Atherosclerosis and Peripheral Arterial Disease

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Disclosures

- No financial disclosures
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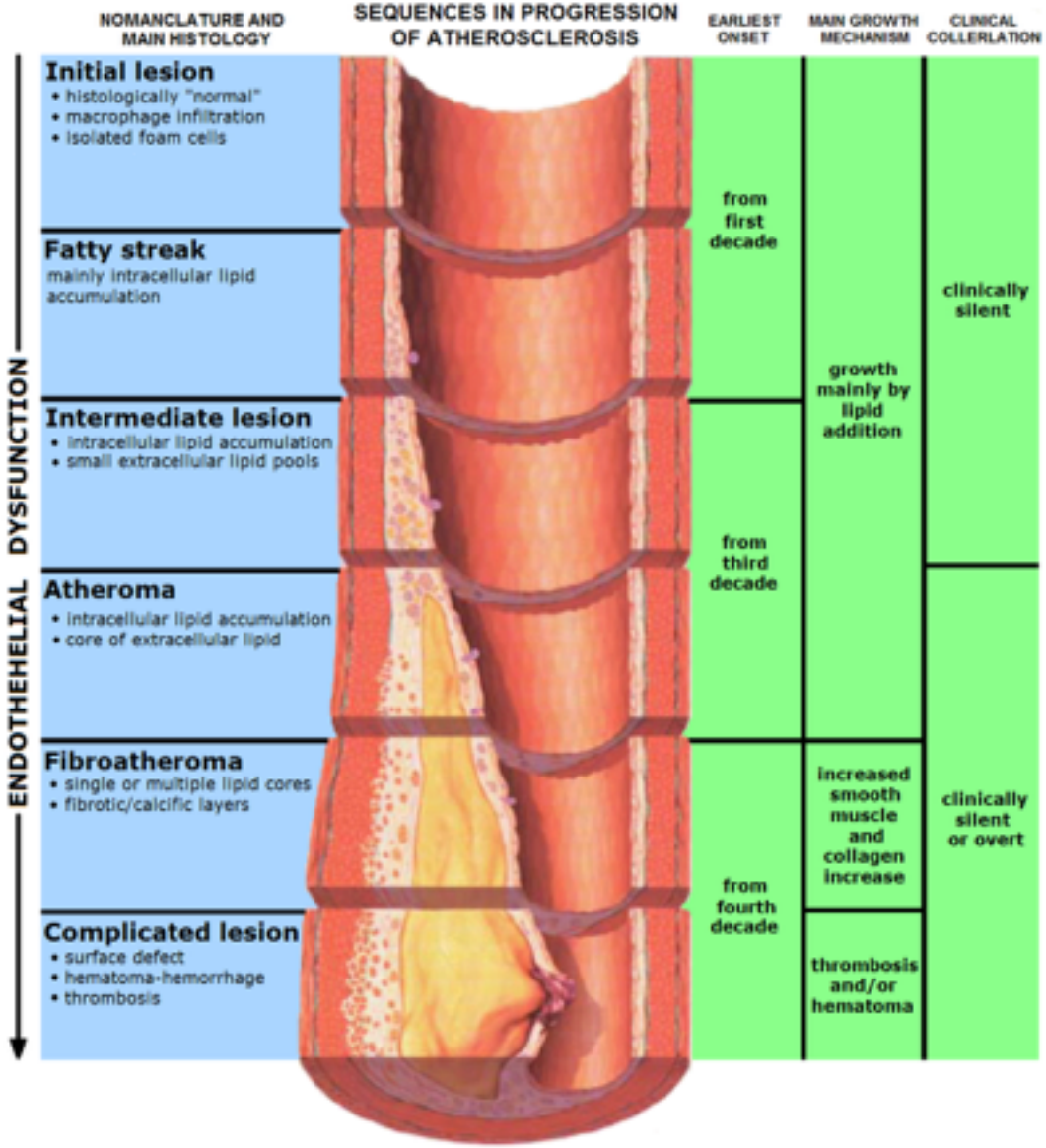
Objectives

- Review the pathophysiology of atherosclerosis
- Discuss specific risk factors and epidemiology for lower extremity peripheral arterial disease
- Discuss presentation of patients with peripheral arterial disease
- Compare different forms of evaluation and work up for peripheral arterial disease
- Discuss and compare potential interventions-open surgical and endovascular

Introduction

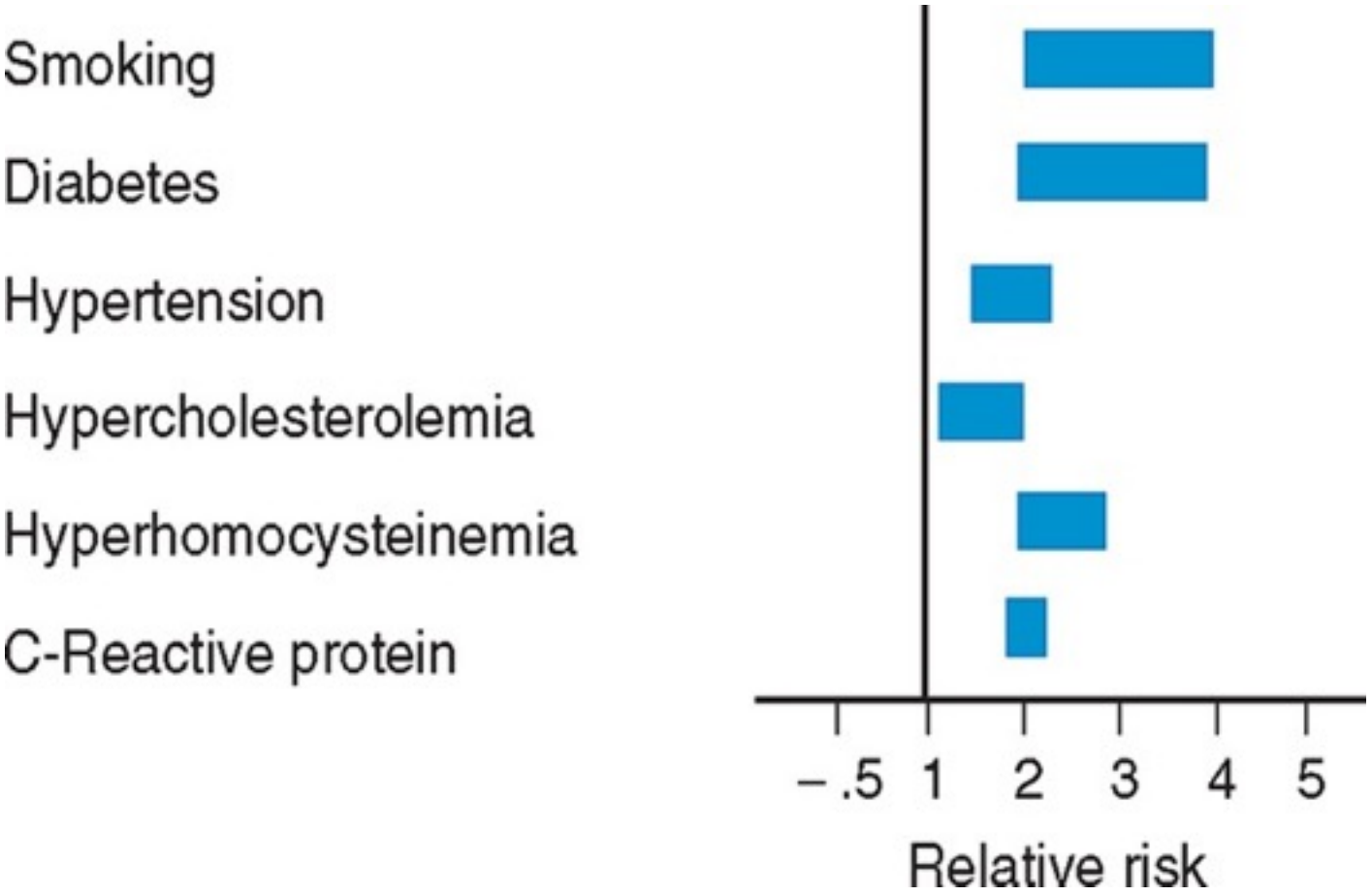
- Definition: thickening of the arterial wall as a result of accumulation of fatty materials
- Greek roots:
  - Athere=gruel
  - skleros=hard


NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly intracellular lipid accumulation
Intermediate lesion
• intracellular lipid accumulation
• small extracellular lipid pools
Atheroma
• intracellular lipid accumulation
• core of extracellular lipid
Fibroatheroma
• single or multiple lipid cores
• fibrotic/calcific layers
Complicated lesion
• surface defect
• hematoma-hemorrhage
• thrombosis
from first decade
from third decade
from fourth decade
growth mainly by lipid addition
increased smooth muscle and collagen increase
thrombosis and/or hematoma
clinically silent
clinically silent or overt

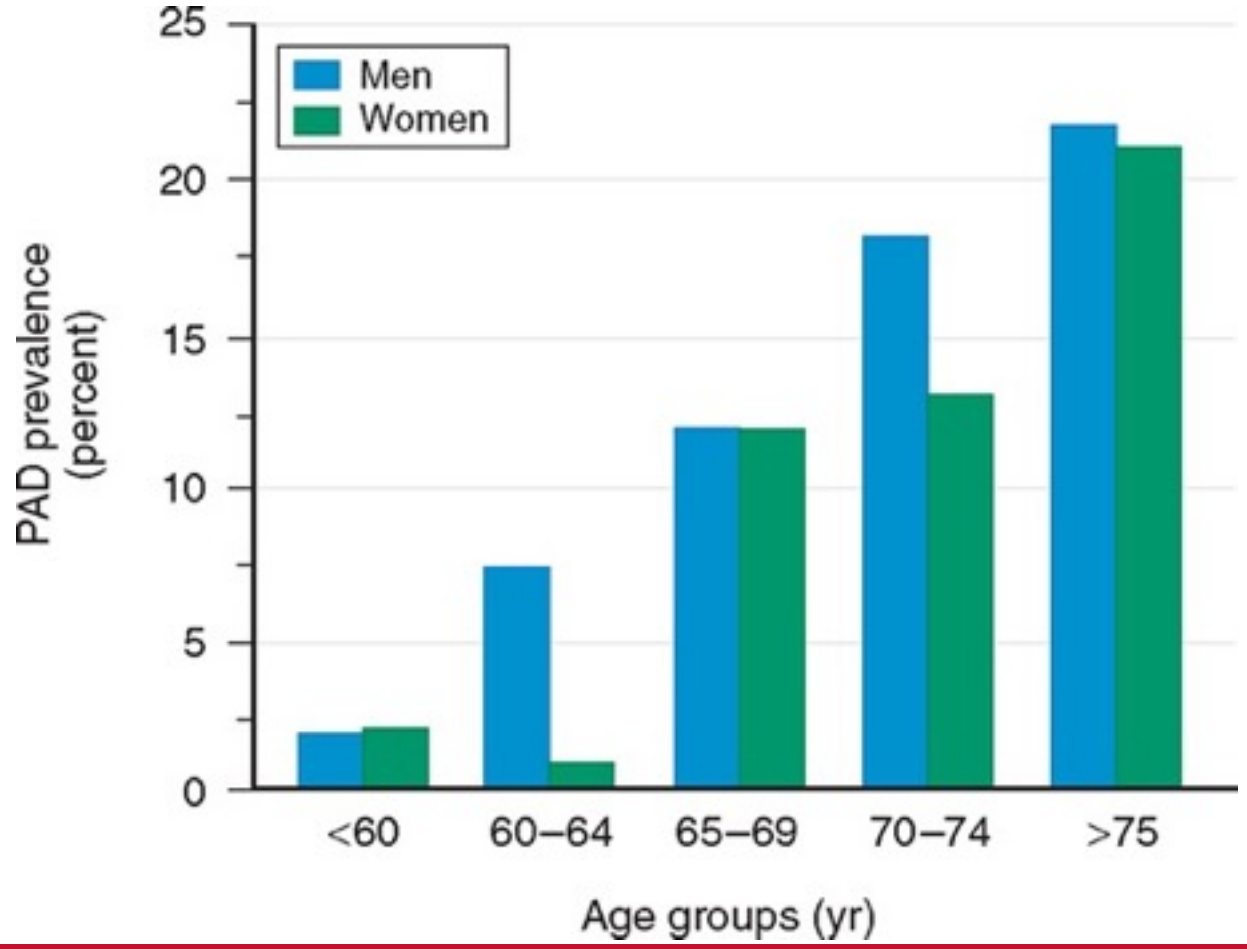
Risk Factors

- Modifiable risk factors
  - Nicotine use (i.e., Tobacco smoking, chewing)
  - Diet (contributing to hyperlipidimia)
  - Hypertension
  - Diabetes
  - Sedentary life style
  - Elevated CRP
  - Hyperhomocysteinemia
- Non modifiable risk factors
  - Age
  - Gender
  - Family history

Relative Risk



Prevalence


Men
Women
PAD prevalence (percent)
25
20
15
10
5
0
<60
60–64
65–69
70–74
>75
Age groups (yr)

Symptoms

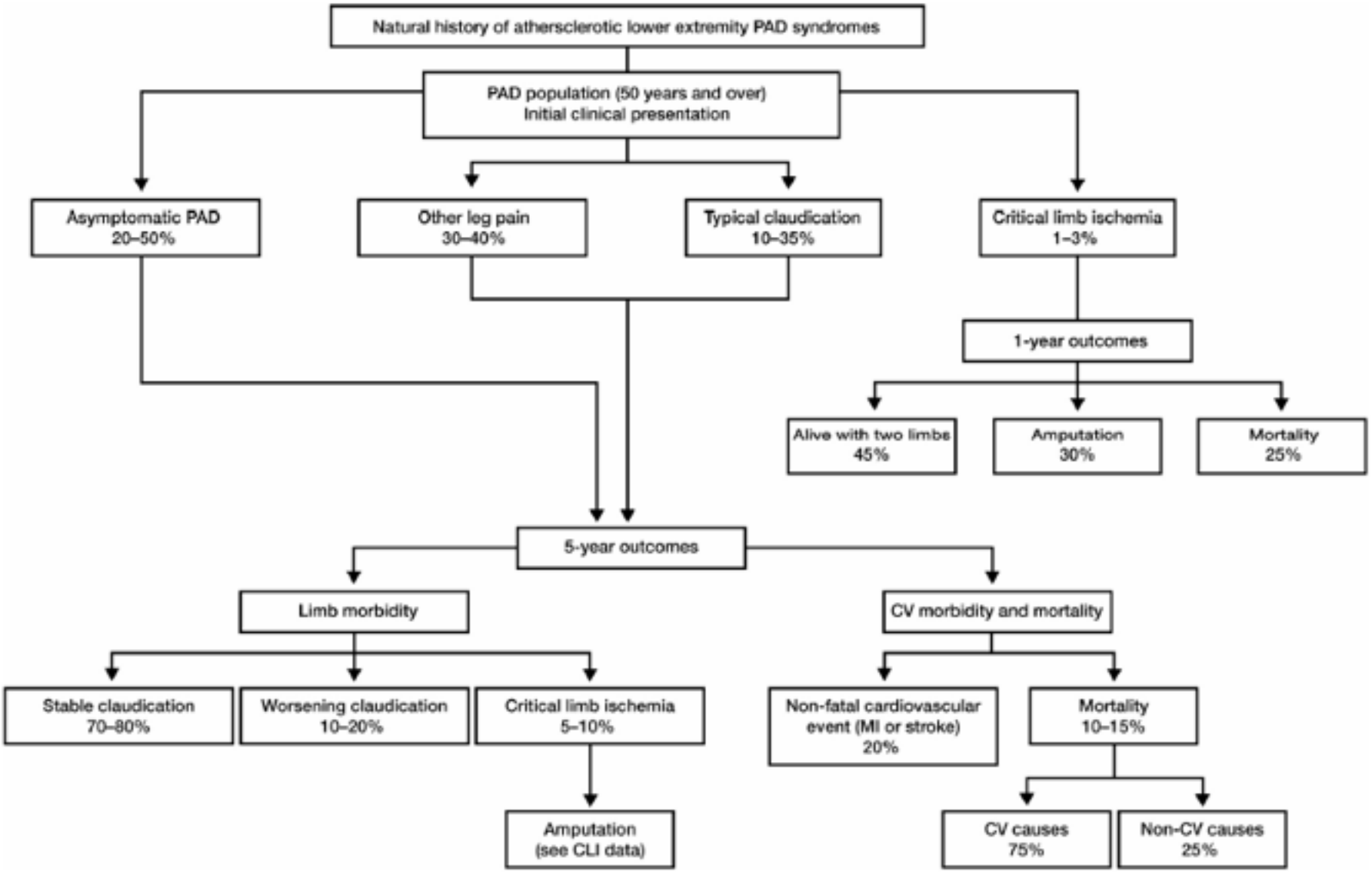
- Asymptomatic
- Intermittent claudication
  - Latin: claudicare “to limp” from clouds “lame”
  - Reproducible, exercise-induced lower extremity pain that is relieved at rest
- Ischemic rest pain
- Tissue loss
  - Minor and major

Symptoms Based on Location of Disease

- Aorto-iliac disease
  - Hip, thigh, buttock claudication
  - Erectile dysfunction
  - Can have calf claudication
- Femoropopliteal Disease
  - Calf and foot claudication

Classification

FONTAINE		RUTHERFORD		
Stage	**Clinical**	**Grade**	**Category**	**Clinical**
I	Asymptomatic	0	0	Asymptomatic
IIa	Mild claudication	I	1	Mild claudication
IIb	Moderate–severe claudication	I	2	Moderate claudication
		I	3	Severe claudication
III	Ischemic rest pain	II	4	Ischemic rest pain
IV	Ulceration or gangrene	III	5	Minor tissue loss
		IV	6	Ulceration or gangrene


Natural history of atherosclerotic lower extremity PAD syndromes
PAD population (50 years and over)
Initial clinical presentation
Asymptomatic PAD
20–50%
Other leg pain
30–40%
Typical claudication
10–35%
Critical limb ischemia
1–3%
1-year outcomes
Alive with two limbs
45%
Amputation
30%
Mortality
25%
5-year outcomes
Limb morbidity
CV morbidity and mortality
Stable claudication
70–80%
Worsening claudication
10–20%
Critical limb ischemia
5–10%
Amputation
(see CLI data)
Non-fatal cardiovascular
event (MI or stroke)
20%
Mortality
10–15%
CV causes
75%
Non-CV causes
25%

Evaluation

- Non-invasive
  - ABI's-Pre & Post exercise
  - Pulse Volume Recording (PVR)/Segmental pressures
  - Arterial duplex
  - MRA
  - CTA
- Invasive
  - Contrast angiography

ABI's

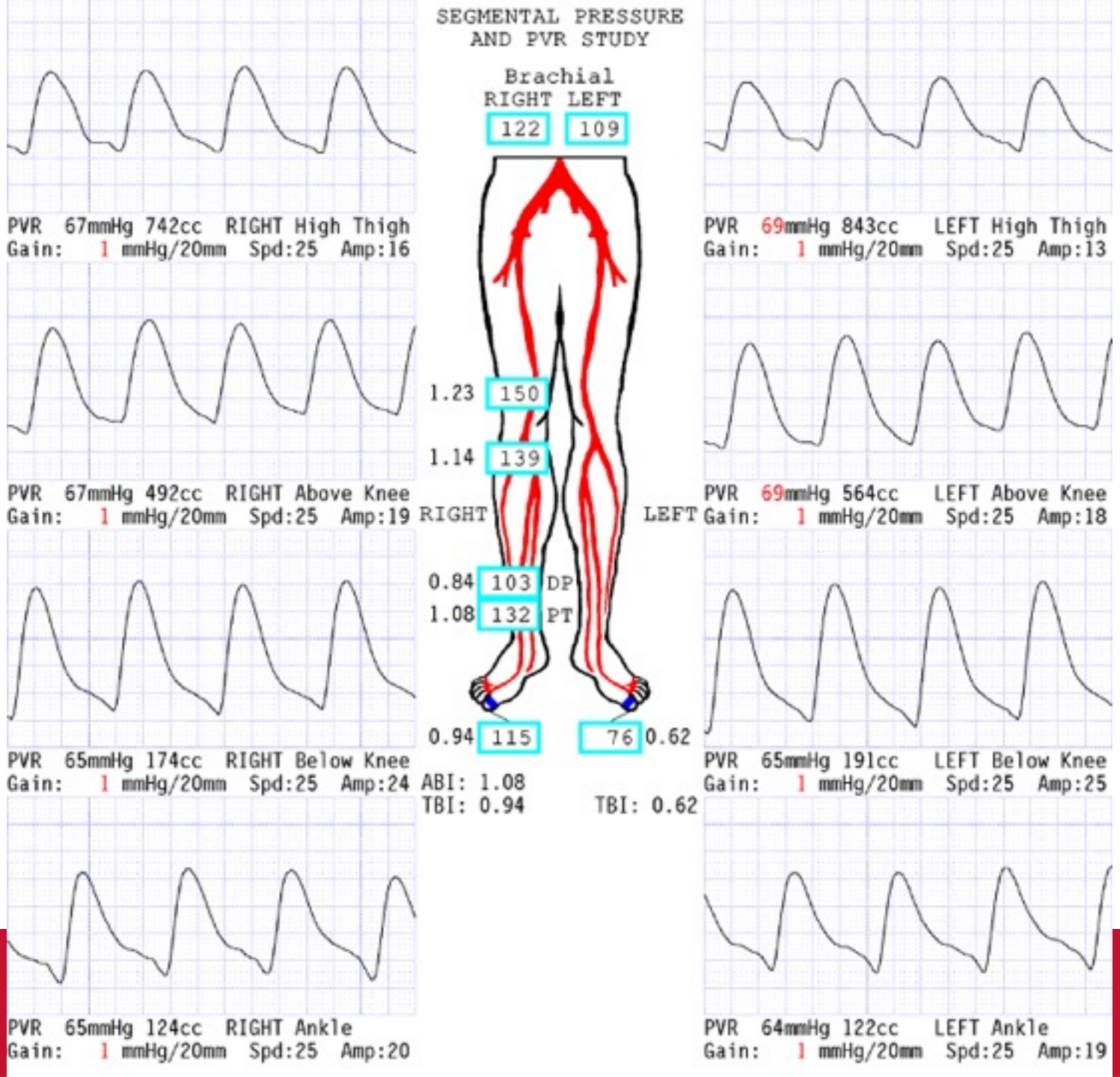
- Ratio of ankle to brachial systolic blood pressure
- Can be limited by medial calcification, significant peripheral edema
- Post-exercise ABI's in patients with suspicion for claudication to confirm diagnosis

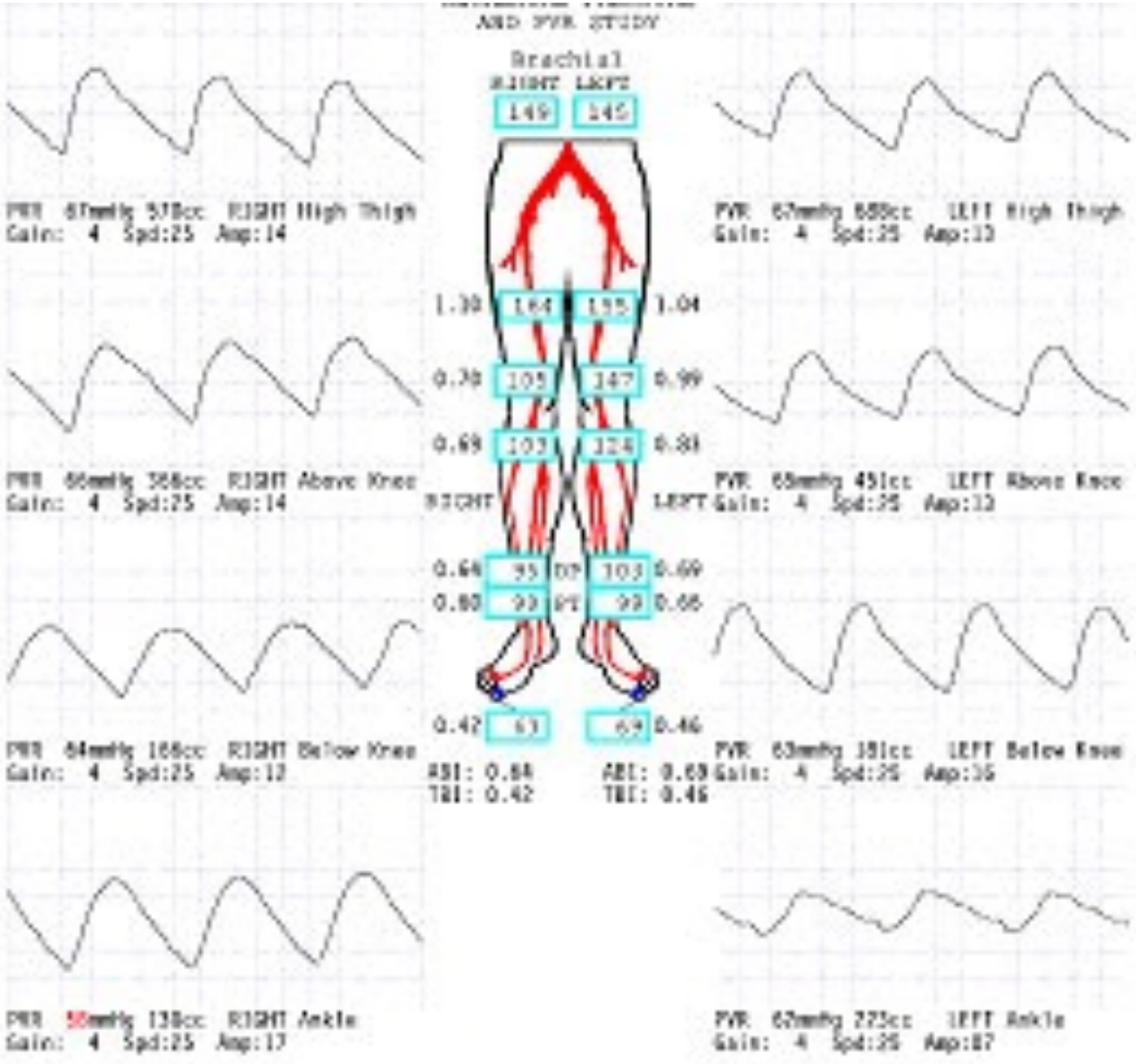
ABI Interpretation

- >1.4: Falsely elevated
- 0.95-1.39: Normal
- 0.75-0.94: Mild arterial insufficiency
- 0.50-0.74: Moderate arterial insufficiency
- <0.50: Severe arterial insufficiency

PVR/Segmental Pressures

- Helps to identify levels of disease
- Compare to proximal segments and contralateral leg
- Technician dependent
- Some limitation with calcified arteries

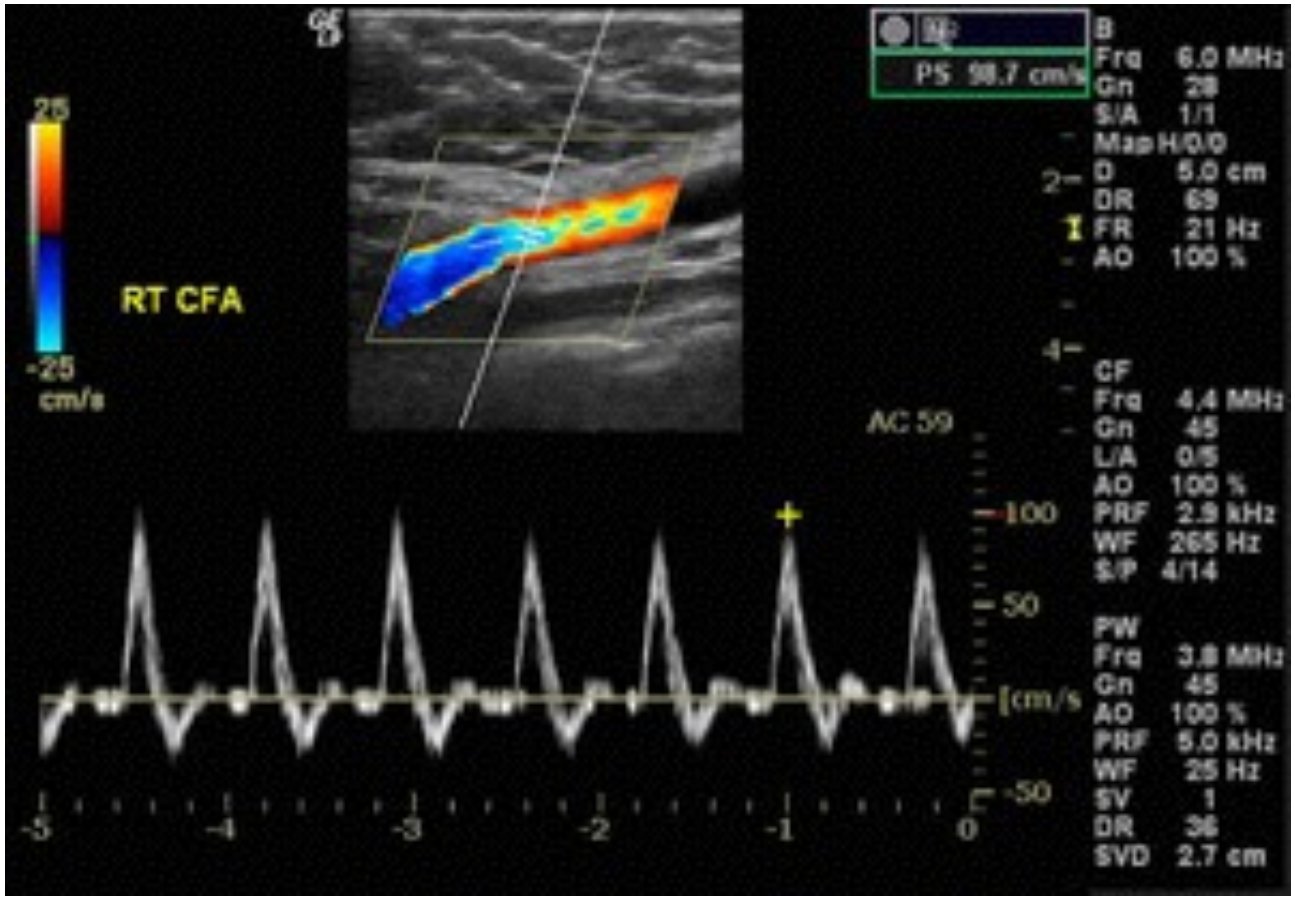

SEGMENTAL PRESSURE
AND PVR STUDY
Brachial
RIGHT LEFT
122 109
PVR 67mmHg 742cc RIGHT High Thigh
Gain: 1 mmHg/20mm Spd:25 Amp:16
PVR 69mmHg 843cc LEFT High Thigh
Gain: 1 mmHg/20mm Spd:25 Amp:13
1.23 150
1.14 139
PVR 67mmHg 492cc RIGHT Above Knee
Gain: 1 mmHg/20mm Spd:25 Amp:19
RIGHT
LEFT
PVR 69mmHg 564cc LEFT Above Knee
Gain: 1 mmHg/20mm Spd:25 Amp:18
0.84 103 DP
1.08 132 PT
PVR 65mmHg 174cc RIGHT Below Knee
Gain: 1 mmHg/20mm Spd:25 Amp:24
PVR 65mmHg 191cc LEFT Below Knee
Gain: 1 mmHg/20mm Spd:25 Amp:25
0.94 115
76 0.62
ABI: 1.08
TBI: 0.94
TBI: 0.62
PVR 65mmHg 124cc RIGHT Ankle
Gain: 1 mmHg/20mm Spd:25 Amp:20
PVR 64mmHg 122cc LEFT Ankle
Gain: 1 mmHg/20mm Spd:25 Amp:19


Brachial
149
145
1.30
164
155
1.04
0.39
105
147
0.99
0.69
103
124
0.81
0.64
95
103
0.69
0.80
99
99
0.66
0.42
63
69
0.46
ABI: 0.84
TBI: 0.42
ABI: 0.68
TBI: 0.46

Arterial Duplex

- Helps to specifically identify location of lesions
- Very technician dependent
- Can be limited by calcification
- Monitor post procedure (surgical or endovascular)

Arterial Duplex



Arterial Duplex

PSV*	Stenosis Severity
Triphasic <100 cm/s	Normal
>30% increase in PSV	20% to 49%
Doubling of PSV(greater than 100% relative to the adjacent proximal segment and reduced systolic velocity distal to the stenosis)	50% to 99%
No Doppler flow in artery	Occluded

MRA

- Tool for patients with renal dysfunction
- Not as limited by heavily calcified lesions
- Time consuming
- Claustrophobia

CTA

- Good evaluation of disease from aorta to popliteal arteries
- Tibial evaluation can be limited especially in calcified tibial
- Less expensive, quicker
- Exposure to contrast and radiation

Contrast Angiography

- Best identifies extent and location of disease
- Can often treat at the same time of the diagnosis
- Invasive
- Iodine based contrast used—can use CO2
- Subjects patient, physician and personnel to radiation

Recommendations: Diagnosis of Peripheral Arterial Disease

		Grade	Level of evidence
2.1.	We recommend using the ABI as the first-line noninvasive test to establish a diagnosis of PAD in individuals with symptoms or signs suggestive of disease. When the ABI is borderline or normal (>0.9) and symptoms of claudication are suggestive, we recommend an exercise ABI.	1	A
2.2.	We suggest against routine screening for lower extremity PAD in the absence of risk factors, history, signs, or symptoms of PAD.	2	C
2.3.	For asymptomatic individuals who are at elevated risk, such as those aged >70, smokers, diabetic patients, those with an abnormal pulse examination, or other established cardiovascular disease, screening for lower extremity PAD is reasonable if used to improve risk stratification, preventive care, and medical management.	2	C
2.4.	In symptomatic patients who are being considered for revascularization, we suggest using physiologic noninvasive studies, such as segmental pressures and pulse volume recordings, to aid in the quantification of arterial insufficiency and help localize the level of obstruction.	2	C
2.5.	In symptomatic patients in whom revascularization treatment is being considered, we recommend anatomic imaging studies, such as arterial duplex ultrasound, CTA, MRA, and contrast arteriography.	1	B

ABI, Ankle-brachial index; *CTA,* computed tomography angiography; *MRA,* magnetic resonance angiography.

Indications for Treatment

- All patients, regardless of symptoms must be medically maximized
- Rutherford 0-3
- Rutherford 4-6

Medical Management of PAD

- Smoking cessation
- Antiplatelets
- Statins
- Diabetes
- Hypertension
- Hyperhomocysteinemia?

Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: Management of asymptomatic disease and claudication

Society for Vascular Surgery Lower Extremity Guidelines Writing Group: Michael S. Conte, MD, (Co-Chair),[a] Frank B. Pomposelli, MD, (Co-Chair),[b] Daniel G. Clair, MD,[c] Patrick J. Geraghty, MD,[d] James F. McKinsey, MD,[e] Joseph L. Mills, MD,[f] Gregory L. Moneta, MD,[g] M. Hassan Murad, MD,[h] Richard J. Powell, MD,[i] Amy B. Reed, MD,[j] Andres Schanzer, MD,[k] and Anton N. Sidawy, MD, MPH,[l] *San Francisco, Calif; Boston and Worcester, Mass; Cleveland, Ohio; St. Louis, Mo; New York, NY; Tucson, Ariz; Portland, Ore; Rochester, Minn; Lebanon, NH; Hershey, Pa; and Washington, D.C.*

Peripheral arterial disease (PAD) continues to grow in global prevalence and consumes an increasing amount of resources in the United States health care system. Overall rates of intervention for PAD have been rising steadily in recent years. Changing demographics, evolution of technologies, and an expanding database of outcomes studies are primary forces influencing clinical decision making in PAD. The management of PAD is multidisciplinary, involving primary care physicians and vascular specialists with varying expertise in diagnostic and treatment modalities. PAD represents a broad spectrum of disease from asymptomatic through severe limb ischemia. The Society for Vascular Surgery Lower Extremity Practice Guidelines committee reviewed the evidence supporting clinical care in the treatment of asymptomatic PAD and intermittent claudication (IC). The committee made specific practice recommendations using the GRADE (Grades of Recommendation Assessment, Development and Evaluation) system. There are limited Level I data available for many of the critical questions in the field, demonstrating the urgent need for comparative effectiveness research in PAD. Emphasis is placed on risk factor modification, medical therapies, and broader use of exercise programs to improve cardiovascular health and functional performance. Screening for PAD appears of unproven benefit at present. Revascularization for IC is an appropriate therapy for selected patients with disabling symptoms, after a careful risk-benefit analysis. Treatment should be individualized based on comorbid conditions, degree of functional impairment, and anatomic factors. Invasive treatments for IC should provide predictable functional improvements with reasonable durability. A minimum threshold of a >50% likelihood of sustained efficacy for at least 2 years is suggested as a benchmark. Anatomic patency (freedom from restenosis) is considered a prerequisite for sustained efficacy of revascularization in IC. Endovascular approaches are favored for most candidates with aortoiliac disease and for selected patients with femoropopliteal disease in whom anatomic durability is expected to meet this minimum threshold. Conversely, caution is warranted in the use of interventions for IC in anatomic settings where durability is limited (extensive calcification, small-caliber arteries, diffuse infrainguinal disease, poor runoff). Surgical bypass may be a preferred strategy in good-risk patients with these disease patterns or in those with prior endovascular failures. Common femoral artery disease should be treated surgically, and saphenous vein is the preferred conduit for infrainguinal bypass grafting. Patients who undergo invasive treatments for IC should be

	Medical treatment for intermittent claudication	Grade	Level of evidence
4.1.	We recommend multidisciplinary comprehensive smoking cessation interventions for patients with IC (repeatedly until tobacco use has stopped).	1	A
4.2.	We recommend statin therapy in patients with symptomatic PAD.	1	A
4.3.	We recommend optimizing diabetes control (hemoglobin A_{1c} goal of <7.0%) in patients with IC if this goal can be achieved without hypoglycemia.	1	B
4.4.	We recommend the use of indicated β-blockers (eg, for hypertension, cardiac indications) in patients with IC. There is no evidence supporting concerns about worsening claudication symptoms.	1	B
4.5.	In patients with IC due to atherosclerosis, we recommend antiplatelet therapy with aspirin (75-325 mg daily).	1	A
4.6.	We recommend clopidogrel in doses of 75 mg daily as an effective alternative to aspirin for antiplatelet therapy in patients with IC.	1	B
4.7.	In patients with IC due to atherosclerosis, we suggest against using warfarin for the sole indication of reducing the risk of adverse cardiovascular events or vascular occlusions.	1	C
4.8.	We suggest against using folic acid and vitamin B_{12} supplements as a treatment of IC.	2	C
4.9.	In patients with IC who do not have congestive heart failure, we suggest a 3-month trial of cilostazol (100 mg twice daily) to improve pain-free walking.	2	A
4.10.	In patients with IC who cannot tolerate or have contraindications for cilostazol, we suggest a trial of pentoxifylline (400 mg thrice daily) to improve pain-free walking.	2	B
4.11.	We suggest the ACEI ramipril (10 mg/d) to improve pain-free and maximal walking times in patients with IC. (ACEIs are contraindicated in individuals with known renal artery stenosis).	2	B

Walking Program

- Walk, walk, walk
- >30 minutes at a time
- >3 times per week
- >6 months in duration
- Supervised vs unsupervised

Surgical Treatment

- Open vs endovascular
- First line therapy for patients with life limiting/disabling claudication
- Failure of medical treatment for claudication
- Treat critical limb ischemia due to risk for limb loss

Principles of Revascularization

- Inflow
  - Optimize hemodynamics to improve patency
- Outflow
  - Number of outflow vessels improve patency
- Conduit
  - Vein
  - Prosthetic

Endovascular Techniques

- Percutaneous Transluminal Angioplasty (PTA)
  - Drug coated balloons
- Stents
  - Drug eluting stents
  - Covered stents/stent grafts
- Atherectomy

Outcomes of Revascularization for AIOD

References (first author)	Modality	FU duration, years	Patency (PAP), %
Yilmaz,[154] Soga,[161] Ichihashi,[160] Indes[139]	PTA + stent	5	63-79
deVries,[157] Rutherford,[146] Reed,[180] Brewster,[182] Chiu[166]	AFB	5	81-93
Cham,[176] Melliere,[177] Van der Vliet,[178] Chiu,[166] Ricco[175]	IFB	5	73-88
Criado,[267] Ricco,[175] Mii[268]	FFB	5	60-83

AFB, Aortofemoral bypass; *FFB,* femorofemoral bypass; *FU,* follow-up; *IFB,* iliofemoral bypass; *PAP,* primary assistant patency; *PTA,* percutaneous transluminal angioplasty.

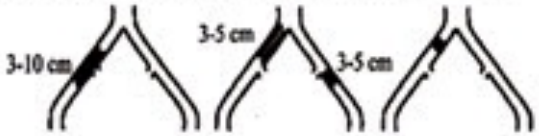
TASC Classification

Type A

Endovascular treatment of choice

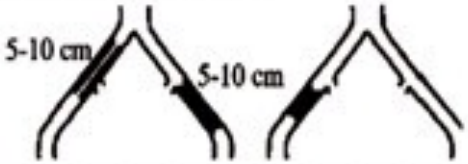
Type B

Currently, endovascular treatment is more often used but insufficient evidence for recommendation



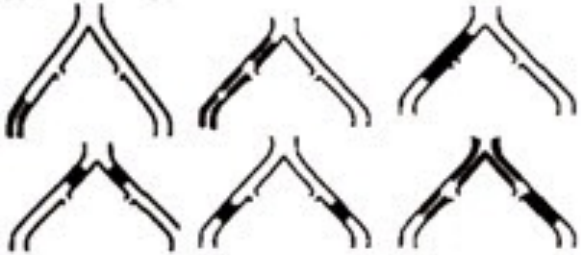
Type C

Currently, surgery treatment is more often used but insufficient evidence for recommendation

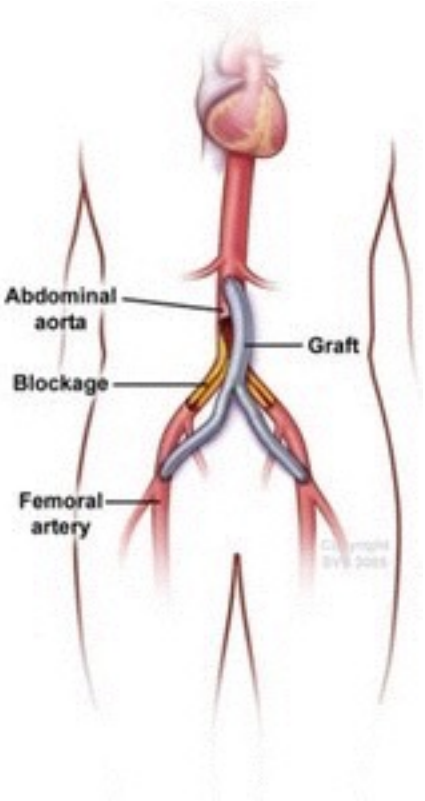


Type D

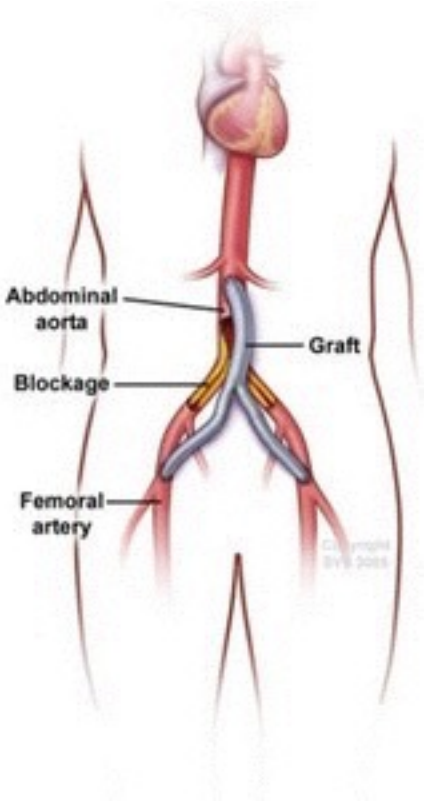
Surgical treatment of choice

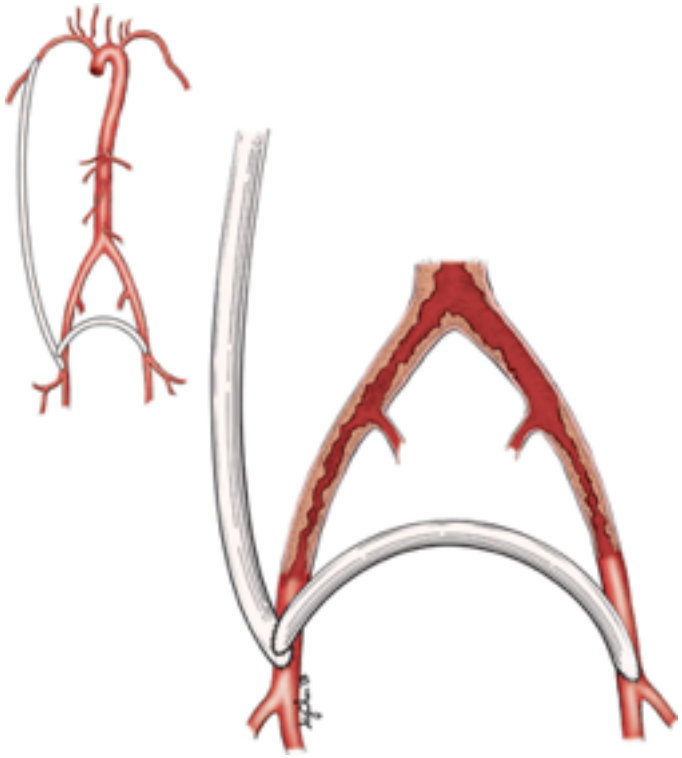


Surgical Revascularization

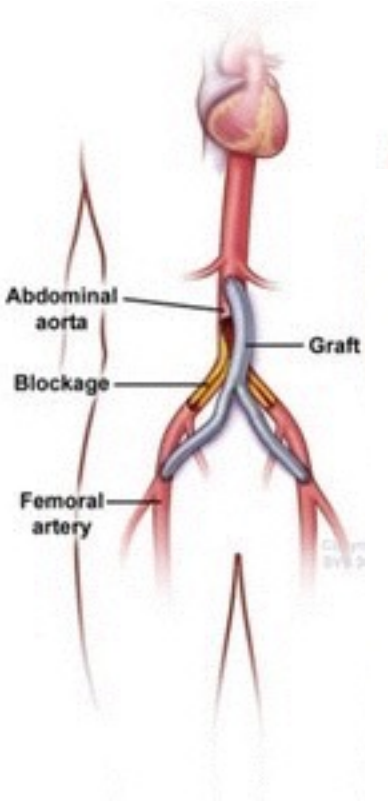


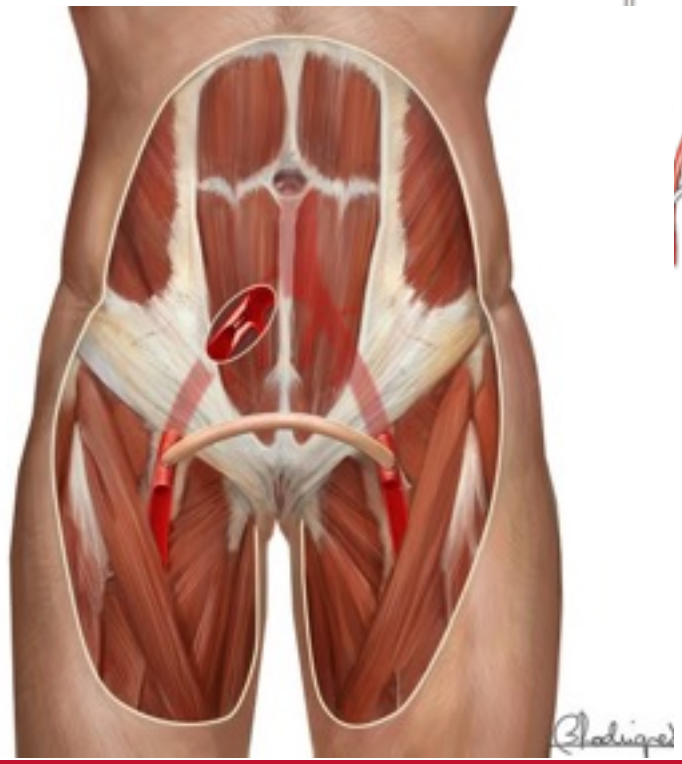
Surgical Revascularization

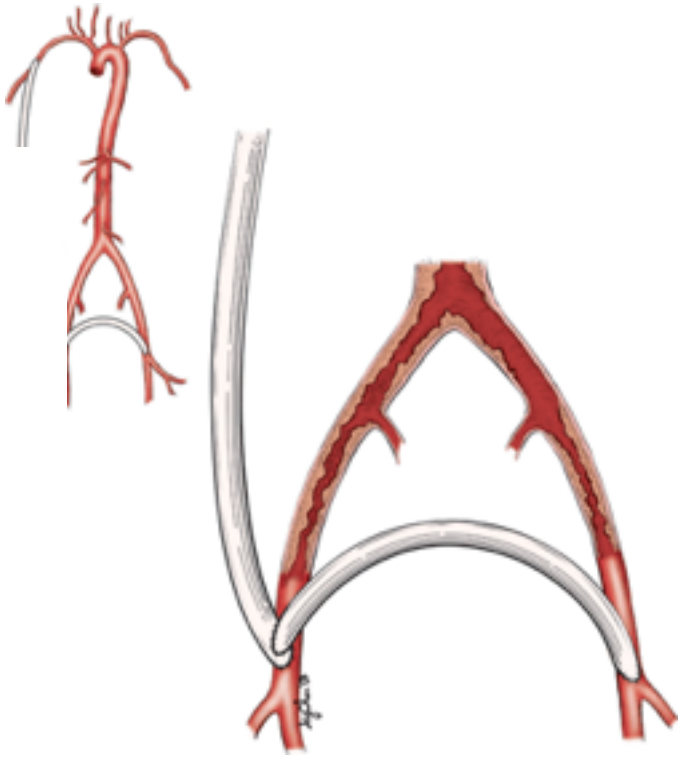




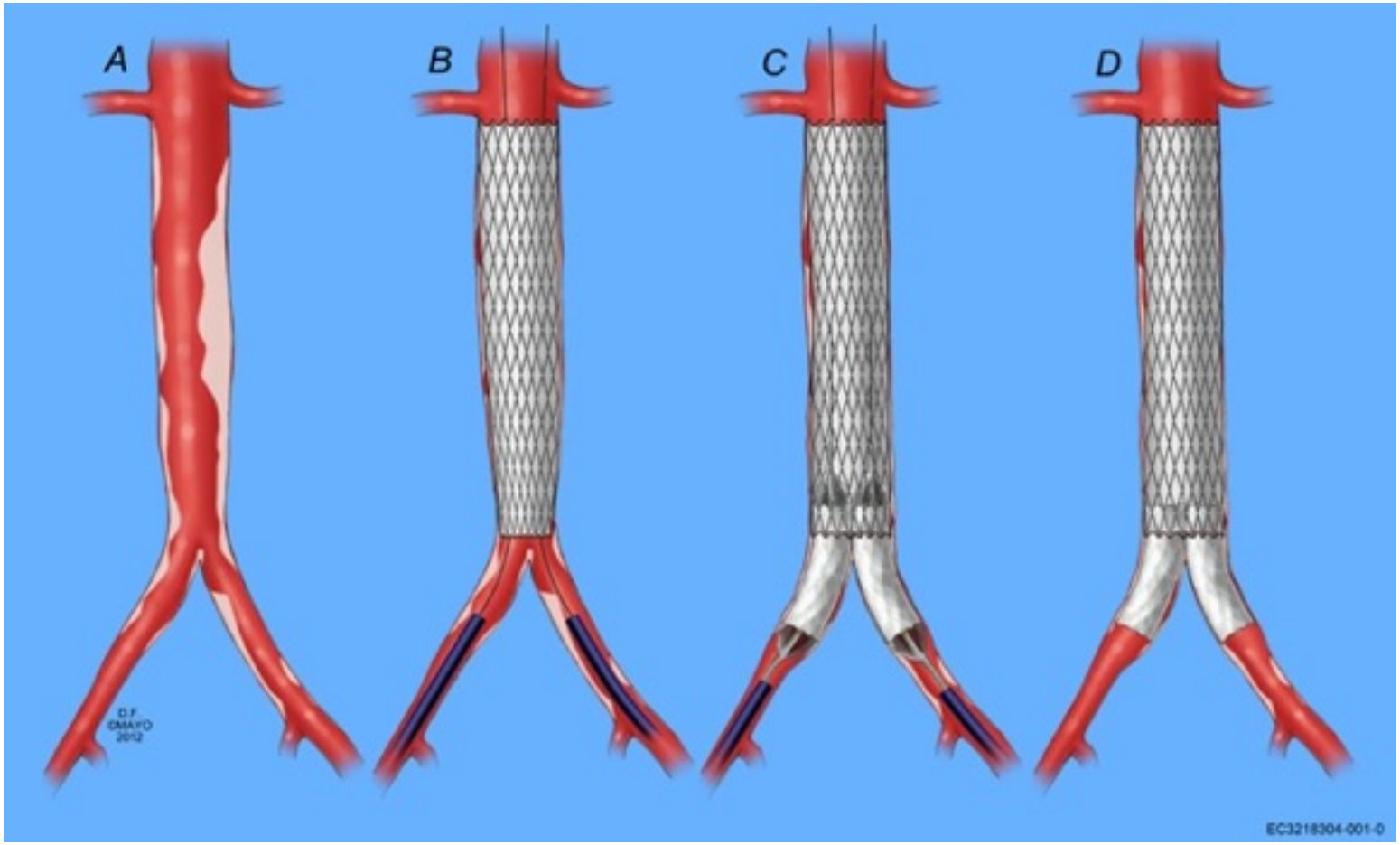
Surgical Revascularization



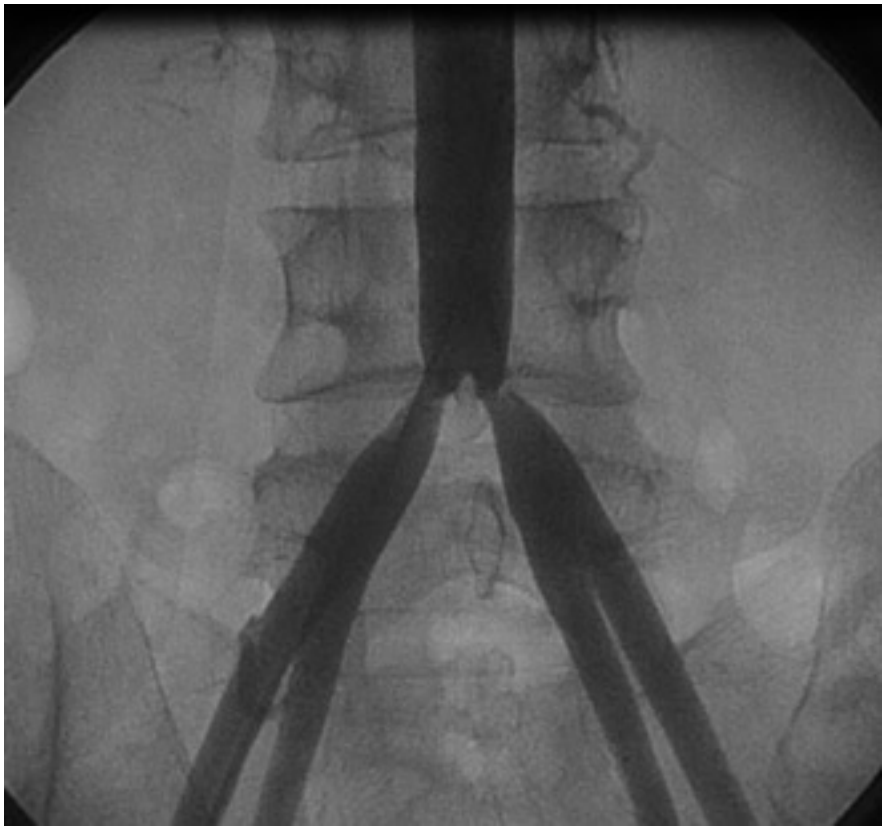




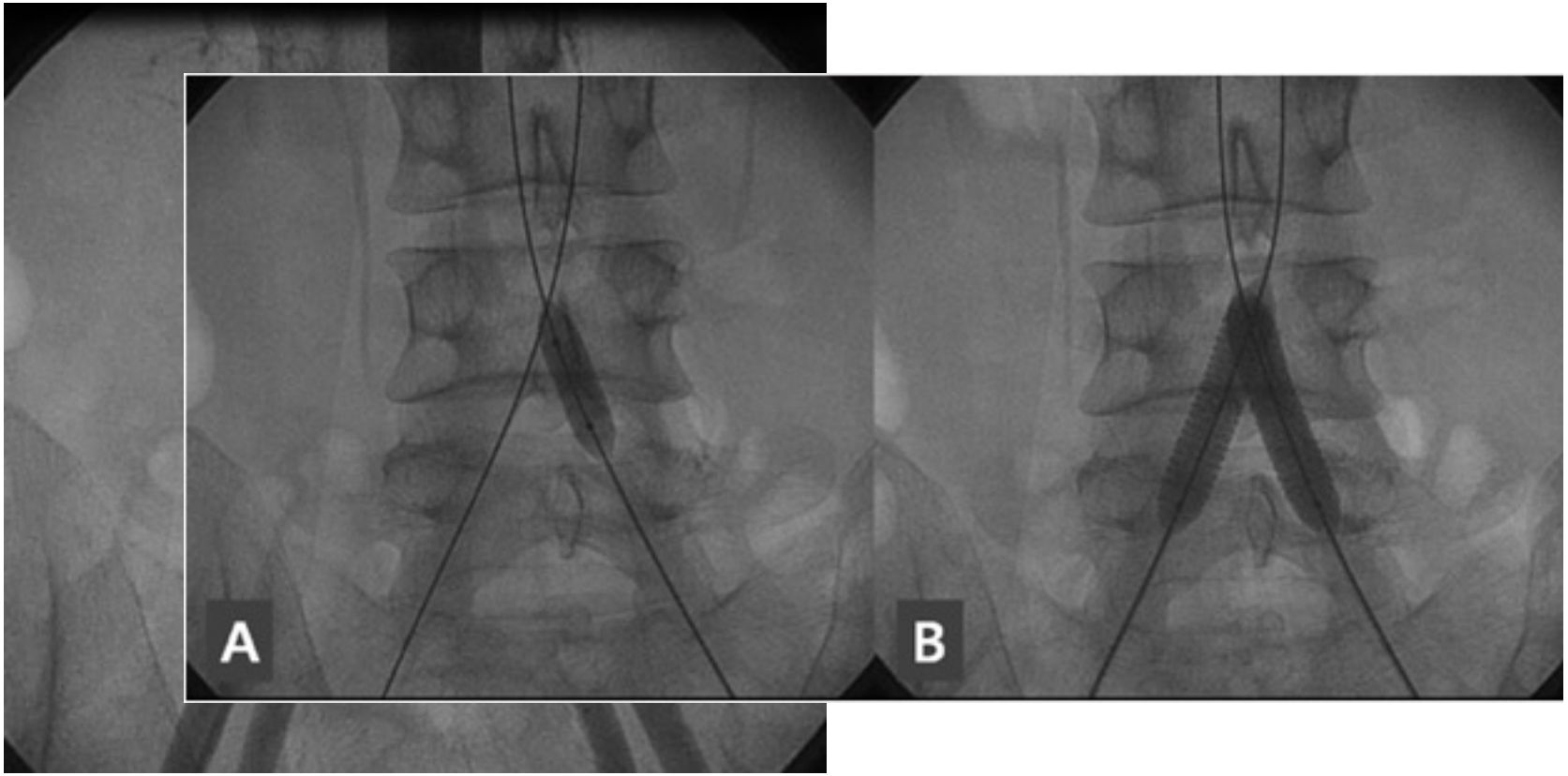
Endovascular Revascularization



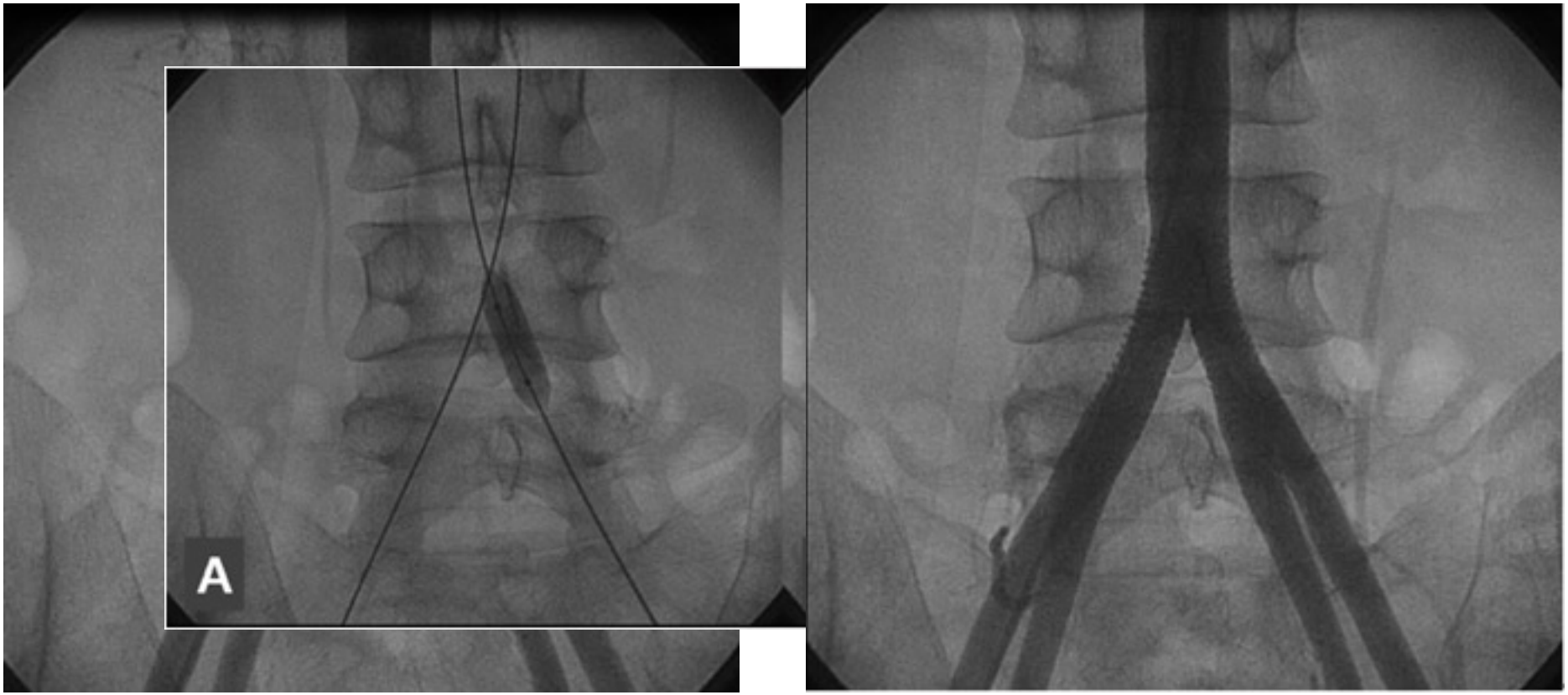
Endovascular Revascularization



Endovascular Revascularization



Endovascular Revascularization



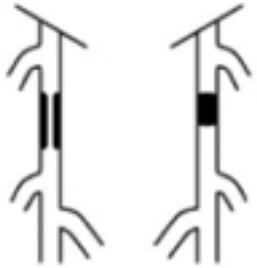
Outcomes of Revascularization for Infrainguinal Disease

References (first author)	Modality	FU duration, years	Patency (PAP), %
Hunink,[193] Muradin,[269] Schillinger[270]	PTA	2	26-68
Schillinger,[270] Laird,[210] Matsumura[211]	PTA + stent	2	51-68
Kedora,[271] Shackles,[272] Geraghty[196]	Covered stent	1	53-77
Pereira,[273] Klinkert[274]	FP vein	5	70-75
Robinson,[275] Klinkert,[274] Pereira[273]	FP prosthetic	5	40-60

FP, Femoropopliteal; *FU,* follow-up; *PAP,* primary patency; *PTA,* percutaneous transluminal angioplasty.

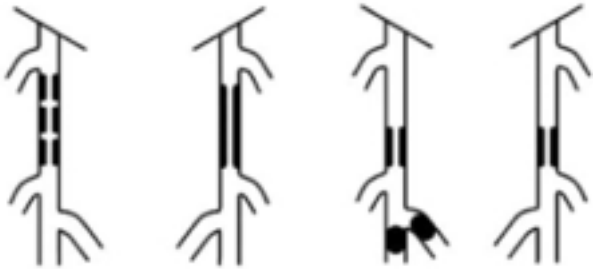
Type A lesions

- Single stenosis ≤10 cm in length
- Single occlusion ≤5 cm in length



Type B lesions:

- Multiple lesions (stenoses or occlusions), each ≤5 cm
- Single stenosis or occlusion ≤15 cm not involving the infrageniculate popliteal artery
- Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass
- Heavily calcified occlusion ≤5 cm in length
- Single popliteal stenosis

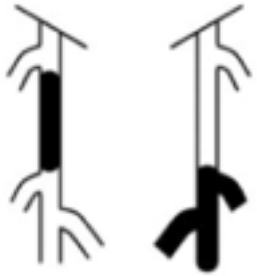


Type C lesions

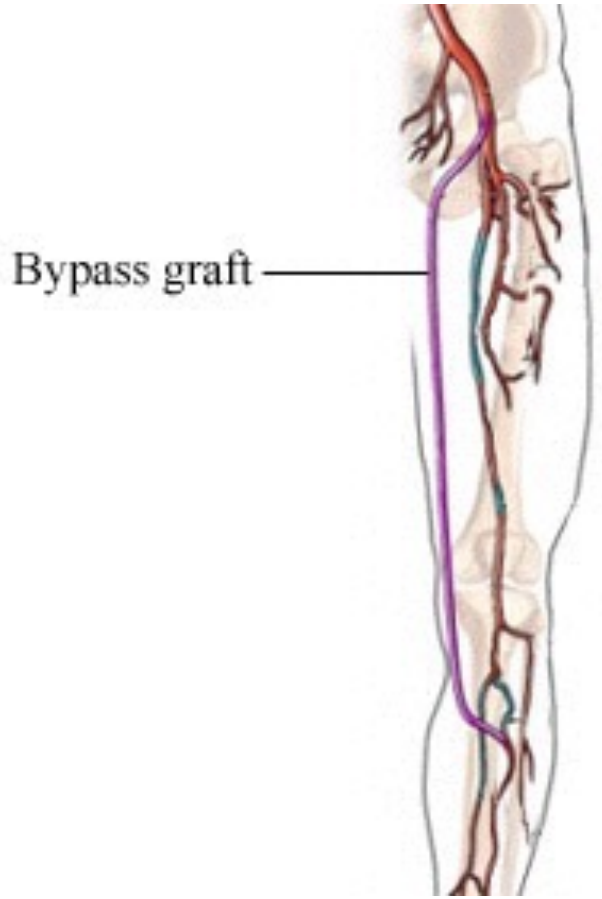
- Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification
- Recurrent stenoses or occlusions that need treatment after two endovascular interventions

Type D lesions

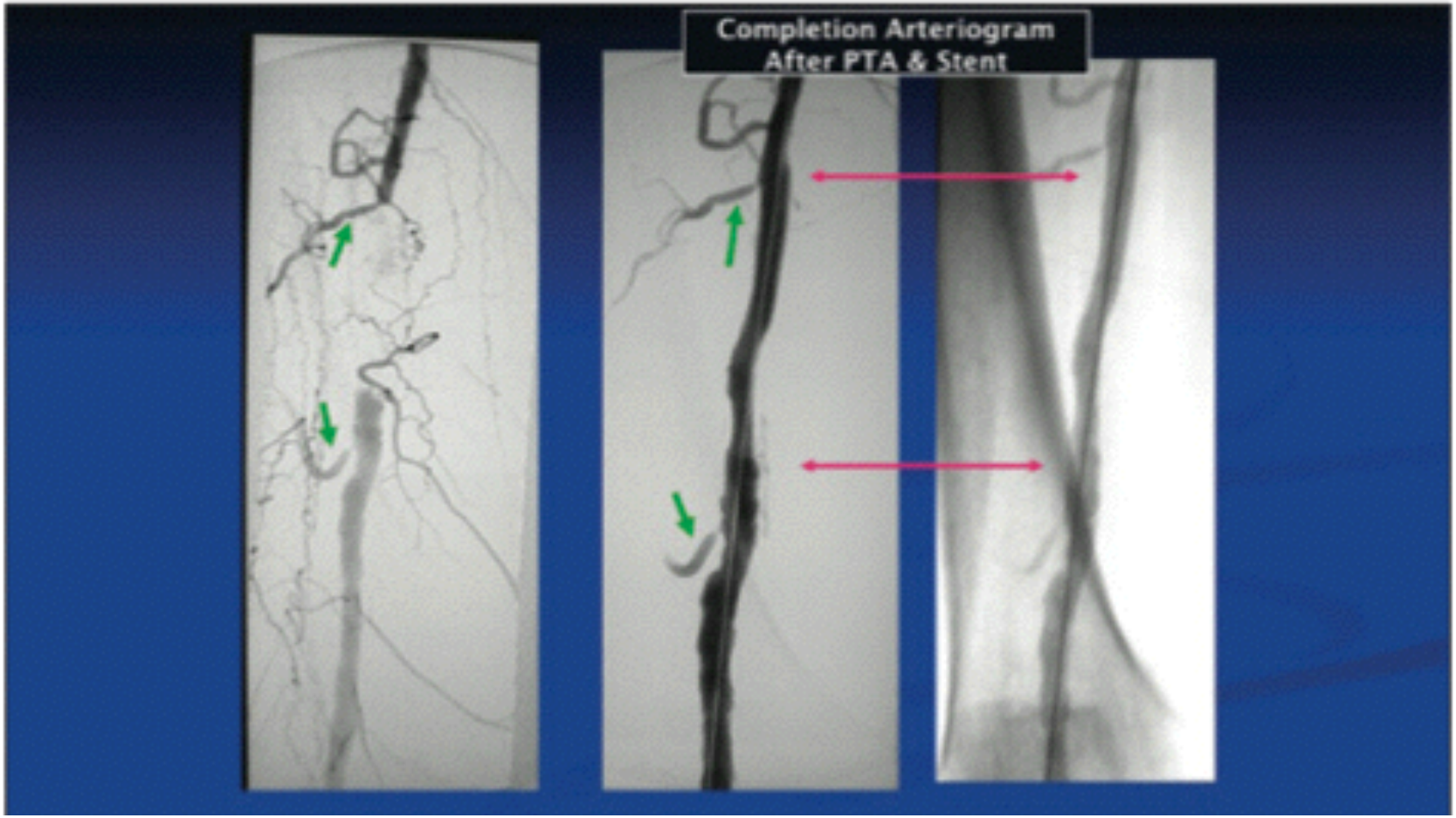
- Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery)
- Chronic total occlusion of popliteal artery and proximal trifurcation vessels



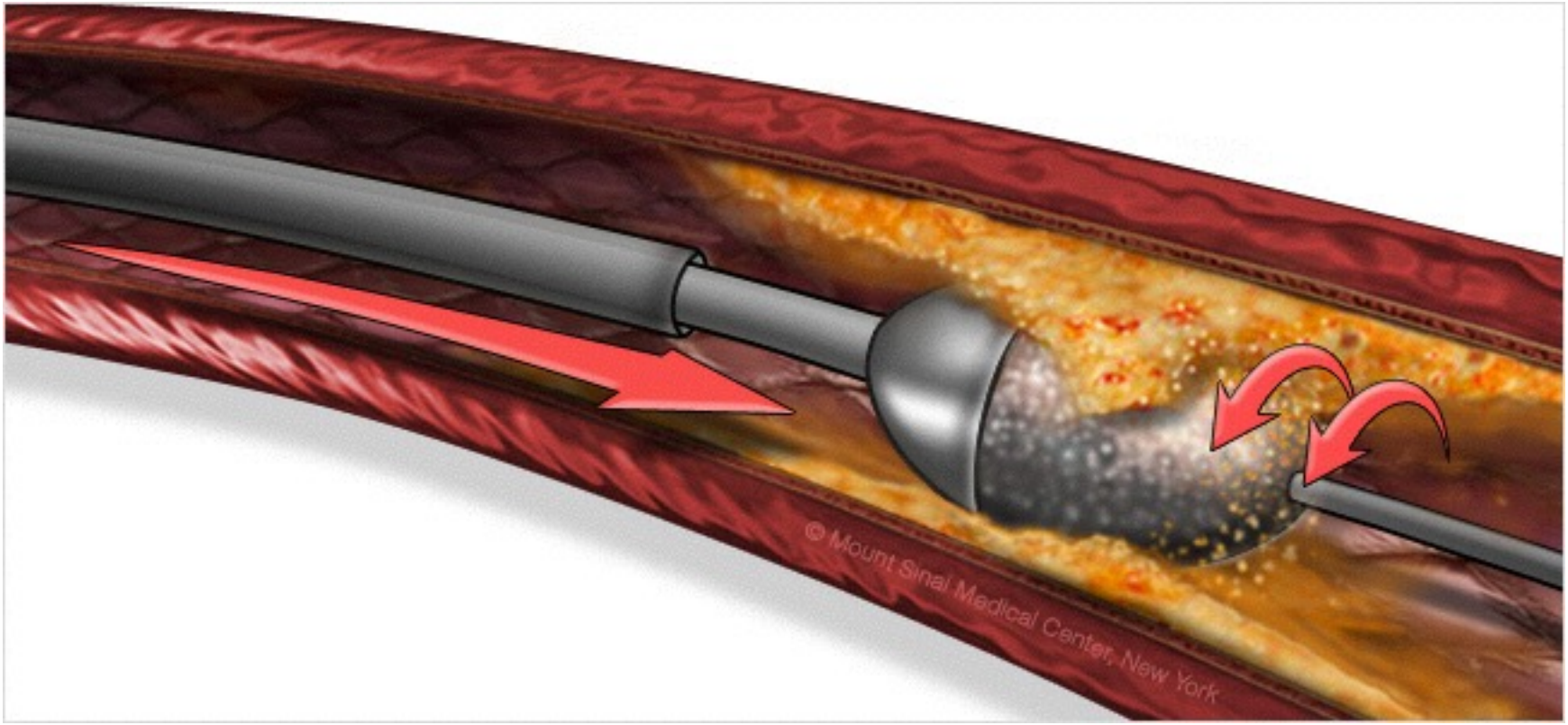
Surgical Revascularization



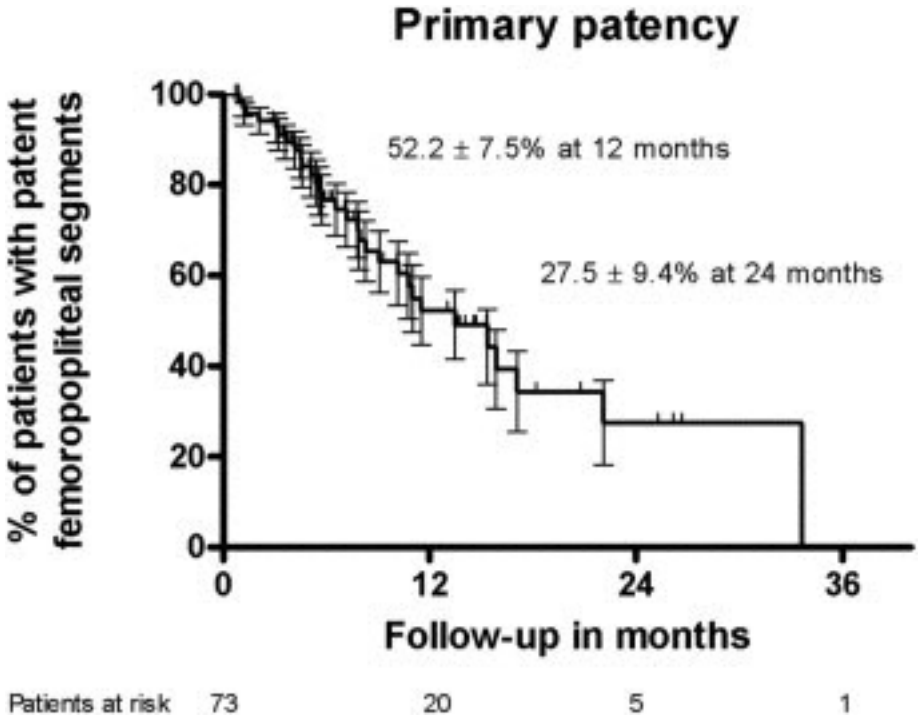
Endovascular Revascularization

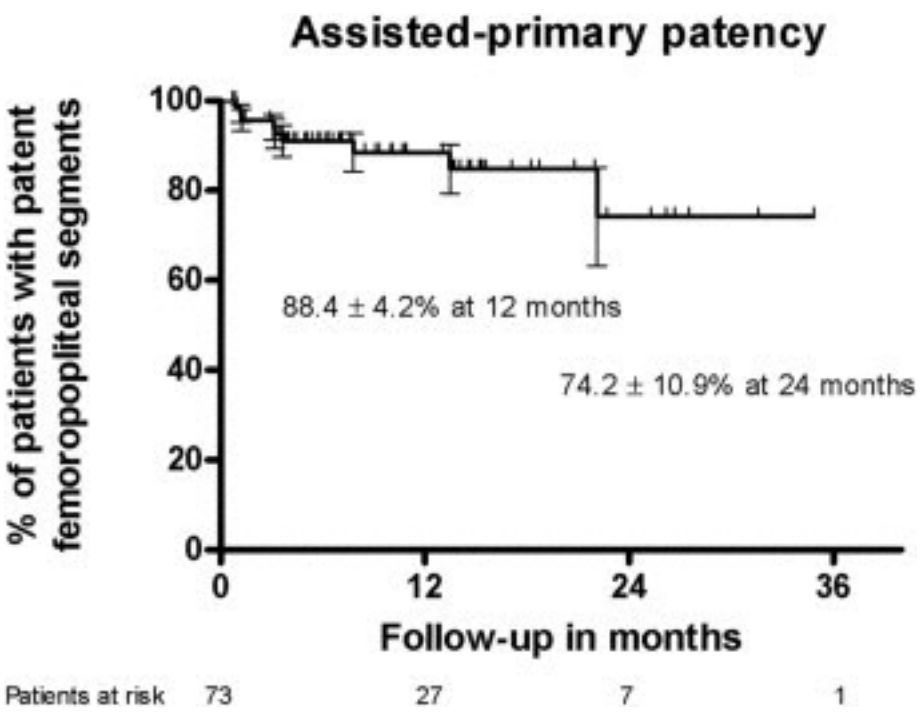


Endovascular Revascularization



Patency of Endovascular Revascularization





Just because we can, should we?

- The Benefit of Revascularization in Nonagenarians with Lower Limb Ischemia is Limited by High Mortality: (Saarinen, E.EJVES.2015;49:420–425.)
- Functional Outcomes After Lower Extremity Revascularization in Nursing Home Residents: (Oresanya L, Zhao S, Gan S, et al. Functional Outcomes After Lower Extremity Revascularization in Nursing Home Residents: A National Cohort Study. *JAMA Intern Med*. Published online April 06, 2015. doi:10.1001/jamainternmed.2015.0486.)
- And of course there is the New York Times Article: "Medicare Payments Surge for Stents to Unblock Blood Vessels in Limbs"

What does the future hold?

- BEST-CLI
- Stem cell therapy

Questions??

Carondelet Heart & Vascular Institute. Be well.