Comparative effectiveness and safety of apixaban versus warfarin in patients with venous thromboembolism

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Purpose. Compared with conventional therapy (enoxaparin followed by warfarin), the direct-acting oral anticoagulant apixaban is thought to offer similar protection against recurrent venous thromboembolism (VTE) with lower bleeding risk. However, evidence regarding the heterogeneity of treatment effect from real-world data is lacking. The study described here aimed to compare the effectiveness and safety of use of apixaban versus warfarin in patients with VTE.

Methods. We conducted a retrospective cohort analysis of commercial and Medicare supplemental databases (data coverage period, 2014-2017) among patients with a diagnosis of VTE who were new users of apixaban or warfarin. We controlled for confounding using propensity score [PS] 1:4 matching. Cox proportional hazard models were used to obtain hazard ratios (HRs) and 95% confidence intervals (CIs). Heterogeneity of treatment effect was assessed among patients with provoked VTE versus unprovoked VTE.

Results. After PS matching, a total of 36,907 patients were included in the cohort (n = 8,094 apixaban users and n = 28,813 warfarin users). In Cox regression models, the use of apixaban versus warfarin was associated with lower risks of recurrent VTE (HR, 0.54; 95% CI, 0.45-0.65) and major bleeding events (HR, 0.67; 95% CI, 0.54-0.84); these results remained consistent in patients with provoked VTE and those with unprovoked VTE.

Conclusion. This population-based analysis of patients with VTE extends results of randomized clinical trials indicating lower risks of development of recurrent VTE and major bleeding events with use of apixaban versus warfarin in real-world settings. The observed benefits of apixaban extended to selected subgroups of the VTE population, including patients with provoked VTE.

Keywords: anticoagulants, effectiveness, safety, VTE

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Venous thromboembolism (VTE), manifest as pulmonary embolism (PE) or deep vein thrombosis (DVT), affects 1 to 3 adults per 1,000 each year in the United States.[1] Among those with initial VTE, 30% will develop a recurrent VTE within 10 years.[1] Anticoagulation therapy can prevent recurrent events but also increases bleeding risk.[2] Due to its relatively low cost, warfarin remains the most commonly prescribed anticoagulant for the treatment of VTE and prevention of recurrent VTE. However, warfarin is cumbersome to use, even as a relatively short-term therapy, owing in part to its many drug interactions and monitoring requirements. Compared to warfarin, direct-acting oral anticoagulants (DOACs) (i.e. edoxaban, apixaban, rivaroxaban, and dabigatran) offer conventional dosing, limited drug–drug interactions, and do not require frequent monitoring.[3,4] Among the approved DOACs, apixaban is considered relatively new and its effectiveness and safety within the VTE population is still being established.[5]

Evidence from the Apixaban for the Initial Management of Pulmonary Embolism and Deep-Vein Thrombosis as First-line Therapy (AMPLIFY) trial, which compared apixaban to conventional treatment (enoxaparin followed by warfarin), found apixaban to be noninferior to warfarin in reducing recurrent VTE and mortality and to be associated with a 69% reduction in the risk of major bleeding.[6] However, head-to-head comparisons of apixaban and warfarin in routine clinical practice are lacking. Randomized clinical trials (RCTs) that examined the efficacy of warfarin within controlled settings were characterized by the close monitoring of warfarin leading to a higher time in the therapeutic range and better adherence.[7,8] Additionally, these trials often focused on selected VTE population and excluded others who might have had concurrent comorbid conditions. Patients with provoked VTE are of interest, in part because they were underrepresented in the key trial (AMPLIFY), and it remains unclear if the benefits of long-term therapy outweigh the potential risks of bleeding from anticoagulation.[6,9,10] Therefore, evidence generated using real-world data can allow for the assessment of the heterogeneity of treatment effect of apixaban among more diverse and complicated VTE populations.

Therefore, the objectives of the study described here were to (1) assess the real-world effectiveness of apixaban versus warfarin for the prevention of recurrent VTE and (2) examine the difference in major bleeding risk in patients with VTE receiving apixaban and warfarin.

KEY POINTS

- Compared with warfarin, apixaban is thought to offer similar protection against recurrent venous thromboembolism but with lower bleeding risk. However, evidence regarding the heterogeneity of treatment effect from real-world data is lacking.
- In this population-based analysis, apixaban use was associated with lower risks of recurrent venous thromboembolism and major bleeding events compared with warfarin.
- Risk reductions with apixaban were consistent across subgroups, including among patients with provoked venous thromboembolism, who have been underrepresented in randomized clinical trials comparing anticoagulants.

Methods

Data source. The study involved a retrospective cohort analysis of data from the period January 2014–December 2017 from the Truven Health MarketScan commercial claims and encounters and Medicare Supplemental database (Truven Health Analytics, Ann Arbor, MI). The database provides a comprehensive assessment of the healthcare experience of enrollees covered by various healthcare plans (e.g., fee-for-service and managed care plans) and retirees in the United States. Healthcare coverage enrollment data are linked with inpatient claims, outpatient claims, and prescription drug claims at the patient level. Data are deidentified and compliant with the Health Insurance Portability and Accountability Act.

Study design and participants. A new-user VTE cohort was used to compare patients initiated on apixaban or warfarin for the treatment of VTE. Inclusion in the study cohort required that patients (1) be 18 years of age or older, (2) meet the definition for VTE during the time period from January 1, 2014, through December 31, 2017, (3) have at least 365 days of continuous enrollment in medical and pharmacy benefits, allowing for a gap not longer than 30 days prior to cohort entry, and (4) fill a prescription for apixaban or warfarin within 30 days following their first VTE diagnosis. We defined VTE as having 1 inpatient claim (any position) or 2 outpatient claims within 1 year of documentation of selected International Classification of Diseases (ICD) codes validated for use in identifying VTE in prior studies[11,12] (codes 415.1, 451.1, 453.2, 453.4, 453.5, 453.8, 453.9, I80.2, I80.3, I80.1, I82.8, I80.9, I82.9, I80.8, O22.3, O22.9, O87.1, I26.9, and I26.0). The baseline period, 12 months period prior to treatment initiation, was used to ascertain baseline comorbidities and prior drug use.

Outcomes. Recurrent VTE (either PE or DVT) was defined by the presence of a VTE ICD code (same as above) in the primary position on inpatient discharge diagnosis.[11,12] Bleeding events, including intracranial hemorrhage and major gastrointestinal (GI) bleeding, were considered major if present on inpatient discharge claims (primary position only) and minor if present on outpatient claims. The ICD (Ninth Revision [ICD-9] or 10th Revision [ICD-10]) codes defining bleeding were previously used and validated in several studies.[5,13-15]

Adjustment for confounders. Potential confounders were measured during the baseline period using inpatient, outpatient, and pharmacy claims; these included comorbidities defined by ICD-9 or ICD-10 codes (e.g., cancer, stroke, thrombocytopenia, chronic kidney disease [CKD]), medications use (e.g., corticosteroids, loop diuretics, estrogens), age, sex, and healthcare utilization (total number of outpatient visits during the preindex period). We also calculated the HAS-BLED score, which predicts bleeding risk in patients receiving anticoagulant treatment.[16]

Follow-up. Follow-up started on the date of the dispensing of the first prescription of apixaban or warfarin. Patients who received apixaban or any other DOACs during the preindex period (i.e., during a 12-month look-back period) or those who had a prescription of apixaban and warfarin on the same date were excluded. Follow-up continued until the occurrence of (1)

an outcome specified above, (2) a gap in enrollment longer than 30 days, (3) discontinuation of index medication, defined as a gap longer than 7 days between consecutive refills, (4) the end of the study period (December 31, 2017), (5) initiation of treatment with the comparator medication, or (6) inpatient death.

Statistical analysis. To control for measured baseline confounders, we developed a propensity score (PS) model to estimate the probability of initiation of apixaban versus warfarin. Covariates included in the model were selected a priori and included risk factors for bleeding, risk factors for recurrent VTE, and measures of healthcare utilization (Table 1). Using the predicted PS from the logistic regression model, we matched new users of apixaban and warfarin (at a 1:4 ratio) through nearest-neighbor matching using a caliper of 0.01. We estimated the association of apixaban and warfarin with recurrent VTE and major bleeding events using Cox proportional hazard models. For the primary outcomes, prespecified subgroup analyses were performed among patients with provoked versus unprovoked VTE, with and without CKD, and by age (<65 years versus ≥65 years). Cohort-defining VTE diagnoses were considered provoked if the patient had pregnancy-related VTE, trauma-related VTE, surgery-related VTE, or hospital admission for 3 or more consecutive days within the 3 months preceding their cohort-defining VTE or had cancer-associated VTE within the 6 months preceding their cohort-defining VTE.[9]

Further, to assess the robustness of the study findings, several sensitivity analyses were performed, including restricting the time between the cohort-defining VTE diagnosis and the first prescription (to intervals of ≤2 days and ≤7 days), stratifying the primary study outcomes by VTE type (PE or DVT), and examining patients who persisted on therapy for more than 90 days. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

Data sharing statement. The data used in the study were obtained from Truven Health Analytics' MarketScan database under a license to the University of Florida College of Pharmacy and are not publicly available.

Results

The online-only data supplement summarizes demographics and clinical characteristics among both groups before PS matching. After matching, a total of 36,907 patients were included in the cohort (8,094 apixaban users and 28,813 warfarin users) (Table 1). After PS matching, patient characteristics were well balanced between apixaban and warfarin users, including mean age (58.9 versus 59.3 years); proportion of men (48.3% versus 47.9%); presence of comorbidities, including cancer (16.2% versus 17.0%) and ischemic heart disease (21.5% versus 20.0%); and baseline medication use, including antiplatelet therapies (6.0% versus 5.5%) and the use of angiotensin-converting enzyme inhibitors (ACEIs) (19.7% versus 19.0%). For all variables, standardized differences were less than 0.1.

Recurrent VTE. Table 2 shows the risk of recurrent VTE with apixaban versus warfarin use in the PS-matched analysis. We identified a total of 129 cases of recurrent VTE among apixaban users, compared to 1,030 cases among warfarin users. The crude incidence of recurrent VTE was 7 per 100 person-years among apixaban users, compared to 11 per 100 person-years among warfarin users. In the Cox proportional hazards model, the use of apixaban versus warfarin was associated with a lower risk of recurrent VTE (hazard ratio [HR], 0.54; 95% confidence interval [CI], 0.45-0.65). As summarized in Table 3, similar findings with regard to recurrent VTE risk with use of apixaban versus warfarin were observed in all subgroup analyses, including in patients with CKD (HR, 0.59; 95% CI, 0.37-0.94) and those without CKD (HR, 0.52; 95% CI, 0.42-0.63) (p interaction = 0.90); in patients less than 65 years of age (HR, 0.53; 95% CI, 0.43-0.66) and those 65 years of age or older (HR, 0.53; 95% CI, 0.44-0.64) (p interaction = 0.63); and in patients with provoked VTE (HR, 0.50; 95% CI, 0.39-0.63) and those with unprovoked VTE (HR, 0.59; 95% CI, 0.44-0.78) (p interaction = 0.56).

Bleeding risk. Table 2 shows the risk of major bleeding with apixaban versus warfarin use in the PS-matched analysis. For the primary safety outcome, the rate of major bleeding was 5 per 100 person-years in the apixaban group, compared to 6 per 100 person-years in the warfarin group. In the Cox proportional hazards model, the use of apixaban was associated with a lower risk of major bleeding compared to warfarin use (HR, 0.67; 95% CI, 0.54-0.84). In the subgroup analyses (Table 3), the association was consistent in patients with baseline CKD (HR, 0.44; 95% CI, 0.27-0.72) and those without CKD (HR, 0.72; 95% CI, 0.56-0.93) (p interaction = 0.09); in those less than 65 years of age (HR, 0.55; 95% CI, 0.39-0.76) and those 65 years of age or older (HR, 0.78; 95% CI, 0.57–1.06) (p interaction = 0.24); and in patients with provoked VTE (HR, 0.61; 95% CI, 0.46-0.81) and those with unprovoked VTE (HR, 0.81; 95% CI, 0.56-1.16) (p interaction = 0.16). Study results remained consistent in several sensitivity analyses, as reported in supplemental Table S2.

For the secondary safety outcome, the rate of minor bleeding was 49 per 100 person-years in the apixaban group, compared to 101 per 100 person-years among warfarin users (Table 2). In the Cox proportional hazards model, the use of apixaban was associated with a lower risk of minor bleeding events compared to warfarin use (HR, 0.41; 95% CI, 0.38-0.44).

Discussion

In this real-world comparative assessment of data from routine clinical practice, the use of apixaban was associated with lower risks of recurrent VTE, major bleeding, and minor bleeding events compared to the use of warfarin. Our findings remained

Table 1. Demographics and Clinical Characteristics of New Users of Apixaban and Warfarin in Propensity Score–Matched Cohorts[a]

Characteristic	Apixaban Group (*n* = 8,094)	Warfarin Group (*n* = 28,813)	STD
Age, mean ± S.D., yr	58.9 ± 16.3	59.3 ± 15.8	0.02
Sex, no. (%)			
Male	3,911 (48.3)	13,814 (47.9)	0.01
Female	4,183 (51.7)	14,999 (52.1)	
Comorbidities, no. (%)			
Cancer	1,312 (16.2)	4,893 (17.0)	0.02
Active cancer[b]	1,168 (14.4)	4,648 (16.1)	0.05
Surgery	1,421 (17.6)	5,223 (18.1)	0.02
Trauma	2,117 (26.2)	7,616 (26.4)	0.01
Antiphospholipid syndrome	9 (0.1)	26 (0.1)	0.01
Hyperlipidemia	3,072 (38.0)	10,634 (36.9)	0.02
Abnormal coagulation	100 (1.2)	644 (2.2)	0.01
Tobacco use	441 (5.4)	1,811 (6.3)	0.04
Respiratory diseases	2,143 (26.5)	7,399 (25.7)	0.02
Liver disease	490 (6.1)	1,410 (4.9)	0.05
CKD	1,087 (13.4)	4,143 (14.4)	0.03
Anemia	1,039 (12.8)	4,428 (15.4)	0.08
Alcohol use disorder	178 (2.2)	568 (2.0)	0.02
Drug use disorder	239 (3.0)	897 (3.1)	0.01
History of bleeding	622 (7.7)	2,710 (9.4)	0.07
Ischemic heart disease	1,739 (21.5)	5,755 (20.0)	0.04
Myocardial infarction	423 (5.2)	1,386 (4.8)	0.02
Stroke	360 (4.4)	1,574 (5.5)	0.05
Heart failure	1,083 (13.4)	2,977 (10.3)	0.09
Varicose veins	232 (2.9)	511 (1.8)	0.07
Thrombocytopenia	259 (3.2)	440 (1.5)	0.09
HAS-BLED score, mean ± S.D.	0.2 ± 0.4	0.2 ± 0.4	0.02
Baseline medications, no. (%)			
Antiplatelet agents	486 (6.0)	1,595 (5.5)	0.02
Corticosteroids	3,206 (39.6)	9,114 (31.6)	0.16
NSAIDs	2,022 (25.0)	6,413 (22.3)	0.06
ACEIs	1,592 (19.7)	5,466 (19.0)	0.02
Aspirin	173 (2.1)	500 (1.7)	0.03
β-Blockers	2,331 (28.8)	7,831 (27.2)	0.04
Calcium channel blockers	1,748 (21.6)	5,932 (20.6)	0.02
SSRIs	1,316 (16.3)	4,375 (15.2)	0.02
PPIs	2,236 (27.6)	7,505 (26.0)	0.04

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Table 1. Demographics and Clinical Characteristics of New Users of Apixaban and Warfarin in Propensity Score–Matched Cohorts[a]

Characteristic	Apixaban Group (*n* = 8,094)	Warfarin Group (*n* = 28,813)	STD
Loop diuretics	1,224 (15.1)	4,196 (14.6)	0.02
Potassium-sparing diuretics	269 (3.3)	904 (3.1)	0.01
Thiazide	120 (1.5)	474 (1.6)	0.01
Vasodilators	162 (2.0)	568 (2.0)	0.00
Estrogens	123 (1.5)	329 (1.1)	0.03
COX-2 inhibitors	268 (3.3)	823 (2.9)	0.03
Outpatient visits, mean ± S.D.	18.4 ± 21.6	18.1 ± 22.5	0.02

[a]STD = absolute standardized difference, CKD = chronic kidney disease, NSAID = nonsteroidal antiinflammatory drug, ACEI = angiotensin-converting enzyme inhibitor, SSRI = selective serotonin reuptake inhibitor, PPI = proton pump inhibitor, COX = cyclooxygenase.
[b]Patients were considered to have active cancer if they had a cancer diagnosis within the 6 months period preceding venous thromboembolism or during treatment with radiotherapy or chemotherapy.

Table 2. Risks of Recurrent VTE, Major Bleeding Events, and Minor Bleeding Events With Use of Apixaban Vs. Warfarin in Propensity Score–Matched Analyses[a]

Outcome and Medication	No. of Patients	Person-Years	No. of Events	Crude Incidence per 100 Person-Years	HR (95% CI)
Recurrent VTE					
Apixaban	8,094	1,803	129	7	0.54 (0.45-0.65)
Warfarin	28,813	9,732	1,030	11	Reference
Major bleeding[b]					
Apixaban	8,094	1,811	90	5	0.67 (0.54-0.84)
Warfarin	28,813	9,820	597	6	Reference
Minor bleeding[c]					
Apixaban	8,094	1,710	830	49	0.41 (0.38-0.44)
Warfarin	28,813	8,169	8,225	101	Reference

[a]VTE = venous thromboembolism, HR = hazard ratio, CI = confidence interval.
[b]Defined as bleeding events requiring hospitalization.
[c]Defined by presence of bleeding in outpatient settings.

consistent across key subgroups of patients, including patients with provoked VTE and those with unprovoked VTE, patients with diagnosed CKD and without CKD, and in patients less than 65 years of age and those 65 years of age or older.

Our findings support and extend the results of previous studies. In the AMPLIFY trial, the only pertinent randomized trial to date, apixaban use led to a 69% reduction of bleeding risk in patients with acute VTE and was noninferior to standard therapy (enoxaparin followed by warfarin) in reducing the risk of recurrent VTE.[6] Our results suggest that under real-world treatment conditions, apixaban was effective (in reducing recurrent VTE) and safe (in reducing bleeding risk) compared to warfarin. It is possible that these findings stem, at least in part, from differences in warfarin management. For example, in our study design we sought to include only new users of warfarin (or apixaban), whereas approximately 1 in 5 AMPLIFY trial participants had prior VTE and, presumably, had been previously treated with warfarin. Because warfarin

Table 3. Risks of Recurrent VTE and Major Bleeding With Use of Apixaban Vs. Warfarin in Propensity Score–Matched Subgroup Analyses[a]

Risk Factor	Medication	No. of Patients	Person-Years	No. of Events	Crude Incidence per 100 Person-Years	Adjusted HR (95% CI)	*p* for Interaction
Subgroup Analysis of Patients With Recurrent VTE							
Baseline VTE							
Provoked	Apixaban	4,188	922	72	8	0.50 (0.39-0.63)	0.56
	Warfarin	15,282	4,222	594	14	Reference	
Unprovoked	Apixaban	3,847	869	55	6	0.59 (0.44-0.78)	
	Warfarin	11,969	4,966	386	8	Reference	
CKD							
Present	Apixaban	1,074	252	20	8	0.59 (0.37-0.94)	0.90
	Warfarin	3,788	1,028	130	13	Reference	
Absent	Apixaban	6,986	1,541	107	7	0.52 (0.42-0.63)	
	Warfarin	24,777	8,485	896	11	Reference	
Age							
<65 years	Apixaban	5,607	1,157	97	8	0.53 (0.43-0.66)	0.63
	Warfarin	19,784	6,481	788	12	Reference	
≥65 years	Apixaban	8,091	1,802	128	7	0.53 (0.44-0.64)	
	Warfarin	28,760	9,567	1,025	11	Reference	
Subgroup Analysis of Patients With Major Bleeding							
Baseline VTE							
Provoked	Apixaban	4,188	929	5	1	0.61 (0.46-0.81)	0.16
	Warfarin	15,282	4,272	372	9	Reference	
Unprovoked	Apixaban	3,847	871	35	4	0.81 (0.56-1.16)	
	Warfarin	11,969	4,994	193	4	Reference	
CKD							
Present	Apixaban	1,074	253	18	7	0.44 (0.27-0.72)	0.09
	Warfarin	3,788	1,025	157	15	Reference	
Absent	Apixaban	6,986	1,548	71	5	0.72 (0.56-0.93)	
	Warfarin	24,777	8,571	441	5	Reference	
Age, yr							
<65	Apixaban	5,607	1,167	40	3	0.55 (0.39-0.76)	0.24
	Warfarin	19,784	6,556	324	5	Reference	
≥65	Apixaban	8,091	641	48	7	0.78 (0.57-1.06)	
	Warfarin	28,760	3,160	262	8	Reference	

[a]VTE = venous thromboembolism, HR = hazard ratio, CI = confidence interval, CKD = chronic kidney disease.

management tends to improve over time, the AMPLIFY trial may have included a population in which warfarin was more likely to be effective and safer, resulting in more conservative risk differences than those documented in our study.

The AMPLIFY trial also enrolled a relatively homogenous population, including mostly patients with unprovoked VTE (90%) and underrepresented several relevant subpopulations that are likely to receive DOAC therapy in routine clinical practice, such as patients with provoked

VTE. Prior studies showed that patients with provoked VTE were at lower risk for recurrent VTE and major bleeding than those with unprovoked VTE, but it is unclear whether or not the risk for recurrent VTE in patients with a provoked VTE event is high enough to warrant drug therapy.[9,10] As a result, it remains unclear whether or not apixaban or warfarin would be preferred if a patient were deemed to have a high enough risk to warrant treatment. Our results strongly suggest that the beneficial effects of apixaban relative to those of warfarin extend to patients with provoked VTE. Furthermore, in our analysis, the observed effectiveness and safety of apixaban versus warfarin were maintained in other subgroup analyses, including patients with CKD versus those without (for the recurrent VTE outcome), and after stratification by age.

There are several clinical implications of the findings reported here. First, our findings suggest that for first-time users of anticoagulants, apixaban may become a preferred agent (relative to warfarin) for reducing the risk of recurrent VTE and bleeding. Second, we found little evidence of heterogeneity in the observed benefits of apixaban use, including among patients with provoked VTE and those with unprovoked VTE, suggesting that apixaban may be suitable for most patients with acute VTE who are at higher risk for adverse health outcomes. Although our findings suggest that apixaban can be a more effective and safer option than warfarin for treatment of patients with VTE, other factors (e.g., drug cost, drug–drug interactions, monitoring requirements) also need to be considered for the selection of an anticoagulant therapy in clinical practice.

Our analysis had several methodological strengths. First, this study was notable for its large sample size; the AMPLIFY trial included a total of 5,395 patients (randomized to warfarin or apixaban), whereas the our analysis included 8,094 users of apixaban alone. Further, our patient cohort was likely more representative of the general VTE population in the United States. The relatively large sample size allowed for the assessment of selected subgroups of the VTE population, for which the results favoring apixaban over warfarin remained consistent. Second, we used a robust PS method resulting in well-balanced patient subgroups, at least for the measured variables. Third, we used an incident-disease, new-user study design, restricting the cohort to patients receiving anticoagulant therapy within 30 days of diagnosis. Such restriction can minimize the bias resulting from differences in disease severity between treatment groups. Nevertheless, there were limitations to our analysis. First, there was a potential for residual confounding due to a lack of clinical information, such as the International Normalized Ratio, a measure commonly used to monitor patients on warfarin therapy. Second, inaccuracy in diagnosis coding was likely to have occurred in our claims data analysis, although we attempted to minimize misclassification by using previously validated codes. Claims data have limitations stemming from the nature of administrative claims for payment purposes. We also did not have data on laboratory results (e.g., creatinine clearance) to corroborate ICD coding. Thus, it is possible that incomplete, missing, or miscoded claims may have impacted the study findings; however, coding errors were likely distributed evenly between the apixaban and warfarin groups. CKD, in particular, is known to be underreported in claims data; however, misclassification of CKD status is unlikely to differ between apixaban and warfarin users and, thus, would not be expected to have biased our results. Third, we defined the study cohort on the basis of diagnosis codes present on inpatient and outpatient claims, which may have captured some prevalent VTE cases. However, our methodology required that patients be treatment naive prior to cohort entry to minimize the inclusion of prevalent cases. Lastly, the data used in the study were not linked to death records, so we were not able to capture fatal events occurring in outpatient settings, although data based on fatal outcomes occurring within the inpatient setting were incorporated as a censoring criterion in the analysis. Finally, our findings may not be generalizable to other VTE populations not covered by commercial or supplemental insurance (e.g., Medicaid recipients, uninsured persons).

Conclusion

This PS-matched analysis of patients with VTE supports the use of apixaban rather than warfarin to reduce the risk of development of recurrent VTE and major bleeding events. The observed benefits of apixaban use extended to selected subgroups of the acute VTE population, including patients with provoked VTE, who were not included to any substantial degree in similar previous studies.

Disclosures

The authors have declared no potential conflicts of interest.

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