

Antithrombotic Therapy Practices in US Hospitals in an Era of Practice Guidelines

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Background: Antithrombotic therapy is efficacious for the prevention of thromboembolic disease, but it necessitates careful risk-benefit assessment.

Methods: Antithrombotic therapy data were retrospectively collected from inpatient medical records at 38 US hospitals. Patients treated for atrial fibrillation, acute myocardial infarction, deep vein thrombosis, or pulmonary embolism and patients given prophylaxis for total knee replacement, total hip replacement, or hip fracture surgery between July 1, 2000, and June 30, 2003, were randomly selected.

Results: The medical records of 3778 patients (53.3% men) were included. The mean patient age was 66.1 years. Of patients with atrial fibrillation at high risk for stroke, only 54.7% received warfarin sodium, and 20.6% received neither aspirin nor warfarin. Of patients with acute myocardial infarction, only 75.5% received aspirin on hospital arrival. After orthopedic surgery procedures, only

85.6% of patients received prophylaxis with a parenteral anticoagulant agent or warfarin. In 49.4% of patients with deep vein thrombosis, pulmonary embolism, or both, unfractionated or low-molecular-weight heparin use was discontinued before an international normalized ratio of 2.0 or greater was achieved for 2 consecutive days. Patients with deep vein thrombosis or pulmonary embolism were rarely discharged from the hospital with bridge therapy (an injectable anticoagulant agent plus warfarin), although the length of hospitalization was significantly shorter than if discharged taking warfarin alone (4.0 vs 8.1 days; $P < .001$).

Conclusions: A significant percentage of hospitalized patients do not receive adequate antithrombotic therapy for the primary and secondary prevention of thromboembolic disease.

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THROMBOSIS IS THE MOST common singular cause of death and a significant public health concern in the United States. Arterial disease accounts for an estimated 1.5 million patients with acute myocardial infarction (AMI)^{1,2} and 780 000 strokes annually.³⁻⁵ Venous disease affects another 2 million patients, with approximately 600 000 of those developing pulmonary embolism (PE).⁶ Acute and chronic illness increases the predisposition to thrombosis. In an era of broadly accepted guidelines for thromboembolic disease, our nation's hospitals can favorably affect disease burden in individuals with inherent risks of initial and subsequent thrombotic events by identifying at-risk individuals and initiating preventive treatment.

*See also pages 1455
and 1469*

We established a national multicenter database for hospitals to assess the patient characteristics, risk factors, and treatment of in-

dividuals with or at risk for thrombotic disease. Primary thrombosis prevention was evaluated in patients with a diagnosis of atrial fibrillation (AF) and in those requiring total knee replacement (TKR), total hip replacement (THR), or hip fracture repair. Secondary prevention was evaluated in patients diagnosed as having AMI, deep vein thrombosis (DVT), or PE.

METHODS

The National Anticoagulation Benchmark and Outcomes Report (EPI-Q Inc) is a national multicenter benchmark database. It was created in December 2002 with input from an advisory board of practicing clinicians in the area of anticoagulation. Hospitals were invited to participate to achieve an approximate balance of 1:1 between academic and community-based providers, with even regional distribution throughout the United States. We included 4 Veterans Affairs medical centers. Seventy-five invitations were issued, and the first 40 hospitals that responded were selected. Two hospitals withdrew from the study because they could not secure trained data collection personnel.

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Group Information: A list of the members of the NABOR Steering Committee appears on page 1464.

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Drs Tapson and Khetan and Mr Colgan have performed research and consulting for AstraZeneca LLP.

STUDY COHORT

Patient medical records were eligible for inclusion based on *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes after hospital discharge. Included were patients discharged with a diagnosis of AMI (ICD-9-CM codes 410.01-410.91), AF (ICD-9-CM code 427.31), PE (ICD-9-CM codes 415.11 and 415.19), DVT (ICD-9-CM code 453.8), pregnancy-related DVT (ICD-9-CM codes 671.00-671.94), pregnancy-related PE (ICD-9-CM codes 673.0-673.8), THR (*Current Procedural Terminology [CPT]* code 81.51), TKR (CPT code 81.54), hip fracture repair (ICD-9-CM codes 820-820.19 or 820.8-820.9 plus CPT code 81.52 for partial hip replacement or 78.55, 79.10, 79.15, 79.30, or 79.35 for internal fixation). Patients were excluded if they were younger than 18 years, were admitted from another acute care hospital where therapy was already instituted, or were discharged to another acute care hospital to continue treatment or if medical records were miscoded.

Lists of patients were generated by each medical center for the study period (January 1, 2002, through June 30, 2003). From these lists, 25 medical records for each of the 4 anticoagulation indications were selected randomly. One medical center included patients treated beginning July 1, 2000, to obtain the requested number of medical records for that site.

Data were abstracted from each medical record using a standard data collection form and data dictionary. Medical record review was performed on site by health system personnel after a training session. Data were entered into the National Anticoagulation Benchmark and Outcomes Report data entry software and were validated by the software program for completeness and consistency of entry, with patient-identifying information removed. On receipt of data at EPI-Q, data were queried again for inconsistencies, and all queries were resolved before data analysis.

STATISTICAL ANALYSIS

Descriptive and univariate methods were used to describe the distribution of patients among anticoagulation categories and to examine indicator performance between the site and the benchmark. Descriptive statistics were used to describe the baseline prevalence of risk factors for bleeding and embolic events, to evaluate treatment selection and use among the antithrombotic indications, and to describe deviation of treatment from nationally accepted evidence-based guidelines. Differences in treatment selection for AF based on classification were examined using a χ^2 test for categorical data. Differences in treatment selection by type of procedure were also examined using a χ^2 test. Differences in length of stay (LOS) were examined using a Mann-Whitney *U* test for nonnormally distributed data.

RESULTS

A total of 3778 patient medical records were included from 21 teaching, 13 community, and 4 Veterans Affairs hospitals located in 28 different states. There were 945, 966, 939, and 928 patients with the diagnoses of AF, AMI, DVT or PE, and orthopedic surgery, respectively. The mean patient age was 66.1 years, ranging from a low of 59.4 years in patients with DVT or PE to a high of 71.5 years in those with AF. Of the total population, 2013 (53.3%) were men. The most frequently reported comorbidities included hypertension, coronary artery disease, a history of AF, and diabetes mellitus (**Table 1**).

PRIMARY PREVENTION

Of the 945 patients with AF, 486 (51.4%) were classified as paroxysmal vs 453 (47.9%) as persistent or permanent. Six patients (0.6%) had insufficient documentation to determine classification. Of this entire group, 321 (34.0%) represented new AF and 622 (65.8%) had documented recurrence. Two patients (0.2%) had insufficient documentation to determine the type of event. Most patients hospitalized with AF (n=814; 86.1%) were classified as having a high stroke risk using the American College of Chest Physicians risk stratification schemata (**Table 2**).⁷ However, there was a large gap between practice and treatment according to guidelines.^{7,8} Of the 814 high-risk patients, only 445 (54.7%) received warfarin sodium. The remainder of the high-risk patients received aspirin alone (n=201) or no treatment at all (n=168) (**Figure 1**). A subset of 419 patients older than 75 years at high risk because of age alone was examined to determine warfarin use. Of these patients, 207 did not receive warfarin. Patients with persistent or permanent AF were more likely to receive warfarin (**Table 3**).

Of the 369 high-risk patients not receiving warfarin, 159 (43.1%) had no documented contraindications. Conversely, 153 (41.5%) were subjectively determined to be at risk for falls, 62 (16.8%) had neuropsychiatric impairment, 54 (14.6%) had previous bleeding, 47 (12.7%) had ulcer disease, and 19 (5.1%) had a history of aneurysm. Of 168 high-risk patients receiving no treatment, 32 (19.0%) were receiving nonsteroidal anti-inflammatory agents and 6 (3.6%) were receiving clopidogrel bisulfate.

Of the 928 patients included who had undergone orthopedic surgery, 358 (38.6%) had TKR, 284 (30.6%) had THR, and 291 (31.4%) had hip fracture repair. Inadequate prophylaxis was administered in 134 patients (14.4%): 77 (8.3%) received only aspirin and 57 (6.1%) received no prophylaxis (**Table 4**). Patients who underwent hip fracture repair were more likely than those who underwent TKR and THR to receive no prophylaxis (13.4% vs 2.8% and 3.2%, respectively; $P < .001$).

Patients who underwent TKR and THR received a mean \pm SD of 3.2 \pm 2.4 and 3.4 \pm 3.0 days of postprocedure anticoagulation therapy, respectively. Only 261 patients who underwent TKR (72.9%) and 206 patients who underwent THR (72.5%) received a prescription for postdischarge anticoagulant agents. Patients who underwent hip fracture repair received a mean \pm SD of 4.7 \pm 5.1 days of postprocedure therapy, and fewer (n=153; 52.6%) received a prescription for postdischarge therapy (**Figure 2**).

SECONDARY PREVENTION

Of 966 patients with AMI, 592 (61.3%) were classified as having unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI) and 365 (37.8%) as having ST-segment elevation myocardial infarction (STEMI). The remaining 9 patients had insufficient documentation to classify. Most patients were men (n=592; 61.3%). Of the total, 501 patients (51.9%) were revascularized, occurring more frequently in patients with STEMI (n=251;

Table 1. Demographics of 3778 Randomly Sampled Patients Admitted to 38 Hospitals

Demographic Characteristic	Atrial Fibrillation (n = 945)	DVT/PE (n = 939)	Orthopedic Surgery (n = 928)	AMI (n = 966)	Total (N = 3778)
Age, mean, y	71.5	59.4	66.8	66.7	66.1
Age range, No. (%)					
≤65 y	270 (28.6)	563 (60.0)	391 (42.1)	441 (45.7)	1665 (44.1)
66-75 y	256 (27.1)	170 (18.1)	224 (24.1)	231 (23.9)	881 (23.3)
>75 y	419 (44.3)	206 (21.9)	313 (33.7)	294 (30.4)	1232 (32.6)
Sex, No. (%)					
M	515 (54.5)	460 (49.0)	429 (46.2)	609 (63.0)	2013 (53.3)
F	430 (45.5)	479 (51.0)	499 (53.8)	357 (37.0)	1765 (46.7)
Coexisting conditions, No. (%)					
Hypertension	632 (6.9)	444 (47.3)	524 (56.5)	663 (68.6)	2263 (59.9)
Coronary artery disease	398 (42.1)	179 (19.1)	169 (18.2)	595 (61.6)	1341 (35.5)
History of atrial fibrillation	622 (65.8)	85 (9.1)	72 (7.8)	117 (12.1)	896 (23.7)
Diabetes mellitus	208 (22.0)	157 (16.7)	123 (13.3)	325 (33.6)	813 (21.5)
Heart failure	325 (34.4)	100 (10.6)	58 (6.3)	277 (28.7)	760 (20.1)
Malignancy	169 (17.9)	257 (27.4)	109 (11.7)	120 (12.4)	655 (17.3)
Renal insufficiency	179 (18.9)	127 (13.5)	78 (8.4)	220 (22.8)	604 (16.0)
Previous CVA, TIA, embolus	153 (16.2)	76 (8.1)	47 (5.1)	127 (13.1)	403 (10.7)
No. of comorbidities, No. (%)					
0	135 (14.3)	279 (29.7)	280 (30.2)	93 (9.6)	787 (20.8)
1	278 (29.4)	270 (28.8)	348 (37.5)	227 (23.5)	1123 (29.7)
2	268 (28.4)	211 (22.5)	199 (21.4)	282 (29.2)	960 (25.4)
≥3	264 (27.9)	179 (19.1)	101 (10.9)	364 (37.7)	908 (24.0)

Abbreviations: AMI, acute myocardial infarction; CVA, cerebrovascular accident; DVT, deep vein thrombosis; PE, pulmonary embolism; TIA, transient ischemic attack.

Table 2. Risk Classification for Vascular Embolic Events in Patients With Atrial Fibrillation*

High-Risk Factors	Moderate-Risk Factors
<ul style="list-style-type: none"> • Previous stroke, transient ischemic attack, or systemic embolic event • History of hypertension • Poor left ventricular systolic function • Aged >75 y • Rheumatic mitral valve disease • Prosthetic heart valve 	<ul style="list-style-type: none"> • Aged 65-75 y • Diabetes mellitus • Coronary artery disease with preserved left ventricular systolic function

*Patients are at high risk if they have any high-risk factor or more than 1 moderate-risk factor, at moderate risk if they have 1 moderate-risk factor, and at low risk if they have no high- or moderate-risk factors.⁷

68.8%) than in those with UA/NSTEMI (n=250; 42.2%) ($P < .001$). Patients with STEMI were more likely to receive glycoprotein IIb/IIIa inhibitor therapy (n=204; 55.9%) vs patients with UA/NSTEMI (n=201; 34.0%) ($P < .001$). Anticoagulation drugs were administered to 493 patients with UA/NSTEMI (83.3%) and 295 patients with STEMI (80.8%) ($P = .47$). Patients receiving aspirin within 24 hours of hospitalization, or within 8 hours of arrival at the hospital or of AMI diagnosis, accounted for 75.5% of the total (n=729). Excluding 120 patients with active peptic ulcer disease or a bleeding history, 643 (76.0%) received aspirin within 8 hours or had documentation of receipt in the previous 24 hours. The proportion of the total discharged from the hospital taking aspirin or warfarin was 88.0% (n=782). Of those not receiving aspirin or warfarin, only

8 (7.5%) received clopidogrel or ticlopidine hydrochloride at hospital discharge.

Of 939 patients diagnosed as having DVT, PE, or both, 32 (3.4%) died during hospitalization. Of these 939 patients, 495 (52.7%) had DVT without diagnosed PE, 267 (28.4%) had PE without diagnosed DVT, and 177 (18.8%) had DVT and PE. Most patients (n=562; 59.8%) received parenteral unfractionated heparin. Low-molecular-weight heparin was also widely used (n=527; 56.1%). There was a small subset of patients (n=78; 8.3%) who received adjusted-dose subcutaneous unfractionated heparin (**Table 5**).

There was inconsistent practice regarding discontinuation of the use of unfractionated heparin or low-molecular-weight heparin. Of the 486 patients who received overlapping (bridge) therapy (a parenteral agent plus warfarin), only 246 (50.6%) had an international normalized ratio (INR) of at least 2.0 for 2 consecutive days before discontinuation of the parenteral agent. In those without 2 consecutive days of a therapeutic INR, only 30.8% had 4 or more days of concurrent treatment. Of 362 patients who were discharged without 2 consecutive days of an INR of 2.0 or greater, 39.5% (n=143) did not receive unfractionated heparin or low-molecular-weight heparin after discharge. Most patients were not discharged from the hospital until the parenteral drug was discontinued (n=460; 50.7%), with only 241 patients (26.6%) being discharged taking a bridge regimen. In patients discharged taking a bridge regimen vs warfarin alone (long-term therapy), mean±SD LOS was significantly shorter (4.0 ± 3.6 days vs 8.1 ± 5.7 days; $P < .001$) (**Figure 3**). A subset of patients (n=134) had either discontinuous treatment or an extended LOS dur-

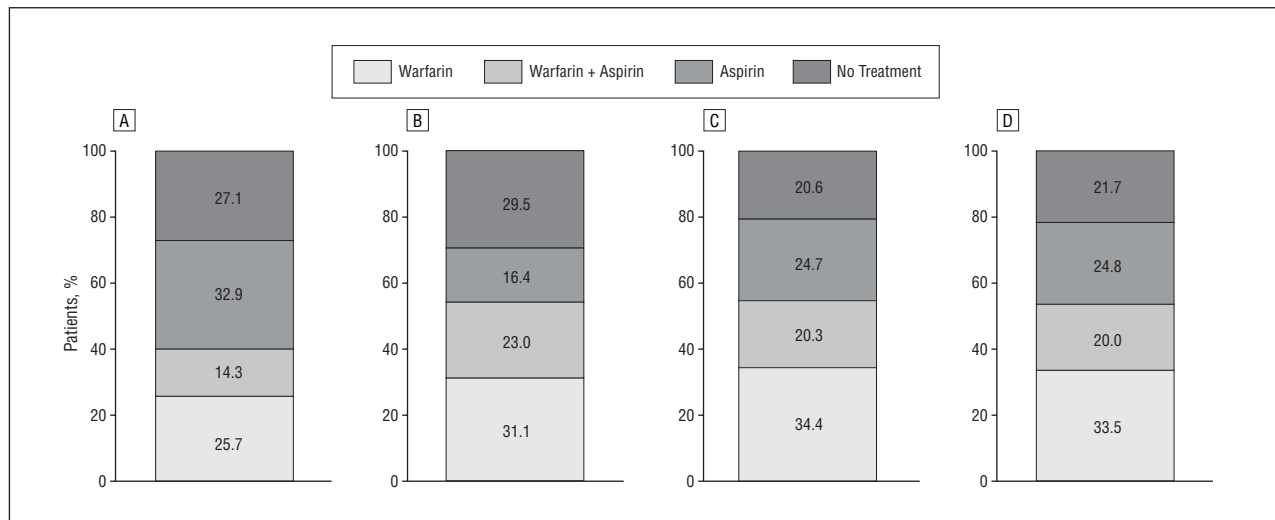


Figure 1. Atrial fibrillation treatment by American College of Chest Physicians risk category⁷: low-risk patients (n=70) (A), moderate-risk patients (n=61) (B), high-risk patients (n=814) (C), and all patients (N=945) (D).

Table 3. Treatment of Atrial Fibrillation by Classification and Type of Event

Treatment	Classification, No. (%)			Type of Event, No. (%)		
	Paroxysmal (n = 486)	Persistent/Permanent (n = 453)	P Value*	First (n = 321)	Recurrent (n = 622)	P Value*
Warfarin	128 (26.3)	189 (41.7)	<.001	83 (25.9)	234 (37.6)	<.001
Warfarin plus aspirin	102 (21.0)	85 (18.8)	.50	68 (21.2)	121 (19.5)	.64
Aspirin alone	145 (29.8)	87 (19.2)	<.001	95 (29.6)	139 (22.3)	<.04
No treatment	111 (22.8)	92 (20.3)	.51	75 (23.4)	128 (20.6)	.36

*By χ^2 test for categorical variables.

ing which treatment was discontinued before hospital discharge. These patients were categorized as “other” and had a mean \pm SD LOS of 12.7 ± 17.8 days.

ANTICOAGULATION MANAGEMENT

Of the 1749 patients who received warfarin at any time during hospitalization, 157 (9.0%) had at least 1 INR value greater than 4.0, 14 (0.8%) experienced major hemorrhage, 120 (6.9%) experienced minor hemorrhage (hematoma, microscopic hematuria, epistaxis, or ecchymosis), and 65 (3.7%) were administered phytonadione. Of the total patient population, 1640 (43.4%) were discharged from the hospital taking warfarin, and 300 of these patients (18.3%) were referred to an anticoagulation management service at discharge. Overall, the mean \pm SD INR at hospital discharge was at the lowest end of the therapeutic range at 2.0 ± 0.9 .

COMMENT

Despite substantial evidence that risk-modifying therapy and appropriate treatment can reduce morbidity and mortality from thrombosis, these findings indicate that there is an important opportunity for improving the primary and secondary prevention of thromboembolic disease. Our re-

sults demonstrate that an unacceptable number of patients with high-risk AF, orthopedic surgery, AMI, or DVT or PE did not receive adequate prophylaxis or treatment. Although our sample of hospitals was geographically balanced, more than half were academic institutions, which is overrepresentative of the population of US hospitals as a whole. However, studies⁹⁻¹¹ suggest that adherence to accepted standards of care is greater at academically affiliated hospitals, and it is possible that our findings actually exceed typical practice in the United States.

Data from longitudinal studies¹² indicate recent increases in the use of warfarin in AF from a low of 12% in 1990 to a high approaching 58% in 2001. The Centers for Medicare & Medicaid Services reported similar findings, with a national median of 57% of patients hospitalized with AF receiving warfarin.¹³ Our findings are comparable, with 57% adherence to treatment guidelines for all risk strata and 54.7% utilization of warfarin in those at high risk for stroke. Most alarming was the observation that 20.6% of high-risk patients received no anticoagulation therapy, with many having no apparent contraindication to warfarin. There is no guideline recommendation that aspirin is indicated for stroke prevention in those older than 75 years or others in the high-risk group, although aspirin was the only prophylaxis provided to 24.7% of the patients in this group.

Table 4. Venous Thromboembolism Prophylaxis in Orthopedic Surgery*

Therapy	Patients, No. (%)		
	TKR (n = 358)	THR (n = 284)	Hip Fx (n = 291)
Warfarin	182 (50.8)	138 (48.6)	74 (25.4)†
Low-molecular-weight heparin	163 (45.5)	129 (45.4)	132 (45.4)‡
Unfractionated heparin	24 (6.7)	14 (4.9)	60 (20.6)§
Aspirin only	28 (7.8)	24 (8.5)	26 (8.9)‡
No prophylaxis	10 (2.8)	9 (3.2)	39 (13.4)§

Abbreviations: Hip Fx, hip fracture repair; THR, total hip replacement; TKR, total knee replacement.

*Four patients underwent 2 procedures during hospitalization.

†Number of patients who underwent Hip Fx was significantly less than for those who underwent TKR and THR ($P < .001$); no significant difference between TKR and THR.

‡No significant differences among TKR, THR, and Hip Fx.

§Number of patients who underwent Hip Fx was significantly greater than for those who underwent TKR and THR ($P < .001$); no significant difference between TKR and THR.

WEIGHING THE RISKS AND BENEFITS OF ORAL ANTICOAGULATION THERAPY WITH WARFARIN

The decision to use warfarin requires consideration of risk and benefit.^{14,15} In AF, randomized trials¹⁶⁻²¹ show virtually no increase in the frequency of major hemorrhage comparing warfarin (1.3%), aspirin (1.0%), and placebo (1.0%) groups, and these trials show an observed rate of intracranial hemorrhage in patients older than 75 years of only 0.8% per year. Yet, it has been shown in the low-risk population that warfarin may not be the favored therapy in individuals with a high risk of upper gastrointestinal tract bleeding or in those concurrently taking nonsteroidal anti-inflammatory drugs.²² Our study shows that among patients hospitalized with AF, those older than 80 years are less likely to receive warfarin, yet AF is responsible for as many as 25% of strokes in individuals aged 75 to 84 years.^{23,24} A potentially poor understanding of the risk-benefit ratio of warfarin suggests the need for practitioner education that promotes primary prevention. Almost 15% of patients who underwent orthopedic surgery received aspirin only or no prophylaxis. No prophylaxis use was most frequently observed in the hip fracture repair cohort, where the incidence was 13.4%.

Warfarin and low-molecular-weight heparin provide effective prophylaxis for orthopedic surgery and are recommended in guidelines.^{25,26} However, even when administered for 7 to 10 days after surgery, the prevalence of asymptomatic DVT remains at 15% for patients with THR and 30% for those with TKR.²⁷ Several studies suggest that the risk of DVT may persist for up to 2 months after THR surgery,²⁶⁻³⁰ and prophylaxis for up to 28 to 35 days has been recommended in the THR and hip fracture surgery setting.²⁶ Although our data are limited in that we did not have posthospitalization data to determine the mean duration of anticoagulation after hospital discharge, we do know that the mean inpatient duration of prophylaxis was less than 5 days and that only

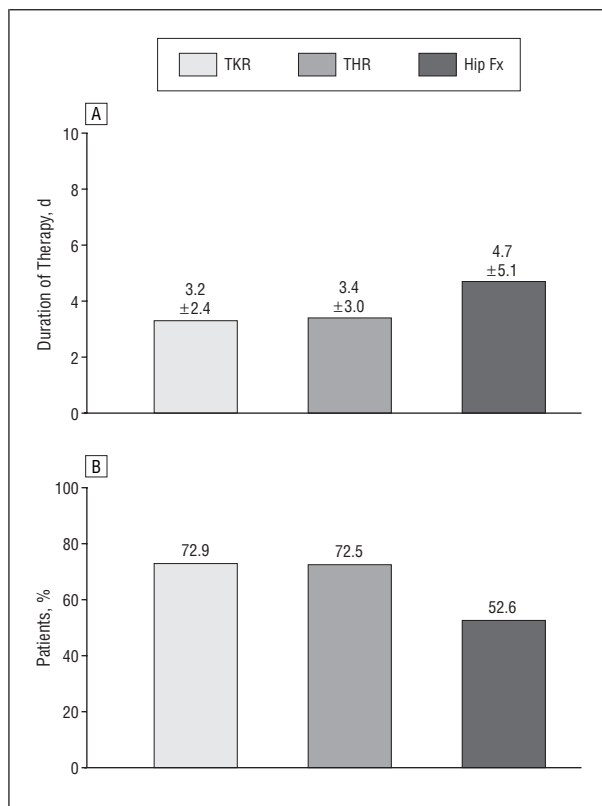


Figure 2. Venous thromboembolism prevention in orthopedic surgery. Mean \pm SD duration of inpatient postprocedure anticoagulation therapy (A) and patients discharged from the hospital with anticoagulation therapy (B) for 358 patients who underwent total knee replacement (TKR), 284 who underwent total hip replacement (THR), and 291 who underwent hip fracture repair (Hip Fx).

slightly greater than 70% of patients who underwent TKR or THR and 50% of those who underwent hip fracture repair were discharged with anticoagulation therapy. These findings indicate that the duration of therapy is inadequate for many patients.

USE OF ASPIRIN AFTER AMI

Aspirin is generally the preferred agent for the secondary prevention of vascular events and death after AMI because of its ease of use, low cost, and proven efficacy. Supporting data³¹⁻³³ indicate that early administration of aspirin improves survival and reperfusion rates over later administration. Therefore, we measured the frequency of aspirin administration within 8 hours of arrival at the hospital or within 8 hours of an event when hospitalized, except in patients who took a routine dose of aspirin within 24 hours of the event. Centers for Medicare & Medicaid Services data¹³ from 2000-2001 demonstrate a higher occurrence of early aspirin administration (85%) than our results (75.5%). The difference is possibly because Centers for Medicare & Medicaid Services indicators define aspirin administration within 24 hours and our results reflect administration within 8 hours. Our findings indicate that improvement is still needed to realize the clinical and public health impact of aspirin therapy.

Table 5. Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) Treatment Selection*

Therapy	Patients, No. (%)			
	DVT (n = 495)	PE (n = 267)	DVT and PE (n = 177)	Total (N = 939)
Low-molecular-weight heparin	286 (57.8)	147 (55.1)	94 (53.1)	527 (56.1)
Unfractionated heparin	256 (51.7)	185 (69.3)	121 (68.4)	562 (59.8)
Adjusted-dose subcutaneous heparin	45 (9.1)	23 (8.6)	10 (5.6)	78 (8.3)
Direct thrombin inhibitor	3 (0.6)	2 (0.7)	1 (0.6)	6 (0.6)

*Includes deaths. Percentages sum to greater than 100% because some patients received multimodality therapy.

BRIDGING FROM PARENTERAL TO ORAL THERAPY IN ACUTE DVT AND PE

Guidelines recommend that unfractionated heparin or low-molecular-weight heparin administration be continued for a minimum of 4 to 5 days and until the INR has been at least 2.0 for a minimum of 2 consecutive days.³⁴ Our data suggest that only half of all patients who initiated warfarin therapy reached an INR of 2.0 or greater for 2 consecutive days before the parenteral agent was discontinued. Only a few patients without a therapeutic INR for 2 consecutive days had 4 days of concurrent unfractionated heparin or low-molecular-weight heparin and warfarin therapy. Concurrent therapy must be long enough to ensure adequate anticoagulation.

We observed that a large proportion of patients with DVT or PE had their hospital discharge delayed until parenteral therapy was discontinued. Only one-fourth were discharged with bridge therapy. The success of outpatient treatment programs demonstrates that DVT may often be safely managed outside the hospital.³⁵⁻³⁸ The mean reduction in LOS was 4.1 days for those discharged with bridge therapy. The low rate of referral to anticoagulation management clinics may have affected the hospital discharge decision. Our results point to a potential economic benefit in the treatment of DVT in the outpatient setting.

IMPLICATIONS

Inconsistent adherence to guidelines and use of anti-thrombotic therapy may reflect differences in physician knowledge, attitudes, and beliefs and system inefficiencies, skewed incentives, organizational culture, or deference to patient preference. Some researchers¹⁶ have suggested that more importance is attached to the perceived risks of therapy than to the benefits, foretelling an unwillingness to accept the risk associated with current therapies. The complex management required to administer an anticoagulant, maintain a therapeutic range, or simply screen for drug interactions and educate patients about diet may also be issues. It is crucial to overcome these potential barriers so that we can better protect patients from initial and recurrent thrombotic events. Failure has too great a price from a greater public health perspective and for individuals unnecessarily afflicted.

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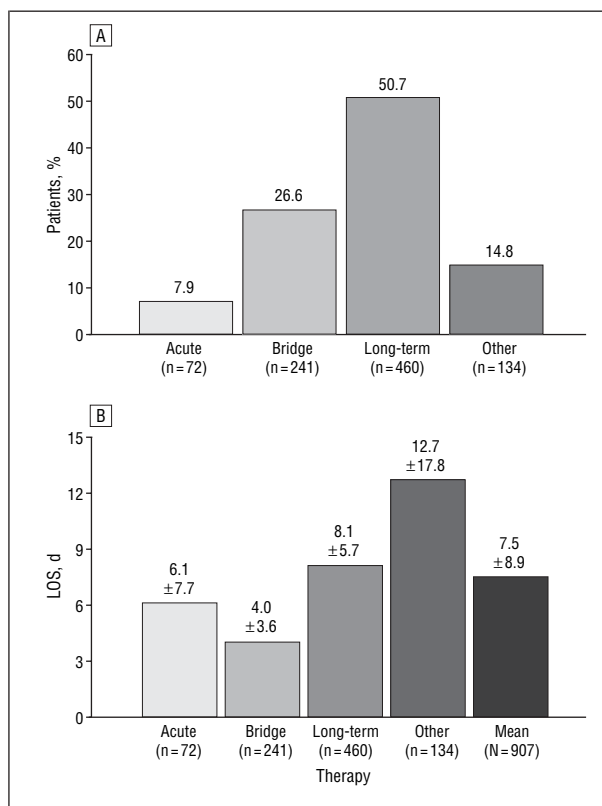


Figure 3. Treatment at hospital discharge (A) and mean \pm SD length of stay (LOS) (B) for patients with deep vein thrombosis, pulmonary embolism, or both. The following were statistically significant by the Mann-Whitney *U* test: acute vs bridge ($P < .01$), acute vs long-term ($P < .01$), and long-term vs bridge ($P < .001$). Acute therapy consists of injectable anticoagulation only; bridge therapy, a parenteral agent plus warfarin sodium; long-term therapy, warfarin alone; and other, either discontinuous treatment or an extended LOS during which treatment was discontinued before hospital discharge.

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REFERENCES

1. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol*. 2002;40:1366-1374.
2. Bick RL. Proficient and cost-effective approaches for the prevention and treatment of venous thrombosis and thromboembolism. *Drugs*. 2000;60:575-595.
3. Gorelick PB, Sacco RL, Smith DB, et al. Prevention of a first stroke: a review of guidelines and a multidisciplinary statement from the National Stroke Association. *JAMA*. 1999;281:1112-1120.
4. Leary MC, Saver JL. Annual incidence of first silent stroke in the United States: a preliminary estimate. *Cerebrovasc Dis*. 2003;16:280-285.
5. Williams GR. Incidence and characteristics of total stroke in the United States. *BMC Neurol*. 2001;1:2-7.
6. Hirsh J, Hoak J. Management of deep vein thrombosis and pulmonary embolism: a statement for healthcare professionals. *Circulation*. 1996;93:2212-2245.
7. Albers GW, Dalen JE, Laupacis A, et al. Antithrombotic therapy in atrial fibrillation. *Chest*. 2001;119(suppl):194S-206S.
8. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary: a Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol*. 2001;38:1231-1266.
9. Allison JJ, Keife CI, Weissman NW, et al. Relationship of hospital teaching status with quality of care and mortality for Medicare patients with acute MI. *JAMA*. 2000;284:1256-1262.
10. Ayanian JZ, Weissman JS, Chasan-Taber S, Epstein AM. Quality of care for two common illnesses in teaching and nonteaching hospitals. *Health Aff (Millwood)*. 1998;17:194-205.
11. Keeler EB, Rubenstein LV, Kahn KL, et al. Hospital characteristics and quality of care. *JAMA*. 1992;268:1709-1714.
12. Stafford RS, Radley DC. The underutilization of cardiac medications of proven benefit, 1990 to 2002. *J Am Coll Cardiol*. 2003;41:56-61.
13. Jencks SF, Huff ED, Cuerdon T. Change in the quality of care delivered to Medicare beneficiaries, 1998-1999 to 2000-2001. *JAMA*. 2003;289:305-322.
14. Gross CP, Vogel EW, Abahy JD, et al. Factors influencing physicians' reported

use of anticoagulation therapy in nonvalvular atrial fibrillation: a cross-sectional survey. *Clin Ther*. 2003;25:1750-1764.

15. Bungard TJ, Ghali WA, Teo KK, et al. Why do patients with atrial fibrillation not receive warfarin? *Arch Intern Med*. 2000;160:41-46.
16. Dhond AJ, Michelen H, Ezekowitz MD. Anticoagulation in the elderly. *Am J Geriatr Cardiol*. 2003;12:243-250.
17. Stroke Prevention in Atrial Fibrillation Investigators. Design of a multicenter randomized trial for the Stroke Prevention in Atrial Fibrillation Study. *Stroke*. 1990;21:538-545.
18. Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low-dose warfarin on the risk of stroke in nonrheumatic atrial fibrillation. *N Engl J Med*. 1990;323:1505-1511.
19. Ezekowitz MD, Bridgers SL, James KE, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation: the Veterans Affairs Cooperative Study. *N Engl J Med*. 1992;327:1406-1412.
20. Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B. Placebo controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation: the Copenhagen AFASAK Study. *Lancet*. 1989;1:175-179.
21. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *J Am Coll Cardiol*. 1991;18:349-355.
22. Man-son-Hing M, Laupacis A. Balancing the risks of stroke and upper gastrointestinal tract bleeding in older patients with atrial fibrillation. *Arch Intern Med*. 2002;162:541-550.
23. Caplan L. Cerebrovascular disease and stroke. In: Cassel CK, Cohen HJ, Larson EB, et al, eds. *Geriatric Medicine*. 3rd ed. New York, NY: Springer-Verlag; 1996: 923.
24. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation: a major contributor to stroke in the elderly: the Framingham Study. *Arch Intern Med*. 1987;147:1561-1564.
25. Bergqvist D, Benoni G, Bjorgell O, et al. Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med*. 1996;335:696-700.
26. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism. *Chest*. 2004;126:338S-400S.
27. Pellegrini VD, Clement D, Lush-Ehmann C, et al. Natural history of thromboembolic disease after total hip arthroplasty. *Clin Orthop*. 1996;333:27-40.
28. Sikorski JM, Hampson WG, Staddon GE. The natural history and aetiology of deep vein thrombosis after total hip replacement. *J Bone Joint Surg Br*. 1981;63:171-177.
29. Trowbridge A, Boese CK, Woodruff B, et al. Incidence of post-hospitalization proximal deep venous thrombosis after total hip arthroplasty: a pilot study. *Clin Orthop*. 1994;299:203-208.
30. Lotke PA, Steinberg ME, Ecker ML. Significance of deep venous thrombosis in the lower extremity after total joint arthroplasty. *Clin Orthop*. 1994;299:25-40.
31. Barbash IM, Freimark D, Gottlieb S, et al; Israeli Working Group on Intensive Cardiac Care, Israel Heart Society. Outcome of myocardial infarction in patients treated with aspirin is enhanced by pre-hospital administration. *Cardiology*. 2002;98:141-147.
32. Freimark D, Matetzky S, Leor J, et al. Timing of aspirin administration as a determinant of survival of patients with acute myocardial infarction treated with thrombolysis. *Am J Cardiol*. 2002;89:381-385.
33. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet*. 1988;2:349-360.
34. Hyers TM, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease. *Chest*. 2001;119(suppl):176S-193S.
35. Levine M, Jent M, Hirsh 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;334:677-681.
36. Koopman MM, Prandoni P, Piovella F, 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;334:682-687.
37. Lindmarker P, Holmstrom M. Use of low molecular weight heparin (dalteparin), once daily, for the treatment of deep vein thrombosis: a feasibility and health economic study in an outpatient setting. *J Intern Med*. 1996;240:395-401.
38. Spyropoulos AC. Outpatient protocols for treatment of venous thromboembolism using low-molecular-weight heparin: to treat or not to treat at home. *Arch Intern Med*. 1999;159:1139-1140.