

# Risk Factors for Deep Vein Thrombosis or Pulmonary Embolus Following Anterior Cruciate Ligament Reconstruction

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**Background:** Nearly 350,000 Americans develop a deep venous thromboembolism (DVT) or pulmonary embolism (PE) annually, and nearly 100,000 Americans die from these events. To date, little research has investigated patient-specific risk factors that increase the rate of DVT/PE following anterior cruciate ligament reconstruction (ACLR).

**Purpose:** To determine relevant patient risk factors for the development of DVT/PE following ACLR.

**Study Design:** Case-control study; Level of evidence, 3.

**Methods:** All instances of ACLR from 2005 to 2014 within the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) prospective database were analyzed. Both univariate analysis and binary logistic regression were performed to determine which patient demographics and surgical factors were associated with DVT or PE following surgery.

**Results:** Of the 9146 patients who underwent ACLR, 46 (0.5%) developed postoperative DVT, 8 (0.1%) developed PE, and 5 (0.05%) developed both. The following variables were associated with the development of DVT or PE on univariate analysis: increased age, a high tibial osteotomy (HTO) performed at the time of ACLR, microfracture performed, the presence of hypertension requiring medical therapy, and the presence of an active wound infection. Independent predictors of DVT or PE on multivariate analysis included HTO (odds ratio [OR], 22.7), the presence of an active wound infection (OR, 11.0), or hypertension requiring medication (OR, 2.2). Meniscal repair was not a risk factor for DVT or PE on univariate or multivariate analysis.

**Conclusion:** In a review of 9146 patients undergoing ACLR, 46 (0.5%) developed DVT in the 30-day postoperative period. Increasing age over 30 years, concomitant HTO or microfracture, hypertension requiring medication, and presence of wound infection were all associated with an increased risk of DVT. The annual incidence of DVT/PE following ACLR reconstruction is low (<1%) and has not changed over time.

**Keywords:** ACL; deep vein thrombosis; pulmonary embolus; VTE; blood clot

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Venous thromboembolism (VTE), encompassing the two interrelated entities deep venous thromboembolism (DVT) and pulmonary embolism (PE), represents a serious postoperative complication. It is estimated that at least 350,000 Americans develop DVT or PE annually and nearly 100,000 Americans die due to VTE-related complications each year.<sup>23</sup> Due to the significant morbidity and mortality associated with VTE, the American Academy of Surgeons (AAOS) developed specific anticoagulation prophylaxis guidelines for hip and knee arthroplasty.<sup>22</sup> Although these guidelines do not extend to nonarthroplasty procedures, chemoprophylaxis is still prescribed routinely for other lower extremity operations, such as anterior cruciate ligament reconstruction (ACLR). According to the survey results by Keller et al,<sup>17</sup> 50.7% of sports medicine fellowship-trained surgeons use chemoprophylaxis following ACLR to protect against the occurrence of VTE; the majority of these surgeons use aspirin, with wide variation in both the dose and duration of treatment.

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ACLR is one of the most common orthopaedic procedures, with nearly 150,000 such operations performed annually in the United States.<sup>19</sup> Any operation places a patient at increased risk for VTE, particularly an operation involving a lower extremity because of the resultant immobility. Although the literature addresses the incidence of VTE following ACLR, specific risk factors predisposing a patient to the development of DVT or PE have not been documented. Small cohort studies and subsequent systematic reviews have described the incidence of VTE following ACLR as between 0.2% and 14%.<sup>8,11,16,27</sup> The variation in the documented incidence is attributable to the diagnostic methods used, the heterogeneity of the population, and the use of chemoprophylaxis. These studies are limited by their size because of the rarity of thromboembolic events, and many of these investigations seek out asymptomatic VTE using postoperative screening, which is not as clinically applicable.

Knowledge of the incidence of VTE following ACLR, as well as classification of patient-specific risk factors, allows surgeons to evaluate their patients' coagulopathic risk and could facilitate the development of a formal prophylactic anticoagulation protocol for nonarthroplasty procedures. The purpose of this study was to describe the incidence of symptomatic VTE following ACLR and to determine specific characteristics that may predispose a patient to the development of DVT or PE; to this end, we used the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database. In particular, we hypothesized that older age and the presence of procedures that limit postoperative weightbearing at the same time as ACLR would lead to an increased rate of VTE.

## METHODS

### Source Data

To study risk factors for DVT or PE following ACLR, we used the ACS NSQIP database. This database is a high-quality, prospectively collected surgical database encompassing approximately 750 medical centers during the period from January 2005 to December 2014. To maintain database quality, hospitals are excluded from ACS NSQIP if their interobserver disagreement rate between clinical reviewers is greater than 5% or if their 30-day follow-up rate is less than 80%. This database provides a highly accurate source of postoperative admission data, patient demographics, and medical comorbidities and has been validated for a large number of orthopaedic procedures to date, including ACLR.

### Data Collection

All cases from January 2005 to December 2014 with the isolated Current Procedural Terminology (CPT) code 29888 ("Arthroscopically aided anterior cruciate ligament repair/augmentation or reconstruction") were included. Additionally, the following CPT codes were included if

occurring simultaneously with ACLR: high tibial osteotomy (HTO) (27457), medial or lateral meniscal repair (29882, 29883), or microfracture (29879). No CPT codes were excluded. A number of patient demographic variables were collected, including age, sex, race, body mass index (BMI), smoking status, operative time, type of anesthesia used during surgery (epidural, general or monitored anesthesia care, and regional blockade), and American Society of Anesthesiologists (ASA) class ranging from 1 (healthy patient) to 4 (potentially life-threatening medical disease).

The primary endpoint assessed was the presence of DVT or PE (VTE) in the 30-day postoperative period. The NSQIP database does not specify the nature of the complication (ie, symptomatic or not symptomatic). Multiple continuous variables were converted to categorical variables for the purposes of data analysis, including age (<20, 20-29, 30-39, 40-49, ≥50 years) and BMI (<18.5, 18.5-24.9, 25-29.9, ≥30). The following medical comorbidities were included in the NSQIP database but were not included in the data analysis because they were not present in any patients undergoing ACLR: ventilator dependence, current pneumonia, presence of ascites or esophageal varices, vascular claudication at rest, coma, central nervous system tumors, disseminated cancer, chemotherapy, and radiotherapy.

Both univariate and multivariate logistic regressions were performed to assess for any patient demographic or surgical variables that represent independent risk factors for DVT or PE.

## Statistical Analysis

Univariate analysis was performed for each individual variable in order to determine which variables to include in the multivariate analysis. Chi-square testing was used for univariate analysis (Table 1). All variables with a *P* value less than .05 were considered significant and ultimately were included in a binary logistic regression model for DVT or PE. Binary logistic regression was performed, and the resulting odds ratios (ORs) with 95% CIs were calculated for all independent predictors of VTE. Results were considered statistically significant with a *P* value lower than the specified cutoff of .05 (SPSS Statistics v21.0; IBM Corporation).

## RESULTS

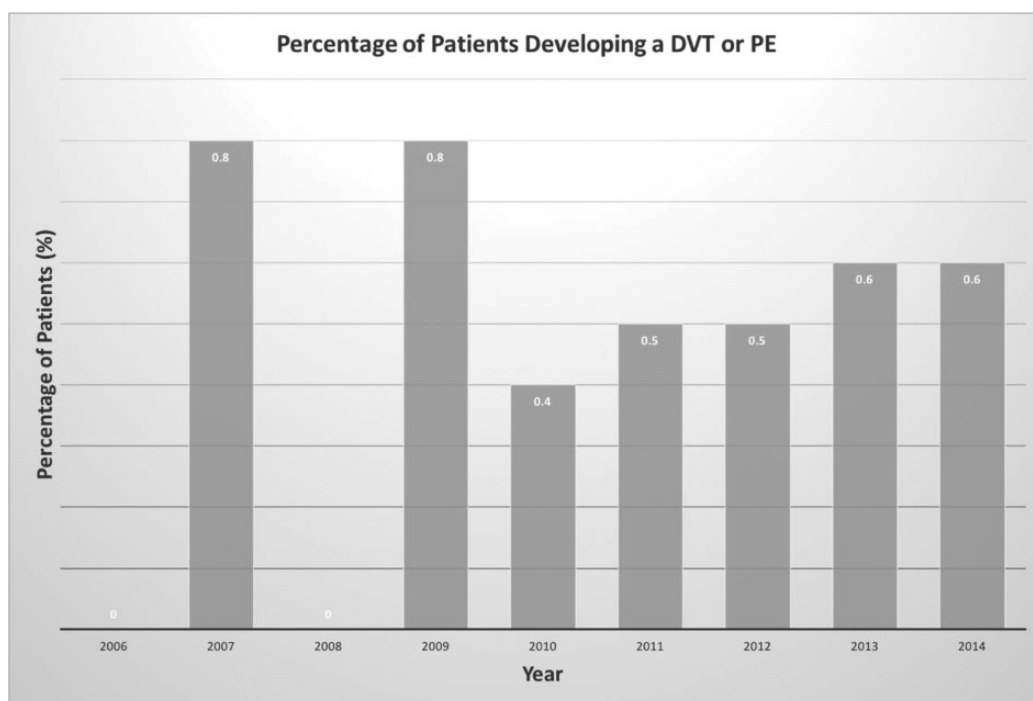
### Univariate Analysis

Of the 9146 patients who underwent ACLR, 46 (0.5%) developed a postoperative DVT, 8 (0.1%) developed PE, and 5 (0.05%) developed both. The variables tested in the univariate analysis are shown in Table 1. The annual DVT/PE rate was below 1% for each year and did not change significantly over time (*P* = .807) (Figure 1). DVTs were diagnosed on average 8.24 days (SD, 5.45 days) following surgery, and PEs were diagnosed on average 12.75 days postoperatively (SD, 6.9 days).

TABLE 1  
Univariate Analysis of Individual Patient Risk Factors for Patients Developing  
DVT or PE Following Anterior Cruciate Ligament Reconstruction<sup>a</sup>

Variable	Patients With DVT or PE, %	Patients Without DVT or PE, %	P Value
Patient demographics			
Sex			.982
Male	65.3	64.1	
Female	34.7	35.9	
Age			.038
<20 y	0	9.0	
20-29 y	28.6	37.6	
30-39 y	28.6	26.5	
40-49 y	30.6	19.2	
≥50 y	12.2	7.7	
Race			.921
White	61.2	58.3	
Asian	4.1	4.5	
Black	6.1	7.2	
Hispanic	2.0	0.8	
Native American	0.0	1.1	
Unknown	26.6	28.1	
Body mass index			.628
<18.5	0.0	2.1	
18.5-24.9	28.6	32.2	
25-29.9	38.8	38.4	
≥30	32.6	27.3	
ASA class			.427
1	40.8	54.5	
2	53.1	41.4	
3	6.1	4.1	
4	0.0	0.0	
Operative variables			
Operation time, min	105.8	102.0	.605
Posterior cruciate ligament reconstruction	0.0	0.5	.626
High tibial osteotomy	2.0	0.1	<.001
Microfracture	6.1	2.4	.045
Meniscal repair	12.2	9.4	.491
Anesthesia			.789
Epidural/spinal	6.1	4.2	
General/monitored anesthesia care	93.9	95.7	
Regional	0.0	0.1	
Surgery within 30 days	0.0	0.1	.965
Medical comorbidities			
Diabetes	0.0	1.6	.370
Smoker	16.3	18.8	.660
Chronic obstructive pulmonary disease	0.0	0.3	.692
Congestive heart failure	0.0	0.0	.941
Previous percutaneous coronary intervention	0.0	0.2	.940
Previous cardiac surgery	0.0	0.1	.947
Angina	0.0	0.0	.968
Hypertension	18.4	6.9	.002
Previous revascularization	0.0	0.0	.973
Dialysis	0.0	0.0	.992
History of transient ischemic attack	0.0	0.1	.961
Hemiplegia	0.0	0.0	.968
History of stroke	0.0	0.0	.973
Paraplegia	0.0	0.0	.971
Open wound	2.0	0.2	.003
Chronic steroid use	0.0	0.4	.667
Loss of 10 pounds prior to surgery	0.0	0.0	.889
Bleeding disorder	0.0	0.3	.719
Pregnancy	0.0	0.0	.995

<sup>a</sup>ASA, American Society of Anesthesiologists; DVT, deep vein thrombosis; PE, pulmonary embolus.



**Figure 1.** Annual rate of deep venous thromboembolism (DVT) or pulmonary embolism (PE) following anterior cruciate ligament reconstruction.

### Patient Demographics

Age ( $P = .038$ ) was the only patient demographic factor that was significantly different for the group of patients experiencing DVT or PE (age range, 18-65 years). In particular, the DVT/PE group had a larger proportion of patients older than 30 years (71.4% vs 53.4% for no DVT/PE). BMI was not significantly different for the VTE group ( $P = .628$ ).

### Operative Variables

With regard to operative variables, the patients who developed DVT or PE were more likely to undergo HTO (2.0% vs 0.1%,  $P < .001$ ) or microfracture (6.1% vs 2.4%,  $P = .045$ ) at the time of ACLR. Meniscal repair did not significantly affect the development of DVT or PE ( $P = .491$ ).

### Medical Comorbidities

The medical comorbidities that were more common in the DVT/PE group included hypertension requiring medication (18.4% vs 6.9%,  $P = .002$ ) and the presence of an open wound infection (2.0% vs 0.2%,  $P = .003$ ) (Table 1).

### Multivariate Analysis

Binary logistic regression revealed multiple independent predictors of VTE following ACLR (Table 2). The variable with the highest ORs for DVT/PE was HTO (OR, 22.7; 95% CI, 2.7-200.0;  $P = .004$ ) at the time of ACLR. Other

TABLE 2

Independent Risk Factors for Deep Vein Thrombosis or Pulmonary Embolus Following Anterior Cruciate Ligament Reconstruction in Multivariate Analysis

Patient Variable	Odds Ratio (95% CI)	<i>P</i>
High tibial osteotomy	22.7 (2.7-200.0)	.004
Active wound infection	11.0 (1.4-83.3)	.023
Hypertension requiring medication	2.2 (1.1-4.8)	.049

significant independent predictors for DVT/PE included active wound infection (OR, 11.0; 95% CI, 1.4-83.3;  $P = .023$ ) and hypertension requiring medication (OR, 2.2; 95% CI, 1.1-4.8;  $P = .049$ ).

### DISCUSSION

Our study found that of 9146 patients undergoing ACLR, 46 (0.5%) developed DVT in the 30-day postoperative period. While this is a relatively small number, it means that on average, a surgeon performing 200 ACLRs per year will encounter 1 DVT per year, a very important finding given the lack of a standardized recommendation for DVT prophylaxis following ACLR. Also, given the variability in patient demographics and risk factors, it may be difficult to determine the true number of DVTs in ACLR patients. The annual fluctuation of VTE found in this study is likely a result of the relative rarity of these events. Cullison et al<sup>15</sup>

used ultrasonography to assess ACLR patients on postoperative days 2 and 3 for DVT. Only 1 patient out of 67 (1.5%) was found to have DVT, which led the authors to recommend against routine DVT prophylaxis following ACLR. Ye et al<sup>27</sup> retrospectively reviewed 171 patients who had undergone arthroscopic ACLR treated without anti-inflammatories or anticoagulants who underwent venous contrast examination on postoperative day 3; the average patient age was 30.1 years. The authors reported that DVT was found in 24 patients (14%) and that the only risk factor for DVT was age beyond 35 years. This led the authors to recommend DVT prophylaxis in patients older than 35 years.

Our study similarly found that increased age was a risk factor for development of DVT; however, we found the age cutoff to occur at 30 years. Jameson et al<sup>15</sup> examined the 90-day complication rates of 13,941 primary ACLRs performed in England from 2008 and 2010; these authors found the DVT and PE rates to be 0.30% and 0.18%, respectively. Unfortunately, the authors did not assess for patient factors contributing to DVT and did not make any recommendations with regard to prophylaxis. However, that investigation serves as a large descriptive study of the rate of DVT following ACLR, similar to ours.

Our study found that concomitant procedures, specifically HTO and microfracture, significantly increased the rate of DVT following ACLR. This seems intuitive, as these procedures add to the operative time and may lead to altered weightbearing status postoperatively, which can increase the risk for venous stasis and VTE. Erickson et al<sup>9</sup> recently reviewed the rates of DVT and PE following HTO, distal femoral osteotomy, and tibial tubercle osteotomy. A low rate of DVT (1.4%; 2/142) was found with these individual procedures; however, this was a relatively small study of DVT rates. Turner et al<sup>25</sup> found that there may be a large difference in clinically diagnosed DVT versus DVT diagnosed by ultrasonography following HTO. In 84 patients, 15% had a clinical diagnosis of DVT while venography demonstrated DVT in 41% of patients postoperatively. While these studies disagree regarding the rate of DVT following HTO, the fact that our study showed a statistically significant increase in the risk of DVT when HTO was performed with ACLR warrants consideration regarding the use of DVT prophylaxis in these patients. Interestingly, meniscal repair did not significantly affect the rate of DVT, potentially indicating that weightbearing status alone was not responsible for the increased DVT risk, although weightbearing in full extension may be increasingly used by surgeons.

Last, our study found that several medical comorbidities were correlated with risk of DVT formation. Open wound infection and the presence of hypertension requiring medication were both significant for DVT and increased its risk. This is important because Americans have a high rate of hypertension, and this rate increases with age. Lacruz et al<sup>18</sup> found that 23% of men between 45 and 55 years of age take antihypertensive medications. Obviously, this is older than the typical ACLR patient. The Centers for Disease Control and Prevention<sup>4</sup> reported a 29.1% prevalence of hypertension in adults over 18 years and a 7.3% prevalence in the 18- to 39-year age group.

Hypertension may contribute to the endothelial damage needed to propagate clot formation. Huang et al<sup>14</sup> recently performed a meta-analysis to examine the correlation between hypertension and DVT following orthopaedic surgery. A total of 16 articles with 68,955 males and 53,057 females were analyzed, and the authors found that hypertension was associated with DVT with an OR of 2.89. This finding shows that the likelihood of an ACLR patient having hypertension is high and should be considered in the decision to use prophylaxis against VTE. Unfortunately, because the NSQIP database does not include several variables that may affect the risk of VTE (eg, altitude, oral contraceptives, tourniquet time), our list of medical comorbidities discussed here is not all-encompassing.

The American College of Chest Physicians currently recommends against DVT prophylaxis after arthroscopic surgery and recommends early mobilization instead.<sup>10</sup> When considering prophylaxis, the Warfarin and Aspirin (WARFASA) study found a 40% risk reduction in DVT formation with aspirin in a group of patients who were previously receiving warfarin, showing that aspirin is an effective method of DVT prophylaxis.<sup>1</sup> This trial was performed in all-comers who had one instance of a previously treated, unprovoked DVT. Similarly, the Aspirin to Prevent Recurrent Venous Thromboembolism (ASPIRE) study (a trial performed among all-comers with one instance of unprovoked DVT) found that aspirin use for DVT prevention reduces the secondary composite outcome of major vascular events following DVT by 34%, without increasing bleeding, which resulted in a significant net clinical benefit.<sup>3</sup>

While an argument could be made against routine DVT prophylaxis in young, healthy ACLR patients, our study showed a significantly increased rate of DVT in patients over 30 years old, those with hypertension requiring medication, and those undergoing concomitant HTO, microfracture, or other procedures that entail delayed weightbearing. Nevertheless, it is imperative that surgical providers weigh the major risks of routine DVT prophylaxis such as aspirin (stomach ulceration, gastrointestinal bleeding, bleeding) and low-molecular-weight heparin (bleeding, heparin-induced thrombocytopenia) prior to instituting it on a routine basis. While these complications may be rare, they cannot be completely prevented in a busy surgical practice. This would lead us to recommend consideration of DVT prophylaxis in these high-risk groups until full weightbearing is achieved. Unfortunately, because the NSQIP database does not document which, if any, types of DVT prophylaxis patients receive, we cannot make causal inferences regarding the prevention of VTE following ACLR, as it is impossible to know whether use of chemoprophylaxis decreased rates of VTE in this study. Furthermore, the growing trend among surgeons in the United States to use chemoprophylaxis following routine ACLR may have contributed to the small number of instances of VTE seen in this study.

## Limitations

This study had several limitations, most of which are related to the inherent limitations of the NSQIP database itself. The data are limited by the time frame of data

collection and the 30-day immediate postoperative period, and the database does not include long-term outcomes. Despite the large number of institutions captured by the NSQIP database, procedures performed in independent surgery centers are not included in this study, so our results may not be fully representative of all arthroscopic ACLR procedures performed. The patients in NSQIP potentially could be older, could have more significant mechanisms leading to multiligamentous injury, or could have more comorbidities than the patient population represented at surgery centers, which could confound data. Additionally, orthopaedic-specific data are not included in the database, such as the type of graft used, the surgeon's use of and preference for DVT prophylaxis, postoperative therapy protocols, and outcome measures specific to arthroscopic ACLR. To that effect, it was unknown how many patients in the database underwent postoperative VTE chemoprophylaxis. Furthermore, we cannot comment on the method of diagnosis of VTE (ie, clinical vs subclinical), as this is not specified in the NSQIP database. In addition, we were unable to determine surgeon experience or hospital volume for arthroscopic ACLR. Despite this, the NSQIP allowed us to determine the incidence of and risk factors for DVT and PE following arthroscopic ACLR, which are not well recorded in the literature to date. The literature has shown the NSQIP to be a high-quality database to study perioperative complications.<sup>2,6,7,12,13,20,21,24,26</sup>

## CONCLUSION

In a review of 9146 patients undergoing ACLR, 46 (0.5%) developed DVT in the 30-day postoperative period. Age over 30 years, concomitant HTO or microfracture, hypertension requiring medication, and presence of wound infection were associated with an increased risk of VTE. Considering these findings, we recommend the use of VTE prophylaxis in these high-risk patient populations.

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