Descriptive Analysis of Venous Thromboembolism in Georgia Trauma Centers Compared with National Trauma Centers Participating in the Trauma Quality Improvement Program

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This study was designed to compare the incidence of venous thromboembolism (VTE) in Georgia trauma centers with other national trauma centers participating in the Trauma Quality Improvement Program (TQIP). The use of chemoprophylaxis and characteristics of patients who developed VTE were also examined. We conducted a retrospective observational study of 325,703 trauma admissions to 245 trauma centers from 2013 to 2014. Patient demographics, rate of VTE, as well as the use, type, and timing of chemoprophylaxis were compared between patients admitted to Georgia and non-Georgia trauma centers. The rate of VTE in Georgia trauma centers was 1.9 per cent compared with 2.1 per cent in other national trauma centers. Overall, 49.6 per cent of Georgia patients and 45.5 per cent of patients in other trauma centers had documented chemoprophylaxis. Low molecular weight heparin was the most commonly used medication. Most patients who developed VTE did so despite receiving prophylaxis. The rate of VTE despite prophylaxis was 3.2 per cent in Georgia and 3.1 per cent in non-Georgia trauma centers. Mortality associated with VTE was higher in Georgia trauma centers compared with national TQIP benchmarks. The incidence of VTE and use of chemoprophylaxis within Georgia trauma centers were similar to national TQIP data. Interestingly, most patients who developed VTE in both populations received VTE prophylaxis. Further research is needed to develop best-practice guidelines for prevention, early detection, and treatment in high-risk populations.

DEEP VENOUS THROMBOSIS (DVT) and pulmonary embolism (PE), collectively referred to as venous thromboembolism (VTE), are a common cause of morbidity, mortality, and increased healthcare costs for hospitalized patients. Trauma patients are a particularly high-risk population who often present with at least one, if not all three, points of Virchow's triad that includes stasis, endothelial injury, and hypercoagulability. Without chemoprophylaxis, the rate of DVT among trauma patients exceeds 50 per cent.[1] Even with chemoprophylaxis, the rate of VTE development during a trauma admission ranges from 2 to 13.9 per cent.[2, 3] Variability in observed rate can be attributed to many things including well documented varied aggressiveness in screening for VTE amongst trauma centers nationally.

PE is among the top three leading causes of mortality in trauma patients who survive beyond the first 24 hours.[1, 4] Estimates of mortality from PE range from 0.38 to 40 per cent.[5, 6] Moreover long term complications from DVT, termed postphlebitic syndrome, occurs in 23 to 60 per cent of patients.[7] A review of the long-term costs of venous thromboembolism found that in-hospital costs were 2.5-fold higher than case-matched controls.[8]

Georgia is one of the few states where all level I and II Trauma Centers participate in the American College of Surgeon's Trauma Quality Improvement Program (TQIP). Over the last two years, all trauma centers medical leadership has participated in monthly TQIP conference calls organized by the state's Committee on Trauma, and this group has formed a state collaborative with the goal to develop the groundwork for

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a state-wide performance improvement program. Initially, the focus was on data quality for all centers.[9] With this background, the collaborative decided to study VTE because it is a significant quality metric for all trauma centers. Recognizing the importance of prevention of VTE after injury, the ultimate goal of the statewide collaborative is to develop and implement an evidence-based consensus protocol to minimize VTE complications across Georgia trauma centers. As the initial phase of the VTE project, the current study was conducted with three aims: 1) identify the rate of VTE for all Georgia hospitals participating in TQIP and compare them with TQIP benchmarks, 2) define trends in the use, type, and timing of chemoprophylaxis in Georgia TQIP hospitals as compared with national norms, and 3) describe the characteristics of cases of VTE for Georgia TQIP hospitals compared with outcomes of VTE across the country.

Methods

Data were collected from the American College of Surgeons TQIP database between 2013 and 2014.[10] The study was approved by the Augusta University Institutional Review Board (IRB 808344–2). All cases that met criteria for entry into the national TQIP database during the study period were included. The American College of Surgeons National Trauma Data Standard was used to define DVT and PE. Venous thromboembolism was defined as the presence of DVT, PE, or both.

We analyzed the following variables from the national dataset: location of hospital (state of Georgia or not), patient age, gender, race, injury type, Injury Severity Score (ISS), hospital length of stay, in-hospital mortality, presence of VTE as a complication, use of chemoprophylaxis, method of chemoprophylaxis, and time from admission to initiation of chemoprophylaxis. Patients with unknown VTE status were excluded from analysis of VTE rate. Chi-squared tests were employed to compare categorical variables. Student's t tests and Wilcoxon rank sum tests were used to compare parametric and nonparametric continuous variables, respectively. Significance level was determined at α level 0.05. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC) and SigmaPlot version 13 (Systat Software Inc., San Jose, CA).

Results

The dataset of interest included 325,703 admissions to 245 Level I and Level II trauma centers, including 14 Georgia trauma centers (n = 14,508) and 231 non-Georgia trauma centers (n = 311,195). Table 1 shows the demographics of these two trauma populations. In general, patients in Georgia centers were slightly younger, more likely to be male, and there was a higher proportion of blacks. Georgia patients tended to stay in

TABLE 1. *Demographics and Outcome in Georgia* versus *Non-Georgia Trauma Centers*

	Georgia Trauma Centers (n = 14,508)	Non-Georgia Trauma Centers (n = 311,195)	*P*
Age, years	49.4 ± 21.5	53.9 ± 22.8	<0.0001
Gender, n (%)			<0.0001
Male	9,424 (65.0)	195,886 (63.0)	
Female	5,081 (35.0)	115,068 (37.0)	
Race, n (%)			
White	9,103 (62.7)	230,815 (74.2)	<0.0001
Black	4,226 (29.1)	36,821 (11.8)	<0.0001
Asian	205 (1.4)	5,601 (1.8)	0.0006
Other	797 (5.5)	29,308 (9.4)	<0.0001
Unknown	177 (1.2)	8,650 (2.8)	<0.0001
Injury type, n (%)			<0.0001
Blunt	12,724 (87.7)	285,523 (91.7)	
Penetrating	1,784 (12.3)	12,724 (8.3)	
ISS	16.5 ± 8.9	16.3 ± 8.8	0.002
Chemical VTE prophylaxis, n (%)			
Yes	7,193 (49.6)	141,584 (45.5)	<0.0001
No	6,342 (43.7)	105,021 (33.8)	<0.0001
Unknown	973 (6.7)	64,590 (20.8)	<0.0001
Time to initiation of chemoprophylaxis, hours	39.1 ± 52.1	32.2 ± 43.1	<0.001
Length of stay, days	8.9 ± 9.9	7.9 ± 9.1	<0.0001
Mortality, n (%)	1,038 (7.2)	20,041 (6.4)	0.0006

Age, ISS, and length of stay are expressed as mean ± standard deviation. Time to initiation of prophylaxis is expressed as median ± interquartile range.

hospital one day longer and had a slightly higher rate of penetrating injury and ISS. They also had a slightly higher overall mortality rate.

Sixty-two patients in Georgia and 13,379 patients in the rest of the country had an "unknown" VTE complication status. This left 312,262 patients, encompassing 14,446 patients from 14 Georgia trauma centers and 297,816 patients from 229 non Georgia trauma centers. The overall rate of VTE in Georgia was not significantly different than the rest of the nation at 1.9 *versus* 2.1 per cent, $P = 0.0751$ (Table 2). The rate of DVT alone in Georgia trauma centers was 1.2 per cent compared with 1.5 per cent in other trauma centers ($P = 0.0082$). The rate of PE alone was 0.6 per cent in Georgia and 0.5 per cent in non-Georgia trauma centers ($P = 0.4719$). The incidence of having both DVT and PE in Georgia trauma centers was 0.2 per cent as compared to 0.1 per cent in the rest of the nation ($P = 0.7992$).

In Georgia, 49.6 per cent of TQIP patients had documented VTE chemoprophylaxis whereas 43.7 per cent did not have documentation of chemoprophylaxis, and 6.7 per cent were unknown (Table 1). Outside of Georgia, 45.5 per cent had documented VTE chemoprophylaxis whereas 33.8 per cent did not have documentation of chemoprophylaxis, and 20.8 per cent had unknown VTE prophylaxis status. VTE developed in 3.2 per cent of Georgia patients and 3.1 per cent of patients at other national centers who received prophylaxis. Low molecular weight heparin (LMWH) followed by heparin were the most commonly used methods of chemoprophylaxis in both study populations (Fig. 1). The median time to initiation of chemoprophylaxis was longer in Georgia at 39.1 hours compared with 32.2 hours in the rest of the nation, $P < 0.001$ (Table 1).

Of the patients who developed VTE, 83.9 per cent of Georgia patients and 70.6 per cent of patients in non-Georgia centers received chemoprophylaxis (Table 3). Again, LMWH was the most common form of chemoprophylaxis. The time to initiation of chemoprophylaxis was longer in Georgia trauma centers at a median of 87.6 *versus* 63.7 hours, $P < 0.001$. The mortality associated with VTE was significantly higher in Georgia centers at 11.3 per cent compared with 7.9 per cent in non-Georgia centers, $P = 0.0425$.

Discussion

Our results indicate that Georgia trauma centers, in aggregate, have a rate of VTE that is nearly identical to

TABLE 2. *Rate of VTE in Georgia and Non-Georgia Trauma Centers*

	Georgia Trauma Centers (n = 14,446)	Non-Georgia Trauma Centers (n = 297,816)	*P*
VTE	274 (1.9)	6,297 (2.1)	0.0751
DVT	173 (1.2)	4,369 (1.5)	0.0082
PE	80 (0.6)	1,519 (0.5)	0.4719
DVT & PE	21 (0.2)	430 (0.1)	0.7992

Rates expressed as n (%).

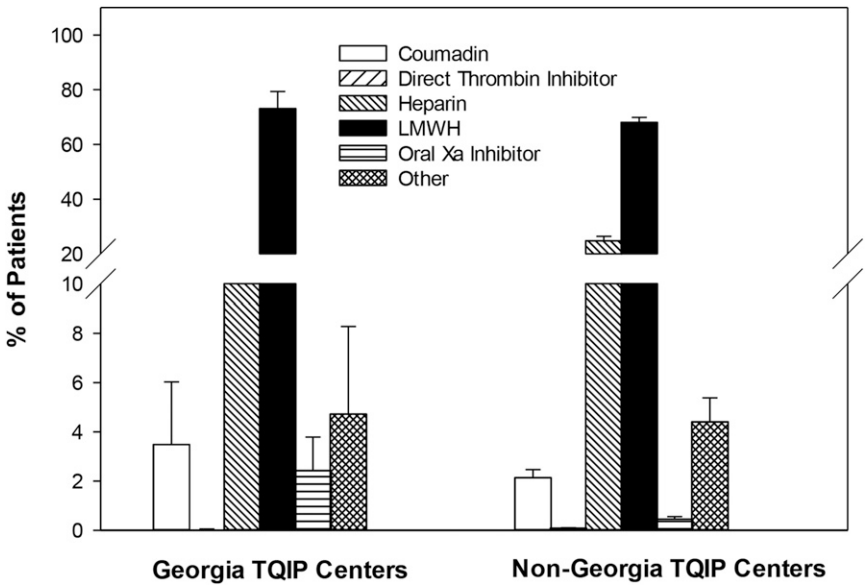

FIG. 1. Type of chemoprophylaxis in Georgia *versus* non-Georgia trauma centers.

TABLE 3. *Characteristics of Cases of VTE in Georgia and Non-Georgia Trauma Centers*

	VTE in Georgia Trauma Centers (n = 274)	VTE in Non-Georgia Trauma Centers (n = 6,297)	*P*
Chemical VTE prophylaxis, n (%)			
No	36 (13.1)	758 (12.0)	0.5841
Unknown	8 (2.9)	1091 (17.3)	<0.0001
Yes	230 (83.9)	4448 (70.6)	<0.0001
Type of chemoprophylaxis, n (%)			
LMWH	173 (75.2)	2848 (64.0)	<0.0001
Heparin	53 (23.0)	1472 (33.1)	0.1216
Coumadin	2 (0.9)	48 (1.1)	0.9519
Direct thrombin inhibitor	0 (0.0)	7 (0.2)	0.5808
Oral Xa inhibitor	2 (0.9)	9 (0.2)	0.0200
Other	0 (0.0)	64 (1.4)	0.0935
Time to initiation of chemoprophylaxis, hours	87.6 ± 143.5	63.7 ± 94.6	<0.001
ISS	23.1 ± 1.1	23.5 ± 1.2	0.890
Mortality, n (%)	31 (11.3)	498 (7.9)	0.0425

Time to initiation of prophylaxis is expressed as median ± interquartile range. ISS is expressed at mean ± standard deviation.

the national average (1.9 *vs* 2.1%) despite a longer length of stay, and a younger and more racially diverse population. Most patients who developed VTE received chemoprophylaxis, but the time to starting prophylaxis was longer in Georgia centers. The rate of VTE during the index admission despite prophylaxis in both Georgia and non-Georgia TQIP centers was similar at 3.2 and 3.1 per cent, respectively. However, the mortality (11.3 *vs* 7.9%) and the time to starting chemoprophylaxis in the population with a VTE diagnosis was significantly higher in Georgia centers compared with other TQIP centers. It is unclear why there is a higher mortality associated with VTE and an overall delay in starting chemoprophylaxis in Georgia. A more detailed analysis is in progress to better elucidate the reasons for these findings. Our rate of unknown status of VTE prophylaxis was significantly lower than the national TQIP norm (6.7 *vs* 20.8%). This we believe, is in no small part, the result of our previously published work on data integrity.[9]

Venous thromboembolism prevention and screening practices vary considerably between and within institutions. There is a general lack of consensus in the literature regarding the ideal method and timing of chemoprophylaxis for trauma patients. Studies on the topic are usually single institutional, often retrospective, and document highly variable rates of VTE (2–13.9%)[2, 3] and methods of chemoprophylaxis. Our observed 3.2 per cent rate of VTE in patients receiving prophylaxis is from a broader population and as such may be a better reflection of the rate.

A 2013 Cochrane Review concluded that VTE prophylaxis is superior to no prophylaxis. The authors found that both mechanical and chemical prophylaxis were shown to decrease DVT with chemical prophylaxis being superior, but there was no evidence that any prophylactic method consistently reduced PE or mortality.[11] There is an ongoing debate about the use of unfractionated heparin (UFH) *versus* LMWH for chemical VTE prophylaxis, after trauma. In a randomized trial, Geerts et al.[12] determined that low molecular weight heparin was superior to UFH when both were dosed twice a day, citing greater effectiveness in preventing VTE and low risks of major bleeding in both groups. However, a more recent study demonstrated no difference between three times a day UFH and daily LMWH.[13] Also Olson et al.[3] found UFH dosed three times a day to be noninferior in efficacy compared with low molecular weight heparin dosed twice a day. The former medication had the added appeal of 20-fold lower costs.[3]

In addition to the medications listed previously, pneumatic compression devices and inferior vena cava (IVC) filters can serve as mechanical VTE prophylaxis. Some of the most recent literature regarding the use of prophylactic IVC filters discourages placement because of lack of reduction in trauma patient mortality and an increase in DVT events.[14] In the ninth edition of the Chest guidelines, the American College of Chest Physicians recommends the use of low dose unfractionated heparin, LMWH, or mechanical prophylaxis, preferably with intermittent pneumatic compression while recommending against routine screening duplex ultrasounds and IVC filters for primary VTE prevention in major trauma patients.[15]

Traumatic brain injury (TBI) represents a subset of the trauma population at an especially high risk for development of VTE, which is likely partially attributable to delays in initiating chemoprophylaxis for fear of exacerbating intracranial hemorrhage. There is mounting evidence suggesting that chemoprophylaxis can be safely administered in TBI patients when started 24 hours after stable head CT.[16] Despite evidence that chemoprophylaxis reduces the incidence of VTE

in TBI patients without concomitant progression of intracranial hemorrhage, a single center's attempt to protocolize the initiation of "early" chemoprophylaxis in TBI was still met with a 20 per cent violation of the protocol.[17] Overall, the literature and national guidelines do not provide clear guidance to practitioners in how best to prevent this common and devastating complication in the context of TBI.

Georgia's TQIP collaborative pursued this initial evaluation of the incidence and outcomes of VTE in our state as an effort to lay the foundation for standardization of the diagnosis, prophylaxis, and therapy for this disease. There are very few state-wide collaboratives focusing on trauma quality improvement initiatives. A review of published regional collaborations for surgical quality improvement found universal reporting of improved clinical outcomes as well as several process measures, including the development infrastructure and establishment of trust among healthcare professionals and between institutions.[18] Collaboratives across institutions that encourage data sharing have also been shown to accelerate adoption of new standards associated with improved outcomes.[19]

Shafi et al.[20] reported finding significant variability in outcomes across trauma centers of similar resource designations and theorized that focus on structures and processes of high-performing trauma centers, as opposed to the availability of optimal resources, is key to improving trauma outcomes. TQIP was designed to provide individual centers with reports of their risk-adjusted outcomes in the form of observed-to-expected (O/E) ratios that can identify areas in which a hospital is a high or low performer in comparison with their peers.[21] The University of Michigan provides an example of improvement in the rate of posttraumatic VTE using a similarly aimed statewide collaborative. The Michigan Trauma Quality Improvement Program was able to identify the University of Michigan as a high outlier within the collaborative and effectively decrease the rate of VTE from 6.2 to 2.2 per cent by implementing a six-point action plan, including standardization of chemoprophylaxis type and dosing as well as monitoring of the time to prophylaxis initiation.[22]

Now that we have defined the scope of the problem of VTE within Georgia Trauma Centers as a whole, the next steps are to identify outliers within the group as well as the current VTE prevention strategies in participating hospitals in an effort to develop a statewide protocol for VTE prevention. The group will also work to review processes and outcomes surrounding special high-risk populations so that they can be stratified to receive more comprehensive prevention as well as earlier detection and treatment.

There are multiple limitations of our retrospective observational study design. Our study specifically focused on VTE prevention in the form of pharmacologic prophylaxis and did not take into account the use of mechanical prophylaxis. The integrity of our data is dependent upon the thoroughness of documentation of complications by individual centers. Exclusion of patients with unknown VTE complication status may bias our results. Another limitation of this study is the inability to discern differences in practice patterns between centers; it is conceivable that centers which routinely screen for DVT would report higher rates of VTE because of the recognition of subclinical disease. We can also infer that differences in the sensitivity of diagnostic equipment between institutions affects the recognition and thus reporting VTE. Unlike the National Surgical Quality Improvement Program, which tracks 30 day outcomes, TQIP only captures complications that occur within the index hospitalization. A cohort study of trauma and orthopedics patients, which followed participants for six months, found that PE occurred at a median of 23 days after injury or surgical intervention, and only 39 per cent of cases of PE were diagnosed during the initial inpatient admission.[5] Furthermore, we are unable to delineate differences in practice of dosing and holding anticoagulation after its initiation for procedures at the individual or institutional level. Lastly, we are unable to determine whether the circumstances in which patients did not receive prophylaxis involved contraindications to anticoagulation, adverse events related to its use, or otherwise.

Conclusions

The Georgia Trauma Collaborative successfully utilized the ACS TQIP dataset to identify and compare the rate of VTE and use of chemoprophylaxis in Georgia to the rest of the nation. Historically, similar-minded collaborations have been catalysts for performance improvement in trauma and surgery. Standardized datasets, such as TQIP, allow for continual data sharing between institutions that is crucial to fostering meaningful relationships. The information gained through these partnerships can be utilized to develop uniform protocols that save lives and cut costs. Future research will be aimed at developing best-practice guidelines for prevention and early treatment of VTE across the state.

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