Risk Factors for Thromboembolic Events After Surgery for Ankle Fractures

Bryce A. Basques, MD, MHS, Christopher P. Miller, MD, Nicholas S. Golinvaux, MD, Daniel D. Bohl, MD, MPH, and Jonathan N. Grauer, MD

Abstract

We conducted a retrospective national-cohort study to determine the incidence of and independent risk factors for venous thromboembolic events (VTEs) after open reduction and internal fixation (ORIF) of ankle fractures.

Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, we identified patients who underwent ORIF for ankle fracture between 2005 and 2012. VTE was defined as the occurrence of a deep vein thrombosis or a pulmonary embolism within the first 30 postoperative days.

Of the 4412 ankle fracture patients who met the inclusion criteria, 33 (0.8%) had a VTE. Multivariate analysis revealed that body mass index (BMI) of 30 to 35 kg/m^2 (odds ratio [OR], 4.77; 95% confidence interval [CI], 1.05-21.72; P = .044), BMI of 35 kg/m^2 or higher (OR, 4.71; 95% CI, 1.03-21.68; P = .046), heart disease (OR, 3.28; 95% CI, 1.20-8.97; P = .020), and dependent functional status (OR, 2.59; 95% CI, 1.11-6.04; P = .028) were independently associated with occurrence of VTE after ankle fracture ORIF.

Patients with higher BMI and patients with heart disease or dependent functional status may be considered for VTE prophylaxis.

Venous thromboembolic events (VTEs), encompassing both deep vein thrombosis (DVT) and pulmonary embolism (PE), are potentially fatal events that can occur after orthopedic surgery.[1] In patients who do not receive prophylaxis, VTE incidence can be as high as 70% for total hip arthroplasty,[2] 26% for hip fracture,[3] and 5% for ankle fracture.[4] Based on the relatively low incidence of VTE after ankle fractures and insufficient evidence for VTE prophylaxis in this population, the American Orthopaedic Foot and Ankle Society and the American College of Chest Physicians do not recommend routine screening or prophylaxis for VTE in patients with ankle fractures.[1,5] Nevertheless, certain patients may be at increased risk for VTE after open reduction and internal fixation (ORIF) of an ankle fracture. In such cases, further consideration for prophylaxis may be warranted.

Other studies of VTEs have identified general risk factors of increased age, obesity, prior thromboembolic disease, oral contraceptive use, multitrauma, varicose veins, and prolonged immobilization, among others.[1,6,7] In orthopedics, most of this research comes from total joint arthroplasty and hip fracture studies. However, there is relatively limited data for ankle fracture. The best studies directly addressing VTE after ORIF of ankle fractures have had important limitations, including missing patient data and suboptimal capture of VTE occurrences,[8-10] possibly leading to underestimates of the incidence of VTEs.

Given the limited data available, we conducted a retrospective national-cohort study to determine the incidence of and independent risk factors for VTEs after ankle fracture ORIF. If patients who are at higher risk for VTE can be identified, they can and should be carefully monitored and be considered for VTE prophylaxis. This information is needed for patient counseling and clinical decision-making.

Materials and Methods

This retrospective study used the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, which captures data from more than 370 participating US hospitals.[11] In ACS-NSQIP, 150 patient variables are collected from operative reports, medical records, and patient interviews by trained clinical reviewers.[11,12] Patients are identified prospectively and randomly sampled at participating hospitals. Routine auditing is performed to ensure high-quality data. Clinical data are collected for the entire 30-day postoperative period, regardless of discharge status during this time.

Patients who underwent ankle fracture ORIF between 2005 and 2012 were identified in the ACS-NSQIP database. They were initially selected by the postoperative diagnosis of ankle fracture (*International Classification of Diseases, Ninth Revision* codes 824.0-824.9). Of these patients, only those with primary *Current Procedural Terminology* codes 27766 (ORIF of medial malleolus fracture), 27769 (ORIF of posterior malleolus fracture), 27792 (ORIF of lateral malleolus fracture), 27814

Authors' Disclosure Statement: The authors report no actual or potential conflict of interest in relation to this article.

(ORIF of bimalleollar fracture), and 27822/27823 (ORIF of trimalleollar fracture) were included in the analysis. Patients with incomplete perioperative data were excluded, leaving 4412 patients (out of the initial 4785) for analysis.

Patient characteristics, including sex, age, height, weight, and history of smoking, were collected from the ACS-NSQIP database. Body mass index (BMI) was calculated from each patient's height and weight. Age was divided into approximately 20-year increments, beginning with age 18 years, in order to compare younger, middle-aged, and elderly groups of patients with ankle fractures. BMI was divided into categories based on the World Health Organization definitions of obesity: under 25 kg/m^2 (normal weight), 25 to 30 kg/m^2 (overweight), 30 to 35 kg/m^2 (class I obesity), and 35 kg/m^2 or over (class II and class III obesity).[13]

Information about medical comorbidities is also available in the ACS-NSQIP database. History of pulmonary disease was defined as a history of dyspnea, severe chronic obstructive pulmonary disease, ventilator-assisted respiration within 48 hours before surgery, or current pneumonia. History of heart disease was defined as a history of congestive heart failure (CHF) or angina within 1 month before admission, myocardial infarction within 6 months before admission, cardiac surgery, or percutaneous coronary intervention. American Society of Anesthesiologists (ASA) classes 3 and above signify severe systemic disease. Steroid use was defined as requiring regular administration of corticosteroid medications within 1 month before surgery. Disseminated cancer was defined as a malignancy that has spread to 1 or more sites besides the primary site.

Functional status was defined as the ability to perform activities of daily living (ADLs) within 30 days before surgery. Best functional status during this period was recorded. ACS-NSQIP defines ADLs as the "activities usually performed in the course of a normal day in a person's life," including bathing, feeding, dressing, toileting, and mobility. An independent patient does not require assistance for any ADLs; a partially dependent patient requires assistance for some ADLs; and a totally dependent patient requires assistance in all ADLs. Partially and totally dependent patients were grouped for analysis. Anesthesia type was separated into general and nongeneral, which includes monitored anesthesia care, spinal anesthesia, and regional anesthesia.

ACS-NSQIP also records the occurrence of multiple events up to 30 days after surgery. For our study, VTE was defined as the occurrence of a DVT or a PE during this period. ACS-NSQIP defines DVT as a new blood clot or thrombus identified within a vein—with confirmation by duplex ultrasonography, venogram, or computed tomography (CT)—that required therapy (anticoagulation, placement of vena cava filter, and/or clipping of vena cava). PE is recorded if ventilation/perfusion (VQ) scan, CT examination, transesophageal echocardiogram, pulmonary arteriogram, CT angiogram, or any other definitive modality is positive.

Statistical analyses were performed with Stata Version 11.2 (StataCorp). Demographic and comorbidity variables were tested for association with occurrence of VTE using bivariate and multivariate logistic regression.

Final multivariate models were constructed with a backward stepwise process that initially included all potential variables and sequentially excluded variables with the highest P value until only those with $P < .200$ remained. Variables with $.050 < P < .200$ were left in the model to control for potential confounding but are not considered significantly associated with the outcome. Statistical significance was established at a 2-sided α of 0.050 ($P < .050$). The fitness of the final logistic regression model was assessed with the C statistic and the Hosmer-Lemeshow goodness-of-fit test.

Table 1. Patient Characteristics

	n	%
Overall	4412	100.0
Age, y		
18-39	1293	29.4
40-59	1636	37.1
≥60	1476	33.5
Male sex	1783	40.4
Body mass index		
<25	927	21.1
25-30	1531	34.9
30-35	1023	23.3
≥35	909	20.7
ASA classes 3 and 4	1253	28.4
History of:		
Diabetes	568	12.9
Smoking	1090	24.7
Pulmonary disease	297	6.7
Heart disease	189	4.3
Hypertension	1570	35.6
Disseminated cancer	7	0.2
Steroid use	87	2.0
Dependent functional status	386	8.8
Fracture type		
Medial malleolus	235	5.3
Lateral malleolus	1143	25.9
Bimalleolar	1705	38.6
Trimalleolar	1329	30.1
Anesthesia type		
General	3788	85.9
Nongeneral[a]	624	14.1

Abbreviation: ASA, American Society of Anesthesiologists.
[a]Included monitored anesthesia care, spinal anesthesia, and regional anesthesia.

Results

For the 4412 ankle fracture patients who met the inclusion criteria, mean (SD) age was 50.9 (18.2) years, and mean (SD) BMI was 30.4 (7.6) kg/m^2. The cohort was 40.4% male. Surgery was performed on 235 patients (5.3%) with medial malleolus fracture, 1143 patients (25.9%) with lateral malleolus

fracture, 1705 patients (38.6%) with bimalleollar fracture, and 1329 patients (30.1%) with trimalleollar fracture. **Table 1** summarizes the patient characteristics.

Of the 33 patients (0.8%) with a VTE recorded within the first 30 postoperative days, 16 (0.4% of all patients) had a DVT recorded, 14 (0.3% of all patients) had a PE recorded, and 3 (0.1% of all patients) had both a DVT and a PE recorded. In 13 (39.4%) of the 33 patients with a VTE, the event occurred after discharge. VTEs were reported a mean (SD) of 11.5 (9.6) days after surgery. No patient in this study died of VTE.

Bivariate logistic regressions were performed to test the association of each patient variable with the occurrence of a VTE. Results are listed in **Table 2**. The bivariate analyses revealed significant associations between VTE after ankle fracture ORIF and the patient variables of age 60 years or older (odds ratio [OR], 2.40; 95% confidence interval [CI], 1.01-5.72), class I obesity (BMI, 30-35 kg/m^2: OR, 5.15, 95% CI, 1.14-23.28), class II and class III obesity (BMI, ≥35 kg/m^2: OR, 6.33, 95% CI, 1.41-28.38), ASA classes 3 and 4 (OR, 3.05; 95% CI, 1.53-6.08), history of heart disease (OR, 5.10; 95% CI, 2.08-12.49), history of hypertension (OR, 2.81; 95% CI, 1.39-5.66), and dependent functional status (OR, 3.39; 95% CI, 1.52-7.56).

Multivariate logistic regression was used to control for potential confounding variables and determine which factors were independently associated with VTEs. Results of this analysis are listed in **Table 2** as well. The multivariate analysis revealed that the patient variables of class I obesity (BMI, 30-35 kg/m^2: OR, 4.77; 95% CI, 1.05-21.72; P = .044), class II and class III obesity (BMI, ≥35 kg/m^2: OR, 4.71; 95% CI, 1.03-21.68; P = .046), history of heart disease (OR, 3.28; 95% CI, 1.20-8.97; P = .020), and dependent functional status (OR, 2.59; 95% CI, 1.11-6.04; P = .028) were independently associated with an increased rate of VTEs. Of note, anesthesia type was not significantly associated with occurrence of VTE on bivariate or multivariate analysis.

The C statistic of the final multivariate model was 0.76, indicating very good distinguishing ability. The Hosmer-Lemeshow goodness-of-fit test showed no evidence of lack of fit.

Discussion

Citing the lack of conclusive evidence and the low incidence of VTE after ankle fracture surgery, current recommendations are to avoid routine VTE prophylaxis in the postoperative management of patients who undergo this surgery.[1,5]

Table 2. Results of Bivariate and Multivariate Logistic Regressions for Influence of Risk Factors on Occurrence of Venous Thromboembolic Events

	Bivariate Analyses[a]		Multivariate Analysis[a,b]	
Risk Factor	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Age, y				
40-59 vs 18-39	0.79 (0.28-2.26)	.659	—	—
≥60 vs 18-39	**2.40 (1.01-5.72)**	**.049**	—	—
Male sex	0.55 (0.26-1.19)	.128	—	—
Body mass index				
25-30 vs <25	2.49 (0.53-11.73)	.250	—	—
30-35 vs <25	**5.15 (1.14-23.28)**	**.033**	**4.77 (1.05-21.72)**	**.044**
≥35 vs <25	**6.33 (1.41-28.38)**	**.016**	**4.71 (1.03-21.68)**	**.046**
ASA classes 3 and 4	**3.05 (1.53-6.08)**	**.001**	2.18 (0.98-4.86)	.056
History of:				
Diabetes	1.21 (0.47-3.14)	.695	0.42 (0.14-1.21)	.111
Smoking	**0.30 (0.09-0.99)**	**.049**	0.34 (0.10-1.14)	.081
Pulmonary disease	2.50 (0.958-6.52)	.061	—	—
Heart disease	**5.10 (2.08-12.49)**	**<.001**	**3.28 (1.20-8.97)**	**.020**
Hypertension	**2.81 (1.39-5.66)**	**.004**	—	—
Steroid use	3.26 (0.77-13.84)	.109	—	—
Dependent functional status	**3.39 (1.52-7.56)**	**.003**	**2.59 (1.11-6.04)**	**.028**
Bimalleolar vs lateral malleolus fracture	1.12 (0.49-2.56)	.792	—	—
Trimalleolar vs lateral malleolus fracture	0.86 (0.34-2.17)	.748	—	—
Nongeneral vs general anesthesia	0.40 (0.09-1.63)	.197	0.31 (0.07-4.85)	.108

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; OR, odds ratio.
[a]Bolding indicates statistical significance (*P* < .05).
[b]Final multivariate model was constructed with backward stepwise process that initially included all potential predictor variables and sequentially excluded variables with highest *P* value until only those with *P* < .20 remained. Variables with .05 < *P* < .20 were left in model to control for potential confounding but are not considered statistically significant. No patients with disseminated cancer or medial malleolus fracture had a venous thromboembolic event, so these variables could not be analyzed with bivariate or multivariate analyses.

However, it is important to identify patients who are at increased risk, as some may benefit from VTE prophylaxis. In the present study, we used the large, high-quality ACS-NSQIP database collecting information from multiple US hospitals to examine risk factors for VTE after ankle fracture ORIF. We identified 4412 patients who underwent ankle fracture ORIF between 2005 and 2012, and found an overall VTE incidence of 0.8%. Multivariate analysis identified obesity, history of heart disease, and dependent functional status as independent risk factors for VTE after ankle fracture ORIF.

This study's 0.8% incidence of VTE after ankle fracture ORIF is consistent with the range (0.29%-5%) reported in other ankle fracture studies.[4,8-10,14-18] We found that VTEs occurred a mean of about 11 days after surgery, and no patient died of VTE.

Obesity (BMI, ≥30 kg/m^2) had the strongest association with VTEs in this study. Obesity, which is a growing public health concern, can make postoperative care and mobilization more difficult.[19] Obesity has previously been associated with VTEs after ankle fractures, and BMI of over 25 kg/m^2 is one of the Caprini criteria for thrombosis risk factor assessment.[6,10] In our study, however, BMI of 25 to 30 kg/m^2 was not associated with an increased VTE rate, indicating that moderately overweight patients may not be at significantly higher risk for VTE (compared with patients with normal BMI) and may not need VTE prophylaxis. VTE prophylaxis after ankle fracture surgery may be considered in patients with BMI over 30 kg/m^2.

History of heart disease was also associated with VTEs in this study. Patients with a history of heart disease were at 3 times the risk for VTE within 30 days of ankle fracture surgery. This association is also consistent with the Caprini criteria, which include acute myocardial infarction and CHF as risk factors for venous thrombosis.[6] Other studies have found associations between CHF and VTE and between cardiovascular risk factors and VTE.[7,20] The association between cardiovascular disease and VTE may derive from the decreased venous flow rate associated with CHF or an overall vascular disease state. These patients may benefit from heightened surveillance and postoperative prophylaxis for VTE.

Dependent functional status was the final risk factor found to be associated with VTE after ankle fracture ORIF. This association likely derives from an inability to mobilize independently, leading to increased venous stasis. Immobilization has been previously associated with increased risk for VTE after ankle surgery.[7,14,16,20] Caretakers should be aware of this increased risk during the postoperative period and diligently monitor these patients for signs and symptoms of VTE. Prophylaxis may also be considered in this patient population.

Several risk factors that were significant on bivariate analysis (increased age; increased ASA class; history of diabetes, pulmonary disease, hypertension) were not significant in the final multivariate model. This finding suggests covariance between these factors and those that were significant in the final multivariate model. In particular, age and increased overall comorbidity (represented by increased ASA class) were not significant in our multivariate model—contrary to findings of other studies.[8-10] It is possible that history of heart disease alone was responsible for the association between overall comorbidity and VTE in those studies. In the present study, separating and controlling for individual comorbidities could have allowed this association to be more precisely characterized.

The characteristics of the ACS-NSQIP database limited our study in several ways. First, although ACS-NSQIP makes significant efforts to collect as many patient variables as possible, some information is not captured. Data about additional factors that may affect VTE risk (eg, history of previous VTE, hypercoagulable state, history of malignancy other than disseminated cancer, tourniquet time, patient position in operating room) were not available. Second, data are collected only on those postoperative adverse events that occur within 30 days after surgery; data on VTEs that occur later are not captured. However, it has been shown that the majority of VTEs occur within the first 30 days after lower extremity trauma and surgery,[21,22] so this follow-up interval was deemed adequate for capture of VTE data. Third, the database does not include information on the prophylactic regimens used for these patients—which may have weakened the associations between predictor variables and VTE risk and led to an underestimated effect size. VTE incidence, as well as the odds of developing a VTE with one of the identified risk factors, may actually be higher than reported in this study.

Conclusion

VTEs are serious complications that can occur after ORIF of ankle fractures. In this study, the overall incidence of VTE after ankle fracture ORIF was 0.8%. Although the American Orthopaedic Foot and Ankle Society and the American College of Chest Physicians do not recommend routine screening or prophylaxis for VTE in patients with ankle fractures,[1,5] the results of this study showed there may be a benefit in emphasizing VTE prophylaxis after ankle fracture ORIF in patients with obesity, history of heart disease, or dependent functional status. At minimum, these patients should be more carefully monitored for development of VTEs.

Dr. Basques, Dr. Miller, Dr. Golinvaux, and Dr. Bohl are Residents, and Dr. Grauer is Associate Professor of Orthopaedics and Rehabilitation, Associate Professor of Pediatrics, Co-Director of Orthopaedic Spine Service, and Co-Director of Yale–New Haven Hospital Spine Center, Department of Orthopaedics and Rehabilitation, Yale University School of Medicine, New Haven, Connecticut.

Address correspondence to: Jonathan N. Grauer, MD, Department of Orthopaedics and Rehabilitation, Yale University School of Medicine, 800 Howard Ave, New Haven, CT 06510 (tel, 203-737-7463; fax, 203-785-7132; email, jonathan.grauer@yale.edu).

Am J Orthop. 2015;44(7):E220-E224.

References

1. American Orthopaedic Foot and Ankle Society. Position statement: the use of VTED prophylaxis in foot and ankle surgery. http://www.aofas.org/medical-community/health-policy/Documents/VTED-Position-Statement-

Approv-7-9-13-FINAL.pdf. Updated 2013. Accessed May 10, 2015.
2. Grady-Benson JC, Oishi CS, Hanson PB, Colwell CW Jr, Otis SM, Walker RH. Routine postoperative duplex ultrasonography screening and monitoring for the detection of deep vein thrombosis. A survey of 110 total hip arthroplasties. *Clin Orthop Relat Res*. 1994;(307):130-141.
3. Salzman EW, Harris WH, DeSanctis RW. Anticoagulation for prevention of thromboembolism following fractures of the hip. *New Engl J Med*. 1966;275(3):122-130.
4. Patil S, Gandhi J, Curzon I, Hui AC. Incidence of deep-vein thrombosis in patients with fractures of the ankle treated in a plaster cast. *J Bone Joint Surg Br*. 2007;89(10):1340-1343.
5. Falck-Ytter Y, Francis CW, Johanson NA, et al; American College of Chest Physicians. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 suppl):e278S-e325S.
6. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon*. 2005;51(2-3):70-78.
7. Mayle RE Jr, DiGiovanni CW, Lin SS, Tabrizi P, Chou LB. Current concepts review: venous thromboembolic disease in foot and ankle surgery. *Foot Ankle Int*. 2007;28(11):1207-1216.
8. Jameson SS, Augustine A, James P, et al. Venous thromboembolic events following foot and ankle surgery in the English National Health Service. *J Bone Joint Surg Br*. 2011;93(4):490-497.
9. SooHoo NF, Eagan M, Krenek L, Zingmond DS. Incidence and factors predicting pulmonary embolism and deep venous thrombosis following surgical treatment of ankle fractures. *Foot Ankle Surg*. 2011;17(4):259-262.
10. Shibuya N, Frost CH, Campbell JD, Davis ML, Jupiter DC. Incidence of acute deep vein thrombosis and pulmonary embolism in foot and ankle trauma: analysis of the National Trauma Data Bank. *J Foot Ankle Surg*. 2012;51(1):63-68.
11. American College of Surgeons National Surgical Quality Improvement Program. *User Guide for the 2012 ACS NSQIP Participant Use Data File*. http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf. Published October 2013. Accessed May 10, 2015.
12. Khuri SF, Henderson WG, Daley J, et al; Principal Investigators of Patient Safety in Surgery Study. Successful implementation of the Department of Veterans Affairs' National Surgical Quality Improvement Program in the private sector: the Patient Safety in Surgery study. *Ann Surg*. 2008;248(2):329-336.
13. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA*. 1999;282(16):1523-1529.
14. Mizel MS, Temple HT, Michelson JD, et al. Thromboembolism after foot and ankle surgery. A multicenter study. *Clin Orthop Relat Res*. 1998;(348):180-185.
15. Solis G, Saxby T. Incidence of DVT following surgery of the foot and ankle. *Foot Ankle Int*. 2002;23(5):411-414.
16. Hanslow SS, Grujic L, Slater HK, Chen D. Thromboembolic disease after foot and ankle surgery. *Foot Ankle Int*. 2006;27(9):693-695.
17. Pelet S, Roger ME, Belzile EL, Bouchard M. The incidence of thromboembolic events in surgically treated ankle fracture. *J Bone Joint Surg Am*. 2012;94(6):502-506.
18. Manafi Rasi A, Kazemian G, Emami Moghadam M, et al. Deep vein thrombosis following below knee immobilization: the need for chemoprophylaxis. *Trauma Mon*. 2013;17(4):367-369.
19. Sabharwal S, Root MZ. Impact of obesity on orthopaedics. *J Bone Joint Surg Am*. 2012;94(11):1045-1052.
20. Kadous A, Abdelgawad AA, Kanlic E. Deep venous thrombosis and pulmonary embolism after surgical treatment of ankle fractures: a case report and review of literature. *J Foot Ankle Surg*. 2012;51(4):457-463.
21. Forsythe RM, Peitzman AB, DeCato T, et al. Early lower extremity fracture fixation and the risk of early pulmonary embolus: filter before fixation? *J Trauma*. 2011;70(6):1381-1388.
22. Bjørnarå BT, Gudmundsen TE, Dahl OE. Frequency and timing of clinical venous thromboembolism after major joint surgery. *J Bone Joint Surg Br*. 2006;88(3):386-391.

This paper will be judged for the Resident Writer's Award.