From the New England Society for Vascular Surgery

Outcomes of infrainguinal bypass determined by age in the Vascular Study Group of New England

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Background: **Many believe extremes of age correlate with poorer outcomes in treatment for lower extremity peripheral arterial disease (PAD). We hypothesized that the youngest patients would have significantly poorer outcomes compared with older cohorts due to the precocious nature of their PAD.**

Methods: **We studied all patients in the Vascular Study Group of New England database undergoing infrainguinal bypass for PAD between 2003 and 2013. Age was grouped by <50 years, 50 to 79 years, and ≥80 years. Our primary outcomes were 1-year freedom from a major adverse limb event (MALE), defined as ipsilateral amputation or need for secondary intervention, and amputation-free survival. A second analysis was performed to analyze the subgroup of patients aged <50 years with critical limb ischemia (CLI), which included a Cox regression model to determine risk factors for MALE or death at 1 year.**

Results: **Of 5265 patients who were treated with infrainguinal bypass for PAD, 324 (6.2%) were aged <50 years. The mean age was 44.6 years, and 66.4% were male. The proportion of African Americans was significantly higher in the youngest age group (<50 years: 6.8% vs 50-79 years: 3.5%, $P = .002$; vs ≥80 years: 3.5%, $P = .013$). More bypasses were done for claudication than acute limb ischemia in patients aged <50 years (33.3% vs 11.4%). More vein grafts were used vs prosthetic (<50 years: 72.1% vs 50-79 years: 65.9%, $P = .024$; vs ≥80 years: 62.6%, $P = .002$). Fewer concomitant proximal procedures were performed compared with the older groups (<50 years: 37.7% vs 50-79 years: 51.1%, $P < .001$; vs ≥80 years: 39.5%, $P = .045$). More young patients returned to the operating room within their initial hospitalization for early graft thrombosis (<50 years: 5.6% vs 50-79 years: 2.9%, $P = .001$; vs ≥80 years: 2.4%, $P = .009$) and revision (<50 years: 4.7% vs 50-79 years: 2.2%, $P = .012$; vs ≥80 years: 1.4%, $P = .002$) compared with the older patients. Overall, MALE-free survival was similar across age groups ($P = .323$), as were patency and amputation rates. When considering only patients with CLI, MALE-free survival in the youngest patients was again similar ($P = .171$) but with significantly more major amputations at 1 year ($P = .022$).**

Conclusions: **For patients aged <50 undergoing infrainguinal bypass surgery, this large series demonstrates similar overall medium-term graft-related outcomes compared with older cohorts. Further, although the youngest patients with CLI have similar MALEs, their amputation rates are higher than in older cohorts. (J Vasc Surg 2015;62:83-92.)**

Peripheral arterial disease (PAD) is defined as atherosclerosis of the noncardiac vessels. Worldwide, >200 million people live with PAD.[1] In the United States and Europe, an estimated 27 million individuals are affected, with ~413,000 hospital admissions annually attributed to PAD.[2] With a 2010 prevalence of 17.6 million, PAD is more common than coronary artery disease in the United States.[3] The annual economic cost is between $164 and $290 billion.[3]

Premature PAD is the onset of peripheral arterial stenosis or occlusion before the age of 50. Its incidence varies between 1.4% and 17%.[4] Earlier studies have suggested that premature lower extremity atherosclerosis presents with more severe symptoms at the time of diagnosis than in older patients[5,6] and manifests as a "virulent" disease with a rapid progression.[7,8] Harris et al[9] reported in 1996 that infrainguinal disease diagnosed in patients aged <50 years carried a poorer outcome than similar disease in older patients. One prospective study of patients with premature PAD followed up for 4 years reported that 40% required multiple interventions due to disease progression or bypass graft failure over a mean follow-up of 6 years.[10] Evidence also suggests that patients with premature PAD have higher rates of repeat operation, limb salvage, and amputation.[6,9]

In the progressive spectrum of PAD, critical limb ischemia (CLI) is the final stage before limb loss. CLI often results from multilevel disease leading to poor collateralization making distal ischemia worse than its less aggressive forms. The incidence of CLI in European patients

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Table I. Patients demographics by age

Variables	*<50 years*	*50-79 years*	P *values*[a]	*≥80 years*	P *values*[a]
Patients, No.[b]	324	4058		883	
Age, mean years	44.56	65.82		84.09	
Height, mean cm	172.94	171.44		168.38	
Weight, mean kg	85.57	81.07		70.71	
Male, No. (%)	215 (66.4)	2781 (68.5)	.227	498 (56.4)	.001
Race, No. (%)					
White	291 (89.8)	3835 (94.5)	.001	840 (95.1)	.001
Black	22 (6.8)	140 (3.5)	.002	31 (3.5)	.013
Asian	0	4 (0.1)		0	
Other	11 (3.4)	79 (2)		12 (1.4)	
BLE symptoms, No. (%)					
Claudication	108 (33.3)	1146 (28.2)	.008	93 (10.5)	<.001
CLI (rest pain, tissue loss)	171 (52.8)	2501 (61.6)	.001	703 (79.6)	<.001
Acute ischemia	37 (11.4)	305 (7.5)	.004	72 (8.2)	.018
Diabetes, No. (%)	135 (41.7)	2119 (52.2)	<.001	401 (45.4)	.137
Dialysis, No. (%)	20 (6.2)	291 (7.2)	.075	48 (5.4)	.097
COPD, No. (%)	57 (17.6)	1150 (28.3)	<.001	201 (22.8)	.03
CAD, No. (%)	62 (19.1)	1459 (36)	<.001	343 (38.9)	<.001
CHF, No. (%)	16 (4.9)	643 (15.9)	<.001	208 (23.6)	<.001
Prior PCI or CABG, No. (%)	45 (13.9)	1365 (33.6)	<.001	258 (29.2)	<.001
Hypertension, No. (%)	206 (63.6)	3544 (87.3)	<.001	790 (89.5)	<.001
Smoking history, No. (%)	290 (89.5)	3561 (87.8)	.201	585 (66.3)	<.001
Prior PVI, No. (%)					
Total interventions	95 (29.3)	1272 (31.3)	.245	196 (22.3)	.007
Ipsilateral inflow PVI	31 (9.6)	551 (13.6)	.041	78 (8.8)	.734
Ipsilateral infrainguinal PVI	58 (17.9)	584 (14.4)	.102	108 (12.2)	.014

BLE, Bilateral lower extremities; *CABG,* coronary artery bypass graft; *CAD,* coronary artery disease; *CHF,* congestive heart failure; *CLI,* critical limb ischemia; *COPD,* chronic obstructive pulmonary disease; *PCI,* percutaneous coronary intervention; *PVI,* percutaneous vascular intervention.

[a]Missing in variables were not included in analysis, percentage was referred to column percentage; *P* values are from the Fisher exact test (all values converted to categoric variables), and $P < .05$ is statistically significant.

[b]Patients receiving bypass for popliteal aneurysms were eliminated; the first procedure per patient was counted in the analysis.

Table II. Secondary outcomes by age at time of discharge

Secondary outcomes[a]	*<50 years, No. (%)*	*50-79 years, No. (%)*	P *values*[b]	*≥80 years, No. (%)*	P *values*[b]
Myocardial infarction	5/324 (1.5)	154/4054 (3.8)	.043	51/879 (5.8)	.001
Wound infection	17/324 (5.3)	193/4054 (4.8)	.685	37/880 (4.2)	.435
Graft infection	3/323 (0.9)	17/4055 (0.4)	.183	2/880 (0.2)	.125
≥3 units pRBC	18/316 (5.7)	230/3862 (6)	1	91/792 (11.5)	.003
Dysrhythmia	4/324 (1.2)	230/3862 (4.1)	.007	56/880 (6.4)	<.001
CHF	3/324 (0.9)	118/4051 (2.9)	.033	44/878 (5)	<.001
Respiratory failure	3/324 (0.9)	89/4053 (2.2)	.157	35/880 (4)	.005
Renal impairment	9/324 (2.9)	171/3961 (4.3)	.247	65/868 (7.5)	.002
Return to the OR					
All indications	47/324 (14.5)	485/4053 (12)	1	110/879 (12.5)	
Bleeding	6/305 (2)	57/3881 (1.5)	.46	9/832 (1.1)	.249
Thrombosis	18/322 (5.6)	116/4045 (2.9)	.011	21/877 (2.4)	.009
Infection	5/322 (1.6)	34/4045 (0.8)	.206	10/877 (1.1)	.564
Revision	15/322 (4.7)	90/4045 (2.2)	.012	12/877 (1.4)	.002
Stroke[c]	1/147 (0.7)	12/1860 (0.7)	1	3/391 (0.8)	1
Ipsilateral amputation[c]	16/203 (7.9)	331/2617 (12.7)	.046	88/558 (15.8)	.004
In-hospital mortality	2/324 (0.6)	59/4057 (1.5)	.321	36/881 (4.1)	.001

CHF, Congestive heart failure; *OR,* operating room; *pRBC,* packed red blood cells.

[a]Patients receiving bypass for popliteal aneurysms were eliminated; the first procedure per patient was counted in the analysis.

[b]Missing in variables were not included in analysis, percentage was referred to column percentage. *P* values are from the χ^2 test, and $P < .05$ is significant.

[c]54% of the data were missing for stroke, and 36% of the data were missing in ipsilateral amputation.

aged <50 years was estimated at 0.24% by Jensen et al.[11] In the United States, Weitz et al[12] estimated the incidence at 1%. However, no population-based studies to date have accurately calculated the incidence of CLI in patients with premature PAD.

The literature on premature PAD is outdated, as most was published in the 1990s. No recently published studies have focused on outcomes of patients with premature PAD, especially in the era of new technologies, including endovascular therapy. We hypothesize that patients with