comparison of 10-mg and 5-mg warfarin initiation nomograms together with low-molecular-weight heparin for outpatient treatment of acute venous thromboembolism. *Ann Intern Med* 2003;138:714-9.
- Segal JB, Bolger DT, Jenckes MW, Krishnan JA, Streiff MB, Engl J, et al. Outpatient therapy with low molecular weight heparin for the treatment of venous thromboembolism: a review of efficacy, safety, and costs. *Am J Med* 2003;115:298-308.
- Boucher M, Rodger M, Johnson JA, Tierney M. Shifting from inpatient to outpatient treatment of deep vein thrombosis in a tertiary care center: a cost minimization analysis. *Pharmacotherapy* 2003;23:301-9.
- O'Brien B, Levine M, Willan A, Goeree R, Haley S, Blackhouse G, et al. Economic evaluation of outpatient treatment with low-molecular-weight heparin for proximal vein thrombosis. *Arch Intern Med* 1999;159:2298-304.
- Spyropoulos AC, Hurley JS, Ciesla GN, de Lissovoy G. Management of acute proximal deep vein thrombosis: pharmacoeconomic evaluation of outpatient treatment with enoxaparin vs inpatient treatment with unfractionated heparin. *Chest* 2002;122:108-14.

- 25. Huisman MV, Buller HR, ten Cate JW, van Royen EA, Vreeken J, Kersten M, et al. Unexpected high prevalence of silent pulmonary embolism in patients with deep venous thrombosis. *Chest* 1989;95:498-502.
- 26. Deitcher SR, Caprini JA. Calf deep venous thrombosis should be treated with anticoagulation. *Med Clin North Am* 2003;87:1157-64.
- 27. Prandoni P, Lensing AWA, Cogo A, Cuppini S, Villalta S, Carta M, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med* 1996;125:1-7.

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