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**Peripheral Arterial Disease:**  
Review and Updates

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## Disclosures

- None relevant to today's talk



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## Outline

- Epidemiology and risk factors
- Pathology and clinical presentation
- Natural history and medical management
- Anatomy of disease
- Interventions options and outcomes
- BASIL-2 and BEST-CLI



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## Epidemiology of Peripheral Arterial Disease (PAD)

- Global prevalence 5.6% affecting 236 million adults
  - US prevalence of 7% affecting 8.5 million adults
- Over 40% of patients with CAD have PAD
  - PAD associated with left main and multivessel CAD
- 25-50% of TAVR patients have PAD



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## Risk Factors for PAD

- Increasing age
- Male sex
- Smoking
- HTN
- DM
- HLD
- Renal insufficiency

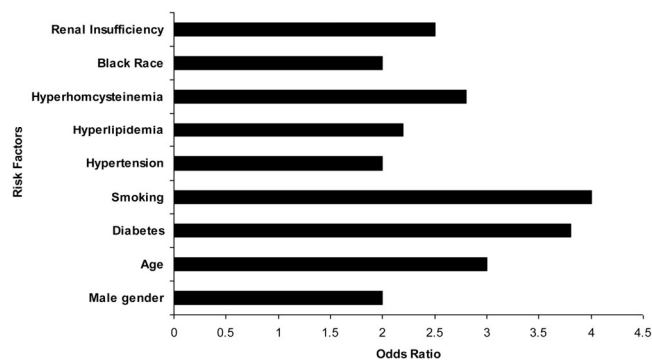


Image source: Conte, Michael S., Frank B. Pomposelli, Daniel G. Clair, Patrick J. Geraghty, James F. McKinsey, Joseph L. Mills, Gregory L. Moneta, et al. "Society for Vascular Surgery Practice Guidelines for Atherosclerotic Occlusive Disease of the Lower Extremities: Management of Asymptomatic Disease and Claudication." *Journal of Vascular Surgery* 61, no. 3 (March 2015): 25-41S.e1. <https://doi.org/10.1016/j.jvs.2014.12.009>.



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## Risk Factors for PAD

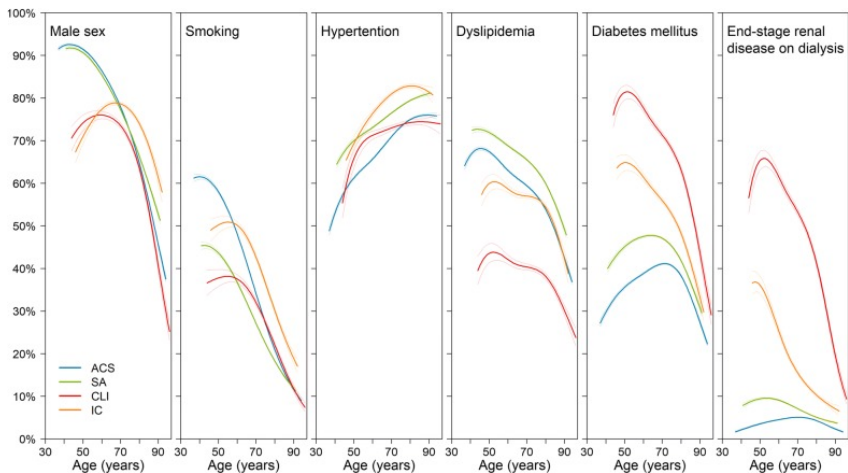


Image source: the J-EVT and J-PCI investigators, Mitsuyoshi Takahara, Osamu Iida, Shun Kohsaka, Yoshimitsu Soga, Masahiko Fujihara, Toshiro Shinke, Tetsuya Amano, and Yuji Ikari. "Diabetes Mellitus and Other Cardiovascular Risk Factors in Lower-Extremity Peripheral Artery Disease versus Coronary Artery Disease: An Analysis of 1,121,359 Cases from the Nationwide Databases." *Cardiovascular Diabetology* 18, no. 1 (December 2019): 155. <https://doi.org/10.1186/s12933-019-0955-5>.



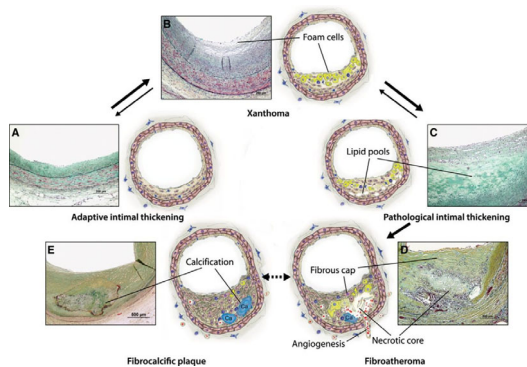
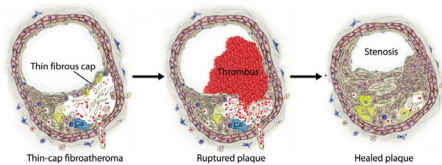
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## Pathology of PAD

- Atherosclerosis
  - Early lesions may regress
  - Progression, rupture/erosion with thrombosis



Images source: Jacob Fog Bentzon. *Circulation Research*. Mechanisms of Plaque Formation and Rupture, Volume: 114, Issue: 12, Pages: 1852-1866, DOI: (10.1161/CIRCRESAHA.114.302721)



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## Pathology of PAD

- Other arterial occlusive disease:
  - Embolism
  - Popliteal artery entrapment syndrome →
  - Popliteal artery aneurysm thrombosis
  - Large or medium vessel vasculitis
  - Cystic adventitial disease
  - Persistent sciatic artery
  - External iliac endofibrosis



Image source: Themes, U. F. O. "21 Popliteal Entrapment Syndrome." Radiology Key, January 8, 2016. <https://radiologykey.com/21-popliteal-entrapment-syndrome/>.



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## Clinical Presentation of PAD

- PAD is conventionally defined as ABI < 0.9, TBI < 0.7 or significant drop in ABI post-exercise
- Clinically:
  - Asymptomatic 75%
  - Intermittent claudication (IC) 20-30%
  - Chronic limb threatening ischemia (CLTI) 1-3%
    - Rest pain > 2 weeks or tissue loss



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## Rutherford Categories of Chronic Limb Ischemia

Grade	Category	Clinical description	Objective criteria
0	0	Asymptomatic-no hemodynamically significant occlusive disease	Normal treadmill or reactive hyperemia test
	1	Mild claudication	Completes treadmill exercise; AP after exercise > 50 mmHg but at least 20 mmHg lower than resting value
I	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete standard treadmill exercise, and AP after exercise < 50 mm Hg
II	4	Ischemic rest pain	Resting AP < 40 mmHg, flat or barely pulsatile ankle or metatarsal PVR; TP < 30 mm Hg
III	5	Minor tissue loss non-healing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP < 60 mm Hg, ankle or metatarsal PVR flat or barely pulsatile; TP < 40 mm Hg
	6	Major tissue loss-extending above TM level, functional foot no longer salvageable	Same as category 5

AP: ankle pressure; PVR: pulse volume recording; TM: transmetatarsal; TP: toe pressure.



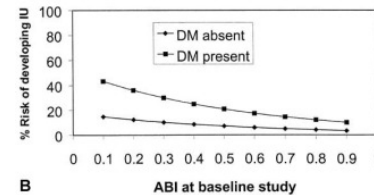
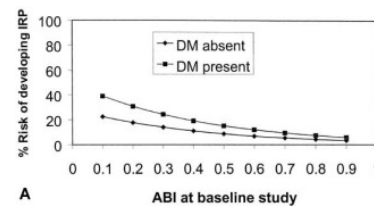
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## Intermittent Claudication

- Natural history of IC over 10 years
  - < 10% any amputation
  - 18% revascularization
  - 23% rest pain
  - 30% tissue loss



Predicted absolute 5-year risk for development of IRP (A) and IU (B).

Image source: Aquino, Rainier, Christopher Johnides, Michel Makaroun, Jeffrey C. Whittle, Visala S. Muluk, Mary E. Kelley, and Satish C. Muluk. "Natural History of Claudication: Long-Term Serial Follow-up Study of 1244 Claudicants." *Journal of Vascular Surgery* 34, no. 6 (December 2001): 962-70. <https://doi.org/10.1067/jvms.2001.119749>.



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## Chronic Limb Threatening Ischemia

- 1 year mortality of 20-25%, 4 year up to 50%
- 1 year major amputation rate of 25% without revascularization
- Presentation:
  - 29% rest pain
  - 45% ulceration
  - 26% gangrene
- Intervention:
  - Non-surgical 29%
  - Revascularization 58%
  - Primary amputation 13%



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## Chronic Limb Threatening Ischemia

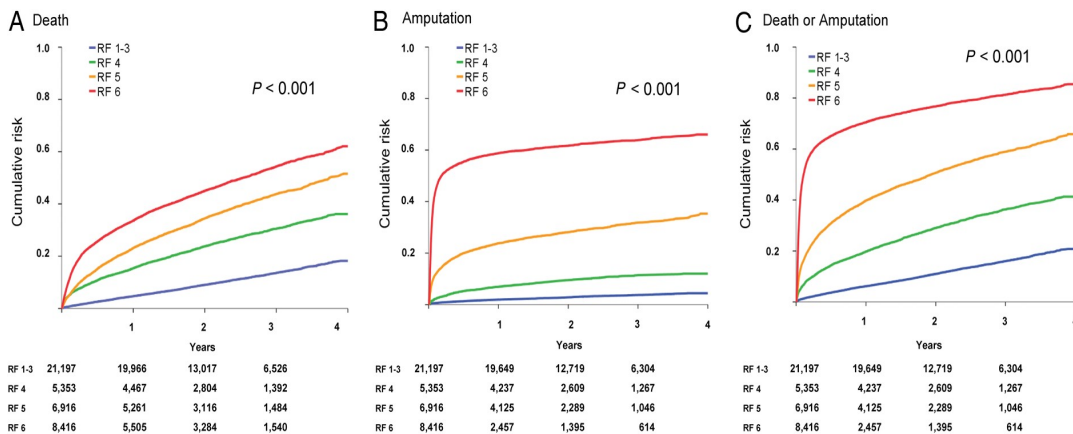


Image source: Reinecke, H., M. Unrath, E. Freisinger, H. Bunzemeier, M. Meyborg, F. Luders, K. Gebauer, N. Roeder, K. Berger, and N. M. Malyar. "Peripheral Arterial Disease and Critical Limb Ischaemia: Still Poor Outcomes and Lack of Guideline Adherence." *European Heart Journal* 36, no. 15 (April 1, 2015): 932-38. <https://doi.org/10.1093/eurh/ahv006>.

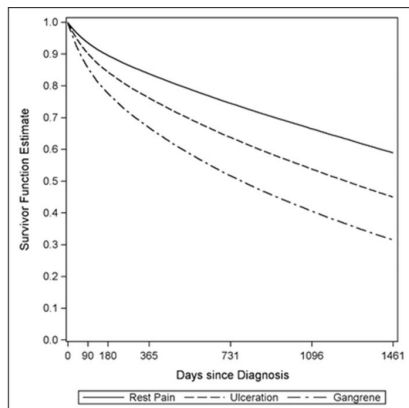


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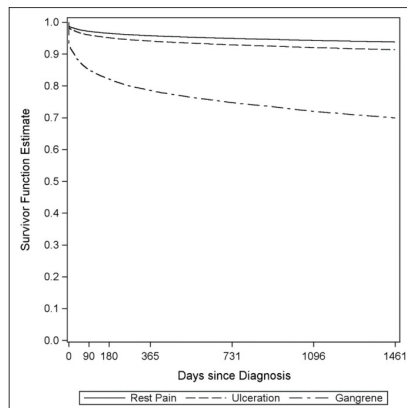


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## Chronic Limb Threatening Ischemia



Patient survival over 4 years following diagnosis of critical limb ischemia



Freedom from major amputation over 4 years following diagnosis of critical limb ischemia

Image source: Mustapha, Jihad A., Barry T. Katzen, Richard F. Neville, Robert A. Lookstein, Thomas Zeller, Larry E. Miller, and Michael R. Jaff. "Determinants of Long-Term Outcomes and Costs in the Management of Critical Limb Ischemia: A Population-Based Cohort Study." *Journal of the American Heart Association* 7, no. 16 (August 21, 2018): e009724. <https://doi.org/10.1161/JAHA.118.009724>.



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## Management of PAD

- Asymptomatic disease
  - Smoking cessation, antihypertensives, glycemic control
  - Antiplatelet +/-
  - Statin
  - Surveillance +/-



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## Management of PAD

- Intermittent Claudication
  - Risk factor modification, statin, Antiplatelet
  - Supervised exercise program
  - Cilostazol
  - Annual surveillance with non-invasive vascular testing



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## Management of PAD

- Intermittent Claudication
  - Revascularize for function NOT limb salvage
  - Intervention for good risk candidates with severe lifestyle limitations with expected durability of intervention > 2 years
  - Consider addition of Xarelto 2.5 BID after procedure



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## Management of PAD

- VOYAGER-PAD

- 6,564 patients randomized to addition of Xarelto 2.5 BID or placebo to usual medical therapy after revascularization procedure
- Reduction in cardiovascular event at 3 years at 17.3% compared to 19.9% (P=0.009) with increase in major bleeding 5.94% versus 4.06% (P=0.007).

First Events Prevented and Caused for 10,000 Patients Treated with Rivaroxaban for One Year

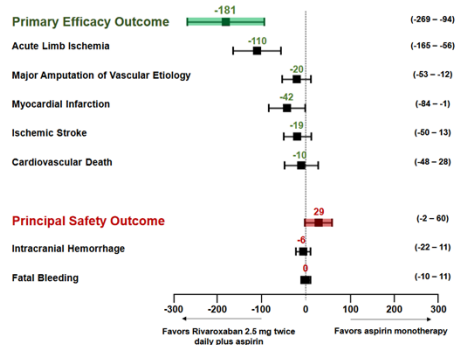


Image source: Bonaca, Marc P., Rupert M. Bowersachs, Sonia S. Anand, E. Sebastian Debus, Mark R. Nehler, Manesh R. Patel, Fabrizio Fanelli, et al. "Rivaroxaban in Peripheral Artery Disease after Revascularization." *New England Journal of Medicine* 382, no. 21 (May 21, 2020): 1994-2004. <https://doi.org/10.1056/NEJMoa2000052>.



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## Management of PAD

- Chronic limb threatening ischemia
  - Revascularization is recommended
  - A multidisciplinary approach with appropriate wound care is recommended
  - 30-50% will not be a candidate for revascularization



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## Anatomy of PAD

- Aortoiliac
- Femoropopliteal
- Infrapopliteal/Infrageniculate/  
Tibial/Crural

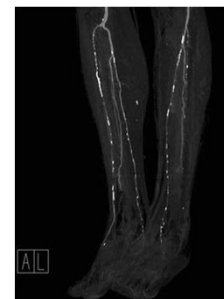
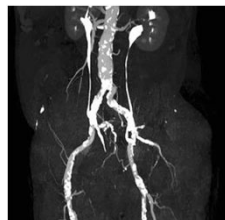


Image source: Horehledo, Barbara, Casper Mihl, Gianluca Milanese, Rutger Brans, Nienke G. Eijvoogel, Babz M. F. Hendriks, Joachim E. Wildberger, and Marco Das. "CT Angiography in the Lower Extremity Peripheral Artery Disease Feasibility of an Ultra-Low Volume Contrast Media Protocol." *CardioVascular and Interventional Radiology* 41, no. 11 (November 2018): 1751-64. <https://doi.org/10.1007/s00270-018-1979-z>.



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## Anatomy of PAD

- Aortoiliac
  - Smoking claudicants
- Femoropopliteal
  - Older smokers
- Tibial
  - DM/ESRD with CLTI
- Multilevel
  - Older smokers

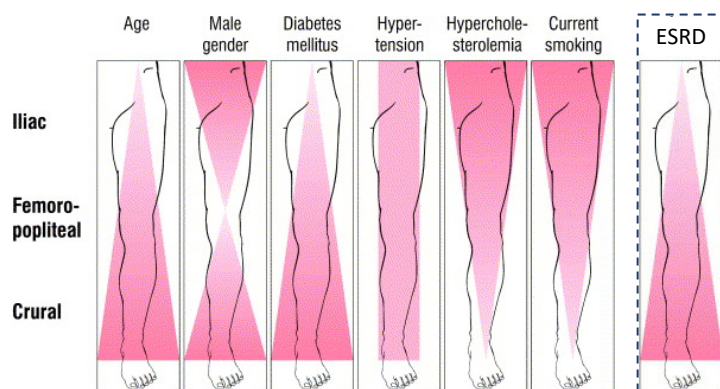


Image source: Diehm, N., A. Shang, A. Silvestro, D.-D. Do, F. Dick, J. Schmidt, F. Mahler, and I. Baumgartner. "Association of Cardiovascular Risk Factors with Pattern of Lower Limb Atherosclerosis in 2659 Patients Undergoing Angioplasty." *European Journal of Vascular and Endovascular Surgery* 31, no. 1 (January 2006): 59-63. <https://doi.org/10.1016/j.ejvs.2005.09.006>.



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## Anatomy of PAD

**A Old age**

Proximal SFA	(P=0.00)
Middle SFA	(P=0.41)
Distal SFA	(P=0.42)
P1	(P=0.75)
P2	(P=0.53)
P3	(P=0.004)

**B Female sex**

Proximal SFA	(P=0.001)
Middle SFA	(P=0.89)
Distal SFA	(P=0.054)
P1	(P=0.001)
P2	(P=0.001)
P3	(P=0.031)

**C Overweight**

Proximal SFA	(P=0.004)
Middle SFA	(P=0.41)
Distal SFA	(P=0.82)
P1	(P=0.19)
P2	(P=0.37)
P3	(P=0.45)

**D Smoking**

Proximal SFA	(P=0.015)
Middle SFA	(P=0.001)
Distal SFA	(P=0.43)
P1	(P=0.030)
P2	(P=0.012)
P3	(P=0.047)

**E Hypertension**

Proximal SFA	(P=0.009)
Middle SFA	(P=0.49)
Distal SFA	(P=0.95)
P1	(P=0.86)
P2	(P=0.10)
P3	(P=0.006)

**F Dyslipidemia**

Proximal SFA	(P=0.04)
Middle SFA	(P=0.007)
Distal SFA	(P=0.030)
P1	(P=0.48)
P2	(P=0.20)
P3	(P=0.12)

**G Diabetes mellitus**

Proximal SFA	(P=0.24)
Middle SFA	(P=0.96)
Distal SFA	(P=0.82)
P1	(P=0.28)
P2	(P=0.15)
P3	(P=0.18)

**H Renal failure on dialysis**

Proximal SFA	(P=0.001)
Middle SFA	(P=0.002)
Distal SFA	(P=0.33)
P1	(P=0.001)
P2	(P=0.001)
P3	(P=0.001)

**ESRD**

Image source: Takahara, Mitsuyoshi, Yoshimitsu Soga, Masahiko Fujiwara, Osamu Iida, and Daito Kawasaki. "Association of Smoking, Diabetes, and Dialysis with the Presence of Popliteal Lesions in Femoropopliteal Artery Disease." *Journal of Atherosclerosis and Thrombosis* 30, no. 10 (October 1, 2023): 1327-35. <https://doi.org/10.5551/jat.64007>.

Image source: Fujiwara, Masahiko. "Angiography and Endovascular Therapy for Femoropopliteal Artery Disease." In *Angiography and Endovascular Therapy for Peripheral Artery Disease*, edited by Yoshiaki Yokoi, Keisuke Fukuda, Masahiko Fujiwara, Akihiro Higashimori, and Osami Kawarada. InTech, 2017. <https://doi.org/10.5772/67181>.

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## Intervention for PAD

- Open and endovascular

Image source: Rowe, Vincent L., William Lee, Fred A. Weaver, and David Etzioni. "Patterns of Treatment for Peripheral Arterial Disease in the United States: 1996-2005." *Journal of Vascular Surgery* 49, no. 4 (April 2009): 910-17. <https://doi.org/10.1016/j.jvs.2008.11.054>.

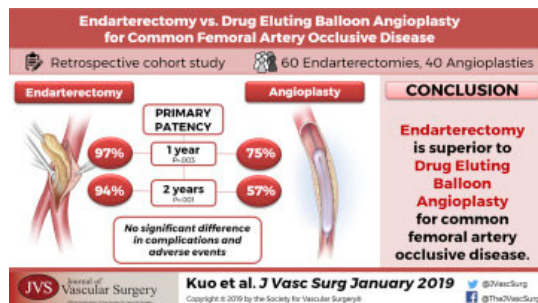
Image source: Guez, David, David R. Hansberry, Carin F. Gonsalves, David J. Eschelmann, Laurence Parker, Vijay M. Rao, and David C. Levin. "Recent Trends in Endovascular and Surgical Treatment of Peripheral Arterial Disease in the Medicare Population." *American Journal of Roentgenology* 214, no. 5 (May 2020): 962-66. <https://doi.org/10.2214/AJR.19.21967>.

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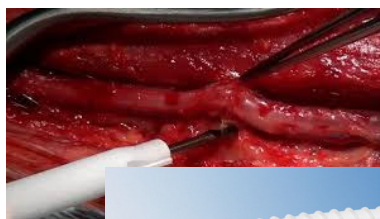
## Intervention for PAD

- Open revascularization
  - Endarterectomy
    - Focal lesion
    - Common femoral, aorta, popliteal, tibial
    - Often used in conjunction with bypass or stent



## Intervention for PAD

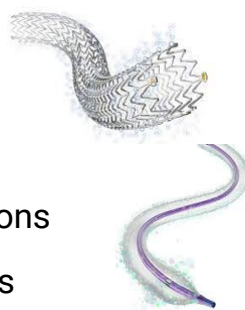
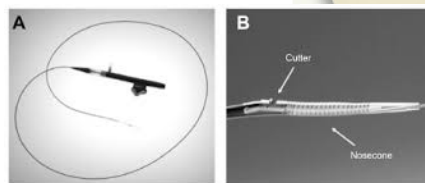
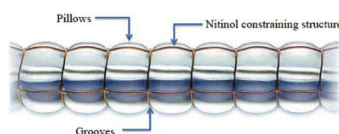
- Open revascularization
  - Bypass: Inflow, outflow, conduit
    - Conduit
      - Autologous
      - Prosthetic
      - Alternative biologics



## Intervention for PAD

- Endovascular Revascularization

- Angioplasty
- Atherectomy
- Stents
- Drug coated balloons
- Drug coated stents



## Intervention for PAD

- Endovascular Adjuncts

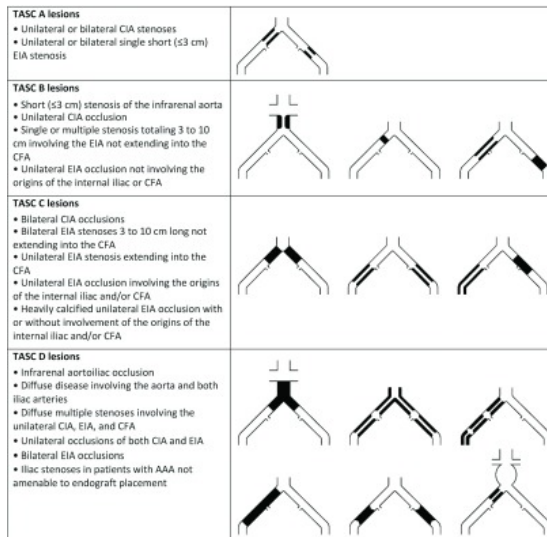
- Wires, catheters, sheaths
- Crossing and re-entry devices
- Intravascular lithotripsy
- Tacking stents
- Intravascular ultrasound
- Embolic protection devices
- Suction and mechanical thrombectomy



## Intervention for PAD

- TransAtlantic Inter-Society Consensus (TASC)
  - 2000 and 2007
- Aortoiliac occlusive disease
  - A – endovascular preferred
  - D – open surgery preferred

Image source: Norgren, L, W.R. Hiatt, J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes. "Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)." *Journal of Vascular Surgery* 45, no. 1 (January 2007): 55-67. <https://doi.org/10.1016/j.jvs.2006.12.037>.



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## Intervention for PAD

- Durability of open intervention for aortoiliac disease

Indication	5-year % patency (range)		10-year % patency (range)		Procedure	5-year % patency (range)
	Claudication	CLI	Claudication	CLI		
Limb based	91 (90–94)	87 (80–88)	86 (85–92)	81 (78–83)	Axillo uni femoral bypass	51 (44–79)
Patient based	85 (85–89)	80 (72–82)	79 (70–85)	72 (61–76)	Axillo bi femoral bypass	71 (50–76)
					Femoral femoral bypass	75 (55–92)

Patency at 5 and 10 years after aortobifemoral bypass

Patency rates at 5 years after extra-anatomic bypass

Images source: Norgren, L, W.R. Hiatt, J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes. "Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)." *Journal of Vascular Surgery* 45, no. 1 (January 2007): 55-67. <https://doi.org/10.1016/j.jvs.2006.12.037>.



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## Intervention for PAD

- Patency after endovascular intervention for aortoiliac disease
  - For TASC A-B, primary and secondary patency rates 5 years are 88% and 97%.
  - Meta-analysis of endovascular treatment of TASC C–D lesions, 5-year primary patency 60% - 86%, secondary patency 80% to 98%



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## Intervention for PAD

- Femoropopliteal occlusive disease
  - A – endovascular preferred
  - D – open surgery preferred

Image source: Norgren, L., W.R. Hiatt, J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes. "Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)." *Journal of Vascular Surgery* 45, no. 1 (January 2007): 55–67. <https://doi.org/10.1016/j.jvs.2006.12.037>

<b>TASC A lesions</b> <ul style="list-style-type: none"><li>• Single stenosis <math>\leq 10</math> cm in length</li><li>• Single occlusion <math>\leq 5</math> cm in length</li></ul>	
<b>TASC B lesions</b> <ul style="list-style-type: none"><li>• Multiple lesions (stenoses or occlusions), each <math>\leq 5</math> cm</li><li>• Single stenosis or occlusion <math>\leq 15</math> cm not involving the infrageniculate popliteal artery</li><li>• Heavily calcified occlusion <math>\leq 5</math> cm in length</li><li>• Single popliteal stenosis</li></ul>	
<b>TASC C lesions</b> <ul style="list-style-type: none"><li>• Multiple stenoses or occlusions totaling <math>&gt;15</math> cm with or without heavy calcification</li><li>• Recurrent stenoses or occlusions after failing treatment</li></ul>	
<b>TASC D lesions</b> <ul style="list-style-type: none"><li>• Chronic total occlusions of CFA or SFA (<math>&gt;20</math> cm, involving the popliteal artery)</li><li>• Chronic total occlusion of popliteal artery and proximal trifurcation vessels</li></ul>	



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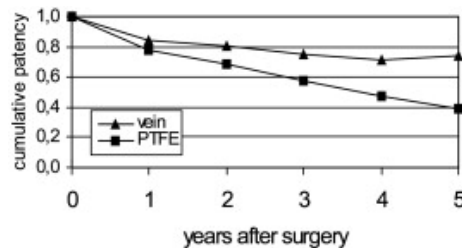


## Intervention for PAD

- Durability of open intervention for femoropopliteal disease

	Claudication	CLI
Vein	80	66
Above-knee PTFE	75	47
Below-knee PTFE	65	65

5-year patency following femoral popliteal bypass



Weighted mean primary patency rates for vein versus PTFE grafts for above knee femoropopliteal bypass

Image source:  
 Klinkert, P, P.N Post,  
 P.J Breslau, and J.H  
 Van Bockel.  
 "Saphenous Vein  
 Versus PTFE for Above-  
 Knee Femoropopliteal  
 Bypass. A Review of  
 the Literature."  
*European Journal of  
 Vascular and  
 Endovascular Surgery*  
 27, no. 4 (April 2004):  
 357-62.  
<https://doi.org/10.1016/j.ejvs.2003.12.027>

Image source: Norgren, L., W.R. Hiatt, J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes. "Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)." *Journal of Vascular Surgery* 45, no. 1 (January 2007): 55-67. <https://doi.org/10.1016/j.jvs.2006.12.037>



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## Intervention for PAD

- Patency after endovascular intervention for femoropopliteal occlusive disease

- Covered stent 5 year patency for >10cm SFA lesions of 62.4%
- Bare metal stent 3 year patency for <8cm SFA lesions 71.0% and >8cm SFA lesions 50.5%
- DCB 3 year patency for SFA lesions <18cm 69.5%
- DES 5 year patency for SFA lesions < 13cm 66.4%



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## Intervention for PAD

- BASIL-2 and BEST-CLI
  - BASIL-2
    - UK, Denmark, Sweden, 2014-2022
    - Vein bypass versus endovascular therapy in 345 CLTI patients
  - BEST-CLI
    - United States, Canada, Finland, Italy, and New Zealand, 2014-2019
    - Bypass versus endovascular therapy, 2 cohorts based on presence of vein, in 1830 CLTI patients, all low surgical risk



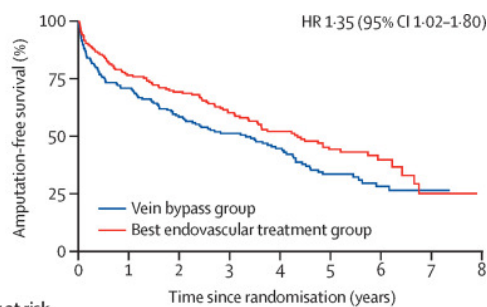
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## Intervention for PAD

- BASIL-2
  - Primary outcome favored endovascular therapy
  - Bypass: 63% amputation/death
  - Endo: 53% amputation/death
  - Driven by higher mortality after bypass, no difference in limb loss



Number at risk	0	1	2	3	4	5	6	7	8
Vein bypass group	172	120	94	78	58	37	19	8	0
Best endovascular treatment group	173	127	112	91	67	47	19	5	0



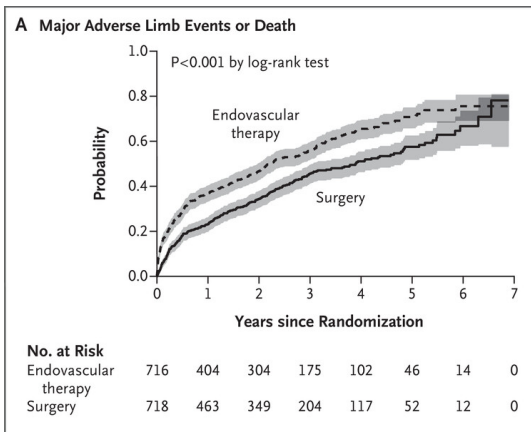
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## Intervention for PAD

- BEST-CLI – Cohort 1
  - Primary outcome favored bypass
  - Bypass: 42.6% MALE/death
  - Endo: 57.4% MALE/death
  - Driven by higher reintervention after endovascular therapy

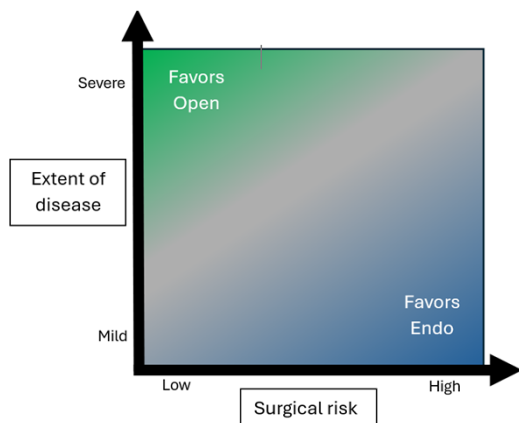


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## Intervention for PAD



GRAND ROUNDS



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Thank you!

