

Premature Peripheral Artery Disease:
 What factors predispose to it, How Should its Treatment Differ, How Does it Influence Treatment Outcomes

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DISCLOSURES

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Premature Peripheral Artery Disease

- ▶ PAD = disease of older adults
- ▶ 200 million worldwide >12 million in United States
 Fowkes et al. *Lancet* 2013;382:1329-40.

Prevalence of PAD by age and gender in adults 40 years and older, United States, 1999-2000

NHANES. *Circulation* 2004;110:738-743

Premature Peripheral Artery Disease

- ▶ Onset before age 50

High Income Countries

Prevalence 3.0% (Male), 3.2% (Female)

Fowkes et al. *Lancet* 2013;382:1329-40.
 Sana et al. *Lancet Glob Health*. 7 (2019). e1020-e1030

Premature Peripheral Artery Disease

- ▶ Risk factors

Traditional	Non-traditional
Smoking	Elevated Lp(a)
Diabetes	Family History of PAD
Hypertension	Genetic predisposition
Dyslipidemia	Hypercoagulability
Metabolic Syndrome	Autoimmune disorders
	HIV infection

Mehta...Alabi O, Sperling. *Trends in CV Medicine* 31(6):351-8

Premature Peripheral Artery Disease

- ▶ Risk factors
 - ▶ Genetic predisposition
 - ▶ Familial hypercholesterolemia
 - ▶ Homocystinuria
 - ▶ Two SNPs
 - ▶ rs10757278 (locus 9p21) → genetic risk factor for CAD Helgadottir et al. *Nat Genet* 2008.
 - ▶ rs1051730 (locus 15q24) → affects nicotine dependence Thorngersson et al. *Nature* 2008.
 - ▶ Hypercoagulability
 - ▶ Factor V Leiden mutation Berard et al. *PLoS ONE* 2013.
 - ▶ The odds of having a Factor V Leiden mutation were five-fold higher among patients with PAD (OR 5.1, 95% CI 1.5-17.4) compared to controls
 - ▶ AT III, protein C, protein S, heparin cofactor II, tissue plasminogen activator release Levy et al. *JVS* 1994.
 - ▶ Stimulant drug abuse Denegri et al. *J Cardiovasc Med* 2016; Bachs et al. *Atherosclerosis* 2017; Tan et al. *Vasc Med* 2019.

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Premature Peripheral Artery Disease

- ▶ Management
 - ▶ Secondary ASCVD prevention
 - ▶ Smoking cessation & comprehensive lifestyle changes
 - ▶ Antithrombotic agents
 - ▶ Lipid lower therapies
 - ▶ Management of other chronic comorbidities
 - ▶ Exercise therapy
 - ▶ Majority of clinical trials did not include young patients

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Premature Peripheral Artery Disease

▶ Outcomes after revascularization

Table 1. Baseline Characteristics During the Year Prior to LIA.

Characteristic	Without revascular assessment (n=1846)	With revascular assessment (n=1919)	P-value
Age (mean ±SD), y	64.9 (12.2)	66.2 (12.1)	<.001
Sex			
Male	438 (23.7%)	458 (23.9%)	0.89
Female	1408 (76.3%)	1461 (76.1%)	
Race			
White	1080 (58.5%)	1124 (58.6%)	0.97
Black	432 (23.4%)	458 (23.9%)	
Hispanic	115 (6.2%)	115 (6.0%)	
Other	219 (11.9%)	219 (11.5%)	
Insurance status			
Medicare	1386 (75.1%)	1434 (74.8%)	
Medicaid	460 (24.9%)	485 (25.2%)	

Alabi O, et al. *JAMA Surg* 2023;158(6):e230479

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Premature Peripheral Artery Disease

▶ Outcomes after revascularization

- ▶ 40% may require multiple reinterventions (Vadivelu et al. *JVS* 1999;30(3):436-445.)
- ▶ Worse patency (Klingthoerfer et al. *JVS* 2016;64:380-388.)
- ▶ 2x the likelihood of bypass occlusion (Tomebalba et al. *JVS* 2019;70(1):175-180.)
- ▶ 4x amputation risk (Tomebalba et al. *JVS* 2019;70(1):175-180.)

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Methods

- ▶ **Study population:** All adults at VQI participating centers undergoing endovascular revascularization for lower extremity peripheral artery disease (PAD) between January 2017 to December 2018
- ▶ **Exclusions:**
 - ▶ Age under 18
 - ▶ Procedure for acute limb ischemia
 - ▶ Hybrid procedures
- ▶ **Data Sources:** Vascular Quality Initiative linked to Medicare claims data

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Methods

- ▶ **Primary Exposure Variable:**
 - ▶ premature PAD (age <50 yrs old)
- ▶ **Primary Outcome Variable:**
 - ▶ Mortality
 - ▶ 30 days, 90 days, 1 year
 - ▶ Major amputation
 - ▶ 30 days, 90 days, 1 year
- ▶ **Analysis:**
 - ▶ Standard demographic comparisons
 - ▶ Competing risk analyses using cumulative incidence functions using the Alaien-Johansen estimator and hierarchical Fine-Gray regression

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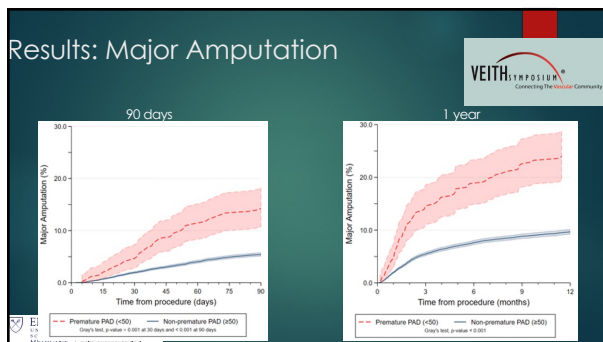
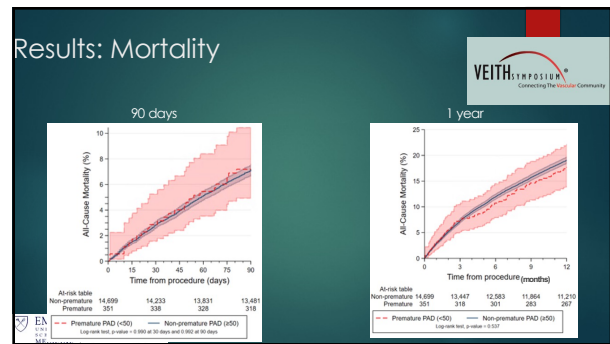
Results

	Total n=15,050	Older Adults n=14,089	Premature PAD n=961	p-value
Age				
Mean (SD)	71.9 (10.2)	72.5 (9.3)	44.2 (4.7)	<0.001
Sex				
Male	8821 (58.6%)	8042 (56.8%)	779 (81.0%)	0.003
Female	6229 (41.4%)	6047 (43.2%)	182 (19.0%)	
Race				
White	11410 (75.8%)	11241 (79.5%)	169 (17.6%)	<0.001
Black	2454 (16.3%)	2323 (16.5%)	131 (13.7%)	
Hispanic	627 (4.2%)	581 (4.1%)	46 (4.8%)	
Other	559 (3.7%)	544 (3.9%)	15 (1.6%)	
Indication for Revascularization				
Classification	5909 (39.2%)	5835 (41.5%)	74 (7.7%)	<0.001
Ischemic Rest Pain	2191 (14.6%)	2130 (15.1%)	61 (6.3%)	
Tissue Loss or Nonhealing Wounds	6953 (46.2%)	6734 (48.0%)	219 (22.8%)	
Preoperative ambulatory status				
Independent	9511 (64.5%)	9314 (66.1%)	197 (20.5%)	0.002
With Assistance	2995 (20.9%)	2864 (20.3%)	131 (13.7%)	
Wheelchair	1190 (7.9%)	1155 (8.2%)	35 (3.6%)	
Bedridden	116 (0.8%)	113 (0.8%)	3 (0.3%)	
Preoperative residential location				
Home	14104 (93.0%)	13773 (97.6%)	331 (34.5%)	0.144
Not Home	946 (6.1%)	316 (2.3%)	20 (2.1%)	

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Results

	1829 N=1829	CRP PADs n=3458	Premature PAD n=201	P-value
Comorbidities				
Obesity (BMI ≥ 30)	499 (27.3)	474 (13.6)	95 (47.6)	<.001
Heart disease				
Coronary artery disease	565 (30.9)	530 (15.2)	122 (60.8)	
Congestive heart failure	269 (14.7)	274 (7.9)	94 (46.9)	0.003
Prior CABG	345 (19.0)	350 (10.1)	64 (31.8)	
Prior PCI	369 (20.2)	360 (10.4)	80 (39.6)	
Chronic lung disease	436 (23.8)	424 (12.3)	64 (31.8)	<.001
Diabetes mellitus	646 (35.4)	623 (18.0)	273 (135)	<.001
Chronic kidney disease Stage 3-5	459 (25.1)	476 (13.8)	42 (20.9)	<.001
On dialysis	193 (10.6)	193 (5.6)	89 (44.3)	<.001
Hypertension	1368 (74.9)	1336 (38.5)	302 (150)	<.001
Prior revascularization	632 (34.6)	635 (18.4)	144 (71.4)	0.688
Prior amputation minor	134 (7.3)	132 (3.8)	67 (33.3)	<.001
Prior amputation major	116 (6.3)	121 (3.5)	75 (37.4)	<.001
Preoperative medications				
Aspirin	1234 (67.6)	1079 (31.2)	269 (133)	0.005
Statins	1141 (62.4)	1027 (29.7)	244 (121)	0.003
Smoking status				
Never	506 (27.7)	585 (16.8)	71 (35.3)	<.001
Former	231 (12.6)	230 (6.7)	61 (30.1)	
Active	693 (37.8)	674 (19.5)	29 (14.6)	



Results

OUTCOMES:	30-days	90-days	1 year	p
Mortality				
All PVDs	2.9%	7.1%	18.6%	NS
Older Adult PAD	2.9%	7.2%	18.6%	NS
Premature PAD	2.8%	7.1%	17.1%	NS
Major Amputation				
All PVDs	2.0%	5.4%	9.2%	.006
Older Adult PAD	1.9%	5.2%	8.9%	<.001
Premature PAD	4.6%	13.7%	21.9%	<.001

Premature PAD Summary

- ▶ Similar risk factors, dissimilar outcomes
- ▶ Plenty of room for investigation and public health awareness
 - ▶ Inflammatory Biomarkers
 - ▶ Proteomics, Transcriptomics, Genomics,
 - ▶ Allostatic load
 - ▶ Population-level screening
 - ▶ And more