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Creation and validation of a simple venous thromboembolism risk scoring tool for thermally injured patients: analysis of the National Burn Repository

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Abstract

Objective—Venous thromboembolism (VTE) has been identified as a major patient safety issue. We report our use of the National Burn Repository (NBR) to create and validate a weighted risk scoring system for VTE.

Methods—Adult patients with thermal injury from the NBR admitted between 1995 and 2009 were included. Independent variables were either known or could be derived at the time of admission, including total body surface area burned (TBSA), inhalation injury, gender, and age. The dependent variable was VTE, a composite variable of patients with deep venous thrombosis and/or pulmonary embolus. The dataset was split into working and validation sets using a random number generator. Multivariable logistic regression identified independent predictors. β – coefficients for independent predictors were used to generate a weighted risk score.

Results—The NBR contained 22,618 patients who met inclusion criteria. The working and validation sets were not statistically different for demographics or risk factors. In the working set, presence of inhalation injury and increased TBSA were independent predictors of VTE. Adjusted β –coefficients were used to generate a weighted risk score which showed excellent discrimination for VTE in both the working (c-statistic 0.774) and validation (c-statistic 0.750) sets. As risk score increased, a linear increase in observed VTE rate was demonstrated in both working and validation sets.

Conclusions—We have created and validated a simple risk score model to predict VTE risk in thermally injured patients using the NBR. The model is based on risk factors easily identified during initial patient contact.

Keywords

Deep venous thrombosis; pulmonary embolus; venous thromboembolism; burn injury; thermal injury; risk factor; National Burn Repository; NBR; DVT; PE; VTE

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Introduction

Venous thromboembolism (VTE) has been identified as a major patient safety issue by clinicians, policymakers, and third-party payers. The United States Surgeon General recently issued a “Call to Action” on DVT and PE ^{1, 2}. The “Call to Action” emphasized VTE risk stratification and prophylaxis as important directions for future research. To fully identify VTE risk in surgical patients, recent publications advocate individualized patient risk assessment ^{3–9}.

The most widely recognized and validated VTE risk tool is the Caprini Risk Assessment Model ¹⁰. The model has been validated to predict VTE risk in general, vascular, and urology patients as well as patients undergoing plastic and reconstructive surgery ^{3, 7}. However, the model was designed to be used in the pre-operative setting, based on risk factors present at baseline. Additionally, the Caprini tool was designed for use in patients having one or, at most, two operations. Other risk factors specific to burn patients, such as TBSA and inhalation injury ^{11–13}, are not considered in existing risk models ^{10, 14–18}. Thus, available risk stratification tools are likely to be poor predictors of VTE risk in the thermally injured population.

Here, we report our use of the National Burn Repository (NBR) to create and validate a weighted risk scoring system for VTE which is specific to thermally injured patients.

Methods

The American Burn Association’s National Burn Repository (NBR) has previously been described in detail ^{19–21}. The NBR is a voluntary data set comprised of burn patients from participating centers in both the United States and Canada. The data is de-identified with respect both to patient-level and hospital-level identifiers. At each NBR site, trained chart reviewers identify eligible patients and perform retrospective chart review for the patient’s initial inpatient stay. Comprehensive patient demographic data as well as both size and etiology of burn injury are obtained. Operative data is coded using ICD-9 procedural codes. Outcomes data for over 110 complications are also included for each patient. Complications data are supported by hospital morbidity and mortality conference data and/or attending physician confirmation. Patient-level data are uploaded to a central server in a de-identified fashion. Datasets are provided to researchers by the American Burn Association upon request.

Patients from the NBR admitted between 1995 and 2009 with age ≥ 18 and length of stay at least 2 days were included in this analysis. Patients with non-thermal injury (such as desquamating skin disease, radiation-associated burns, and electrical injury) and patients who died within 3 days of admission were excluded. Exclusion criteria are demonstrated graphically in Figure 1.

Thermally injured patients have multiple recognized risk factors for VTE. Many of these, such as central venous line insertion and pneumonia, occur during hospitalization. The NBR does not contain a time-to-event variable for complications or ICD-9 procedural codes. We were unable to determine whether in-hospital risk factors for VTE occurred before or after VTE was diagnosed. Thus, our independent variables included those which were either known or could be derived at the time of admission. Independent variables used in this analysis included TBSA burned, inhalation injury, gender, and age. To facilitate risk model creation in a clinically relevant fashion, the continuous variables TBSA and age were empirically transformed to categorical variables. Inhalation injury can be diagnosed in many ways; the method or methods of diagnosis are recorded in the NBR. For this study, inhalation injury was diagnosed in one of three ways, specifically direct visualization of the

airway (e.g. fiberoptic bronchoscopy) and/or clinical examination (e.g. carbonaceous sputum or singed nasal hairs) and/or clinical history (e.g. history of closed space injury).

Patients with deep venous thrombosis (DVT) and/or pulmonary embolus (PE) were identified using the complications data set. A VTE variable was created as a composite of patients with DVT and/or PE. VTE was the dependent variable of interest in our multivariable logistic regression models.

The dataset was divided into working and validation sets using a random number generator. The working and validation sets were comprised of 75% and 25% of the total number of patients, respectively. Bivariate statistics were performed to compare the working and validation sets to ensure failure of randomization had not occurred.

We performed multivariable logistic regression to identify independent predictors of VTE. A weighted risk scoring system was then generated. For independent predictors, weighted scores were generated by dividing the β –coefficients by the smallest β –coefficient, multiplying by two and rounding to the nearest integer³². The derived risk scoring system was then re-applied to the working set to examine VTE incidence stratified by risk score. Risk score for TBSA 5–9% was empirically changed from “3” to “2” as this change drastically improved model fit. The derived risk scoring system was then applied to the validation set. VTE incidence stratified by risk score was examined in the validation set and compared to data derived from the working set.

The aggregate weighted risk score was then used as the single independent variable in a logistic regression model with VTE as the dependent variable. This was performed for working and validation sets separately. The amount of variability in VTE explained by the weighted risk score was examined using the c-statistic, defined as the area under the receiver-operator curve (AUROC). The c-statistics for the working and validation sets were compared.

The STATA11 statistical package (StataCorp LP, College Station, Texas) was used to clean, merge, and analyze the data sets provided by the American Burn Association.

Results

The NBR contained a total of 22,618 adult patients with thermal injury who met inclusion criteria (Figure 1). Among these patients, the overall incidence of VTE was 0.97%.

From all patients, 16,851 patients (~75% of the total) were randomized to the working set and 5,761 patients (~25% of the total) were randomized to the validation set. No statistical differences between the working and validation sets were seen for gender, mean age, mean TBSA, presence of inhalation injury, or incidence of VTE (Table 1).

Multivariable logistic regression was used in the working set to identify factors independently associated with VTE. Presence of inhalation injury and increased TBSA were independent predictors of VTE. Age and gender were not significantly associated with VTE when controlling for other independent variables (Table 2). For independent predictors, the adjusted β –coefficients from the regression model were used to generate a weighted risk score (Figure 2). The risk score showed excellent discrimination for VTE in both the working set (c-statistic 0.774) and subsequently in the validation set (c-statistic 0.750).

A stratified analysis of VTE rate by weighted risk score is shown in Figure 3. There was a linear increase in observed VTE rate as risk score increased. This trend was present for both the working set, in which the model was derived, and the validation set, a pristine data set

which was not used in model derivation. At maximum risk score (risk score = 8), the observed incidence of VTE was 5.1% for the entire NBR data set. At individual risk scores, the observed incidence of VTE was very similar between the working and validation sets (Figure 3).

Discussion

VTE risk score for thermally injured patients

We have used the National Burn Repository to create and validate a risk-scoring system for VTE after thermal injury. The risk score is simple and based on two factors easily ascertained at admission: TBSA burned and presence of inhalation injury. The scoring system was validated in a pristine data set which was separate from data used to derive the risk score. In both our working and validation sets, a linear increase in VTE risk occurs as risk score increases. Patients with TBSA of 50–65% and inhalation injury were at highest risk for VTE, with an observed inpatient risk of 5.1%; this rate is comparable to highest-risk patients in general, vascular, urology, and plastic surgery^{3,7}. Our prior work using the NBR has demonstrated a linear relationship between TBSA and death²¹. Increased risk of death likely explains why our risk score model weights TBSA >65% less heavily than TBSA 50–65%.

Burn injuries that are clinically diagnosed as partial thickness at the time of admission may progress to full thickness injuries within several days. Our risk model was based on risk factors that could be derived at the time of admission and thus the distinction between partial and full thickness injury was not made in the risk model. The NBR does contain data for TBSA, total partial thickness injury, and total full thickness injury. For completeness, we did examine relative contributions of partial and full thickness injury to VTE risk. Our analysis did not indicate that full thickness burns placed patients at higher risk than partial thickness injury (data not shown).

VTE has been highlighted by major policymakers and payers as both a patient safety and quality of care issue. In his 2008 “Call to Action” for DVT and PE, then-Surgeon General Steven K. Galson stressed the creation of data-driven guidelines for VTE risk stratification and prophylaxis². The Surgical Care Improvement Project (SCIP), a national partnership whose goal is to improve the quality of surgical care through reduction in post-operative complications, has identified VTE prevention and receipt of appropriate VTE prophylaxis as indicators of quality care²².

VTE has been discussed in the popular media and among hospital payers as an in-hospital complication which may be potentially preventable. As such, the Centers for Medicare and Medicaid Services (CMS) has considered all VTE events for addition to their list of “never events”: those post-operative complications deemed potentially preventable for which CMS will not pay if acquired in-hospital. At present, VTE after selected major orthopaedic procedures is considered to be potentially preventable^{23, 24}.

We have previously used the NBR to examine factors independently associated with VTE after thermal injury²¹. Multivariable logistic regression identified three independent predictors of VTE, including TBSA, total number of inpatient operations, and total number of ICU days. However, these results were criticized by some because the total number of ICU days and total number of operations remained unknown until hospital discharge. Thus, only at the conclusion of a patient’s hospitalization could their inpatient VTE risk be fully understood; at that time, any opportunity to provide prophylaxis had passed. We also attempted to build a rudimentary method to stratify patients into “low”, “medium”, and

“high” risk categories based on admission risk factors. However, we did not create a true weighted risk scoring system.

We received valuable feedback from colleagues at several national meetings. Our colleagues specifically asked for a way to estimate VTE risk “up front”, so that appropriate prophylaxis could be provided at the time of admission. Thus, we have created our risk tool using risk factors which are known or can be derived at admission. As shown by the AUROC, the model explains at least 75% of the variability in VTE. The remainder of variation in VTE may be explained by factors which occur during hospitalization (see the *Limitations* section below).

Limitations

We have previously discussed limitations of the NBR for examinations of VTE in both thermally²¹ and electrically²⁵ injured populations. However, several items are noteworthy from this project.

The NBR does not contain data on receipt of mechanical or pharmacologic VTE prophylaxis. Thus, the NBR cannot be used to demonstrate whether prophylactic measures can prevent VTE in high-risk patients after thermal injury.

Based on the AUROC, our risk-score model explains at least 75% of the variability in the VTE outcome. The model is based only on risk factors which are either known or can be immediately derived at the time of admission. Thermally injured patients acquire multiple risk factors for VTE during hospitalization^{10, 11, 21, 26, 27}. However, the NBR does not have “time to complication” or “time to procedure” variables. While infectious complications, multiple operations, and central venous catheters, among others, likely contribute to VTE risk, the NBR cannot identify the temporal relationship of complications to VTE diagnosis. Thus, risk factors acquired in-hospital could not be included in this risk score model. This represents an important direction for further research.

Our previous work examined VTE in the 1995–2007 dataset. We showed no clear relationship between VTE diagnosis and time²¹. However, VTE was diagnosed much more frequently in 2008–2009 data when compared to other years in which greater than 1,000 patients were placed in the database (Figure 4). This indicates a chronology bias^{28,29}, possibly due to a heightened awareness of VTE via literature from major policymakers and payers^{2, 22, 24, 30}. As a result, we could not use the 2008–2009 data as our validation cohort. Instead, we randomly assigned patients to the working or validation sets using a random number generator.

Future Directions

Using the NBR, we have identified both increased TBSA and presence of inhalation injury as independent predictors of VTE after thermal injury. Important future directions for research include 1) identifying acquired/in-hospital risk factors for VTE after thermal injury, 2) condensing known data regarding risk factors present on admission and those which develop in-hospital into a single, validated risk scoring system and 3) examining the utility of chemoprophylaxis in burn patients to prevent VTE. The NBR currently lacks a “time to complication” or “time to procedure” variable. Were these variables added, researchers could identify complications or procedures which occurred prior to diagnosis of VTE and could be considered VTE risk factors. Given that over 5,000 patients are added to the NBR annually, one year of data would be sufficient to validate a new risk scoring system that condensed admission and acquired/in-hospital risk factors.

At present, there is no randomized, controlled trial (RCT) data which examines chemoprophylaxis effectiveness for VTE prevention after thermal injury. Should an RCT on chemoprophylaxis be proposed, the risk-scoring system created and validated in this manuscript would serve as an excellent tool to identify patients at high risk for VTE. Of note, standard prophylactic dosing of enoxaparin, a low-molecular weight heparin, has been shown to be inadequate in patients with large TBSA. Appropriate enoxaparin prophylaxis dose has been shown to correlate linearly with TBSA³¹. Thus, a proposed RCT should consider using antifactor Xa levels to guide prophylactic enoxaparin dosing.

Conclusions

We have created and validated a simple risk score model to predict VTE risk in thermally injured patients using the NBR. The model is based on risk factors easily identified during initial patient contact and demonstrates a linear increase in VTE risk as risk score increases. Future work should focus on identifying acquired/in-hospital risk factors, incorporating acquired/in-hospital risk factors into the risk model presented in this manuscript and examining the utility of chemoprophylaxis for VTE prevention in high-risk thermally injured patients.

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Figure 1.
Exclusion criteria for National Burn Repository analysis.

Two Point Risk Factors		Four Point Risk Factors	
☐ Inhalation Injury	☐ TBSA 5-9%	☐ TBSA 10-19%	
Five Point Risk Factors		Six Point Risk Factors	
☐ TBSA 20-49%	☐ TBSA >65%	☐ TBSA 50-65%	
TOTAL SCORE _____			
Total Score		Inpatient VTE Rate	
0-4		<1.0%	
5		~2.0%	
6		~3.0%	
7		~3.5%	
8		~5.0%	

Figure 2.
Weighted, validated risk scoring model for VTE after thermal injury.

Figure 3.
Stratified analysis of VTE by weighted risk score in working and validation sets.

Figure 4. Frequency of VTE stratified by admission year. Data is shown for high-volume (>1,000 cases/year) contribution years only.

Table 1

Comparison of working and validation sets.

	Working set (N=16,851)	Validation set (N=5,761)	p value
Female gender, %	30.9%	31.4%	0.49
Age, mean	45.6	45.6	0.90
TBSA, mean	12.5	12.4	0.78
Inhalation injury, %	14.5%	13.7%	0.10
VTE, %	0.97%	0.97%	0.99

Table 2

Adjusted odds ratios for VTE using multivariable logistic regression. Constant for the logistic equation was -6.87.

	Beta coefficient	Adjusted odds ratios (95% CI)	p value
TBSA burned			
<5%	Reference	Reference	-----
5–9%	1.40	4.05 (1.84–8.91)	0.001
10–19%	2.06	7.83 (3.79–16.14)	<0.001
20–34%	2.67	14.51 (7.03–29.93)	<0.001
35–49%	2.62	13.76 (6.10–31.02)	<0.001
50–65%	2.84	17.02 (6.98–41.53)	<0.001
>65%	2.51	12.23 (5.08–29.50)	<0.001
Inhalation injury	0.94	2.57 (1.82–3.63)	<0.001
Age			
18–39	Reference	Reference	-----
40–60	0.26	1.29 (0.86–1.94)	0.21
>60	0.28	1.33 (0.89–1.98)	0.16
Female gender	0.11	1.12 (0.79–1.58)	0.53

Table 3

Observed rate of VTE stratified by risk score in working set (N=16,851)

Risk Score	Patients with VTE	Total Patients	Rate of VTE
0	2	5,493	0.04%
2	26	3,924	0.66%
4	30	3,281	0.91%
5	48	2,426	1.98%
6	18	639	2.82%
7	31	919	3.37%
8	9	169	5.33%