

# Risk Factors of Premature PAD and Associated Outcomes

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## OBJECTIVES:

- Patients with premature peripheral arterial disease (PAD) are at high risk for major amputation after lower extremity revascularization (LER).
- Diabetes mellitus (DM) and smoking are common and widely considered risk factors, but their impact on outcomes has not been well studied.
- This paper aims to better characterize individual risk factors contributing to premature PAD and their associated outcomes.

## METHODS:

- The Vascular Quality Initiative databases for peripheral vascular interventions, infrainguinal bypass, and suprainguinal bypass were reviewed.
- Only patients with premature PAD (age ≤ 50) were included.
- Patients were stratified into 3 groups based on risk factor: DM only, smoking only, and Other (no DM or smoking).
- Patients with concomitant DM and smoking were excluded.

## RESULTS:

**Table I : Baseline Characteristics**

Characteristic	DM N = 2,080 (21.6%)	Smoking N = 6,498 (67.6%)	Other N = 1,037 (10.8%)	p-value
Age, years (mean ± SD)	44 ± 8 <sup>c,d</sup>	44 ± 8 <sup>b,d</sup>	39 ± 11 <sup>c,b</sup>	<0.001 <sup>a</sup>
Female sex	946 (45.5%) <sup>c</sup>	2,522 (38.8%) <sup>b,d</sup>	476 (45.9%) <sup>c</sup>	<0.001 <sup>a</sup>
Race				<b>0.002<sup>a</sup></b>
White	941 (45.3%) <sup>c,d</sup>	5,037 (77.4%) <sup>b,d</sup>	606 (58.5%) <sup>b,c</sup>	
African American	785 (37.7%) <sup>c,d</sup>	1,200 (18.5%) <sup>b,d</sup>	297 (28.6%) <sup>b,c</sup>	
Other	352 (16.9%) <sup>c,d</sup>	259 (3.9%) <sup>b,d</sup>	134 (12.9%) <sup>b,c</sup>	
Hispanic	368 (17.7%) <sup>c,d</sup>	174 (2.7%) <sup>b,d</sup>	115 (11.1%) <sup>b,c</sup>	<0.001 <sup>a</sup>
Body mass index (mean ± SD)	32 ± 8 <sup>d</sup>	28 ± 7	29 ± 8 <sup>b</sup>	<0.001 <sup>a</sup>
Insulin Requiring Diabetes	1,602 (77.1%)	-	-	<0.001
Non-insulin Requiring Diabetes	478 (22.9%)	-	-	<0.001
Coronary artery disease	553 (26.6%) <sup>c,d</sup>	1,164 (17.9%) <sup>b,d</sup>	99 (9.6%) <sup>b,c</sup>	<0.001 <sup>a</sup>
ESRD	866 (41.6%) <sup>c,d</sup>	219 (3.4%) <sup>b,d</sup>	182 (17.5%) <sup>b,c</sup>	<0.001 <sup>a</sup>
Prior LER	595 (28.6%)	1,870 (28.8%)	264 (25.4%)	0.2
Prior major amputation	250 (12.0%) <sup>c,d</sup>	201 (3.1%) <sup>b</sup>	27 (2.6%) <sup>b,c</sup>	<0.001 <sup>a</sup>
<b>Procedural details</b>				
Indication				<0.001 <sup>a</sup>
Acute limb Ischemia	98 (4.8%) <sup>c,d</sup>	623 (12.2%) <sup>b</sup>	137 (14.2%) <sup>b</sup>	
Claudication	438 (22.1%) <sup>c,d</sup>	3,156 (58.9%) <sup>b</sup>	559 (56.9%) <sup>b</sup>	
CLTI	1,495 (73.9%) <sup>c,d</sup>	1,563 (28.9%) <sup>b</sup>	278 (28.9%) <sup>b</sup>	
Type of Procedure				<b>0.03<sup>a</sup></b>
Endovascular Intervention	1,834 (88.3%) <sup>c,d</sup>	4,430 (68.1%) <sup>b,d</sup>	705 (67.9%) <sup>b,c</sup>	
Suprainguinal bypass	30 (1.4%) <sup>c,d</sup>	1,040 (16.1%) <sup>b,d</sup>	86 (8.4%) <sup>b,c</sup>	
Infrainguinal bypass	216 (10.3%) <sup>c,d</sup>	1,028 (15.8%) <sup>b,d</sup>	246 (23.7%) <sup>b,c</sup>	
Urgency				<b>0.024<sup>a</sup></b>
Elective	1,456 (70.0%)	5,001 (76.9%)	716 (69.0%)	
Urgent	564 (27.1%) <sup>c,d</sup>	1,143 (17.7%) <sup>b,d</sup>	206 (19.9%) <sup>b,c</sup>	
Emergent	55 (2.7%) <sup>c,d</sup>	347 (5.4%) <sup>b,d</sup>	115 (11.1%) <sup>b,c</sup>	

Bold, statistically significant difference for P<0.05 and P<0.017 after the post hoc analysis  
<sup>a</sup>Post hoc analysis significant differences between: DM/Non-Smoking<sup>b</sup>, Smoking/Non-DM<sup>c</sup>, and Non-Smoking/Non-DM<sup>d</sup>.

**Table II: Perioperative complications**

Perioperative 30-day outcomes	DM N = 2,080 (21.6%)	Smoking N = 6,498 (67.6%)	Other N = 1,037 (10.8%)	p-value
Renal complications	54 (3.2%) <sup>d</sup>	118 (2.4%)	13 (1.5%) <sup>b</sup>	<b>0.034<sup>a</sup></b>
Thrombosis	13 (0.9%) <sup>c,d</sup>	142 (4.7%) <sup>b</sup>	17 (3.1%) <sup>b</sup>	<0.001 <sup>a</sup>
30-day mortality	18 (0.9%) <sup>c</sup>	19 (0.3%) <sup>b</sup>	4 (0.4%)	<b>0.016<sup>a</sup></b>
30-day major amputation	93 (5.4%) <sup>c,d</sup>	25 (0.4%) <sup>b</sup>	31 (3.0%) <sup>b</sup>	<b>0.022<sup>a</sup></b>

Bold, statistically significant difference for P<0.05 and P<0.017 after the post hoc analysis  
<sup>a</sup>Post hoc analysis significant differences between: DM/Non-Smoking<sup>b</sup>, Smoking/Non-DM<sup>c</sup>, and Non-Smoking/Non-DM<sup>d</sup>.

**Table III: Long-term outcomes**

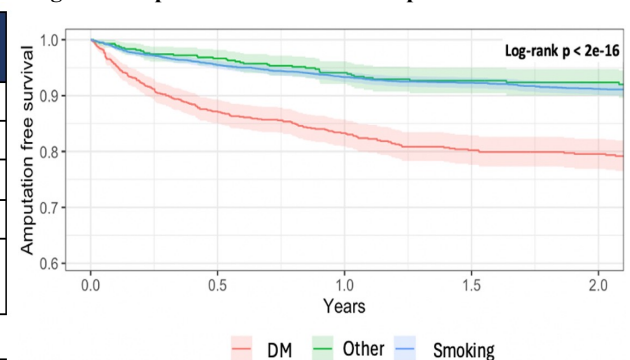
Long-term outcomes	DM N = 1,355 <sup>1</sup> (19.9%)	Smoking N = 4,735 <sup>1</sup> (69.4%)	Other N = 730 <sup>1</sup> (10.7%)	p-value
Reintervention	121 (13.1%)	462 (13.3%)	65 (12.3%)	0.9
Major amputation	202 (20.2%) <sup>c,d</sup>	249 (7.6%) <sup>b</sup>	34 (6.1%) <sup>b</sup>	<0.001 <sup>a</sup>
MALE	300 (29.1%) <sup>c,d</sup>	663 (17.1%) <sup>b</sup>	92 (16.2%) <sup>b</sup>	<0.001 <sup>a</sup>
Mortality	236 (17.4%) <sup>c,d</sup>	317 (6.7%) <sup>b</sup>	42 (5.8%) <sup>b</sup>	<0.001 <sup>a</sup>

<sup>1</sup>The sample size differed due to loss to follow-up  
<sup>a</sup>Post hoc analysis significant differences between: DM/Non-Smoking<sup>b</sup>, Smoking/Non-DM<sup>c</sup>, and Non-Smoking/Non-DM<sup>d</sup>.

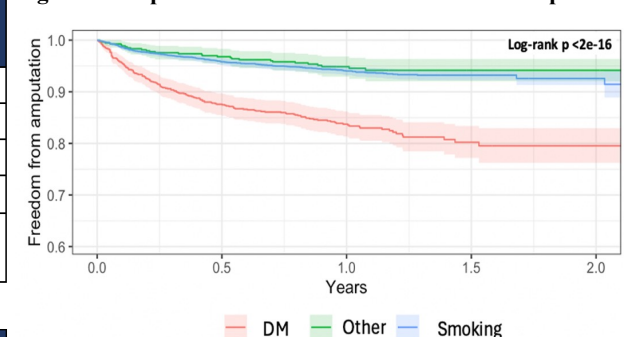
**Table IV: Cox Regression Analysis for Major Amputation**

Characteristic	Hazard Ratio	95% Confidence Interval
Smoking	1.28	0.76-2.17
Diabetes Mellitus	<b>1.86</b>	<b>1.09-3.17</b>
BMI	<b>0.98</b>	<b>0.96 - 0.99</b>
Hispanic	<b>1.66</b>	<b>1.06 - 2.59</b>
Assisted ambulation	<b>1.64</b>	<b>1.19 - 2.26</b>
Non-ambulatory	<b>1.88</b>	<b>1.16 - 3.06</b>
Prior major amputation	<b>1.52</b>	<b>1.11-2.09</b>
Preoperative Anticoagulant	<b>1.58</b>	<b>1.16-2.16</b>
Acute limb ischemia (vs IC)	<b>8.32</b>	<b>4.82-9.41</b>
Chronic Limb Threatening Ischemia (vs IC)	<b>4.64</b>	<b>2.8-7.69</b>

**Figure I. Kaplan-Meier curve for amputation-free survival**



**Figure II. Kaplan-Meier curve for freedom from amputation**



## CONCLUSION:

- The risk factors of premature PAD significantly impact outcomes of LER.
- DM is highly associated with amputation prior to and after revascularization.
- Other risk factors need further characterization to better understand this virulent form of PAD.