Deep Venous Thrombosis and Pulmonary Embolism After Lower Extremity Amputation in Patients with Diabetes

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Background

- Lower extremity amputation (LEA) is a feared complication of diabetic foot disease [1] and a leading cause of hospitalization in patients with diabetes mellitus (DM). [2]
- Deep venous thrombosis (DVT) and pulmonary embolism (PE) are associated with significant post-operative morbidity and mortality. Identification and prophylactic treatment of at-risk patients can reduce the incidence of DVT/PE. [3]
- Past studies have investigated the association between DM and DVT/PE, with mixed results. [4-6]

Aim and Methods

- **This study aims to identify risk factors for DVT and PE in patients with diabetes mellitus undergoing a lower extremity amputation.**
- A retrospective analysis of 36,445 LEA cases from the American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP) database was performed. 23,380 patients with DM and 13,065 patients without DM were included in this study.
- ACS-NSQIP records complications during the first 30 days after surgery.

TABLE 1. Patient demographics and comorbidities by presence of diabetes mellitus

	Overall N = 36,445		DM N = 23,380		No DM N = 13,065	
Parameter	**Value**	**(%)**	**Value**	**(%)**	**Value**	**(%)**
Patient Factors						
Age, median, years [a]	65.0	(56.0-75.0)	65.0	(56.0-74.0)	66.0	(56.0-77.0)
Male Gender	23,499	(64.5)	15,382	(65.8)	8,117	(62.1)
Smoking	10,558	(29.0)	5,602	(24.0)	4,956	(37.9)
Race						
Asian or Pacific Islander	679	(1.86)	501	(2.14)	178	(1.36)
Black or African-American	9,862	(27.1)	6,524	(27.9)	3,338	(25.5)
Native American	257	(0.71)	184	(0.79)	73	(0.59)
White	22,584	(62.0)	14,140	(60.5)	8,444	(64.6)
Unknown/Not Reported	3,063	(8.40)	2,031	(8.69)	1,032	(7.90)
Ethnicity						
Hispanic	2,837	(7.78)	2,230	(9.54)	607	(4.65)
Non-Hispanic	31,485	(86.4)	19,793	(84.7)	11,692	(89.5)
Unknown/Not Reported	2,123	(5.83)	1,357	(5.80)	766	(5.86)
BMI, median [a]	27.4	(23.3-32.7)	28.7	(24.6-34.1)	25.1	(21.5-29.8)
Pre-op Functional Status						
Independent	20,954	(57.5)	13,351	(57.1)	7,603	(58.2)
Partially Dependent	11,206	(30.7)	7,412	(31.7)	3,794	(29.0)
Totally Dependent	4,009	(11.0)	2,443	(10.4)	1,566	(12.0)
Unknown	276	(0.76)	174	(0.74)	102	(0.78)
Steroid Use	2,316	(6.35)	1,370	(5.86)	946	(7.24)
Laboratory values [a]						
Albumin	2.74	(2.20-3.30)	2.70	(2.20-3.20)	2.80	(2.30-3.40)
BUN	21.0	(13.0-34.0)	23.0	(15.0-36.9)	16.9	(11.0-27.0)
Creatinine	1.19	(0.80-2.38)	1.31	(0.90-2.95)	0.95	(0.70-1.50)
PT	14.2	(12.2-16.1)	14.3	(12.3-16.1)	14.2	(12.2-16.2)
PTT	33.8	(29.5-40.3)	33.6	(29.5-39.8)	34.0	(29.6-41.7)
INR	1.2	(1.10-1.33)	1.2	(1.10-1.33)	1.2	(1.08-1.34)
WBC	10.1	(7.70-13.6)	10.3	(7.90-13.9)	9.71	(7.40-13.1)
Comorbidities						
HTN requiring therapy	29,256	(80.3)	20,172	(86.3)	9,084	(69.5)
PVD	12,123	(64.9)	8,054	(67.8)	4,069	(60.0)
Dialysis	7,456	(20.5)	5,679	(24.3)	1,777	(13.6)
Previous MI	955	(5.1)	644	(5.4)	311	(4.6)
Previous CVA/Stroke	3,814	(19.4)	2,499	(21.0)	1,315	(19.4)
Complication						
DVT/Thrombophlebitis	398	(1.09)	220	(0.94)	178	(1.36)
Pulmonary Embolism	157	(0.43)	87	(0.37)	70	(0.54)

BMI = Body-Mass Index; HTN = Hypertension; PVD = Peripheral Vascular Disease; MI = Myocardial Infarction; CVA = Cerebrovascular Accident
[a]Median and Interquartile Range (IQR 25th to 75th percentile) presented for continuous laboratory values
Two patients had contralateral amputation (1 BKA and 1 AKA); Three patients had previously had a BKA

Data Analysis and Results

TABLE 2: DVT and PE in patients undergoing Lower Extremity Amputation

	Overall N = 36,445	DM N = 23,380	No DM N = 13,065	
Parameter	**Value (%)**	**Value (%)**	**Value (%)**	**P-value**
Complication, N (%)				
DVT/Thrombophlebitis	398 (1.09)	220 (0.94)	178 (1.36)	**0.0002**
Pulmonary Embolism	157 (0.43)	87 (0.37)	70 (0.54)	**<0.0001**

TABLE 3. Risk factors for DVT and PE in post-LEA patients with diabetes

	DVT		PE	
Parameter	**OR[a]**	**(95% CI)**	**OR[a]**	**(95% CI)**
Patient Factors				
Age > 65	1.02	(0.78, 1.33)	1.04	(0.68, 1.59)
Female sex	**1.49**	**(1.15, 1.95)**	**1.64**	**(1.08, 2.51)**
BMI > 30	1.03	(0.78, 1.34)	0.88	(0.56, 1.38)
Smoking status	0.96	(0.70, 1.31)	0.83	(0.49, 1.39)
Diabetes Management				
Insulin use	1.10	(0.80, 1.52)	0.78	(0.49, 1.25)
Non-insulin control	0.80	(0.54, 1.18)	1.28	(0.75, 2.18)
Oral agents	1.18	(0.73, 1.92)	1.16	(0.53, 2.51)
Comorbidities				
PVD	1.03	(0.69, 1.55)	0.92	(0.50, 1.69)
HTN	1.05	(0.71, 1.55)	0.83	(0.47, 1.47)
Acute renal failure[b]	1.52	(0.93, 2.46)	0.82	(0.30, 2.23)
Prior MI	**2.55**	**(1.45, 4.50)**	1.19	(0.37, 3.85)
Prior CVA/Stroke	1.10	(0.65, 1.87)	1.34	(0.62, 2.87)
Dialysis[c]	**1.52**	**(1.15, 2.02)**	0.99	(0.61, 1.62)
Pre-Op Functional Status				
Independent vs. Dependent[d]	**0.60**	**(0.46, 0.79)**	**0.52**	**(0.34, 0.80)**
Partially dependent[e]	**1.37**	**(1.01, 1.86)**	1.45	(0.89, 2.37)
Completely dependent[e]	**2.59**	**(1.81, 3.70)**	**3.36**	**(1.97, 5.72)**

[a]Values greater than 1 signify increased odds, while values less than 1 signify decreased odds. Significant ratios are in bold
[b]Compromise of renal function within 24 hours prior to surgery
[c]Peritoneal dialysis, hemodialysis, hemofiltration, hemodiafiltration or ultrafiltration performed within 2 weeks prior to surgery for acute or chronic renal failure.
[d]Independent status compared to any level of dependence.
[e]Compared to independent functional status.

Diabetes and DVT/PE After LEA

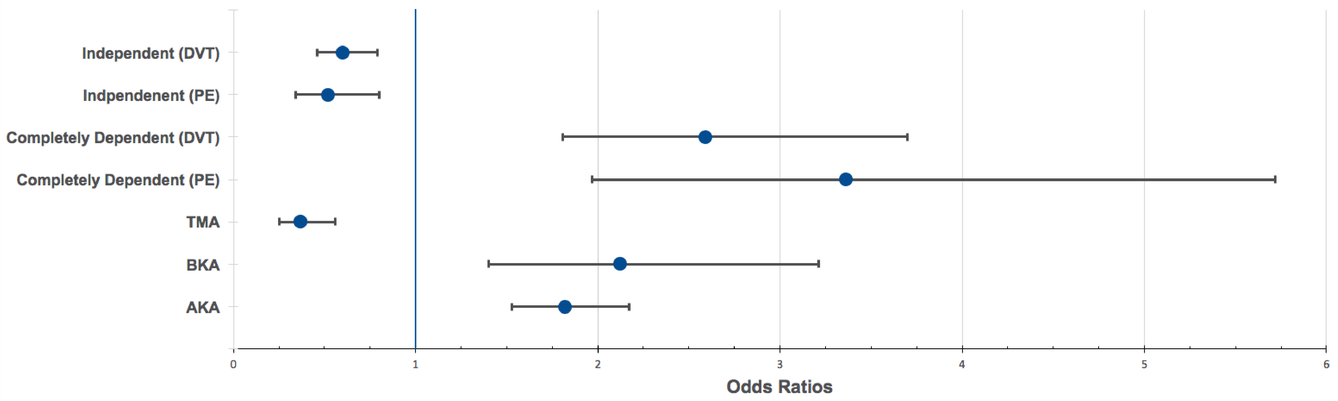
- In patients undergoing an LEA, DM was associated with a slight **decrease** in the incidence of DVT and PE. (Table 2)
- This decrease in DVT and PE risk appears to be driven by a higher proportion of patients with completely dependent functional status in the No DM group ($p<0.0001$ [a]). (Table 1)

[a] *Chi-squared test of homogeneity for categorical variables*

Functional Status and Level of Amputation

- **Completely dependent patients were 2.59 times more likely to develop a DVT, and 3.36 times more likely to develop a PE.** (Figure 1)
- **Patients with a below or above knee amputation were 2.12 and 1.82 times more likely to experience a DVT/PE compared to transmetatarsal amputations.** (Figure 1)

Figure 1: Functional Status and Level of Amputation Associated with Increased DVT/PE Risk



TMA = Transmetatarsal Amputation; BKA = Below Knee Amputation; AKA = Above Knee Amputation
BKA and AKA OR compared to more proximal amputation
TMA, BKA, and AKA ORs calculated for combined DVT/PE risk

Conclusion and Discussion

- **Diabetes mellitus is not an independent risk factor for DVT/PE in patients undergoing a lower extremity amputation.**
- Prior studies suggest that the connection between DVT/PE and DM is due to an inflammatory, prothrombotic state induced by hyperglycemia. [7] One hypothesis for the absence of increased risk associated with DM in this study is that patients requiring an LEA are in an inflammatory, prothrombotic state, irrespective of DM status.
- **Pre and post operative functional status has an impact on DVT/PE risk.** This emphasizes the importance of rapid intervention, limb sparing procedures, and early ambulation in surgical management of diabetic foot ulcers.

Limitations and Future Research

- The ACS-NSQIP does not record HgA1c or serum glucose levels. A future study will evaluate glycemic control and risk of DVT/PE in diabetic patients.
- The ACS-NSQIP also does not record prophylactic antithrombotic protocols. We assume that the two groups received similar perioperative DVT/PE prophylaxis. No statistically significant difference in pre-operative PT, PTT, and INR was noted between the two groups. (Table 1)

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