Open and Endo Revascularization In Young Patients With PAD: What Works, What Doesn't, and How Should Treatment be Modified?

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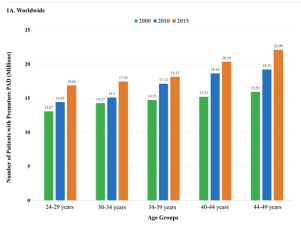
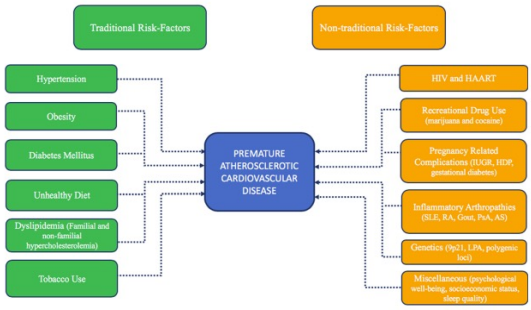
PREMATURE ASCVD AND PAD: AN ESCALATING CHALLENGE

- Premature PAD affects approximately 2% (1-7%) of adults <50
  - May be under-reported
- Increasing worldwide prevalence
- CV mortality and secondary prevention in young patients are not improving



A. Mehta, D.S. Dhindsa and A. Hooda et al./Trends in Cardiovascular Medicine 31 (2021) 351–358

PREMATURE ATHEROSCLEROTIC CARDIOVASCULAR DISEASE



REVASCULARIZATION FOR PREMATURE PAD

- Long –recognized challenge for revascularization
  - Small vessel size, inflammation, vasospasm, thrombophilia
  - Need for reintervention and reoperation
  - More difficult in females?
- Optimal medical management unclear

> Surgery. 1984 Nov;96(5):863-9.

Atherosclerosis in the young: a virulent disease

R A McCready, A E Vincent, R W Schwartz, G L Hyde, S S Mattingly, W O Griffen Jr

RESULTS OF BYPASS IN YOUNG PATIENTS

Factors associated with early failure of infrainguinal lower extremity arterial bypass

Niten Singh, MD, Anton N. Sidawy, MD, Kent J. DeZee, MD, Richard F. Neville, MD, Cameron Akbari, MD, and William Henderson, PhD, *Washington, DC* (J Vasc Surg 2008;47:556-61.)

- 14,788 patients undergoing infrainguinal bypass in VA medical centers
- Outcome: graft failure at ≤ 30 days

Table III. Age and early graft failure

	Univariate analysis of age and graft failure			*Multivariate logistic regression analysis of age and graft failure*[a]		
Age (years)	*Bypasses, no.*	*Failures, no.*	*Failure, %*	*OR*[b]	*95% CI*	P
<51	1035	85	8.21[c]	2.2	1.6-3.0	<.001
51-60	3248	171	5.26[c]	1.4	1.2-1.6	<.001
61-70	5354	242	4.52	1.1	0.96-1.3	<.150
>70	5151	225	4.37	Ref	Ref	Ref
Total	14,788	723	4.9			

CI, Confidence interval; *OR*, odds ratio.
[a]Age ≥70 as reference.
[b]Odds ratios adjusted for anesthesia type, diabetic mellitus, African American race, hematocrit, and operation type.
[c]$P < .001$ on χ^2.

ENDOVASCULAR RX IN YOUNG PATIENTS

Impact of endovascular options on lower extremity revascularization in young patients

Cassius Iyad Ochoa Chaar, MD, Michel S. Makaroun, MD, Luke K. Marone, MD, Robert Y. Rhee, MD, George Al-Khoury, MD, Jae S. Cho, MD, Steven A. Leers, MD, and Rabih A. Chaer, MD, *Pittsburgh, Pa*

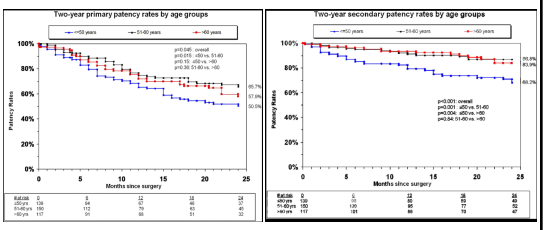
- 298 patients
  - Group A (<50): 139 limbs in 97 patients
    - Increased smoking and hypercoagulable state
  - Group B (51-60): 151 limbs in 103 patients
  - Group C (>60): 119 limbs in 98 patients

Table III. Lower extremity revascularization procedures in the three age groups

Procedure	*Group A (≤50 years)*	*Group B (51-60 years)*	*Group C (>60 years)*
Bypass			
Prosthetic	27	24	6
Autogenous	23	25	37
Other open[a]	2	6	—
Hybrid[b]	5	4	1
Angioplasty	3	10	17
Stenting	29	59	38
Atherectomy[c]	4	6	4
Lysis	5	. . .	. . .
Cryoplasty	1	2	. . .

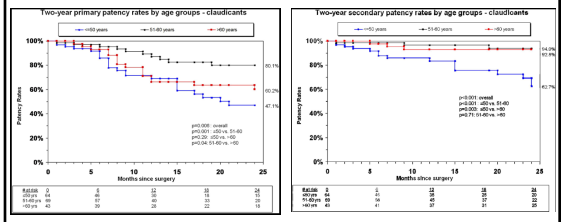
- Indications similar between groups (≈ 55% CLI)
- Group A:
  - More aortoiliac dz
  - Lesions had higher TASC class

REDUCED PATENCY IN YOUNG PATIENTS



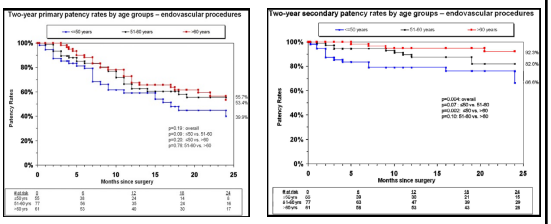
Journal of Vascular Surgery 2012 56703-713.e3DOI: (10.1016/j.jvs.2012.01.073)

WORST PATENCY SEEN IN YOUNG CLAUDICANTS



- No difference in patency between age groups for CLI patients

PATENCY WORSE AFTER ENDOVASCULAR PROCEDURES



- Trend toward lower primary patency and lower secondary patency after open procedures

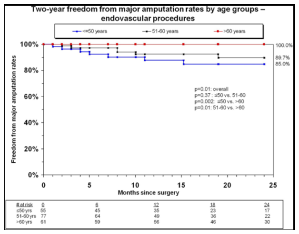
PROGRESSION TO CLTI AND AMPUTATION IN YOUNG PATIENTS

22/97 patients ≤ 50 progressed from claudication to CLTI after intervention over a mean of 22 months

15 open | 7 endo

3 reinterventions /pt

10% amputation rate at 2 years after revascularization for claudication in patients ≤ 50

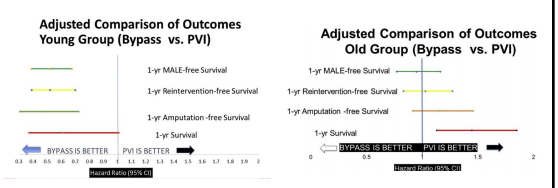


- Amputation rate in claudicants worse than natural history of disease ?
- Significantly lower freedom from amputation after endo revascularization in patients ≤ 50

Younger patients have worse outcomes after peripheral endovascular interventions for suprainguinal arterial occlusive disease

Michael C. Madigan, MD,[a] Alik Farber, MD,[b] Denis V. Rybin, PhD,[c] Gheorhge Doros, PhD,[c] William P. Robinson III, MD,[a] Jeffrey J. Siracuse, MD,[b] Jens Eldrup-Jorgensen, MD,[d] *and* Mohammad H. Eslami, MD, MPH,[a] *Pittsburgh, Pa; Boston, Mass; Greenville, NC; and Portland, Me*

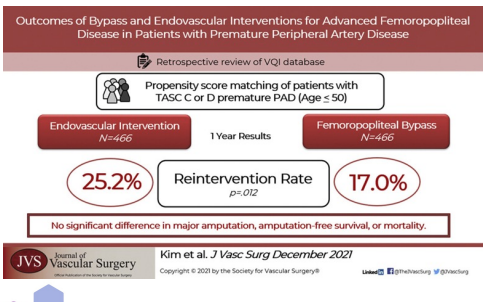
- Propensity-matched comparison of ENDO vs. Open Aortoiliac revascularizations in VQI 2010-2017
- 3062 cases in the ≥60-year group (1021 bypass; 2041 PVI)
- 2548 cases in the <60-year group (1697 bypass; 851 PVI)



(J Vasc Surg 2021;73:1715-22.)

Outcomes of bypass and endovascular interventions for advanced femoropopliteal disease in patients with premature peripheral artery disease

Tanner I. Kim, MD,[a] Yawei Zhang, MD, PhD, MPH,[b,c] Jonathan A. Cardella, MD,[a] Raul J. Guzman, MD,[a] *and* Cassius Iyad Ochoa Chaar, MD, MS,[a] *New Haven, Conn*



RISK FACTORS FOR POOR OUTCOME?

Outcomes of open and endovascular infra-inguinal revascularization are poor in young patients with atherosclerotic peripheral artery disease but do not differ between genders

Fang Yuan[1], Margaret C Trocol[2], W Darrin Clouse[3] and William P Robinson[4]

- Objective: determine effect of gender on infrainguinal revascularization in young patients with premature PAD
  - Patients < 55 at a single institution between 2011-2019
  - 81 infrainguinal revascularizations (35 open, 46 endo) in 37 M and 31 F
  - 65% CLTI (no difference between men and women)
  - Women: younger, higher BMI, increased DM and HLD
  - Mean f/u = 806 days

Table 3. Thirty-day outcomes in young patients receiving revascularization procedures, stratified by gender.

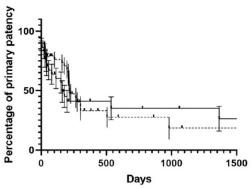
	Total, *n* = 81	Male, *n* = 45	Female, *n* = 36	*p* value
Wound infection (%)	1 (1.2%)	0 (0.0%)	1 (2.8%)	0.2606
Wound dehiscence (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
MACE (major adverse cardiovascular event)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
CVA or MI	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Mortality	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
MALE (major adverse limb event)	13 (16.0%)	5 (11.1%)	8 (22.2%)	0.1758
Loss of patency	14 (17.3%)	6 (13.3%)	8 (22.2%)	0.2931
Reintervention	12 (14.8%)	5 (10.9%)	7 (19.4%)	0.2756
Amputation	1 (1.2%)	0 (0.0%)	1 (2.8%)	0.2606

CVA: cerebrovascular accident; MI: myocardial ischemia; MACE: major adverse cardiovascular event; MALE: major adverse limb event; SD: standard deviation.

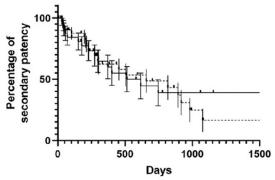
2022 Nov 15:17085381221140160

NO DIFFERENCE IN PATENCY BETWEEN MEN AND WOMEN

1-year Primary Patency = 34 ± 6 %



1-year Secondary Patency = 62 ± 6 %



NO DIFFERENCE IN MAJOR ADVERSE LIMB EVENTS BETWEEN MEN AND WOMEN

1-year MALE-free survival = 47 ± 6 %

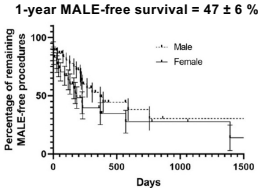


Table 4. Long-term outcomes in young patients receiving revascularization procedures, stratified by gender.

	Total, *n* = 81	Male, *n* = 45	Female, *n* = 36	*p* value
Mean Follow-up days (SD)	806.2 (784.8)	676.0 (660.5)	968.9 (900.3)	0.0954
Postop duplex/ABI follow-up (%)	73 (90.1%)	41 (91.1%)	32 (88.9%)	0.7391
Mean postop ABI (SD)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.5769
Mean ABI change (SD)	0.3 (0.2)	0.4 (0.2)	0.2 (0.2)	0.042
MALE (%)	44 (54.3%)	23 (51.1%)	21 (58.3%)	0.5167
Reintervention (%)	42 (51.9%)	23 (51.1%)	19 (52.8%)	0.8814
Mean number of reinterventions (SD)	1.2 (1.9)	0.8 (1.1)	1.7 (2.5)	0.0338
Major amputation (%)	11 (13.6%)	5 (11.1%)	6 (16.7%)	0.4683
Minor amputation (%)	16 (19.8%)	7 (15.6%)	9 (25.0%)	0.2888
Stenosis (%)	24 (29.6%)	11 (24.4%)	13 (36.1%)	0.2532
Occlusion (%)	30 (37.0%)	16 (35.6%)	14 (38.9%)	0.7576
New ulcer (%)	6 (7.4%)	2 (4.4%)	4 (11.1%)	0.2549
Death (%)	12 (14.8%)	6 (13.3%)	6 (16.7%)	0.6748
Bypass after index endovascular procedure (%)	16 (34.8%)	8 (33.3%)	8 (36.4%)	0.8293

SD: standard deviation; MALE: major adverse limb events; ABI: ankle-brachial index.

CONCLUSIONS FROM OUR STUDY

- Females and males < 55 with premature PAD have similar outcomes (30-day morbidity, long-term patency and MALE) after infrainguinal revascularization
- Poor outcomes compared to historical cohorts of older patients with PAD
  - 35% PP at 1 year
  - 50% reintervention at 1 year
  - 14% amputation rate over 2-3 year follow up (65% CLTI)
  - 15% mortality rate over 2-3 year follow up
- Need improved patient selection and strategies for premature PAD!

RISK FACTORS FOR POOR OUTCOME?

The progressive nature of peripheral arterial disease in young adults: A prospective analysis of white men referred to a vascular surgery service

R. James Valentine, MD, Mark R. Jackson, MD, J. Gregory Modrall, MD, Kenneth E. McIntyre, MD, and G. Patrick Clagett, MD, *Dallas, Tex*

- 51 white men age < 45
- Mean f/u 74 months
- Objective: Determine risk factors for poor outcome (defined as more than one revascularization or amputation)
  - REDO = more than 1 intervention
  - Stable = Disease stable with 0 or 1 intervention

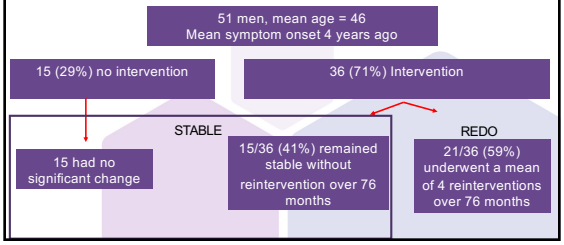


Table II. Comparison of demographics and risk factors between the two study groups

	REDO	*STABLE*	*P value*
No. of patients	21	30	
Age at onset (years)	39 ± 0.5	43 ± 2	<.001
Smoking			.11
Continued	19 (90%)	23 (77%)	
Stopped	1 (5%)	7 (23%)	
Never	1 (5%)	—	
Hypertension	12 (57%)	16 (53%)	NS
Diabetes mellitus	5 (24%)	6 (20%)	NS
Dyslipidemia	8 (38%)	10 (33%)	NS
Mean no. of risks	2.7 ± 0.3	2.2 ± 0.2	NS

Table IV. Comparison of serum markers between the two groups

	REDO	*STABLE*	*P value*
Lp(a) (mg/dL)	51 ± 11	27 ± 5	.032
Lp(a), >30 mg/dL	12 (57%)	9 (30%)	.053
No. with hypercoagulable states	7 (33%)	9 (30%)	NS
Mean no. with hypercoagulable states	0.38 ± 0.13	0.33 ± 0.1	NS
Homocysteine (μmol/L)	19 ± 2	16 ± 1	.12

Multivariate Predictors of Reintervention/Amputation:

- Age at diagnosis: HR 1.4 (95% CI 1.1-1.8)
- Initial ABI <. 0.5: HR 6.4 (95% CI 1.5-27)

- Higher Lipoprotoein a levels in REDO
- Age (<43) and severity of ischemia at intervention predict progression of PAD in young patients

THE ROLE OF ANTICOAGULATION?

- Patients < 50 who underwent lower extremity revascularization (both bypass and PVI) in the VQI
- Compared the outcomes of antiplatelet Rx only vs antiplatelet + anticoagulation in propensity-matched patients

Anticoagulation in Patients with Premature Peripheral Artery Disease Undergoing Lower Extremity Revascularization

Tanner I. Kim,[1,2] Andrew DeWan,[3] Michael Murray,[4] He Wang,[5] Arya Mani,[6] Carlos Mena-Hurtado,[6] Raul J. Guzman,[7] and Cassius Iyad Ochoa Chaar,[7] Honolulu, Hawaii, and New Haven, Connecticut

Ann Vasc Surg 2024; 105: 150–157

Table IV. One year outcomes of patients on antiplatelet medications only and antiplatelet plus anticoagulation after propensity matching

	Antiplatelet only	Antiplatelet and anticoagulation	
Outcomes	$N = 1{,}256$	$N = 628$	P value
Reintervention	111/676 (16.4%)	61/273 (22.3%)	0.032[a]
Ipsilateral major amputation	76/901 (8.4%)	40/398 (10.1%)	0.347
Mortality	44 (3.5%)	42 (6.7%)	0.002[a]
Major adverse limb events	161/674 (23.9%)	86/272 (31.6%)	0.014[a]
Amputation-free survival	788/901 (87.5%)	322/398 (80.9%)	0.001[a]

[a]Denotes P value < 0.05. Lower numbers depicted due to missing data from long-term follow-up.

Anticoagulation + antiplatelet was associated with higher reintervention and mortality at 1 yr

SUMMARY OF CURRENT REVASCULARIZATION EVIDENCE

- Young age associate with early bypass graft failure
  - Acceptable long-term results
- Young age associated with endovascular failure and reintervention
- Revascularization in young claudicants associated with high rates of conversion to CLTI and amputation
  - worse than natural history of claudication?
- Open revascularization performs better than endo
  - Aortoiliac and infrainguinal disease
  - Limited data with selection bias
- Anticoagulation in addition to antiplatelet does not improve outcomes in young patients
  - Limited data in select patients
  - Patient < 50 not included in most trials (e.g., Voyager PAD)

HOW SHOULD WE APPROACH PREMATURE PAD IN YOUNG PATIENTS?

- *Aggressively investigate and treat unusual risk factors*
  - *Lipoprotein a*
- *Optimize lifestyle changes, medical therapy, and exercise for claudication*
  - *Much higher threshold for revascularization!*
  - *Never revascularize for claudication if medical status not optimized*
- *Open surgery is preferable to endovascular when revascularization is required (CLTI)*
- *Can approach revascularization in women and men similarly*

- Ongoing Needs:
  - Understand biologic, medical, or technical factors which influence the outcome of conservative management and revascularization (open and endo)

Thank you!