Trends of Inpatient Venous Thromboembolism in United States Before and After the Surgeon General's Call to Action

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Venous thromboembolism (VTE) is an important cause of morbidity and mortality in the United States (US). The increasing rates of VTE in the US resulted in the surgeon general issuing a call to action to reduce VTE in 2008. The objective of our study was to analyze the national trends of inpatient VTE in the US from 2004 to 2013 (5 years before and after 2008). We used the dataset National Inpatient Sample, Healthcare Cost and Utilization Project and measured trends of inpatient VTE by annual % change using joinpoint regression software. From 2004 to 2013 the National Inpatient Sample contained data on 78 million hospitalizations (weighted n = 385 million). In these 1.6 million had a diagnosis of VTE (2.0%, weighted n = 7.7 million) including 1.2 million with deep venous thrombosis (DVT) (1.53%, weighted n = 5.9 million) and 588,878 with pulmonary embolism (PE) (0.74%, weighted n = 2.8 million). Joinpoint regression analysis showed that rates of DVT and PE are increasing consistently from 2004 to 2013(1.27% to 1.80% for DVT and 0.52% to 0.92% for PE). The increasing rates of DVT and PE were consistent in all subgroups except few exceptions. In conclusion inpatient VTE rates continue to rise even after 5 years from the surgeon general's a call to action except in certain high-risk patients. Further research is needed to curb the VTE in patients especially among those perceived to be at lower risk of VTE. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;124:960−965)

Venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) is an important cause of morbidity and mortality in the United States (US). The increasing rates of VTE in the US lead to The Surgeon General issuing a call to action to reduce VTE in 2008.[1] After 2008, several organizations have issued guidelines on VTE prophylaxis based on various risk factors in patients admitted to hospital which includes risk assessment reminders and suitable actions based on evidence.[2,3] However, it is unknown whether the rates of VTE have changed since 2008. The objective of this study is to determine the national trends of inpatient VTE, DVT, and PE in the US from 2004 to 2013 (5 years before and after The Surgeon General's a call to action).

Methods

We used the National Inpatient Sample (NIS), one of the largest publicly available inpatient dataset in US for our analysis. NIS is published by Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality.[4] NIS represents a 20% stratified random sample of discharges from all hospitals, excluding rehabilitation and long-term acute care hospitals. NIS is drawn from all states participating in HCUP, representing more than 95% of the US population and uses National Health Survey Strata to weigh each participating hospital. Discharge weights are provided for each entry and are used to project to a nationally representative population. The details of NIS method have been previously published by the HCUP.[5]

All patients available in the NIS data were included in the study. VTE was defined by ICD9 codes 451 to 453 (DVT) and 415.1 (PE).[6] Annual rates (per 100 hospitalization) of inpatient VTE were calculated from 2004 to 2013 by patient characteristics (age, gender, and race), hospital type, insurance type, and certain high-risk groups (Padua score[7] ≥ 4, patients with cancer, patients who underwent major operative procedures [OR] or trauma, patients with previous history of VTE, patients with history of thrombophilia, and patients with immobility). Subgroup analysis was performed to evaluate for variations in trends. Approximate Padua score was calculated using ICD9 codes for risk stratification (Supplement Table 1). Trend weights provided by HCUP were used to generate national estimates.[5]

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See page 964 for disclosure information.

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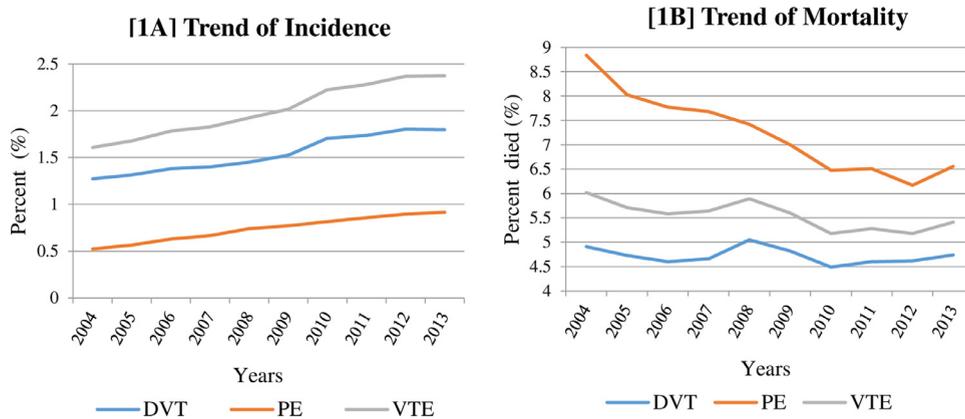E-mail address: kmehta2@kumc.edu (K.D. Mehta).

Figure 1. Trends of incidence (A) and mortality (B) of inpatient venous thromboembolism (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE) in United States from 2004 to 2013. Abbreviations: DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

Although there are other VTE risk assessment models (Caprini score, Kucher model, Geneva risk score, and IMPROVE score); previous studies have shown that they are difficult to compare and none is an ideal risk assessment model.[8] Hence, we chose Padua score as an example for patients with high risk of VTE.

SAS 9.3 (SAS Institute Inc., Cary, North Carolina) was used to calculate annual rates of VTE per 100 hospitalization. Joinpoint regression program was used to detect significant changes in the direction and magnitude of trend of VTE and related-inpatient mortality.[9] Joinpoint regression uses the grid search method to detect points at which statistically significant changes (p <0.05) occur in the direction and magnitude of trend under the assumption of constant variance and uncorrelated errors.[10] In this study "0" joinpoint represents no change in the trend and "1" joinpoint represents change in either magnitude or direction depending on the positive or negative slope. Positive slope means increasing rates and negative slope means decreasing rates.

Results

From 2004 to 2013 the NIS contained data on 78 million hospitalizations (weighted n = 385 million). In these 1.6 million had a diagnosis of VTE (2.0%, weighted n = 7.7 million) including 588,878 with PE (0.74%, weighted n = 2.8 million) and 1.2 million with DVT (1.53%, weighted n = 5.9 million). Joinpoint regression analysis showed that

rates of DVT are increasing consistently from 1.27% in 2004 to 1.80% in 2013 with no significant change in the direction and magnitude (Figure 1 and Table 1). Similarly, rates of PE are also increasing from 0.52% in 2004 to 0.92% in 2013 with marginal decline in magnitude of slope in recent years (Figure 1 and Table 1). The amount of patients with high risk of VTE (Padua score ≥ 4) was 15.0% and they contributed to 34.1% of total VTE events. Patients with a high risk of VTE increased from 12.46% to 18.21% from 2004 to 2013 (p <0.001). In patients with VTE, the inpatient mortality rates are decreasing consistently from 2004 to 2013 with no significant change in the direction and magnitude (Figure 1 and Table 1). The inpatient mortality rate was higher in high-risk VTE group compared with low-risk group (7.77% vs 3.07%, p <0.0001 for DVT and 11.40% vs 5.07%, p <0.0001 for PE), although overall tread is decreasing in both groups (Supplement Figure 1).

The subgroup analysis showed that the rates of DVT and PE continued to increase either without any change in magnitude or marginal drop in magnitude for most of the subgroups by age categories, gender, race, hospital type (teaching status, location, and bed size), insurance type as well as VTE risk factors (Tables 2 and 3, Figure 2, Supplement Figure 1 to 4). The exceptions were 75 to 84 years of age, 85 and more than 85 years of age, urban nonteaching hospital, Medicare primary payer, male gender, patients with high-risk VTE (Padua score ≥ 4), patients with history of thrombophilia, major OR, and trauma subgroups in which the rates of DVT have started

Table 1

The trends of incidence and mortality of inpatient venous thromboembolism (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE) measured by annual percentage change (APC) using joinpoint regression analysis from 2004 to 2013 (n = 1.6 million, weighted n = 7.7 million)

Subgroups	No. of joinpoint	Joinpoint year	p Value*	Timeframe 1	Slope of timeframe 1 (APC) (%)	Timeframe 2	Slope of timeframe 2 (APC) (%)
Total population							
DVT	0	-	0.58	2004-2013	+4.4	-	-
PE	1	2008	0.001	2004-2008	+9.1	2008-2013	+4.7
VTE	0	-	0.1411	2004-2013	+4.8	-	-
Mortality							
DVT	0	-	0.8831	2004-2013	−0.4	-	-
PE	-	-	-	-	-	-	-
VTE	0	-	0.110	2004-2013	−3.6	-	-

APC = annual percentage change; - = not available; DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.
* p Value of joinpoint regression at 95% confidence interval <0.05.

Table 2

The trends of deep vein thrombosis (DVT) measured by annual percentage change (APC)* using joinpoint regression analysis from 2004 to 2013. (n = 1.2 million, weighted n = 5.9 million)

Subgroups	No. of joinpoint	Joinpoint year	p Value[†]	Timeframe 1	Slope of timeframe 1 (APC)* (%)	Timeframe 2	Slope of timeframe 2 (APC)* (%)
Total population	0	-*	0.58	2004-2013	+4.4	-	-
Age (years)							
0-14	0	-	0.175	2004-2013	+7.8	-*	-
15-24	0	-	0.624	2004-2013	+6.0	-	-
25-34	0	-	0.673	2004-2013	+4.8	-	-
35-44	0	-	0.524	2004-2013	+3.9	-	-
45-54	0	-	0.469	2004-2013	+3.9	-	-
55-64	0	-	0.555	2004-2013	+3.5	-	-
65-74	0	-	0.065	2004-2013	+3.3	-	-
75-84	1	2011	0.036	2004-2011	+3.92	2011-2013	−0.18
≥85	1	2011	0.023	2004-2011	+3.85	2011-2013	−1.41
Sex							
Male	1	2011	0.003	2004-2011	+5.69	2011-2013	+0.12
Female	0	-	0.220	2004-2013	+3.3	-	-
Races							
White	0	-	0.102	2004-2013	+3.8	-	-
Black	0	-	0.054	2004-2013	+4.7	-	-
Hispanic	0	-	0.106	2004-2013	+6.0	-	-
Asian/Pacific islander	1	2006	0.007	2004-2006	+17.0	2006-2013	+3.7
Native American	0	-	0.501	2004-2013	+5.3	-	-
Other races	0	-	0.158	2004-2013	+6.6	-	-
Hospital bed size							
Small	0	-	0.443	2004-2013	+3.6	-	-
Medium	0	-	0.317	2004-2013	+3.9	-	-
Large	0	-	0.233	2004-2013	+4.4	-	-
Hospital location							
Rural	0	-	0.154	2004-2013	+2.8	-	-
Urban-nonteaching	1	2011	0.011	2004-2011	+4.79	2011-2013	−3.35
Urban-teaching	0	-	0.386	2004-2013	+4.5	-	-
Payment method							
Medicare	1	2011	0.046	2004-2011	+3.99	2011-2013	−0.56
Medicaid	0	-	0.612	2004-2013	+5.8	-	-
Private insurance	0	-	0.077	2004-2013	+4.3	-	-
Self-pay	0	-	0.287	2004-2013	+6.9	-	-
No other charges	0	-	0.496	2004-2013	+4.5	-	-
Other payment methods	0	-	0.662	2004-2013	+2.5	-	-
High-risk VTE *,[‡]							
Yes	1	2011	0.006	2004-2011	+5.0	2011-2013	−0.6
No	0	-	0.21	2004-2013	+2.6	-	-
Cancer							
Yes	0	-	0.53	2004-2013	3.4	-	-
No	0	-	0.071	2004-2013	4.0	-	-
Major OR* procedure or trauma							
Yes	1	2011	0.004	2004-2011	+6.4	2011-2013	−1.6
No	0	-	0.33	2004-2013	+3.6	-	-
Previous VTE							
Yes	0	-	0.34	2004-2013	+3.5	-	-
No	0	-	0.07	2004-2013	+3.4	-	-
History of thrombophilia							
Yes	1	2011	0.04	2004-2011	-0.2	2011-2013	−4.9
No	0	-	0.14	2004-2013	+3.9	-	-
Immobility							
Yes	1	2010	0.005	2004-2010	+9.1	2010-2013	+1.6
No	0	-	0.09	2004-2013	+4.0	-	-
Obesity							
Yes	1	2007	0.54	2004-2007	+1.7	2007-2013	+5.5
No	1	2011	0.04	2004-2011	+4.54	2011-2013	−1.05

* Abbreviation: - = not available; APC = annual percentage change; OR = operative room; VTE = venous thromboembolism.

[†] p Value of joinpoint regression at 95% confidence interval <0.05.

[‡] High-risk VTE was defined as patients with Padua score >=4.

Table 3
The trends of pulmonary embolism (PE) measured by annual percentage change (APC)* using joinpoint regression analysis from 2004 to 2013. (n = 588,878, weighted n = 2.8 million)

Subgroups	No. of joinpoint	Joinpoint year	p Value[†]	Timeframe 1	Slope of timeframe 1 (APC)* (%)	Timeframe 2	Slope of timeframe 2 (APC)* (%)
Total population	1	2008	0.001	2004-2008	+9.1	2008-2013	+4.7
Age (years)							
0-14	0	-*	0.352	2004-2013	+5.5	-	-
15-24	1	2011	0.024	2004-2011	+9.8	2011-2013	−0.88
25-34	1	2010	0.008	2004-2010	+8.8	2010-2013	+2.9
35-44	1	2010	0.002	2004-2010	+10.3	2010-2013	+2.2
45-54	1	2009	0.0002	2004-2009	+9.2	2009-2013	+3.8
55-64	1	2008	0.0002	2004-2008	+8.8	2008-2013	+3.1
65-74	1	2008	0.0002	2004-2008	+8.4	2008-2013	+2.7
75-84	1	2008	0.0002	2004-2008	+7.9	2008-2013	+2.5
≥85	1	2008	0.0002	2004-2008	+8.1	2008-2013	+1.8
Sex							
Male	1	2009	0.0009	2004-2009	+9.7	2009-2013	+2.9
Female	1	2009	0.003	2004-2009	+8.0	2009-2013	+2.7
Races							
White	1	2009	0.0002	2004-2009	+9.0	2009-2013	+2.4
Black	1	2008	0.002	2004-2008	+11.0	2008-2013	+4.5
Hispanic	1	2008	0.024	2004-2008	+14.6	2008-2013	+5.1
Asian/Pacific islander	1	2007	0.0002	2004-2007	+22.8	2007-2013	+4.5
Native American	0	-	0.053	2004-2013	+8.3	-	-
Other races	1	2010	0.042	2004-2010	+10.41	2010-2013	−1.94
Hospital bed size							
Small	1	2006	0.034	2004-2006	+19.5	2006-2013	+5.7
Medium	1	2007	0.010	2004-2007	+11.0	2007-2013	+4.8
Large	1	2009	0.001	2004-2009	+8.5	2009-2013	+2.6
Hospital location							
Rural	1	2010	0.001	2004-2010	+8.4	2010-2013	+3.3
Urban-nonteaching	1	2009	0.0007	2004-2009	+9.5	2009-2013	+2.3
Urban-teaching	1	2008	0.008	2004-2008	+9.2	2008-2013	+3.7
Payment method							
Medicare	1	2008	0.0002	2004-2008	+8.0	2008-2013	+2.6
Medicaid	1	2010	0.044	2004-2010	+11.2	2010-2013	+3.7
Private insurance	1	2010	0.0006	2004-2010	+9.6	2010-2013	+0.4
Self-pay	1	2011	0.035	2004-2011	+12.0	2011-2013	+2.9
No other charges	0	-	0.671	2004-2013	+8.7	-	-
Other payment methods	1	2011	0.028	2004-2011	+8.91	2011-2013	−4.11
High-risk VTE *[,‡]							
Yes	1	2008	0.0002	2004-2008	+8.9	2008-2013	+1.5
No	1	2010	0.003	2004-2010	+7.4	2010-2013	+1.7
Cancer							
Yes	1	2007	0.0004	2004-2007	+10.3	2007-2013	+3.2
No	1	2010	0.003	2004-2010	+8.1	2010-2013	+1.6
Major OR* procedure or Trauma							
Yes	1	2009	0.0009	2004-2009	+8.2	2009-2013	−0.3
No	1	2009	0.003	2004-2009	+9.1	2009-2013	+3.8
Previous VTE*							
Yes	0	-	0.11	2004-2013	+4.4	-	-
No	1	2009	0.002	2004-2009	+8.3	2009-2013	+2.2
History of Thrombophilia							
Yes	1	2008	0.0002	2004-2008	+4.4	2008-2013	−4.9
No	1	2009	0.002	2004-2009	+8.4	2009-2013	+3.0
Immobility							
Yes	1	2009	0.002	2004-2009	+11.1	2009-2013	+2.6
No	1	2009	0.002	2004-2009	+8.8	2009-2013	+2.9
Obesity							
Yes	1	2010	0.001	2004-2010	+6.42	2010-2013	+0.82
No	1	2008	0.001	2004-2008	+9.29	2008-2013	+2.96

* Abbreviation: - = not available; APC = annual percentage change; OR = operative room; VTE = venous thromboembolism.
[†] p Value of joinpoint regression at 95% confidence interval <0.05.
[‡] High-risk VTE was defined as patients with Padua score >=4.

Trend of mortality with high risk VTE subgroups

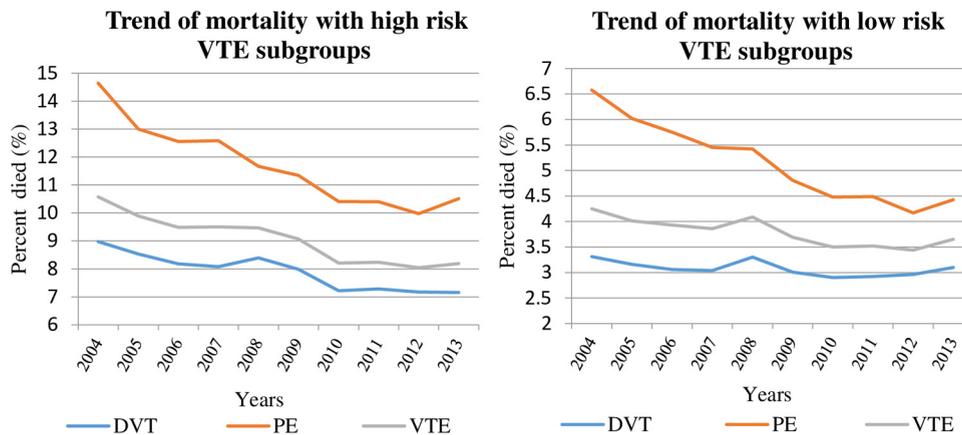## Trend of mortality with low risk VTE subgroups

Figure 2. Trends of inpatient mortality in patients with VTE, PE, and DVT by risk of VTE subgroups. Abbreviations: DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

to decrease in recent years. In patients with PE, patients categorized according to 15 to 24 years of age, other payment methods, other races, patients with a history of thrombophilia, major OR, and trauma patients subgroups had decreased rates of PE in recent years (Table 3).

Discussion

Since The Surgeon General issued a call to action to reduce VTE in 2008, several hospitals have introduced VTE prevention programs. The VTE prevention programs tend to focus on high-risk patients and involve using prophylactic anticoagulants and attempts to increase the mobility of the patients. The results of this study show that, despite these initiatives, VTE rates continue to rise except in certain high-risk patients. The collaborative efforts to prevent VTE have certainly reduced the VTE rates in high-risk patients (advanced age, Padua score ≥ 4, patients who underwent major OR or trauma, and patients with history of thrombophilia). However, patients with estimated Padua score ≥4 contributed to less than half of VTE events and the VTE rates continue to rise in patients perceived to be at lower risk of VTE. This suggests an existence of "Rose Paradox,"[11] where intervention directed at high-risk patients may not reduce the burden of VTE in population.

The continued rise in VTE rates could be partly due to higher utilization of diagnostic tests (CT angiogram, V/Q scan, and duplex ultrasonography) in recent years. However, the imaging studies are more likely to be over used in high-risk patients. So, overutilization of imaging studies is unlikely to explain increasing VTE rates in low-risk patients. Although increasing population can be attributed to increase in incidence of VTE, proportional increase in number of admissions can be seen. In recent years, several hospitals have introduced automated electronic medical record prompts to start VTE prophylaxis or have employed designated personnel to identify high-risk patients and provide them with VTE prophylaxis.[12] Such interventions could have led to better adherence of VTE prevention guidelines in high-risk patients which can explain the decline in VTE noted in this study in high-risk patients.

Most of the VTE risk prediction systems rely on generating scores for VTE risk based on preselected variables.[7,13]

However, unknown factors which can potentially affect the VTE risk will not be part of any such system which relies on previously known risk factors. The artificial intelligence techniques such as deep learning,[14] which does not rely on prespecified variables may provide more promising approach to identify patients at risk of VTE. However, this approach is yet to be developed and eventually tested in real world setting.

Our study has several limitations. The NIS does not contain data on medications and radiologic tests. So, we are unable to study utilization of VTE prophylaxis or radiologic tests. Since, the NIS does not contain patient identifiers; we are unable to verify the documented diagnoses for patients. Validity of approximate Padua score could not be established based on available studies and Padua might underestimate VTE risk in obese patients hospitalized for acute illness. Majority of DVT's are treated as outpatient which are not captured in NIH data and we are unable differentiate patients hospitalized with DVT versus new inpatient DVT's. However, despite these limitations, the large size of the dataset and nationally representative sampling technique make the results comparable across the time frame of the study.

In conclusion, The Surgeon General's a call to action in 2008, the VTE rates have continued to rise except in certain high-risk patients. This study re-emphasizes the need to curb the increasing trend of inpatient VTE, especially in those who are perceived to be at lower risk of VTE.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.06.015.

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