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Transaction Number: 18055
Username: hyin Name: Hongjun Yin Status: Faculty
ISSN/ISBN:
NotWantedAfter: 03/02/2009
Accept Non English: Yes
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Request Type: Article - Article

Loan Information

LoanAuthor:
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NotWantedAfter: 03/02/2009

Article Information

PhotoJournalTitle: The American journal of orthopedics.
PhotoJournalVolume: 36
PhotoJournalIssue: 4
Month:
Year: 2007
Pages: 193-197
Article Author:
Article Title: Factors Associated With Thromboprophylaxis for Orthopedic Patients and Their Impact

Citation Information

Cited In:
Cited Title:
Cited Date:
Cited Volume:
Cited Pages:

OCLC Information

ILL Number: 48856647
OCLC Number: 31091622
Lending String: *VZB,UBM,WQM,WQM
Original Loan Author:
Original Loan Title:
Old Journal Title: The American Journal of Orthopedics
Call Number:
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Notes

12/4/2008 10:35:33 AM hyin PubMed ID: 17515185

48856647

STATUS: IN PROCESS 20081205 **OCLC #:** 31091622

REQUEST DATE: 20081204 **NEED BEFORE:** 20090103 **SOURCE:** ILLiad

BORROWER: ZLI **RECEIVE DATE:** **DUE DATE:**

RENEWAL REQ: **NEW DUE DATE:** **SPCL MES:**

LENDERS: VZB, *UBM, WQM, WQM

LHR SUMMARY: v.24-(1995-)
UNIFORM TITLE: American journal of orthopedics (Belle Mead, N.J.)
TITLE: The American journal of orthopedics.
ISSN: 1078-4519
IMPRINT: Belle Meade, N.J. : Excerpta Medica, c1994-
ARTICLE: : Factors Associated With Thromboprophylaxis for Orthopedic Patients and Their Impact on
Outcome
VOLUME: 36
ISSUE NUMBER: 4
ISSUE DATE: 2007
PAGES: 193-197
VERIFIED: <TN:18055><ODYSSEY:148.4.41.146/ILL> OCLC
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to go through our firewall.-zli.

PATRON: Yin, Hongjun

An Original Study

Factors Associated With Thromboprophylaxis for Orthopedic Patients and Their Impact on Outcome

James E. Muntz, MD, Paul J. O'Connor, RPh, MBA, Hongjun Yin, PhD, and F. Randy Vogenberg, RPh, PhD

Abstract

We conducted a study to identify the factors affecting inpatient thromboprophylaxis use and to assess the impact of pharmacologic prophylaxis on the incidence of postsurgical venous thromboembolism (VTE). Our ultimate goal was to close the gap in knowledge about the need for thromboprophylaxis, including aspirin use. Although prophylaxis was effective in reducing VTE risk in orthopedic patients, it seemed to be underused at some hospitals, and use of aspirin alone in these patients continues despite guidelines recommending otherwise.

Every year, the number of hip and knee replacements rises. In 2001, in the United States, 165,000 short-stay hospital patients had discharge diagnoses of total hip arthroplasty (THA), and 326,000 had discharge diagnoses of total knee arthroplasty (TKA).[1] Current trends suggest that, with the aging Baby Boom population and increasing life expectancies, these numbers will continue to rise. Of patients undergoing TKA without thromboprophylaxis, 40% to 84% experience deep venous thrombosis (DVT), and up to 7% have pulmonary embolic events.[2] Similarly, of patients undergoing THA, 45% to 57% experience DVT, up to 30% have a pulmonary embolism (PE),[3] and up to 6% have a fatal PE.[4] Although thromboprophylaxis (also referred to as *prophylaxis* here) with unfractionated heparin, low-molecular-weight heparin (LMWH), or warfarin[2] has been shown to significantly decrease the risk that postsurgical hip and knee replacement patients will develop DVT or PE, it is far from universally prescribed. Only 83% of the 11,728 patients studied by Anderson and colleagues[2] received thromboprophylaxis, as we defined it, after hip or knee replacement.

More than 201,000 first lifetime cases of venous thromboembolism (VTE) present each year, with surgery being the greatest risk factor.[5] Reported rates of DVT in patients undergoing knee arthroscopy alone are as high as 17.9%.[6] Patients undergoing orthopedic surgery are at especially high risk. Without prophylaxis, one half of orthopedic patients will develop DVT, which causes 90% of all pulmonary emboli to form.[2] The long-term effects of VTE include excess mortality, recurrent VTE, and postthrombotic syndromes.[7,8] Risk factors for VTE are increasing age, surgery requiring anesthesia for more than 30 minutes, prolonged immobilization, cerebrovascular accident, cardiac dysfunction, cancer, fracture (pelvis, femur, or tibia), obesity, pregnancy or recent delivery, estrogen therapy, inflammatory bowel disease, paralysis, varicose veins, and genetic factors.[2,9,10]

Two medical record reviews conducted to study thromboprophylaxis use yielded little useful information for identifying factors associated with thromboprophylaxis use in physician practice.[3,11] In our study, described in this article, we wanted to identify the factors affecting inpatient thromboprophylaxis use and assess the impact of pharmacologic prophylaxis on postsurgical VTE incidence. Our ultimate goal was to close the gap in knowledge about the need for thromboprophylaxis, including use of aspirin.

Methods

Our study tapped administrative databases with diagnoses and procedures coded in *ICD-9-CM* (*International Classification of Diseases, Ninth Revision, Clinical Modification*) from 15 geographically diverse hospitals across the United States.

From these databases, we identified 5828 hip replacement procedures (*ICD-9* procedure codes 815.1, 815.2, and 815.3) and 5900 knee replacement procedures (codes 815.4 and 815.5). To allow 90-day follow-up, we excluded patients who had surgery within 90 days before the data-collection period. We included patients discharged between October 1, 1999, and September 1, 2002. Patients

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Am J Orthop. 2007;36(4):193-197.

Table I. Patient Age and Sex

Patient Group	No. Discharges	Age (y)		Female (%)
		Mean	SD	
Hip replacement	5828	66.9	15.1	59.1
Knee replacement	5900	66.4	11.0	64.0
Receiving prophylaxis	9769	67.1	12.8	61.6
Not receiving prophylaxis	1959	64.4	14.8	61.2

Table II. Factors Associated With Thromboprophylaxis Use*

Model	Factors Considered†	Significant Factors (Odds Ratio, *P*)
1		
Comorbidity aggregated	Age	Age (1.01, <.01)
	Sex	Hip vs knee (1.24, <.01)
	Procedures	LOS (4.21, <.01)
	No. comorbidities	No. comorbidities (0.92, <.01)
	Logarithm of LOS	
2		
Comorbidity considered separately	Age	Age (1.01, <.01)
	Sex	Hip vs knee (1.27, <.01)
	Procedures	LOS (4.43, <.01)
	31 dichotomous variables on comorbidity	Dementia (0.53, <.01)
	Logarithm of LOS	Metastatic solid tumor (0.45, .01)
		Valvular disease (0.78, <.05)
		Obesity (0.84,<.05)
		Drug abuse (0.70, <.01)
		Psychosis (0.53, <.01)
		Depression (0.78, .02)
		Fluid and electrolyte disorders (0.61, <.01)
3		
Age categorized	Age (categorized)	Age (1.06, <.01)
	Sex	Significant factors as in model 2
	Procedures	
	31 dichotomous variables on comorbidity	
	Logarithm of LOS	
4		
Aspirin considered	Age (categorized)	Age (1.04, <.01)
	Sex	Hip vs knee (1.42, <.01)
	Procedures	LOS (5.71, <.01)
	31 dichotomous variables on comorbidity	Dementia (0.52, <.01
	Logarithm of LOS	Metastatic solid tumor (0.31, <.01)
	Aspirin use	Depression (0.60, .04)
		Myocardial infarction (2.12, <.01)
		Aspirin (0.05, <.01)
		Mild to moderate diabetes (1.23, .03)
		Fluid and electrolyte disorders (0.67, <.01)

*LOS indicates length of stay. †Procedures = hip replacement, knee replacement.

who underwent both hip and knee replacement procedures were excluded. Table I shows the age and sex composition of the study group.

For the purposes of this study, we used American College of Chest Physicians (ACCP) guidelines[12] to help identify patients who received thromboprophylaxis. All patients with any coded diagnosis of DVT or PE were excluded from the analysis. Therefore, we considered the remaining subset of patients who received an anticoagulant—unfractionated heparin, LMWH, or warfarin—as receiving prophylaxis. The data collected did not include LMWHs other than enoxaparin and dalteparin.

Logistic regression was performed to model the association between thromboprophylaxis use and the factors of age, sex, procedure (hip or knee replacement), comorbidities, and length of stay (LOS). Our selection of these factors for analysis was based on our review of the literature and on the availability of the information in the database.

For modeling purposes and to better allow for comparisons of patient age, we categorized age in either 1- or 5-year increments (<45, 45-49, 75-79, ≥80). Because of the skewed distribution of LOS, we put a logarithm of LOS, which is close to normal distribution, into the model analysis.

In a concurrent study, we found that aspirin, compared with anticoagulants, was associated with higher risk for readmission—an indication that aspirin use might influence thromboprophylaxis use. Therefore, aspirin use was included as a factor. *Aspirin* included aspirin 81 mg, and aspirin 325 mg. We selected and classified comorbidities using the combined set of Charlson's method[13] and the study by Elixhauser and colleagues.[14] As a result, we considered 31 comorbidities: myocardial infarction (MI), peripheral

Table III. Patients Who, With or Without Certain Disease, Received Aspirin (%)

Has Disease	Disease					
	Valvular Disease	Obesity	Drug Abuse	Psychosis	Myocardial Infarction	Mild to Moderate Diabetes
Yes	15.46	14.27	15.26	19.85	22.69	10.94
No	8.25	8.02	8.18	8.42	8.01	8.26

vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, moderate to severe liver disease, mild to moderate diabetes, diabetes with chronic complications, paralysis, renal disease, malignancy without metastasis (including lymphoma and leukemia), metastatic cancer, AIDS, congestive heart failure, cardiac arrhythmias, hypothyroidism, valvular disease, hypertension, neurologic disorders (excluding paralysis), coagulopathy, obesity, weight loss, fluid and electrolyte disorders, anemia, alcohol abuse, drug abuse, psychoses, and depression.

We also used χ^2 tests to assess the association between thromboprophylaxis and VTE incidence (*ICD-9* diagnosis codes 451.11, 451.19, 451.2, 451.83, and 997.2) during the 90 days after surgery discharge. This assessment excluded from outcome evaluation those patients with VTE at surgery admission. As data are not available for patients seeking care from other facilities after surgery discharge, we assumed readmission to the same hospital where patients had surgery if they developed VTE during the 90 days after discharge.

Results

Rate of thromboprophylaxis use varied across the 15 hospitals (Figure). Eight hospitals had a prophylaxis rate of almost 100%. The lowest rate among the hospitals was 26%.

Physicians were more likely to prescribe thromboprophylaxis for older patients and for patients with longer LOS (Table II). In addition, hip replacement patients (vs knee replacement patients) were more likely to receive prophylaxis. Patients with more comorbidity; patients with dementia, metastatic solid tumor, depression, or fluid and electrolyte disorders (vs patients without these diseases); and patients receiving aspirin were all less likely to receive thromboprophylaxis. Findings on valvular disease, obesity, drug abuse, psychosis, MI, and mild to moderate diabetes seemed inconsistent across the models (we discuss these inconsistent findings in the Discussion section). According to χ^2 test results, patients receiving prophylaxis were less likely to develop VTE during the 90 days after discharge ($P = .015$).

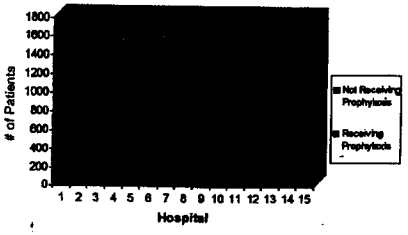

Figure. Thromboprophylaxis use at 15 hospitals.

To test the sensitivity of these results to bias from hospitals with very high prophylaxis rates, we performed an additional analysis excluding the 8 hospitals that the initial analysis identified as having a prophylaxis rate of almost 100%. The preceding results still held, except for slight changes in magnitude of *P* values (ie, statistically significant factors remained significant).

Discussion

As the prophylaxis rate was low, some hospitals need to promote use of thromboprophylaxis in orthopedic patients (Figure), especially knee replacement patients, who, with other variables controlled, are less likely than hip replacement patients to receive prophylaxis.

Patients with dementia were less likely to receive prophylaxis as well. A positive correlation was found between the prophylaxis rates for dementia (mean, 83.2%; SD, 6.6%) and age (mean, 66.4%; SD, 13.1%). Such fragile patients overall were less likely to receive thromboprophylaxis, though older patients were more likely to receive thromboprophylaxis in general, as shown by the odds ratios for age in all 4 models (Table II). In addition, we found increasing age and longer LOS associated with more use of prophylaxis—consistent with what the ACCP guideline suggest.[12] Longer LOS is a good but imperfect substitute for longer immobilization. Further study is necessary to elucidate the reasoning behind these practice patterns.

That a patient with more comorbidity was less likely to receive prophylaxis is surprising. Metastatic cancer, a major risk factor for thrombosis, was associated with less prophylaxis use. Dementia, fluid and electrolyte disorders, and depression were also found negatively associated with prophylaxis use. Valvular disease, obesity, drug abuse, and psychosis were found associated with less prophylaxis use in models 2 and 3 (Table II), yet this relation was not supported when aspirin was included in the model (model 4, Table II). In addition, when we considered aspirin in model 4, we found MI and mild to moderate diabetes to be positively associated with prophylaxis use, which may suggest that patients with these comorbidities were more likely to receive aspirin. This assumption was confirmed by the cross-tabulation results for the above 6 diseases:

Table IV. Percentage of Patients Who Received Prophylaxis, Aspirin, or Neither, by No. of Comorbidities*

	No. of Comorbidities						
	0	1	2	3	4	5	6
Prophylaxis (only)	82.95 (81.9)	86.09 (81.49)	83.61 (80.83)	82.47 (78.76)	84.88 (78.38)	86.36 (78.64)	79.37 (64.29)
Aspirin (only)	6.07 (5.02)	6.07 (4.60)	7.28 (4.50)	11.13 (7.42)	12.87 (6.37)	13.06 (5.34)	24.60 (9.52)
Neither	12.02	12.44	10.89	10.11	8.75	8.31	11.11

*No. of patients with 7 or more comorbidities is too small to give meaningful results.

Table V. Deep Venous Thrombosis Incidence Among Patients Who Received Aspirin, Prophylaxis, or Neither

Prophylaxis Only	Aspirin Only	Neither
0.87% (82/9407)	0.78% (5/641)	2.20% (29/1318)

valvular disease, obesity, drug abuse, psychosis, myocardial infarction, mild to moderate diabetes (Table III). In general, we found that the more comorbidity a patient had, the more likely the patient received aspirin (Pearson r, 0.30; $P<.001$) (Table IV). Aspirin usage was particularly associated with prophylaxis use among patients with mild to moderate diabetes. This is likely because physicians are aware that cardiac dysfunction and obesity are risk factors for thrombosis.

We can conclude that physicians were less apt to give anticoagulants to patients with more comorbidity. In fact, physicians were more likely to give antiplatelet medications (eg, aspirin) to patients with more comorbidity. Chi-square tests showed that DVT incidence in the aspirin group did not significantly differ from that in the prophylaxis group but was significantly lower than in the no-anticoagulant group ($P<.01$) (Table V). Further study is needed to determine why physicians avoid administering anticoagulants to patients taking aspirin. Such practice choices may result from higher confidence or familiarity with aspirin or from concerns about bleeding with combination therapy. To date, there is not enough evidence on the relative risk for bleeding in patients who receive both an antiplatelet and an anticoagulant; however, investigators have found that, though aspirin is more effective than placebo, it is less effective than the anticoagulants recommended by ACCP.[2,12] Still, some orthopedic surgeons continue to use aspirin for thromboprophylaxis. Although physicians report prophylaxis use, data show that only 30% of patients receive adequate prophylaxis according to the new ACCP guidelines.[12]

Study Limitations

Study limitations include those inherent in using administrative databases for analysis—lack of specific detailed information on data points, such as dosing, length of prophylaxis therapy, and type or frequency of monitoring.

Some patients in this study may not have received DVT/PE prophylaxis, so the actual prophylaxis rate may be overstated or understated. This study focused only on pharmacologic prophylaxis; forms of mechanical intervention were not addressed. In addition, as this was a retrospective, observational study rather than a prospective, randomized, controlled study, we could not evaluate unobserved confounding factors. Last, VTE incidence during the 90 days after discharge was captured only when a patient was admitted to the same hospital.

Conclusions

Although prophylaxis is effective in reducing VTE risk in orthopedic patients, it seems underused at some hospitals, and use of aspirin in these patients continues despite guidelines recommending otherwise. Aspirin prophylaxis and its clinical and economic impact should call for more study and consensus on its appropriate roles. In addition, further study is needed to effectively elucidate the predictors of physicians' prescribing behavior and/or decision making regarding critical thromboprophylaxis decisions.

Authors' Disclosure Statement and Acknowledgments

The development of this analyses and manuscript was under a doctoral student fellowship program to conduct independent research, and utilized data gathered through Aon Consulting's Clinical Effectiveness Initiative. This initiative was funded through an unrestricted research grant from Sanofi Aventis. Authors Muntz and Vogenberg are occasional speakers on clinical related topics and receive honoraria from Sanofi Aventis.

The authors thank Leo K. Lichtig, PhD, and Christe S. Bruderlin, MS, for their research, editorial assistance, and article preparation.

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