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Does diabetes type increase the odds of venous thromboembolism following traumatic injury?

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ABSTRACT

Background Venous thromboembolism (VTE) remains a clinically significant complication after trauma even though screening and prophylaxis strategies for at-risk patients have substantially reduced incidence. Our study sought to determine if diabetes, a condition that promotes thrombi formation, is associated with developing a VTE in trauma patients.

Methods The registries of 2 level I and a level II trauma centers were retrospectively reviewed for consecutively admitted trauma patients over a 6-year period. Demographics, VTE risk factors, injury characteristics, and VTE incidence were univariately compared between patients with insulin-dependent diabetes mellitus (IDDM), non-insulin-dependent diabetes mellitus (NIDDM), and no diabetes. Stepwise logistic regression was performed to identify independent predictors of VTE; results were further stratified by age (<65 and ≥65 years) and presented as adjusted ORs (AOR).

Results Of the 26 934 total patients, 779 (2.9%) had IDDM, 2052 (7.6%) had NIDDM, and the remaining 89.5% were without diabetes. VTE incidence was 3.6%, 2.4%, and 2.2%, in IDDM, NIDDM, and non-diabetes, respectively (p=0.02). After adjustment for established and significant risk factors, neither IDDM (AOR=1.43, 95% CI 0.95 to 2.15, p=0.09) nor NIDDM (AOR=1.03, 95% CI 0.75 to 1.40, p=0.88) was associated with increased odds of developing a VTE. Patients ≥65 years developed VTE more frequently than those <65 years (2.5% vs 2.1%, p=0.04). Among patients <65 years, IDDM was significantly predictive of VTE (AOR=1.86, 95% CI 1.01–3.41, p=0.045), but NIDDM was not. For patients ≥65 years, neither type of diabetes was predictive of VTE.

Conclusions VTE incidence was ~2 times higher among injured patients <65 years with IDDM versus no diabetes. Overall, we did not find an increased risk of VTE in patients with any diabetes. Additional studies are needed before a recommendation on VTE screening or prophylaxis in IDDM can be made.

Level of evidence Level III, therapeutic/care management.

BACKGROUND

Venous thromboembolism (VTE), a collective diagnostic term to encompass both deep vein thrombosis (DVT) and pulmonary embolism (PE), is a significant complication after traumatic injury that may lead to disability or death. Aggressive screening and prophylaxis strategies provided to patients deemed high risk have effectively reduced the frequency of VTE in the trauma population.[1 2] Increased age, obesity, smoking, pregnancy, history of VTE, blood transfusion, surgery, hospitalization over 48 hours, mechanical ventilation, and the following injury-specific characteristics are recognized VTE risk factors for trauma patients: pelvic/lower extremity trauma, head trauma, venous injury, femur or tibia fracture, and spinal cord injury.[1 3–9] Diabetes mellitus (diabetes), an increasingly common comorbidity, has rarely been studied as a potential independent risk factor for VTE development in trauma populations and these studies did not differentiate the diabetes type,[10 11] despite the condition's physiological disposition to thrombophilia.[12 13]

Diabetes is a systemic, chronic illness characterized by prolonged elevation of glucose levels, causing the endothelial cells lining the blood vessels to absorb unhealthy levels of glucose. Over time, this pattern leads to permanent damage of blood vessels, with subsequent endothelial dysfunction, altered platelet activation, and increased blood coagulability, resulting in increased risk of thrombi formation.[12 13] In non-trauma populations, the association between diabetes and VTE remains inconclusive. Several studies have found an increased likelihood of the development of VTE among patients with diabetes,[14–17] while other large-scale studies failed to identify a link between diabetes and VTE or PE.[18–20]

In the current study, we sought to determine if diabetes was an independent predictor of VTE following a traumatic injury. With this information, it is our hope that we identify if patients with preinjury diabetes should be recognized as a high-risk subgroup of trauma patients that would benefit from aggressive VTE screening and prophylaxis strategies.

METHODS

We conducted a retrospective cohort study of all adult (≥18 years old) trauma patients consecutively admitted to two metropolitan area level I trauma centers (hospitals 1 and 2) and one metropolitan level II trauma center (hospital 3). Patients were excluded if they were readmitted for a previous trauma (n=468) or if their hospital stay was <1 day (n=1124). The trauma registries (TraumaBase, Clinical Data Management, Evergreen, CO), broad sets of data prospectively collected by trained personnel at each hospital, were used to obtain 6 years of data from each of the level I trauma centers (1/1/2008–12/31/2013) and 3 years of data from the level II trauma center (1/1/2011–12/31/2013). This study was approved by each hospital's respective Institutional Review Boards.

The primary outcome was the development of a VTE while hospitalized, defined as a DVT, PE, or

both. All hospitals tested symptomatic patients. In addition, hospital 1 screened any patient considered high risk for the development of VTE, defined as those who received anesthesia for more than 1 hour (if prophylaxis was not started preoperatively), were on prolonged bed rest prior to admission, had a history of prior DVT, sustained a hip fracture, or had their prophylaxis with compression devices discontinued for more than 8 hours. The variation in screening, where only one of the three hospitals (33%) had a specific protocol to screen asymptomatic trauma patients for DVT, is similar to the results of a survey among National Trauma Data Bank hospitals. This survey found only 28% of the responding hospitals had written guidelines regarding DVT screening in asymptomatic patients.[21] Each institution had their own prophylaxis protocol or allowed for physician discretion in prophylaxis administration (table 1). We also examined in-hospital mortality.

The primary exposure variable was diabetes status, defined in two ways: (1) the presence or absence of any diabetes, and (2) insulin-dependent diabetes mellitus (IDDM), non-insulin-dependent diabetes mellitus (NIDDM), or no diabetes. During the study period, the trauma registries at hospitals 1 and 2 differentiated the diabetes type. Within the comorbidity variable, there were options at hospital 1 to record diabetes as 'IDDM' and 'NIDDM'. At hospital 2, diabetes was recorded as 'IDDM' and 'DM'. At hospital 3, both types of diabetes were lumped into one category called 'diabetes'. A research nurse at hospital 3 performed a chart review to document whether the patient had type 1 or 2 diabetes. Patients categorized as NIDDM, DM, or type 2 diabetes made up the NIDDM group; patients categorized as IDDM or type 1 diabetes made up the IDDM group. All classifications were based on chart documentation, not laboratory values.

Additional covariates examined included the following demographic and injury characteristics: elderly age (<65 vs ≥65 years), sex (male or female), smoking status (yes/no), history of alcohol abuse (yes/no), Injury Severity Score (ISS, <16 vs ≥16), the presence of pre-existing comorbidities in addition to diabetes, the presence of specific comorbidities (coagulopathy, obesity, cancer, cardiac disease, cerebrovascular accident, and pregnancy), undergone a surgical procedure, placement of a central line, mechanical ventilation (yes/no), hospital length of stay (LOS), admission to the intensive care unit (yes/no), infection (yes/no), hip fracture, region of injury (neck/spine, abdominal/pelvic, chest, external, limb, face, head) where the Abbreviated Injury Score (AIS) was ≥2, and multiple injuries (two or more injury regions with an AIS≥2). Obesity was defined as BMI (kg/m^2) ≥30 (hospital 1), BMI≥40 between 2008 and 2011 and a BMI≥30 for 2012–2013 (hospital 2); or if it was recorded by the nurse or physician in the medical history (hospital 3).

Differences by diabetes status were examined using Pearson's χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. Stepwise multivariate logistic regression analysis was performed to calculate the OR for diabetes type on the development of VTE, with entry and exit criteria of p=0.2 and 0.05, respectively. All covariates were available for inclusion in the logistic regression, with the exception of history of coagulopathy as this likely represents an intermediate variable on the causal pathway. Since diabetes type differs by age and increasing age is a risk factor for diabetes, the data were also analyzed by age strata (<65 and ≥65 years). In multivariate logistic regression models that attempted to control for center effect, hospital 3 was removed from all analyses due to potential misclassification of diabetes type. Data analyses were performed using SAS (V.9.3, Cary, North Carolina, USA).

RESULTS

During the study period, a total of 26 934 new adult trauma patients were admitted and hospitalized for a minimum of 1 day. In total, 601 (2.2%) patients developed VTE; 449 (1.7%) had DVT, 114 (0.4%) a PE, and 38 (0.1%) sustained both DVT and PE. The in-hospital mortality among patients with VTE was 5.7% in comparison to 3.3% of patients without VTE (p=0.002).

Table 1 Hospitals' guidelines for DVT prophylaxis within trauma patients

Hospital 1	Mechanical compression devices and TEDS applied, unless patient suffered leg fracture or has poor arterial perfusion of legs
	Trauma patients with multiple DVT risk factors, especially prior DVT, should receive subcutaneous heparin 5000 units every 12 hours.* Spinal cord injury patients should receive subcutaneous heparin, adjusted to maintain a PTT=35–40. Treatment may be discontinued when spasticity develops. Risk factors for DVT include:

- ► Age >40+bed rest >3 days
- ► Prior DVT
- ► Coma (GCS<7)
- ► Spine fracture
- ► Quadriplegia/paraplegia
- ► Pelvic fracture
- ► Leg/hip fracture
- ► Cancer
- ► CHF
- ► General surgery+bed rest
- ► Lupus anticoagulant
- ► Hereditable coagulation deficiencies
- ► Nephrotic syndrome
- ► Stroke
- ► Urological surgery
- ► Myocardial infarction
- ► Older age
- ► Obesity
- ► Oral contraception
- ► Pregnancy/postpartum
- ► Ulcerative colitis/inflammatory bowel disease
- ► Sepsis
- ► Myeloproliferative disease
- ► Varicose veins
- ► Smoking

Hospital 2	Patients >16 years—mechanical compression devices and TEDS applied to uninjured leg or both legs if possible
	All patients not at risk for bleeding with anticipated stay >48 hours and non-ambulatory should receive chemical prophylaxis. Patients initially at risk for further bleeding can have chemical prophylaxis started within 72 hours of injury.
	Trauma patients without contraindications should receive enoxaparin (30 mg, subcutaneous, twice per day) unless a dose adjustment is needed due to geriatric age, weight, or renal failure. Patients with epidural catheters and ICP monitors will receive 40 mg of subcutaneous enoxaparin once a day. Enoxaparin is held 24 hours prior to placement of epidural or ICP.
	Preoperative chemical prophylaxis will not be held for surgical procedures unless requested by surgeon.
Hospital 3	No formal prophylaxis protocol. Treated per physician opinion

*Per communication with the trauma services department, the current practice has changed without an update to the protocol; it is standard procedure to use enoxaparin for chemical prophylaxis.
CHF, congestive heart failure; GCS, Glasgow Coma Scale; ICP, intracranial pressure; PTT, partial thromboplastin time; TEDS, thromboembolism deterrent stockings.

Of the adult trauma patients, 89.5% were without diabetes, 2.9% had IDDM, and 7.6% had NIDDM. The incidence of VTE varied by diabetes status with 3.6% of patients with IDDM, 2.4% of patients with NIDDM, and 2.2% of patients without diabetes developing VTE (p=0.02).

The risk factors associated with VTE significantly varied depending on diabetes status, yet no group was without risk (table 2). Patients without diabetes were most often smokers, had a history of alcohol abuse, and sustained multiple injuries; whereas, patients with IDDM and NIDDM were older and had more pre-existing comorbidities, including obesity.

In univariate analysis, patients with any diabetes had significantly higher odds of VTE compared with patients without diabetes (OR=1.28, 95% CI 1.00 to 1.63, p=0.046). This association did not remain significant in multivariate regression analysis (adjusted OR (AOR)=1.15, p=0.29; table 3).

Unadjusted analysis by diabetes type showed that patients with IDDM had increased odds of VTE compared with patients without diabetes (OR=1.68, 95% CI 1.14 to 2.48, p=0.01), but patients with NIDDM did not (OR=1.13, 95% CI 0.84 to 1.51, p=0.43). In multivariate regression analysis, neither IDDM (AOR=1.43, p=0.09) nor NIDDM (AOR=1.03, p=0.88) were associated with increased odds of developing VTE. The covariates that were independently associated with developing VTE were many of the established risk factors for VTE: age, male sex, obesity, ISS≥16, an injury to a limb or hip, multiple injuries, undergone a surgical procedure, the placement of a central line, mechanical ventilation, and infection (table 3).

As expected, the incidence of VTE varied with age; elderly patients experienced more VTE than non-elderly patients (2.5% vs 2.1%, p=0.04). Elderly patients also had higher rates of diabetes (table 2). Thus, we explored the data further by each age stratum.

Patients <65 years old

The subset of patients <65 years included 16 877 patients, of which 15 781 (93.5%) did not have diabetes, 340 (2.0%) had IDDM and 756 (4.5%) had NIDDM. The incidence of VTE within the subgroup <65 years was 3.8%, 2.5%, and 2.0% for patients with IDDM, NIDDM, and no diabetes, respectively. Unadjusted, patients with any diabetes (OR=1.45, 95% CI 1.00 to 2.09, p=0.049) and IDDM (OR=1.92, 95% CI 1.09 to 3.37, p=0.02) had significantly increased odds of developing VTE, but NIDDM was not associated with VTE (OR=1.24, 95% CI 0.78 to 1.98, p=0.36). After adjustment, neither patients with any diabetes (AOR=1.41, p=0.08) nor NIDDM (AOR=1.21, p=0.44) had an increased risk of VTE, while those with IDDM (AOR=1.86, p=0.045) continued to have increased odds of developing VTE in comparison to patients without diabetes (table 4).

Patients ≥65 years old

The subset of patients ≥65 years included 10 057 patients, of which 8322 (82.8%) did not have diabetes, 439 (4.4%) had IDDM, and 1296 (12.9%) had NIDDM. The incidence of VTE among the patients ≥65 years was 3.4% for patients with IDDM, 2.4% among patients with NIDDM, and 2.4% in patients without diabetes. Unadjusted, neither any diabetes (OR=1.10, 95% CI 0.79 to 1.51, p=0.58) nor type—IDDM (OR=1.42, 95% CI 0.83 to 2.43, p=0.20) and NIDDM (OR=0.99, 95% CI 0.67 to 1.44, p=0.94)—was associated with developing a VTE. Any diabetes, IDDM, and NIDDM remained unassociated with developing a VTE after adjusting for covariates (table 5).

Table 2 Risk factors and outcomes by diabetes type			
Clinical characteristics, n (%)	**No diabetes (n=24 103)**	**IDDM (n=779)**	**NIDDM (n=2052)**	**p***
Hospital†				<0.001
1	11 909 (90.9%)	426 (3.3%)	771 (5.9%)	
2	8034 (87.8%)	334 (3.7%)	781 (8.5%)	
3	4160 (88.9%)	19 (0.4%)	500 (10.7%)	
Elderly, ≥65 years	8322 (34.5%)	439 (56.4%)	1296 (63.2%)	<0.001
Male	14 092 (58.5%)	430 (55.2%)	1081 (52.7%)	<0.001
Smoker	4088 (17.0%)	87 (11.2%)	193 (9.4%)	<0.001
Alcohol abuse	2925 (12.1%)	51 (6.6%)	115 (5.6%)	<0.001
Pre-existing comorbidities‡	15 558 (64.6%)	690 (88.6%)	1869 (91.1%)	<0.001
Coagulopathy	1747 (7.3%)	115 (14.8%)	310 (15.1%)	<0.001
Obesity	1147 (4.8%)	111 (14.3%)	285 (13.9%)	<0.001
Cancer	80 (0.3%)	3 (0.4%)	9 (0.4%)	0.71
Cardiac disease	2347 (9.7%)	162 (20.8%)	526 (25.6%)	<0.001
Cerebrovascular accident	536 (2.2%)	50 (6.4%)	114 (5.6%)	<0.001
Pregnancy	143 (0.6%)	0 (0%)	1 (0.1%)	0.001
ISS≥16§	4912 (20.4%)	112 (14.4%)	428 (20.9%)	<0.001
Hip fracture	2722 (11.3%)	127 (16.3%)	319 (15.6%)	<0.001
Region of injury				
Neck/spine¶	4105 (17.0%)	117 (15.0%)	278 (13.6%)	<0.001
Abdominal/pelvic¶	1808 (7.5%)	23 (3.0%)	87 (4.2%)	<0.001
Chest¶	4741 (19.7%)	135 (17.3%)	360 (17.5%)	0.02
External¶	415 (1.7%)	8 (1.0%)	19 (0.9%)	0.01
Limb¶	11 453 (47.5%)	414 (53.2%)	970 (47.3%)	0.01
Face¶	1774 (7.4%)	28 (3.6%)	90 (4.4%)	<0.001
Head¶	6888 (28.6%)	170 (21.8%)	578 (28.2%)	<0.001
Multiple injuries	6278 (26.1%)	134 (17.2%)	384 (18.7%)	<0.001
Surgical procedure	10 638 (44.1%)	360 (46.2%)	810 (39.5%)	<0.001
Placement of a central line	1773 (7.4%)	65 (8.3%)	173 (8.4%)	0.13
Mechanical ventilation	2597 (10.8%)	77 (9.9%)	184 (9.0%)	0.03
Hospital LOS, median (IQR)	3 (2–6)	4 (3–7)	4 (2–6)	<0.001
Admitted to ICU	7854 (32.6%)	252 (32.4%)	683 (33.3%)	0.80
Infection	450 (1.9%)	18 (2.3%)	53 (2.6%)	0.06
No complications	21 496 (89.2%)	667 (85.6%)	1788 (87.1%)	<0.001
VTE	523 (2.2%)	28 (3.6%)	50 (2.4%)	0.02
DVT	422 (1.8%)	24 (3.1%)	41 (2.0%)	0.02
PE	135 (0.6%)	5 (0.6%)	12 (0.6%)	0.95
In-hospital death§	791 (3.3%)	26 (3.3%)	86 (4.2%)	0.09

*Significant p values (p<0.05) are displayed in bold.
†Row percent presented for hospital.
‡Pre-existing comorbidities does not include diabetes.
§Missing ISS on 77 patients and death outcome on 1 patient.
¶AIS≥2.
AIS, Abbreviated Injury Score; DVT, deep vein thrombosis; ICU, intensive care unit; IDDM, insulin-dependent diabetes mellitus; ISS, Injury Severity Score; LOS, length of stay; NIDDM, non-insulin-dependent diabetes mellitus; PE, pulmonary embolism; VTE, venous thromboembolism.

Finally, we attempted to control for the study center by adding the hospital into the multivariate logistic regression models for patients of all ages, as well as the subsets of patients under and over 65 years of age. Our results persisted when excluding hospital 3, where there is potential misclassification, and controlling for center differences at hospitals 1 and 2; among patients under 65 years, IDDM was significantly predictive of VTE (AOR=1.92, 95% CI 1.04 to 3.52, p=0.04). Otherwise, any diabetes and type of diabetes were not predictive of developing VTE.

Table 3 Multivariate predictors of a venous thromboembolism, all ages

	AOR	95% CI	p*
Model 1: any diabetes and adjustment for covariates			
Any diabetes	1.15	0.89 to 1.49	0.29
Age≥65	1.67	1.37 to 2.02	<0.001
Male	1.39	1.15 to 1.68	0.001
Obesity	1.63	1.23 to 2.16	0.001
ISS≥16	1.42	1.12 to 1.81	0.005
Limb injury†	1.58	1.28 to 1.95	<0.001
Face injury†	0.67	0.49 to 0.91	0.01
Multiple injuries	1.40	1.11 to 1.77	0.01
Surgical procedure	3.55	2.78 to 4.52	<0.001
Hip injury†	1.32	1.02 to 1.71	0.03
Placement of a central line	1.55	1.21 to 1.99	0.001
Mechanical ventilation	3.48	2.70 to 4.47	<0.001
Infection	2.00	1.47 to 2.72	<0.001
Model 2: IDDM and adjustment for covariates			
IDDM	1.43	0.95 to 2.15	0.09
Age≥65	1.71	1.39 to 2.10	<0.001
Male	1.49	1.23 to 1.82	<0.001
Obesity	1.68	1.24 to 2.27	0.001
ISS≥16	1.40	1.09 to 1.81	0.01
Limb injury†	1.57	1.26 to 1.96	<0.001
Face injury†	0.66	0.48 to 0.91	0.01
Multiple injuries	1.40	1.09 to 1.79	0.01
Surgical procedure	3.44	2.67 to 4.43	<0.001
Hip injury†	1.38	1.05 to 1.80	0.02
Placement of a central line	1.54	1.19 to 2.00	0.001
Infection	2.08	1.51 to 2.85	<0.001
Mechanical ventilation	3.53	2.71 to 4.59	<0.001
Model 3: NIDDM and adjustment for covariates			
NIDDM	1.03	0.75 to 1.40	0.88
Age≥65	1.77	1.47 to 2.13	<0.001
Male	1.35	1.12 to 1.64	0.002
Obesity	1.65	1.23 to 2.21	0.001
ISS≥16	1.65	1.32 to 2.06	<0.001
Limb injury†	1.90	1.56 to 2.32	<0.001
Surgical procedure	3.62	2.83 to 4.61	<0.001
Placement of a central line	1.54	1.19 to 1.98	0.001
Mechanical ventilation	3.48	2.69 to 4.50	<0.001
Infection	2.00	1.46 to 2.74	<0.001

*Significant p values (p<0.05) are displayed in bold.
†AIS≥2.
AIS, Abbreviated Injury Score; AOR, adjusted OR; IDDM, insulin-dependent diabetes mellitus; ISS, Injury Severity Score; NIDDM, non-insulin-dependent diabetes mellitus.

Table 4 Multivariate predictors of a venous thromboembolism, patients under the age of 65 years

	AOR	95% CI	p*
Model 4: any diabetes and adjustment for covariates			
Any diabetes	1.41	0.95 to 2.09	0.08
Male	1.51	1.16 to 1.96	0.002
Obesity	1.76	1.25 to 2.47	0.001
ISS≥16	1.58	1.19 to 2.09	0.002
Limb injury†	1.85	1.44 to 2.37	<0.001
Surgical procedure	3.38	2.42 to 4.72	<0.001
Hip injury†	1.57	1.05 to 2.36	0.03
Placement of a central line	1.53	1.13 to 2.08	0.01
Mechanical ventilation	4.04	2.94 to 5.53	<0.001
Infection	2.35	1.62 to 3.43	<0.001
Model 5: IDDM and adjustment for covariates			
IDDM	1.86	1.01 to 3.41	0.045
Male	1.52	1.16 to 2.00	0.003
Obesity	1.78	1.24 to 2.55	0.002
ISS≥16	1.53	1.14 to 2.05	0.005
Limb injury†	1.79	1.39 to 2.31	<0.001
Surgical procedure	3.42	2.42 to 4.83	<0.001
Hip injury†	1.63	1.07 to 2.46	0.02
Placement of a central line	1.49	1.09 to 2.04	0.01
Mechanical ventilation	4.06	2.93 to 5.62	<0.001
Infection	2.53	1.73 to 3.70	<0.001
Model 6: NIDDM and adjustment for covariates			
NIDDM	1.21	0.74 to 1.99	0.44
Male	1.45	1.11 to 1.90	0.01
Obesity	1.76	1.24 to 2.50	0.002
ISS≥16	1.63	1.22 to 2.17	0.001
Limb injury†	1.93	1.49 to 2.48	<0.001
Surgical procedure	3.28	2.33 to 4.60	<0.001
Hip injury†	1.56	1.02 to 2.37	0.04
Placement of a central line	1.49	1.09 to 2.03	0.01
Mechanical ventilation	4.09	2.97 to 5.64	<0.001
Infection	2.26	1.54 to 3.32	<0.001

*Significant p values (p<0.05) are displayed in bold.
†AIS≥2.
AIS, Abbreviated Injury Score; AOR, adjusted OR; IDDM, insulin-dependent diabetes mellitus; ISS, Injury Severity Score; NIDDM, non-insulin-dependent diabetes mellitus.

DISCUSSION

Our findings suggest that IDDM is an independent risk factor for developing a VTE among adult trauma patients under the age of 65. Otherwise, we found no significant relationships between the development of VTE and patients with 'any diabetes', NIDDM, or patients with IDDM who are older than 65 years. These findings deserve further study as they may be influenced by the low incidence of NIDDM (7.6%) and high incidence of IDDM (2.9%) in our population. Additionally, since VTE occurs in a small percentage of trauma patients, these findings should be replicated in a larger study.

Overall, the incidence of VTE in our population of adult trauma patients hospitalized for more than 1 day (2.2%) is comparable to previously published studies that eliminated minor traumas,[10 22] but higher than a large study using the American College of Surgeons National Trauma Data Bank, which reported VTE incidence of just 0.36% when considering all injury severity levels.[1] Our study reinforced the following risk factors as being associated with developing VTE after trauma: age, sex, obesity, major trauma, surgery, placement of a central line, mechanical ventilation, limb injury, and infection.[1 3–9 23 24] The most significant predictors of VTE in our overall population were those undergoing a surgical procedure, mechanical ventilation, and having an infection; these predictors were found across all models, independent of definition of diabetes. Thus, even with similar adjustments, our analysis identified IDDM increased the risk of VTE whereas NIDDM did not.

Existing trauma literature does not separate diabetes types when examining the risk for VTE. However, an association between diabetes and VTE was found in a meta-analysis that examined the incidence and risk factors for VTE among patients who had surgical treatment of fractures below the hip (RR=1.46, 95% CI 1.27 to 1.68; p=0.000).[11] And, Paffrath et al[22] found an independent association of concomitant

Table 5 Multivariate predictors of a venous thromboembolism, patients 65 years and older

	AOR	95% CI	p*
Model 7: any diabetes and adjustment for covariates			
Any diabetes	1.06	0.76 to 1.48	0.74
Multiple injuries	1.74	1.28 to 2.36	**<0.001**
Surgical procedure	4.78	3.46 to 6.59	**<0.001**
Placement of a central line	1.76	1.15 to 2.71	**0.01**
Mechanical ventilation	2.77	1.86 to 4.13	**<0.001**
Model 8: IDDM and adjustment for covariates			
IDDM	1.25	0.72 to 2.17	0.43
Male	1.48	1.10 to 1.98	**0.01**
Limb injuries†	1.49	1.07 to 2.09	**0.02**
Multiple injuries	1.54	1.10 to 2.17	**0.01**
Surgical procedure	3.85	2.67 to 5.54	**<0.001**
Placement of a central line	1.82	1.14 to 2.91	**0.01**
Mechanical ventilation	2.94	1.87 to 4.61	**<0.001**
Model 9: NIDDM and adjustment for covariates			
NIDDM	0.98	0.66 to 1.45	0.91
Multiple injuries	1.84	1.34 to 2.52	**0.001**
Surgical procedure	5.01	3.59 to 7.01	**<0.001**
Placement of a central line	1.70	1.09 to 2.64	**0.02**
Mechanical ventilation	2.72	1.80 to 4.10	**<0.001**

*Significant p values (p<0.05) are displayed in bold.
†AIS≥2.
AIS, Abbreviated Injury Score; AOR, adjusted OR; IDDM, insulin-dependent diabetes mellitus; ISS, Injury Severity Score; NIDDM, non-insulin-dependent diabetes mellitus.

diseases, which included diabetes, renal failure, malignancies, and coagulation disorders, with the development of VTE (OR=1.98, 95% CI 1.39 to 2.83, p<0.005).

While the association between diabetes and VTE in non-trauma populations is inconsistent, one study identified a relationship between age, type 1 diabetes and increased risk for VTE. An analysis of the National Hospital Discharge Survey by Stein et al[15] found that patients with diabetes aged 20–49 faced an increased risk of VTE, and this risk was only apparent in younger patients without additional comorbid conditions that also increase the risk of VTE.

Perhaps a contributing factor to the inconsistent association of diabetes with VTE is failure to identify the at-risk group. In the non-trauma literature, when Stein et al[15] examined VTE by age deciles, it was the patients under the age of 50 in which diabetes was a risk factor for VTE; this risk was not apparent in any decile above 50. On the contrary, the Heart and Estrogen/progestin Replacement Study (HERS), conducted in postmenopausal women under the age of 80 with coronary disease, found no independent association between diabetes and VTE.[20] Within the trauma literature, studies examining VTE risk after trauma appear to account for age, sex, injury characteristics, and treatment,[1] [3] [6] [8] but less often consider concomitant pre-existing conditions,[7] [22] or specifically diabetes.[10] [11]

The 2002 Eastern Association for the Surgery of Trauma guidelines found spinal fractures and spinal cord injury to be the only proven risk factors for development of VTE following traumatic injury. Age is recognized as a risk factor, yet the cut-off determining risk remains unclear. As of the 2002 guidelines, other traditional risk factors had yet to be supported in larger studies or demonstrated significance in meta-analyses.[25] As type 1 diabetes continues to rise,[26] [27] large-scale, prospective research is needed to determine the impact diabetes type and other recognized risk factors may have on VTE development.

Our study is not without limitations. Given the retrospective nature of the study and the use of a pre-existing database, we were unable to specify whether VTE was found because of screening or due to symptoms, we do not know which confirmatory studies were performed for the diagnosis of VTE, and we were unable to identify which patients received prophylaxis, missed doses of prophylaxis, or account for the reasons behind patients receiving or not receiving prophylaxis. Each of the three trauma centers had differences in their prophylaxis protocols, thus each facility could have provided prophylaxis to different patients. Differences in the incidence of VTE were observed between the three study centers. The differences by site may be due to differences in demographic or injury characteristics at each hospital, differences in the prophylaxis protocols, and surveillance bias as hospital 1 was the only institution that screened for VTE in asymptomatic patients.[8] [28–30] We attempted to account for these differences by examining demographics, injury characteristics, and institution in the multivariate models. Second, based on our definitions of diabetes at hospital 3, where type 1 diabetes equals IDDM and type 2 diabetes equals NIDDM, we recognize the possibility of bias due to misclassification of diabetes type. For instance, a person with type 2 diabetes could require the use of insulin; in our study, this patient would be misclassified as NIDDM. We performed an additional analysis excluding hospital 3 and adjusting for center differences for hospitals 1 and 2, and demonstrated that IDDM was still associated with an increase in developing VTE in patients <65 years. Even with this limitation, we feel the outcomes by diabetes type are of interest to present and a unique aspect of our study because it has not been studied in the trauma population. Nevertheless, we recommend that additional research should be conducted on diabetes type and VTE before conclusions can be made. Third, the definition of obesity varied across sites, but due to the strong associations between obesity and both diabetes and VTE, we wanted to capture obesity as best we could. Fourth, the median LOS for all patients was 3–4 days. There is a chance that we may have missed cases of VTE that occurred after the patients were discharged from the hospital. Finally, our study excluded patients under 18 years of age even though children have a higher incidence of type 1 diabetes than adults,[31] who would require insulin, hence the results are only applicable for adult trauma populations. Strengths of this study are the large patient sample and multicenter population.

In a study of nearly 27 000 patients, we found patients under the age of 65 with IDDM faced an increased rate of VTE development. Overall, we did not find that patients with any diabetes had an increased risk for developing VTE after trauma. We cannot make a recommendations on VTE screening or prophylaxis in IDDM due to limitations of our study, but we encourage future research to examine the risk of VTE by diabetes type.

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