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A predictive nomogram-based model for lower extremity compartment syndrome after trauma in the United States: a retrospective case-control study

Blake Callahan, MD[1,2,3], Darwin Ang, MD[1,2], Huazhi Liu, MS[2]

[1]Department of Surgery, University of Central Florida College of Medicine, Orlando, FL, USA
[2]Department of Surgery, HCA Ocala Hospital, Ocala, FL, USA
[3]Department of Emergency, WellStar Kennestone Regional Medical Center, Marietta, GA, USA

Purpose: The aim of this study was to utilize the American College of Surgeons Trauma Quality Improvement Program (TQIP) database to identify risk factors associated with developing acute compartment syndrome (ACS) following lower extremity fractures. Specifically, a nomogram of variables was constructed in order to propose a risk calculator for ACS following lower extremity trauma.

Methods: A large retrospective case-control study was conducted using the TQIP database to identify risk factors associated with developing ACS following lower extremity fractures. Multivariable regression was used to identify significant risk factors and subsequently, these variables were implemented in a nomogram to develop a predictive model for developing ACS.

Results: Novel risk factors identified include venous thromboembolism prophylaxis type particularly unfractionated heparin (odds ratio [OR], 2.67; 95% confidence interval [CI], 2.33–3.05; P<0.001), blood product transfusions (blood per unit: OR 1.13 [95% CI, 1.09–1.18], P<0.001; platelets per unit: OR 1.16 [95% CI, 1.09–1.24], P<0.001; cryoprecipitate per unit: OR 1.13 [95% CI, 1.04–1.22], P=0.003).

Conclusions: This study provides evidence to believe that heparin use and blood product transfusions may be additional risk factors to evaluate when considering methods of risk stratification of lower extremity ACS. We propose a risk calculator using previously elucidated risk factors, as well as the risk factors demonstrated in this study. Our nomogram-based risk calculator is a tool that will aid in screening for high-risk patients for ACS and help in clinical decision-making.

Keywords: Compartment syndromes; Wounds and injuries; Extremities; Clinical decision-making

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Correspondence to
Blake Callahan, MD
Department of Surgery, University of Central Florida College of Medicine, 431 SW 1st Ave, Ocala, FL 34471, USA
Tel: +1-407-266-1000
Email: blakecallahan13@gmail.com

INTRODUCTION

Background

Acute compartment syndrome (ACS) is an emergent condition where pressure within the confined spaces of intramuscular septa rises enough to compromise blood flow to the musculature housed within these compartments [1]. The rise in pressure and neurovascular compromise, in turn, leads to necrosis of tissue,

often resulting in permanent tissue damage. The condition arises most frequently after extensive soft tissue injury or extremity bone fractures. A significant proportion of compartment syndrome cases involve the lower extremities, with the region below the knee being the most frequently affected [2].

ACS requires timely recognition and surgical intervention to prevent tissue necrosis and permanent injury [3]. Given this narrow therapeutic window, it is essential to identify risk factors for developing traumatic ACS, but current known risk factors are mostly limited to general conditions such as age, sex, extremity fracture, and fracture classification, although other variables have been established outside of trauma [4]. Identifying further risk factors would enable the development of more trauma-specific risk calculators, which would hopefully improve surveillance in high-risk individuals and shorten the time needed to diagnose ACS.

Objectives

The study conducted a large retrospective case-control analysis using data gathered from the American College of Surgeons Trauma Quality Improvement Program (TQIP) database [5]. We sought to establish further risk factors for lower extremity compartment syndrome after traumatic bone fractures as well as to establish a risk calculator for the condition.

METHODS

Ethics statement

This study was approved by the HCA DataClear and PubClear research and publication authorization process (No. 1396). Informed consent was waived due to the retrospective nature of the study and the deidentification of the database data.

Data source

This study was a retrospective case-control study utilizing the TQIP database for the years 2007 to 2019. This database contains demographic and treatment variables collected from patients from over 875 trauma centers throughout the United States. This dataset consists only of deidentified data, and thus, this study was given exempt status after a formal review from our Institutional Review Board.

Patient selection

We selected a subset of patients from the TQIP database to include those with lower extremity fractures. This was achieved by retrieving patients who had been diagnosed with lower extremity fractures including femur, tibia, or fibula fractures by using International Classification of Disease (ICD) 9th and 10th Revision codes including S72, S82, 821, and 823.

Case and control groups

The case and control groups were constructed using ICD diagnosis codes. The case group comprised patients with the outcome of extremity compartment syndrome during hospitalization (T79A and T79.A0, 958.90, 958.91, 958.92) among those with lower extremity fractures. The control group consisted of patients with lower extremity fractures, in whom extremity compartment syndrome did not occur. The case group contained 2,629 patients with compartment syndrome and the control group consisted of 762,083 patients without compartment syndrome.

Variables and multivariable analysis

Continuous data were expressed as mean with standard deviation or median, and differences between the two groups were compared. Parametric data expressed as proportions were evaluated by using the chi-square test, and the Student t-test was applied to continuous variables. Nonparametric data were assessed using the Fisher exact test for proportions and the Wilcoxon rank-sum test for continuous variables. Statistical analyses were conducted using SAS ver. 9.4 (SAS Institute Inc). Risk factors or predictor variables were considered significant if the P-values were less than 0.004, which was determined based on a Bonferroni correction for 11 predictor variables. These variables were subjected to multivariable analysis, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each to evaluate the associated risk of developing compartment syndrome.

For each group in the study, we examined several variables potentially associated with the risk of developing extremity compartment syndrome. These variables included age, sex, height, body mass index (BMI), type of venous thromboembolism (VTE) prophylaxis, time to procedure start, presence of burns, and the amounts of various blood products transfused. These variables are presented in Table 1. "Time to procedure start" is defined as the interval from when the patient was seen in the emergency department to the start of surgery. Although "time to procedure start" is included in Table 1, we did not incorporate it into our multivariable analysis in Table 2 due to its limited availability in the TQIP dataset. This variable was only recorded for 14.4% of patients in the dataset and was therefore excluded from further analysis. To evaluate the absolute risk of developing lower extremity compartment syndrome, a nomogram was constructed using a method described by Zlotnik and Abraira [6]. This approach has been previously utilized for estimating risk after tibial

Table 1. Extremity trauma variables according to the occurrence of compartment syndrome

Variable	Compartment syndrome		P-value
	Present (n=2,629)	Absent (n=762,083)	
Age (yr)	41.1±15.7	56.6±21.0	<0.001
Sex (%)			<0.001
Male	83.4	51.2	
Female	16.6	48.8	
Race/ethnicity (%)			
Asian	1.8	1.5	0.100
Black	19.8	12.8	<0.001
Hispanic	13.2	9.2	<0.001
White	61.3	73.4	<0.001
Other	3.9	3.1	0.020
Body mass index (kg/m^2) (%)			
<20	4.5	8.4	<0.001
20–35	77.1	75.4	0.040
>35	18.5	16.2	0.002
Height (cm)	170.7±23.0	168.1±17.7	<0.001
Weight (kg)	90.1±33.1	82.4±28.5	<0.001
Time to procedure (hr)	85.0±110.1	50.3±82.1	<0.001
VTE prophylaxis type (%)			
Heparin	12.6	7.2	<0.001
Low-molecular-weight heparin	58.6	51.0	<0.001
Other	4.1	7.1	<0.001
None	24.7	34.7	<0.001
VTE prophylaxis (%)			<0.001
Yes	75.3	65.3	
No	24.7	34.7	
Lowest systolic blood pressure (mmHg)	88.6±27.7	87.4±25.7	0.340
Burn (%)	0.04	0.04	0.910
Blood transfusion (%)			<0.001
Yes	16.1	4.6	
No	-	-	
Transferred blood (U)	0.48±1.56	0.12±0.77	<0.001
Transferred plasma (U)	0.28±1.19	0.07±0.60	<0.001
Transferred platelet (U)	0.13±0.67	0.02±0.29	<0.001
Transferred cryoprecipitate (U)	0.05±0.46	0.01±0.18	<0.001
Diabetes (%)	8.0	16.7	<0.001
Hypertension (%)	19.9	39.6	<0.001
Renal insufficiency (%)	0.5	2.3	<0.001

Values are presented as mean±standard deviation, unless otherwise indicated.
VTE, venous thromboembolism.

plateau fractures [7]. This nomogram is shown in Fig. 1.

RESULTS

Upon examining the demographic data, the results suggest associations with compartment syndrome that are consistent with previous studies [1]. Male sex is associated with higher odds of developing the condition (OR, 3.30; 95% CI, 2.96–3.68; P < 0.001), and individuals with a BMI greater than 35 kg/m^2 also had increased odds of developing compartment syndrome (OR, 1.55; 95% CI, 1.26–1.90; P < 0.001).

New variables evaluated in this study included VTE prophy-

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Table 2. Multivariable regression analysis of predictors of compartment syndrome

Variable	Estimate	OR	95% CI	P-value
Age (yr) (every 1-yr increase)	−0.027	0.97	0.97–0.98	<0.001
Sex				
Female	Reference	-	-	-
Male	0.597	3.30	2.96–3.67	<0.001
Body mass index (kg/m^2)				
<20	Reference	-	-	-
20–35	0.059	1.36	1.13–1.64	0.120
>35	0.189	1.55	1.26–1.90	<0.001
Height (cm) (every 1-cm increase)	−0.004	0.996	0.994–0.998	<0.001
VTE prophylaxis type				
None	Reference	-	-	-
Heparin	0.577	2.67	2.33–3.05	<0.001
Low-molecular-weight heparin	−0.017	1.47	1.34–1.62	0.640
Other	−0.155	1.28	1.04–1.58	0.040
Surgery				
No	Reference	-	-	-
Yes	0.187	1.45	1.33–1.59	<0.001
Burn				
No	Reference	-	-	-
Yes	−0.289	0.56	0.08–4.01	0.570
Transferred blood (U) (every 1-U increase)	0.124	1.13	1.09–1.18	<0.001
Transferred plasma (U) (every 1-U increase)	−0.010	0.99	0.94–1.04	0.710
Transferred platelet (U) (every 1-U increase)	0.151	1.16	1.09–1.24	<0.001
Transferred cryoprecipitate (U) (every 1-U increase)	0.118	1.13	1.04–1.22	0.003
Diabetes				
No	Reference	-	-	-
Yes	−0.086	0.84	0.72–0.98	0.030
Hypertension				
No	Reference	-	-	-
Yes	−0.019	0.96	0.86–1.08	0.520
Renal insufficiency				
No	Reference	-	-	-
Yes	−0.447	0.41	0.24–0.71	0.002

OR, odds ratio; CI, confidence interval; VTE, venous thromboembolism.

laxis type, whether surgery took place, whether burns were present, and whether a patient received blood, plasma, platelet, or cryoprecipitate transfusions. Heparin VTE prophylaxis was positively associated with compartment syndrome (OR, 2.67; 95% CI, 2.33–3.05; P < 0.001). The data also suggested that compartment syndrome was more likely to occur following surgery (OR, 1.45; 95% CI, 1.33–1.59; P < 0.001). Blood, platelet, and cryoprecipitate transfusions were modestly higher in the group with compartment syndrome. These variables are shown in Tables 1 and 2. As noted in the Methods section, time to procedure was found to have a significant association with the development of compartment syndrome, but this variable was excluded from the formal analysis due to limited data availability. The available data suggested that patients who developed compartment syndrome had a significantly longer time to their first operation than patients who did not develop compartment syndrome (85.0 ± 110.1 hours vs. 50.3 ± 82.1 hours, P < 0.001). This implies that patients who developed compartment syndrome did not receive early salvage procedures. It is likely that most, if not all, patients who developed compartment syndrome underwent salvage procedures such as fasciotomy or external fixation after the condition was diagnosed, as this is standard of care for the condition. To support

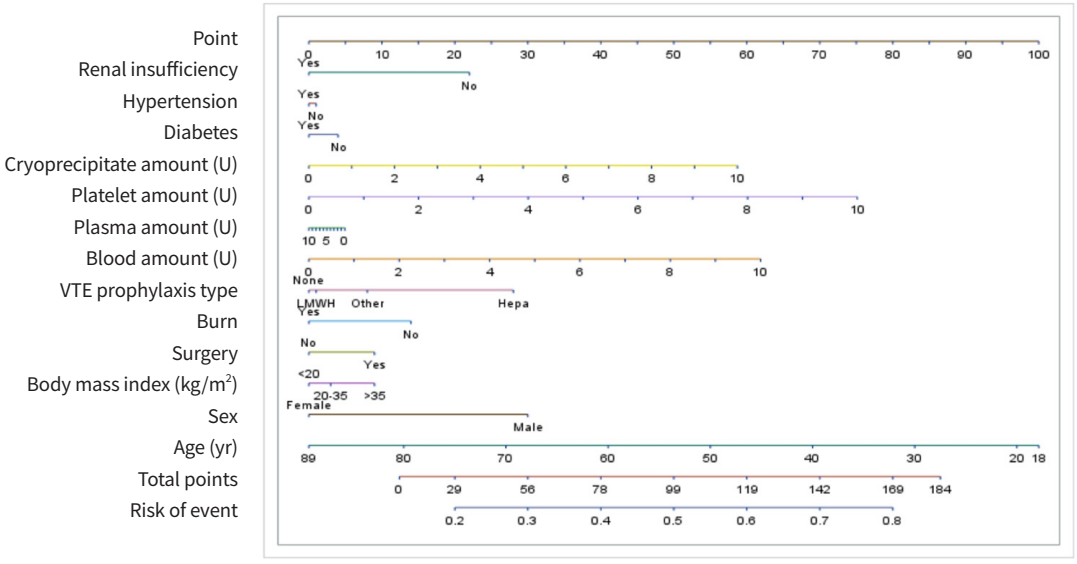

Fig. 1. A predictive nomogram for lower extremity acute compartment syndrome in trauma patients with lower extremity fracture(s). The vertical line from each variable intersecting the top blue line (0–100) estimates the score for each variable. The sum of the variable points is the total number of points (bottom red line). A vertical line between the bottom red line and the bottom risk of event blue line estimates the absolute risk of developing compartment syndrome during the hospital admission. VTE, venous thromboembolism.

this notion—namely, that patients in the ACS group underwent more salvage procedures than the control group—a further subanalysis was performed post hoc, focusing specifically on ICD-10 codes for tibial external fixation device application. External tibial fixation devices were applied to 15.4% of patients in the ACS group versus 2.7% of patients who did not develop ACS.

Utilizing the nomogram, one can estimate the risk of developing compartment syndrome. This is done by drawing a vertical line at each variable corresponding to the patient's condition and intersecting this line with the horizontal line at the top that represents the points for that variable. The points for each variable are then summed to obtain a total score. This total score is compared to the risk of events line (blue) at the bottom of the nomogram. The point at which the total score intersects with the estimated risk line indicates the patient's estimated risk. For a more objective measure of estimated risk, one can use the following formula: "risk = (total points + 21.174) / 237.49." Additionally, a user-friendly worksheet derived from the data presented in the nomogram is available for reference (see table in Material S1).

The following is an example of this nomogram being used for a fictional patient and is visually demonstrated in Fig. 2:

A 28-year-old man with a femoral shaft fracture was admitted to the emergency department. He had a BMI of 27 kg/m^2 and required 1 unit of packed red blood cells upon admission. Subsequently, he underwent open reduction and internal fixation of the femur fracture in the operating room. He was administered low-molecular-weight heparin both preoperatively and postoperatively. The patient's scores, as derived from the nomogram, are as follows: 85 points for age, 22 points for the absence of renal insufficiency, 30 points for being male, 3 points for BMI, 9 points for undergoing surgery, 6 points for receiving 1 unit of blood, and 0 points for all other variables. The sum of these points is 155. When this total is compared to the estimated risk line at the bottom of the nomogram, it corresponds to an approximate 78% risk for this patient's admission.

DISCUSSION

Blood product transfusions have been identified as positive predictors of compartment syndrome in this study. The literature extensively reports that excessive volume resuscitation with crystalloids and blood products can contribute to the development of abdominal compartment syndrome [8]. The rationale behind this association is that increased intravascular volume, coupled with heightened vascular permeability following trauma, results in interstitial edema of soft tissues due to Starling forces [8].

The question of whether the same conclusion could be drawn for extremity compartment syndrome has been very sparsely explored to date. Branco et al. [2] previously demonstrated that packed red blood cells are a risk factor for ACS. However, this study also found platelets and cryoprecipitate to be as strong of a

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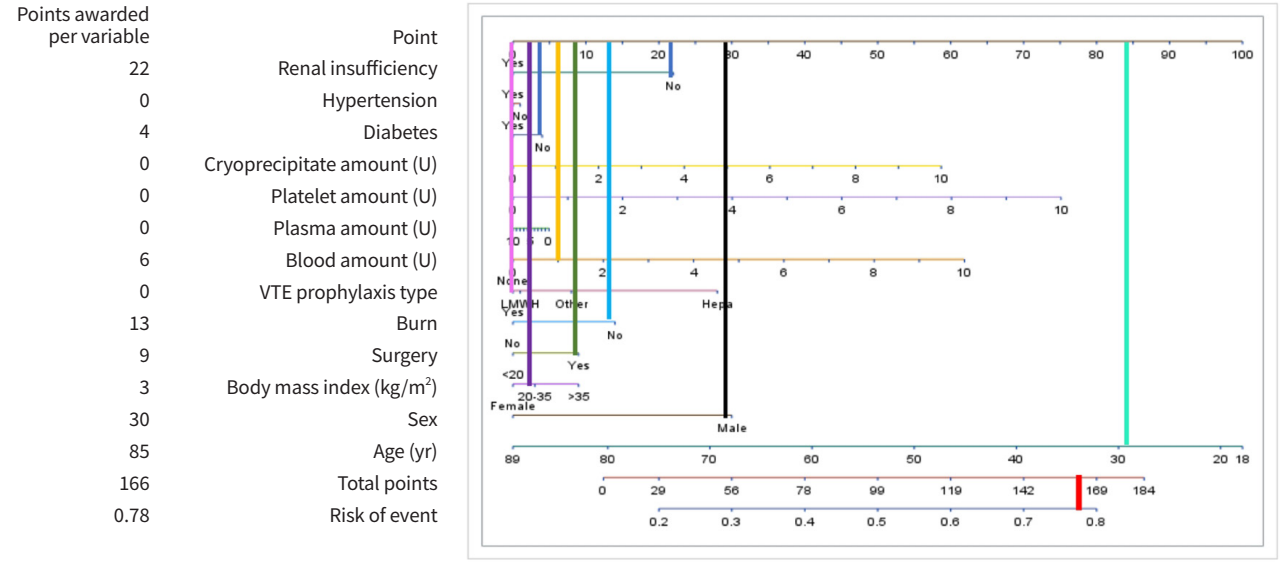

Fig. 2. A visual example of the fictional patient discussed in the Results section as superimposed on our predictive nomogram. VTE, venous thromboembolism.

predictor as packed red blood transfusion. Crystalloid infusion was not evaluated in this study due to a lack of data availability within the TQIP database.

Another novel finding in this study is that VTE prophylaxis with heparin emerged as a risk factor for ACS. The theoretical risk associated with chemoprophylaxis is that patients may experience bleeding into the surgical site, which could lead to ACS postoperatively. Our results suggest an association between the use of heparin and the development of ACS. In contrast, the use of low-molecular-weight heparin or other anticoagulation methods did not show a significant association with ACS. A review of the literature did not uncover previous studies where this was a significant finding, although there are case reports that suggest anticoagulation alone can lead to extremity ACS [9,10].

This novel finding may reflect baseline patient characteristics, such as illness severity and comorbidities, that prevent the use of more common types of VTE prophylaxis, including modalities like low-molecular-weight heparin. Despite these potential intuitive explanations for the association with ACS, the type of VTE prophylaxis could be a valuable variable in risk estimation.

Our predictive nomogram for estimating ACS in patients with lower extremity fractures (Fig. 1) could serve as a valuable aid in clinical decision-making and as a surveillance tool. While the classic physical examination findings of compartment syndrome are highly specific for the condition, the sensitivity of the physical exam is low, leading to many cases being undiagnosed or diagnosed late [11]. The complexity of diagnosis increases when patients are sedated or intubated for other coexisting conditions; in these instances, a surveillance tool such as our nomogram can increase clinicians' awareness.

Risk calculators have become well-established tools for many medical conditions, with the most effective ones being derived from extensive datasets through statistical modeling [12]. Our nomogram was developed using the TQIP database, which is large and comprehensive.

Limitations

There are several limitations to this study. First, this study focused on associations and not causation. Although the case-control study is comprehensive in its power due to the large size of the TQIP database, it represents a retrospective analysis rather than a prospective randomized controlled trial. Second, as previously mentioned, the risk factors identified may be secondary to other disease processes or patient comorbidities that actually reflect the risk for ACS. However, determining the mechanism is beyond the scope of this project. Instead, we present variables that are predictive of ACS outcomes within a specific population. Additionally, like any risk calculator, future studies will be required to prospectively validate the results of the nomogram. In the interim, we propose that this tool can be incorporated into the clinical armamentarium for assessing the need to further investigate ACS or the risk of ACS. Finally, several meta-analyses have identified additional risk factors for compartment syndrome that were not examined in this study. Risk factors previously suggested to be associated with the develop-

ment of ACS, but not included in our study, include tibial plateau fractures of Schatzker types IV–VI, polytrauma, gunshot wounds with fracture and vascular injury, combined forefoot and midfoot injury, Injury Severity Score, and AO Foundation/Orthopaedic Trauma Association (AO/OTA) type C fractures [7,13,14]. Further retrospective analyses could incorporate these already known risk factors and refine the granular prediction of risk for compartment syndrome after extremity fractures. Other future studies may expand the scope of the analysis to investigate upper extremity fractures and whether the risk calculator tool can be generalized to patients with all extremity fractures.

Conclusions

Predicting compartment syndrome in the lower extremities following trauma has traditionally been based on broad risk factors, lacking precise or standardized methods for risk stratification. This study contributes to the growing body of evidence suggesting that the use of heparin and blood product transfusions may be additional risk factors to consider during the risk stratification of lower extremity ACS. We propose a novel risk calculator that incorporates both previously published risk factors and those identified in this study. These calculations could provide a more accurate risk estimation and, hopefully, assist in making more informed clinical decisions for this limb-threatening condition.

ARTICLE INFORMATION

Author contributions

Conceptualization: BC, DA; Data curation: all authors; Formal analysis: all authors; Methodology: all authors; Project administration: BC; Visualization: BC, HL; Writing–original draft: BC, DA; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Data availability

Data analyzed in this study are available from the corresponding author upon reasonable request.

Supplementary materials

Material S1. Risk calculator for lower extremity compartment syndrome after trauma.

Supplementary materials are available from https://doi.org/10.20408/jti.2023.0077.

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