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ORIGINAL RESEARCH

Influence of the duration of hospital length of stay on frequency of prophylaxis and risk for venous thromboembolism among patients hospitalized for acute medical illnesses in the USA

Alpesh Amin MD, MBA[1], W Richey Neuman MD, MPH[2], Melissa Lingohr-Smith PhD[3], Brandy Menges PhD[3], Jay Lin PhD, MBA[3]

[1]Univeristy of California, Irvine, School of Medicine, Irvine, CA, USA; [2]Portola Pharmaceuticals, South San Francisco, CA, USA; [3]Novosys Health, Green Brook, NJ, USA

Abstract

Background: We evaluated whether the duration of hospital stay influences venous thromboembolism (VTE) prophylaxis patterns and VTE risk during hospitalization and post-discharge among patients hospitalized for acute illnesses in the USA.

Methods: Patients hospitalized for acute illnesses were identified from the US MarketScan Commercial and Medicare databases (January 1, 2012–June 30, 2015). Patients were stratified by index hospital length of stay (LOS), with study groups with 1–3 day, 4–6 day, and ≥7 day LOSs. Use of VTE prophylaxis and VTE event rates during and after hospitalization (6-month follow-up) were evaluated.

Results: Of the overall population, 8647 had a 1–3 day LOS, 5551 had a 4–6 day LOS, and 3697 had a ≥7 day LOS. A greater proportion of patients with a 1–3 day LOS (66.2%) did not receive any VTE prophylaxis in comparison to patients with a 4–6 day LOS (55.0%) and ≥7 day LOS (48.8%; $p<0.001$). Proportions of patients with VTE events during the index hospitalization increased with longer hospital LOS (1–3 day LOS: 0.5%; 4–6 day LOS: 1.3%; ≥7 day LOS: 5.4%), as did proportions of patients with VTE events during the 6-month follow-up (1–3 day LOS: 2.4%; 4–6 day LOS: 2.7%; ≥7 day LOS: 4.2%).

Conclusion: Among this study population of hospitalized acutely ill patients in the USA, VTE pharmacologic prophylaxis was underutilized, regardless of the duration of hospital stay. However, the risk for VTE events was substantial, with nearly 10% of those with a ≥7 day LOS having suffered a VTE event within 6 months.

Keywords: acute illness, hospitalization, venous thromboembolism, VTE prophylaxis, VTE risk.

Citation

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Introduction

According to the American College of Chest Physicians (ACCP) 2012 criteria, nearly 7.3 million acutely ill hospitalized patients were at risk for venous thromboembolism (VTE) in the USA in 2014.[1,2] Many patients hospitalized for acute medical illnesses are at increased risk for VTE events while they are hospitalized and for an extended duration following hospital discharge.[3,4] Compared to hospitalized control cases, medical costs within the first 3 months of hospitalization are estimated to be increased by approximately $17,000 (2011 USD) for patients who have a VTE event during or after a recent hospitalization.[5]

The evidence-based ACCP guidelines recommend that acutely medically ill hospitalized patients who have an increased risk of thrombosis receive pharmacological prophylaxis during hospitalization to reduce the incidence of VTE.[2] However, some relatively recent studies have not demonstrated that greater provision of VTE prophylaxis among this patient population is associated with a decline in VTE events.[3,6,7] Thus, there is some uncertainty in the medical community on the necessity for the use of such VTE pharmacologic prevention tactics. As the risk for VTE is elevated for hospitalized acutely ill patients and VTE is associated with poor patient outcomes, it is widely recognized that better strategies of VTE prophylaxis are needed.[8,9]

Acutely ill patients hospitalized for longer durations may be at increased risk for VTE events due to greater illness severity, older age, greater comorbidity, and longer periods of immobility, among other factors. The objectives of this

study were to evaluate whether the duration of hospital stay influences VTE prophylaxis patterns and risk for VTE during hospitalization and post-discharge among patients hospitalized for acute medical illnesses in the USA.

Methods

Study population

Patients hospitalized for acute medical illnesses were identified from the Truven Health Analytics MarketScan Commercial and Medicare databases between January 1, 2012, and June 30, 2015. Acute medical illnesses included heart failure, respiratory diseases, ischemic stroke, cancer, infectious diseases, and rheumatic diseases and were identified by International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes. The acute medically illnesses were based on ACCP guidelines and other existing clinical trial populations.[2,10,11]

The MarketScan claims data include inpatient and outpatient information, laboratory data, and detailed hospital drug data, reflecting real-world treatment patterns and costs. In compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), the databases utilized for this study consist of fully de-identified data sets, with synthetic identifiers applied to patient-level and provider-level data to protect the identities of both the patients and data contributors. Patient consent was not obtained because the databases contained de-identified information. The MarketScan claims databases were further linked to the MarketScan Hospital Drug Database to provide the details of healthcare services, resource utilization, and costs for patients in the inpatient and outpatient settings.

The earliest hospitalization for acute medical illnesses to occur during the index identification period was defined as the index hospitalization. Patients were required to have 6 months of continuous medical and prescription insurance coverage prior to the index hospitalization (baseline period). Patients were additionally required to have 6 months of continuous insurance coverage after the index admission date (follow-up period). Patients were excluded if they had a pregnancy diagnosis during the baseline period or at the index hospitalization, death during the index hospitalization, or hip or knee replacement surgery during the index hospitalization. After inclusion and exclusion criteria were applied, patients were stratified by index hospital length of stay (LOS), with study groups of patients with 1–3 day, 4–6 day, and ≥7 day LOSs. These LOS categories were designated because among the overall study population the median LOS was equal to 4 days and the mean LOS equal to 4.8 days. Thus, the three LOS categories used in this study represented the shorter (i.e. less than median value), medium, and longer LOS categories.

Demographics, patient clinical characteristics, and hospital characteristics

Patient demographics, clinical characteristics, and hospital characteristics were evaluated during the 6-month baseline period and index hospitalization for each study group.

VTE prophylaxis patterns

The proportions of patients who received and did not receive inpatient and/or outpatient VTE pharmacologic prophylaxis were determined. VTE prophylaxis in the inpatient setting was determined based on pharmacy records for enoxaparin, warfarin, direct-acting oral anticoagulants (DOACs: apixaban, dabigatran, rivaroxaban, edoxaban), fondaparinux, or unfractionated heparin (UFH) during the index hospitalization. VTE prophylaxis in the outpatient setting was determined based on pharmacy claims for the previously listed anticoagulants within 15 days after VTE diagnosis. Among patients who received inpatient and/or outpatient prophylaxis, the proportions of patients who received enoxaparin only, warfarin only, enoxaparin and warfarin combined, a DOAC only, and 'other' VTE prophylactic drug combinations or drugs (e.g. other anticoagulant combinations, fondaparinux, etc.) were evaluated.

VTE events

The proportions of patients with VTE events during the index hospitalization and within 6 months of hospital discharge were evaluated for each study group. A VTE event during the index hospitalization was based on the presence of an ICD-9-CM code for deep vein thrombosis (DVT) and/or pulmonary embolism (PE) at either primary or secondary position of discharge diagnosis codes. A VTE event during the post-discharge follow-up period was defined by the presence of a primary or secondary ICD-9-CM code for DVT and/or PE during an emergency room or inpatient admission, or on an outpatient claim with 1 or more of the following confirmatory events: a pharmacy claim for enoxaparin, fondaparinux, or UFH within 15 days after VTE diagnosis; or a pharmacy claim for warfarin or DOACs (apixaban, dabigatran, rivaroxaban, edoxaban) within 15 days after VTE diagnosis, and no evidence of atrial fibrillation or atrial flutter in the 6 months preceding the outpatient diagnosis for DVT and/or PE.[4] Cumulative VTE rates by time were also evaluated for each study group of patients with 1–3 day, 4–6 day, and ≥7 day LOSs with Kaplan–Meier analysis.

All-cause and VTE-related hospital readmissions

The proportions of patients with all-cause and VTE-related hospital readmissions in the 6-month post-discharge follow-up period were determined for each study group.

Statistical analyses

Descriptive statistics were utilized to evaluate differences in demographics, clinical characteristics, hospital characteristics, and VTE prophylaxis patterns between the study groups with different LOSs. ANOVA and chi-square tests were used to detect statistically significant differences in continuous and categorical variables, respectively. Multivariable logistic regression analyses were conducted to evaluate the influence of longer hospital LOSs on the likelihood of receiving any VTE prophylaxis in the inpatient or outpatient settings. Covariates in the regression models included gender, region, index acute medical illness, pre-index comorbidities (atrial fibrillation, VTE, major bleeding), and hospital characteristics, including admission source, urban/rural, teaching status, and bed size. Cumulative rates for VTE events occurring after the index hospital admission date were evaluated using Kaplan–Meier analysis for each study group. A critical value of 0.05 was used to determine statistical significance. All statistical analyses were carried out using SAS 9.4.

Results

Study population

Patient demographics, clinical, and hospital characteristics of the study population stratified by hospital LOSs are shown in Table 1. Of the overall population (n=17,895), 8647 (48.3%) had a 1–3 day LOS, 5551 (31.0%) had a 4–6 day LOS, and 3697 (20.7%) had a ≥7 day LOS. Mean index hospital LOSs for patients with 1–3 day LOS, 4–6 day LOS, and ≥7 day LOS were 2.2 days, 4.8 days, and 11.1 days, respectively. Patients with longer hospital LOSs were older (≥7 days: 62.8 years versus 4–6 days: 61.5 years versus 1–3 days: 54.5 years, $p<0.001$) and had greater comorbidity as measured by Charlson Comorbidity Index score (≥7 days: 2.6 versus 4–6 days: 2.3 versus 1–3 days: 1.9, $p<0.001$).

Across the study groups, most hospitals were urban (86–89%), nonteaching (95–96%), of large size (300 to ≥500 beds, 65–73%), and located in the South Census region (75–81%), reflecting the distribution of hospital records contained in the database.

VTE prophylaxis

A greater proportion of patients with a 1–3 day LOS (66.2%) did not receive any VTE prophylaxis in comparison to patients with a 4–6 day LOS (55.0%) and ≥7 day LOS (48.8%; $p<0.001$). More patients with a ≥7 day LOS (10.7%) received both inpatient and outpatient VTE prophylaxis than patients with a 4–6 day LOS (7.5%) and 1–3 day LOS (5.3%) years of age. Of patients who received inpatient VTE prophylaxis, most in any study group received enoxaparin only (1–3 day LOS: 80.5%; 4–6 day LOS: 76.3%; ≥7 day LOS: 71.6%, $p<0.001$; Table 2). In the outpatient setting, warfarin only was the most frequent anticoagulant patients received (1–3 day LOS: 41.3%; 4–6 day LOS: 44.4%; ≥7 day LOS: 46.3%, $p=0.11$; Table 2).

After controlling for differences in patient and hospital characteristics, the findings of the regression analysis showed

Table 1. Demographics, clinical, and hospital characteristics of study groups.

	LOS: 1–3 days n=8647		LOS: 4–6 days n=5551		LOS: ≥7 days n=3697		*p*-value
Age (years)							
Mean ± SD	54.5±23.3		61.5±19.6		62.8±17.1		<0.001
Median	58		63		63		
	n	%	n	%	n	%	
Age group (years)							<0.001
<18	872	10.1	185	3.3	36	1.0	
18–29	454	5.3	219	4.0	123	3.3	
30–39	549	6.4	267	4.8	206	5.6	
40–49	1004	11.6	548	9.9	331	9.0	
50–59	1738	20.1	1099	19.8	798	21.6	
60–64	1036	12.0	745	13.4	538	14.6	
65–69	615	7.1	462	8.3	333	9.0	
70–74	584	6.8	487	8.8	322	8.7	
75–79	584	6.8	447	8.1	350	9.5	
≥80	1211	14.0	1092	19.7	660	17.9	

(Continued)

Table 1. ***(Continued)***

	LOS: 1–3 days n=8647		LOS: 4–6 days n=5551		LOS: ≥7 days n=3697		*p*-value
Gender							<0.001
Female	4669	54.0	3208	57.8	2037	55.1	
Male	3978	46.0	2343	42.2	1660	44.9	
Health plan							<0.001
Comprehensive	3776	43.7	3039	54.8	2141	57.9	
HMO	1053	12.2	453	8.2	278	7.5	
CDHP	572	6.6	274	4.9	163	4.4	
EPO	9	0.1	2	0.0	1	0.0	
POS	406	4.7	212	3.8	133	3.6	
POS w/capitation	43	0.5	35	0.6	23	0.6	
PPO	2409	27.9	1354	24.4	854	23.1	
Missing/unknown	379	4.4	182	3.3	104	2.8	
Index hospitalization LOS (days)							<0.001
Mean ± SD	2.2±0.8		4.8±0.8		11.1±6.3		
Median	2		5		9		
Charlson comorbidity index (CCI), pre-index hospitalization							<0.001
Mean ± SD	1.9±2.2		2.3±2.4		2.6±2.5		
Median	1		2		2		
CCI score group	n	%	n	%	n	%	<0.001
CCI=0	2868	33.2	1463	26.4	794	21.5	
CCI=1–2	3350	38.7	2126	38.3	1392	37.7	
CCI=3–4	1426	16.5	1055	19.0	784	21.2	
CCI≥5	1003	11.6	907	16.3	727	19.7	
Census region							<0.001
South	6463	74.7	4320	77.8	2978	80.6	
North central	1283	14.8	778	14.0	457	12.4	
West	715	8.3	347	6.3	205	5.6	
Northeast	186	2.2	106	1.9	57	1.5	
Urban/rural status							<0.001
Urban	7472	86.4	4843	87.3	3287	88.9	
Rural	1175	13.6	708	12.8	410	11.1	
Teaching status							0.01
Yes	441	5.1	226	4.1	162	4.4	
No	8206	94.9	5325	95.9	3535	95.6	
Number of beds							<0.001
<200	1640	19.0	1013	18.3	531	14.4	
200–299	1349	15.6	807	14.5	463	12.5	
300–499	3574	41.3	2465	44.4	1777	48.1	
≥500	2084	24.1	1266	22.8	926	25.1	

CDHP, consumer-driven health plan; EPO, exclusive provider organization; HMO, health maintenance organization; LOS, length of stay; POS, point of service; PPO, preferred provider organization; SD, standard deviation.

Table 2. VTE prophylaxis treatments of study groups.

Inpatient VTE prophylaxis	**LOS: 1–3 days n=2709 (31.3%)**		**LOS: 4–6 days n=2357 (42.5%)**		**LOS: ≥7 days n=1777 (48.1%)**		***p*-value**
Anticoagulants	n	%	n	%	n	%	<0.001
Enoxaparin only	2180	80.5	1798	76.3	1273	71.6	
Enoxaparin + warfarin	101	3.7	129	5.5	132	7.4	
DOAC only	55	2.0	48	2.0	31	1.7	
Warfarin only	367	13.6	363	15.4	313	17.6	
Other[a]	6	0.2	19	0.8	28	1.6	
Outpatient VTE prophylaxis	**LOS: 1–3 days n=668 (7.7%)**		**LOS: 4–6 days n=558 (10.1%)**		**LOS: ≥7 days n=512 (13.9%)**		***p*-value**
Anticoagulants	n	%	n	%	n	%	0.11
Enoxaparin only	82	12.3	55	9.9	39	7.6	
Enoxaparin + warfarin	55	8.2	38	6.8	39	7.6	
DOAC only	91	13.6	87	15.6	60	11.7	
Warfarin only	276	41.3	248	44.4	237	46.3	
Other[a]	164	24.6	130	23.3	137	26.8	

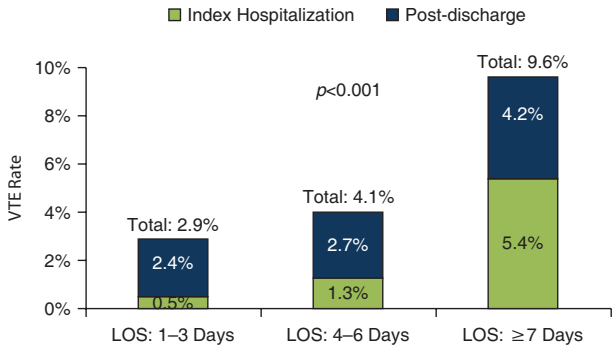
DOAC, direct oral anticoagulant; LOS, length of stay; VTE, venous thromboembolism.
[a]Includes other anticoagulant combinations not listed earlier as well as the use of other anticoagulants, such as fondaparinux.

that patients with a 4–6 day LOS (odds ratio [OR]: 1.6; confidence interval (CI): 1.5–1.7; $p<0.001$) and those with a ≥7 day LOS (OR: 2.1; CI: 2.0–2.3; $p<0.001$) had significantly greater likelihoods for receiving VTE prophylaxis than patients with only a 1–3 day LOS. Other patient and hospital characteristics associated with a greater likelihood for receiving VTE prophylaxis included being female versus male (OR: 1.1, $p=0.001$), having had a prior VTE event (OR: 2.8, $p<0.001$), rural versus urban hospital (OR: 1.4, $p<0.001$), and larger hospital size (200–299 versus 1–199 beds OR: 1.7, $p<0.001$; 300–499 versus 1–199 beds OR: 1.5, $p<0.001$; ≥500 versus 1–199 beds OR: 1.1, $p=0.035$).

VTE events

The proportions of patients with VTE events during the index hospitalization increased with longer hospital LOS (1–3 day LOS: 0.5%; 4–6 day LOS: 1.3%; ≥7 day LOS: 5.4%), as did the proportions of patients with VTE events during the 6-month follow-up period (1–3 day LOS: 2.4%; 4–6 day LOS: 2.7%; ≥7 day LOS: 4.2%) (Figure 1).

Figure 1. Proportions of patients with VTE events during the index hospitalization and within 6 months of hospital discharge of study population stratified by hospital LOS.



LOS, length of stay; VTE, venous thromboembolism

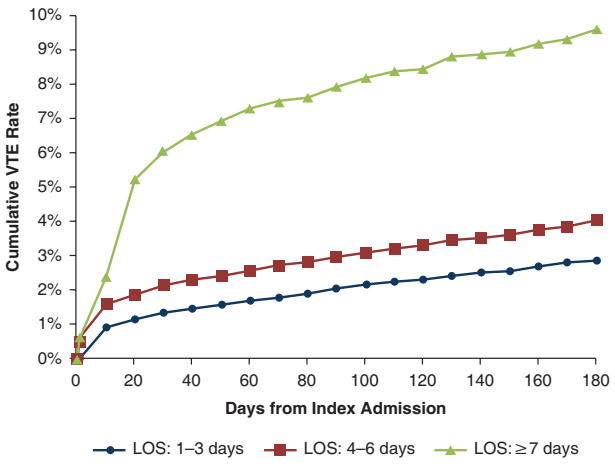
Cumulative VTE rates

Cumulative VTE event rate within 40 days of index hospital admissions was highest among patients hospitalized for ≥7 days (6.6%), followed by among those hospitalized for 4–6 days (2.3%), and among those hospitalized for 1–3 days (1.5%) (Figure 2). Among all study groups, VTE risk remained elevated up to 30–40 days after hospital admission. During the 6-month follow-up, the proportion of VTE events occurring within 40 days of index admissions was highest for patients with a ≥7 day LOS (68.2%), followed by for patients with a 4–6 day LOS (57.3%), and patients with a 1–3 day LOS (51.4%).

Hospital readmissions

Within 6 months of hospital discharge, 22.5% (n=1949), 28.0% (n=1553), and 34.8% (n=1288) of the study groups with a 1–3 day LOS, 4–6 day LOS, and ≥7 day LOS, respectively, had a hospital readmission for any cause. Of the hospital readmissions for any cause, 6.0% (n=117), 6.0% (n=93), and 9.8%

Figure 2. Cumulative VTE event rates during the follow-up period of the study population stratified by hospital LOS.



LOS, length of stay; VTE, venous thromboembolism

(n=126) were VTE-related among the study groups with a 1–3 day LOS, 4–6 day LOS, and ≥7 day LOS, respectively.

Discussion

In this retrospective analysis of nearly 18,000 patients hospitalized between January 2012 and June 2015 in the USA for acute medical illnesses, 48.3% had a 1–3 day LOS, 31.0% had a 4–6 day LOS, and 20.7% had a ≥7 day LOS. After controlling for differences in patient and hospital characteristics, those who had longer hospital LOSs were more likely to have received VTE prophylaxis than patients with only a 1–3 day LOS; however, one-half to two-thirds of patients within the study groups did not receive any VTE pharmacologic prophylaxis in the inpatient or outpatient setting. Also, patients with a ≥7 day LOS more frequently received VTE prophylaxis in both the inpatient and outpatient setting than patients with shorter durations of hospital LOS, but the proportion was still relatively low at 11%.

Of those patients who received VTE prophylaxis, most were administered enoxaparin in the inpatient setting and warfarin in the outpatient setting. DOACs were used to a limited extent in either setting. A strength of this study is the realistic capture of VTE prophylaxis patterns routinely practiced among a large population of patients who may be at increased risk for VTE. Although the duration of hospital stay is not predetermined at the time of the admission, it is generally assumed to correlate with patient disease severity across multiple disease conditions. Thus, the findings of this study provide useful information that details the VTE prophylaxis patterns of patients in the particular LOS categories of this study. Although the time period of our study was not long enough to identify temporal trends in VTE prophylaxis patterns, the results of our recent study on the overall population of hospitalized acutely ill patients were that 38.0 and 10% received inpatient and outpatient VTE prophylaxis.[12] This inpatient VTE prophylaxis rate is somewhat lower than that observed across other earlier conducted studies of hospitalized at-risk patients in the USA, in which rates ranged between 40 and 60%.[4,13–15] Among our study population, not all hospitalized acutely ill patients may have been considered at high risk for VTE based on the criteria of the ACCP (2012) and recommended to receive pharmacologic prophylaxis.[2] However, it is possible that a majority of those with longer hospital LOSs would have met such criteria, as they were older, had greater comorbidity, and were likely immobilized for a significant period of time.

The frequency of VTE events during both the index hospitalization and in the 6 months following hospital discharge was highest for patients with a ≥7 day LOS (9.6%), followed by those with a 4–6 day LOS (4.1%) and those with a 1–3 day LOS (2.9%). The majority of VTE events (51–68%) that occurred happened within the first 40 days after hospital admission for all study groups, with cumulative VTE rates within this time period being 1.5, 2.3, and 6.6% for patients with 1–3 day, 4–6 day, and ≥7 day LOS, respectively. Hospital readmissions that were VTE-related were also the most prevalent among patients with a ≥7 day LOS. Other characteristics of patients with longer LOS (i.e. greater disease severity, longer immobility) may have contributed to their greater risk for a VTE event, as well as their greater likelihood for receiving VTE prophylaxis; however, as mentioned the VTE prophylaxis rates for patients with a ≥7 day LOS were still low emphasizing the significant unmet need of this patient group.

The findings of our study show that among hospitalized acutely ill patients in the USA, VTE pharmacologic prophylaxis is underutilized, regardless of the duration of hospital stay. Although even when VTE pharmacologic prophylaxis, primarily in the inpatient setting, is received more frequently, the risk for VTE remains high, especially in the first 40 days following hospital discharge. In this study, VTE event rates were more than 2–3 times higher for patients with a ≥7 day LOS than patients with shorter hospital stays. These observations are similar in certain aspects to that of Merah and investigators who identified acutely ill immobilized patients who had a symptomatic VTE event from the international RIETE (Registro Informatizado Enfermedad TromboEmbolica) database.[9] In this latter study, outcomes of all-cause-death, fatal PE, VTE recurrences, and major bleeding did not significantly differ between patients who did (37%) and did not receive VTE prophylaxis during their period of immobility.[9] The findings of Merah et al and our study suggest that currently used VTE prophylaxis strategies may not only be underutilized, but also that they may not be used appropriately (e.g. suboptimal duration) and/or may be ineffective for reducing VTE risk for many acutely ill hospitalized patients. Likewise, using data collected from the Rochester Epidemiology Project, Heit et al reported that when VTE prophylaxis during hospitalization was increased from 40 to 90%, VTE attack rates did not significantly

change.[3] Despite these rather negative studies, some other recent studies conducted in England have demonstrated that when hospitals comply with nationally developed VTE risk assessment tools and provide VTE prophylaxis to those determined to be most at risk there is a significant decline in the occurrence of hospitalization-related VTE.[16–18]

To address the unmet need for standardized and validated VTE risk assessment tools and prophylaxis strategies among acutely ill hospitalized patients in the USA, new paradigms are actively being implemented.[19] These paradigms involve the incorporation of validated Risk Assessment Models (RAMs) during hospital admission, which will be used to identify acutely ill hospitalized patients who are at increased risk for VTE and would benefit most from receiving VTE prophylaxis.[19] The use of these newly developed and standardized VTE RAMs for US hospitals was mandated by the Center for Medicare and Medicaid Services (CMS) as of January 1, 2017.[19]

There is also a need for more efficacious VTE prophylaxis medications in that they not only reduce the risk for VTE over commonly used anticoagulant medications, but also do not impart a greater risk for bleeding, which is important for many acutely ill hospitalized patients. Toward these goals, the Acute Medically Ill VTE Prevention With Extended-Duration Betrixaban (APEX) trial, recently showed that extended-duration betrixaban compared to standard-duration enoxaparin was associated with reduced risk for VTE (5.3 versus 7.0%; relative risk: 0.76; CI: 0.63–0.92; p=0.006) and no significant increase in the risk for major bleeding (0.7 versus 0.6%; relative risk: 1.19; 95% CI: 0.67–2.12; p=0.55).[10] Furthermore, in a follow-up analysis of participants in the APEX trial, extended-duration betrixaban versus standard-duration enoxaparin was also associated with a reduced risk of VTE-related rehospitalization at 42 days (0.25 versus 0.75%) and at 77 days (0.45 versus 1.04%).[20]

Potential limitations

Retrospective, observational, claims database analyses have certain limitations. First, claims within the MarketScan commercial and Medicare supplemental databases may not generalize to patients insured by Medicaid. Also, the majority of claims in the MarketScan databases are from patients located in the South Census region and may not be generalizable to other US geographic regions. However, the MarketScan databases are generally considered robust in data, and such information is likely representative of real-world patterns associated with routine clinical practice. In claims databases, there is not reliable information to differentiate from VTE present at admission versus VTE that developed during hospital stays. Especially in the case of those patients with short (1–3 days) LOS, the proportion of VTE events that were present at hospital admission may be higher. In this study, we measured all diagnosed VTE events. Despite this limitation our data display a clear trend that increasing hospital LOS is associated with greater risk for VTE. Additionally, the degree of VTE risk could not be discerned for patients in this study due to current limitations of the databases. Furthermore, other events (e.g. cancer diagnosis, knee or hip surgery, etc.) that may have occurred during the follow-up period of the study population may impact VTE risk. Due to the retrospective, observational nature of this study and other limitations of the MarketScan databases, a causal relationship between such events and the occurrence of VTE cannot be established. Some patients in the study population, particularly in the inpatient setting, may have received a prescription for warfarin or a DOAC for a condition other than VTE prophylaxis, such as atrial fibrillation, and this could have led to an overestimation of VTE prophylaxis in the study population. Also, VTE prophylaxis rates may be higher when mechanical VTE prophylaxis is considered, which was not measured in this study, as the data sources do not contain reliable information on mechanical VTE prophylaxis. The observational design of this study is susceptible to various biases, such as information or classification bias (e.g. identification of false-positive VTE events). Lastly, as this study was a retrospective, observational analysis, causality between VTE prophylaxis and VTE event occurrence cannot be established.

Conclusion

In this study, acutely ill hospitalized patients with a longer LOS were more likely to have received VTE prophylaxis than patients with a shorter LOS; however, approximately one-half to two-thirds of patients within the study groups with different LOSs did not receive any VTE pharmacologic prophylaxis in the inpatient or outpatient setting. Among this study population of acutely ill hospitalized patients, the risk for VTE events was substantial, with nearly 10% of those with a ≥7 day LOS having suffered a VTE event within 6 months of hospital admission (68% occurred within 40 days of index admissions). Greater utilization of appropriate VTE pharmacologic prophylaxis regimens among these hospitalized acutely ill patients who are older, have greater comorbidity, and are likely to have reduced immobility for a longer time, may provide a significant benefit and help to reduce the clinical and economic burden of VTE.

Contributions: All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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Correspondence: Alpesh Amin, School of Medicine University of California, Irvine, UCIMC, 101 The City Drive South Building 58, Room 110, ZC-4076H, Mail Code: 4076, Irvine, CA 92868, USA. anamin@uci.edu

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