Mount Sinai Health Partners:
Frontline Excellence in Ambulatory Chronic Disease Management

Module 3: COPD and Vascular Disease

Tuesday, September 21, 2021

Course Director
Arshad K. Rahim, MD, MBA, FACP

Provided by
Mount Sinai Health Partners (MSHP) and the
Icahn School of Medicine at Mount Sinai

Icahn School of Medicine at Mount Sinai

Health Partners

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Please find below the compiled information we have received on disclosure of relevant financial relationships from activity faculty and planners. The following faculty/planners have reported that they have no relevant financial relationships to disclose:

David Steiger, MD
Soma Brahmanandam, MD
Arshad K. Rahim, MD, MBA, FACP
Lisa Bloch, MS

Faculty Disclosures

The following faculty/planners have reported that they have relevant financial relationships to disclose:

Peter Faries, MD
Professor of Surgery, Diagnostic, Molecular and Interventional Radiology
Icahn School of Medicine at Mount Sinai

Dr. Faries is a consultant/advisor for Abbott.

Jeffrey Olin, DO
Professor of Medicine, Cardiology, Nephrology
Icahn School of Medicine at Mount Sinai

Dr. Olin is a consultant/advisor for Janssen Pharmaceuticals.

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Complete the course evaluation and download your certificate (or verification of attendance for non-physicians) after September 28, 2021

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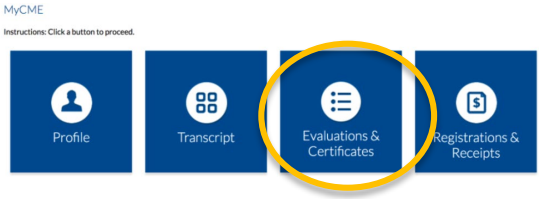
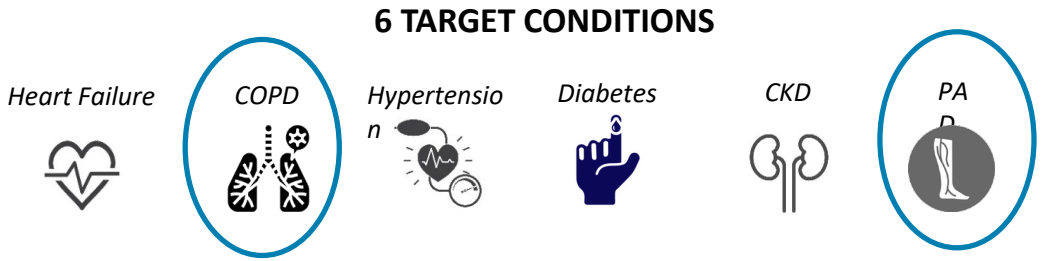
Go to "***My CME***" button on the top right

Click "***Evaluations and Certificates***" – online evaluation will be open at the end of the course. There will be one tab for each day.



Mount Sinai Approach to Condition Management for VBC Success



Deliver highest quality and value of ambulatory care for 6 target conditions that impact the communities we help care for and drive performance in VBC contracts

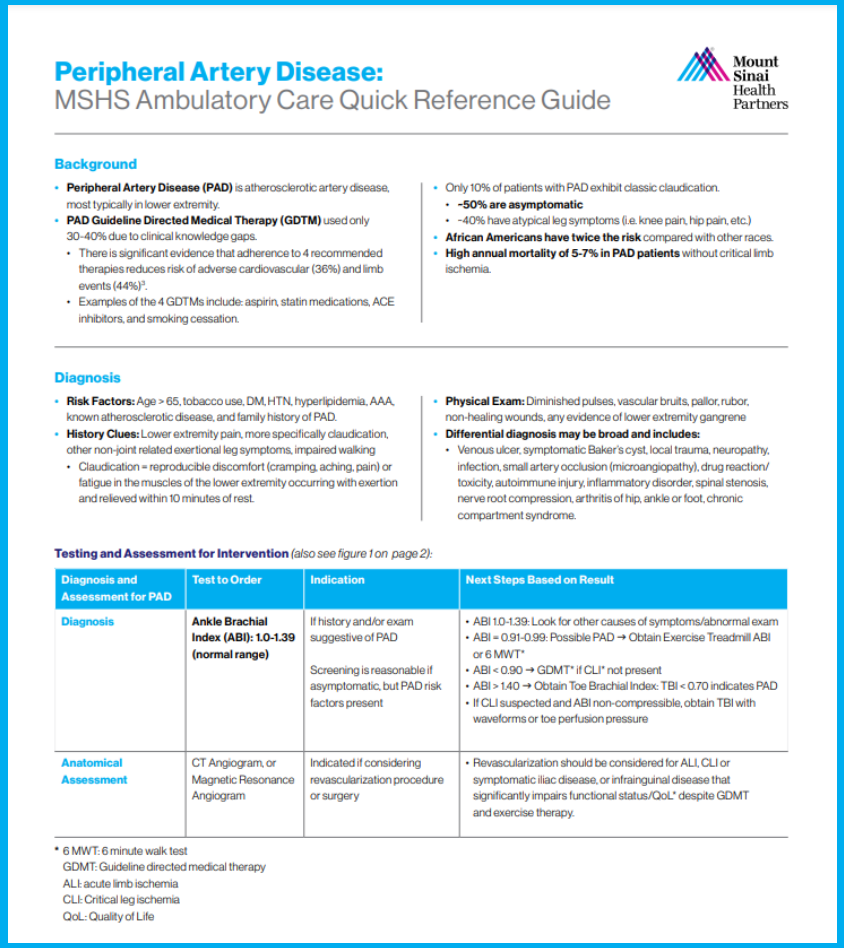
How?

1. **Establish care standards to deliver consistent and coordinated care, throughout the MSHS and the CIN, across all dispersed sites of care, preventing need for excessive ER and IP usage**

2. **Data-supported targeting to identify populations and those most impactable**

Refer to the following resources:

https://mshp.mountsinai.org/web/mshp/quick-guides



Peripheral Artery Disease:
MSHS Ambulatory Care Quick Reference Guide

Mount Sinai Health Partners

Background

- **Peripheral Artery Disease (PAD)** is atherosclerotic artery disease, most typically in lower extremity.
- **PAD Guideline Directed Medical Therapy (GDTM)** used only 30-40% due to clinical knowledge gaps.
  - There is significant evidence that adherence to 4 recommended therapies reduces risk of adverse cardiovascular (36%) and limb events (44%)[3].
  - Examples of the 4 GDTMs include: aspirin, statin medications, ACE inhibitors, and smoking cessation.
- Only 10% of patients with PAD exhibit classic claudication.
  - **~50% are asymptomatic**
  - ~40% have atypical leg symptoms (i.e. knee pain, hip pain, etc.)
- **African Americans have twice the risk** compared with other races.
- **High annual mortality of 5-7% in PAD patients** without critical limb ischemia.

Diagnosis

- **Risk Factors:** Age > 65, tobacco use, DM, HTN, hyperlipidemia, AAA, known atherosclerotic disease, and family history of PAD.
- **History Clues:** Lower extremity pain, more specifically claudication, other non-joint related exertional leg symptoms, impaired walking
  - Claudication = reproducible discomfort (cramping, aching, pain) or fatigue in the muscles of the lower extremity occurring with exertion and relieved within 10 minutes of rest.
- **Physical Exam:** Diminished pulses, vascular bruits, pallor, rubor, non-healing wounds, any evidence of lower extremity gangrene
- **Differential diagnosis may be broad and includes:**
  - Venous ulcer, symptomatic Baker's cyst, local trauma, neuropathy, infection, small artery occlusion (microangiopathy), drug reaction/ toxicity, autoimmune injury, inflammatory disorder, spinal stenosis, nerve root compression, arthritis of hip, ankle or foot, chronic compartment syndrome.

Testing and Assessment for Intervention *(also see figure 1 on page 2)*:

Diagnosis and Assessment for PAD	Test to Order	Indication	Next Steps Based on Result
Diagnosis	**Ankle Brachial Index (ABI): 1.0-1.39 (normal range)**	If history and/or exam suggestive of PAD Screening is reasonable if asymptomatic, but PAD risk factors present	• ABI 1.0-1.39: Look for other causes of symptoms/abnormal exam • ABI = 0.91-0.99: Possible PAD → Obtain Exercise Treadmill ABI or 6 MWT* • ABI < 0.90 → GDMT* if CLI* not present • ABI > 1.40 → Obtain Toe Brachial Index: TBI < 0.70 indicates PAD • If CLI suspected and ABI non-compressible, obtain TBI with waveforms or toe perfusion pressure
Anatomical Assessment	CT Angiogram, or Magnetic Resonance Angiogram	Indicated if considering revascularization procedure or surgery	• Revascularization should be considered for ALI, CLI or symptomatic iliac disease, or infrainguinal disease that significantly impairs functional status/QoL* despite GDMT and exercise therapy.

* 6 MWT: 6 minute walk test
GDMT: Guideline directed medical therapy
ALI: acute limb ischemia
CLI: Critical leg ischemia
QoL: Quality of Life

Frontline Excellence in Ambulatory Chronic Disease Management

Module 3: COPD and Vascular Disease
September 21, 2021

6:00 - 6:05 pm **Welcome and Opening**
Arshad K. Rahim, MD, MBA, FACP

6:05 - 6:40 pm **Peripheral Artery Disease: Ambulatory Excellence**
Peter Faries, MD
Jeffrey Olin, DO
Soma Brahmanandam, MD

6:40 - 6:50 pm **Audience Q&A**

6:50 - 7:20 pm **COPD: Ambulatory Excellence**
David Steiger, MD

7:20 – 7:30 pm **Audience Q&A and Closing Remarks**

Frontline Provider Excellence in Ambulatory Chronic Disease Management: Peripheral Artery Disease (PAD)

Jeffrey W. Olin, D.O., F.A.C.C., F.A.H.A., M.S.V.M.
Professor of Medicine (Cardiology)
Director of Vascular Medicine &
the Vascular Diagnostic Laboratory
Icahn School of Medicine at Mount Sinai

Soma Brahmanandam, MD
Medical Director, Quality and Patient Safety
Mount Sinai Queens
Assistant Professor, Surgery, Vascular Surgery
Icahn School of Medicine at Mount Sinai

Mount Sinai Health Partners

September 21, 2021

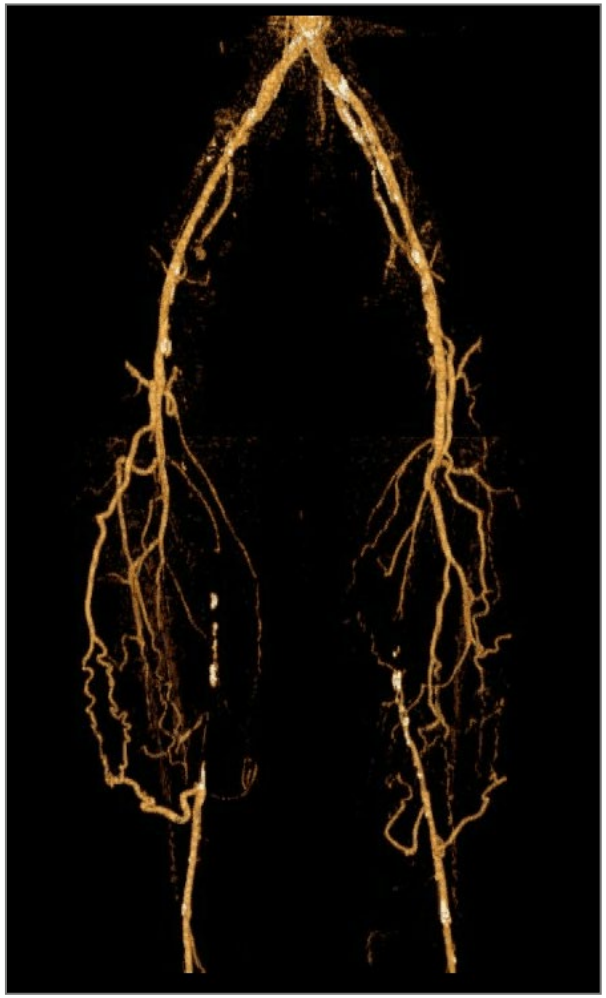
Agenda

1. Introduction to PAD and Diagnosis
2. Medical Management
3. Surgical Interventions for PAD
4. Case Study

Introduction to PAD

Peripheral Artery Disease (PAD)

- The presence of a stenosis or occlusion in the aorta or arteries of the lower limbs
- Usually caused by atherosclerosis
- May impair walking or cause critical limb threatening ischemia
- Associated with an increased risk of myocardial infarction, stroke and death

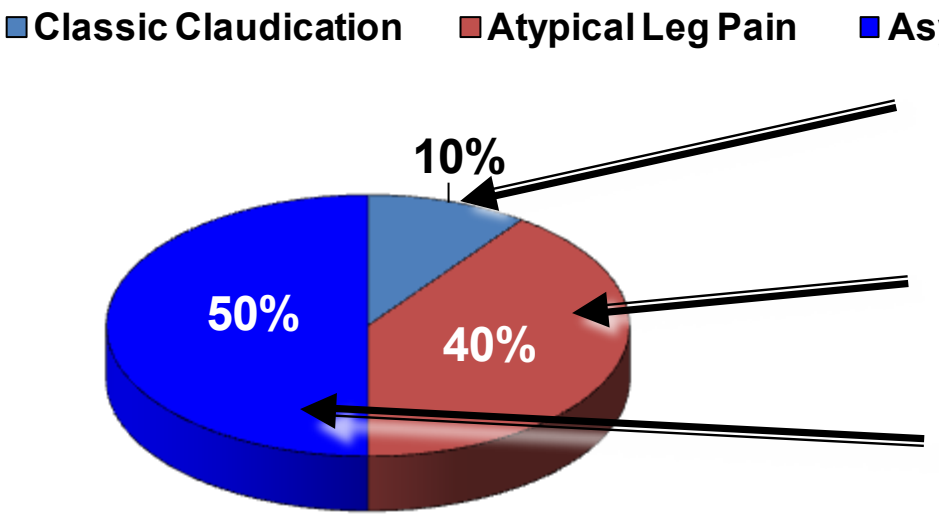


Intermittent Claudication

Aching, pain, tiredness, tightness, cramping in the buttocks, thigh, calf or foot brought on by exercise and relieved by rest

- Reproducible with a consistent level of exercise from day to day
- Completely resolves within 2–5 minutes after the exercise has stopped
- Occurs again at the same distance once walking has resumed

Some Not So Well Known Facts



- Only 8%–10% of patients with peripheral arterial disease (PAD) have “classic” claudication
- ~40% of patients with PAD have “atypical” leg symptoms
- ~50% of patients with PAD are asymptomatic with regard to the leg

PAD Evaluation

PHYSIOLOGIC TESTING Functional assessment – ***is there an arterial flow problem?***	• Ankle-Brachial Index (Toe-Brachial Index) • Pulse Volume Recordings • Segmental Limb Pressures • Continuous Wave Doppler ***Can be performed at rest and with exercise***
IMAGING Imaging assessment of the arterial circulation – ***allows identification of the lesion anatomically***	• Duplex Ultrasonography • CT or MR angiography • Catheter-based angiography

Spectrum of PAD

What are the symptoms of peripheral artery disease and terms used to describe the severity of disease?

Claudication

- Reproducible pain in a muscle bed with exertion, that is relieved with rest.
- *Location of pain identifies area of stenosis*
  - *Aorto-iliac, buttock pain, SFA-popliteal, calf pain*

Rest Pain

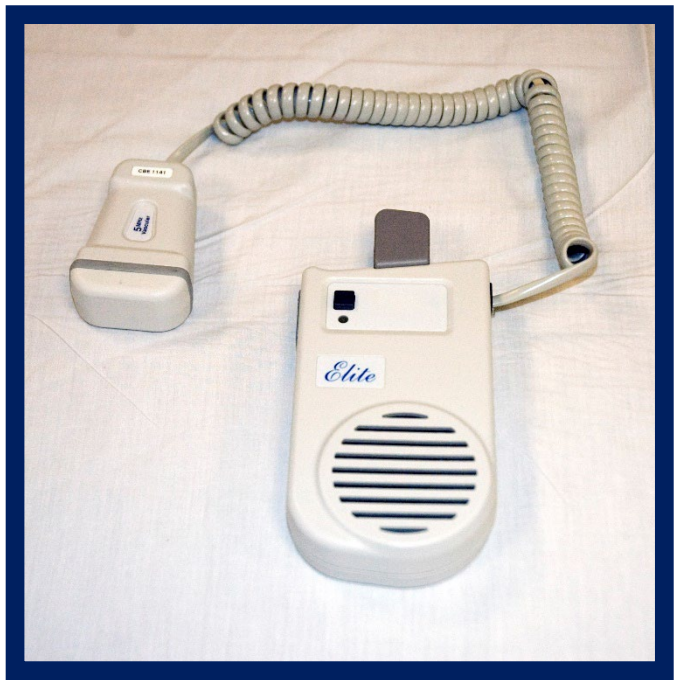
- Foot pain worsens with elevation and dependency relieves discomfort

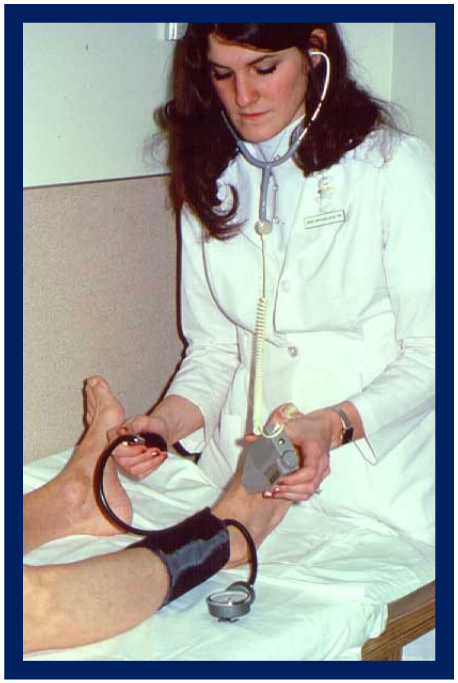
Tissue Loss

- Inability to heal ulcers, blisters and progression to gangrene

Testing for PAD: Ankle – Brachial Index

$$ABI = \frac{\text{Pressure measured Dorsalis Pedis or Posterior Tibial Artery}}{\text{“Normal” Brachial Pressure}}$$

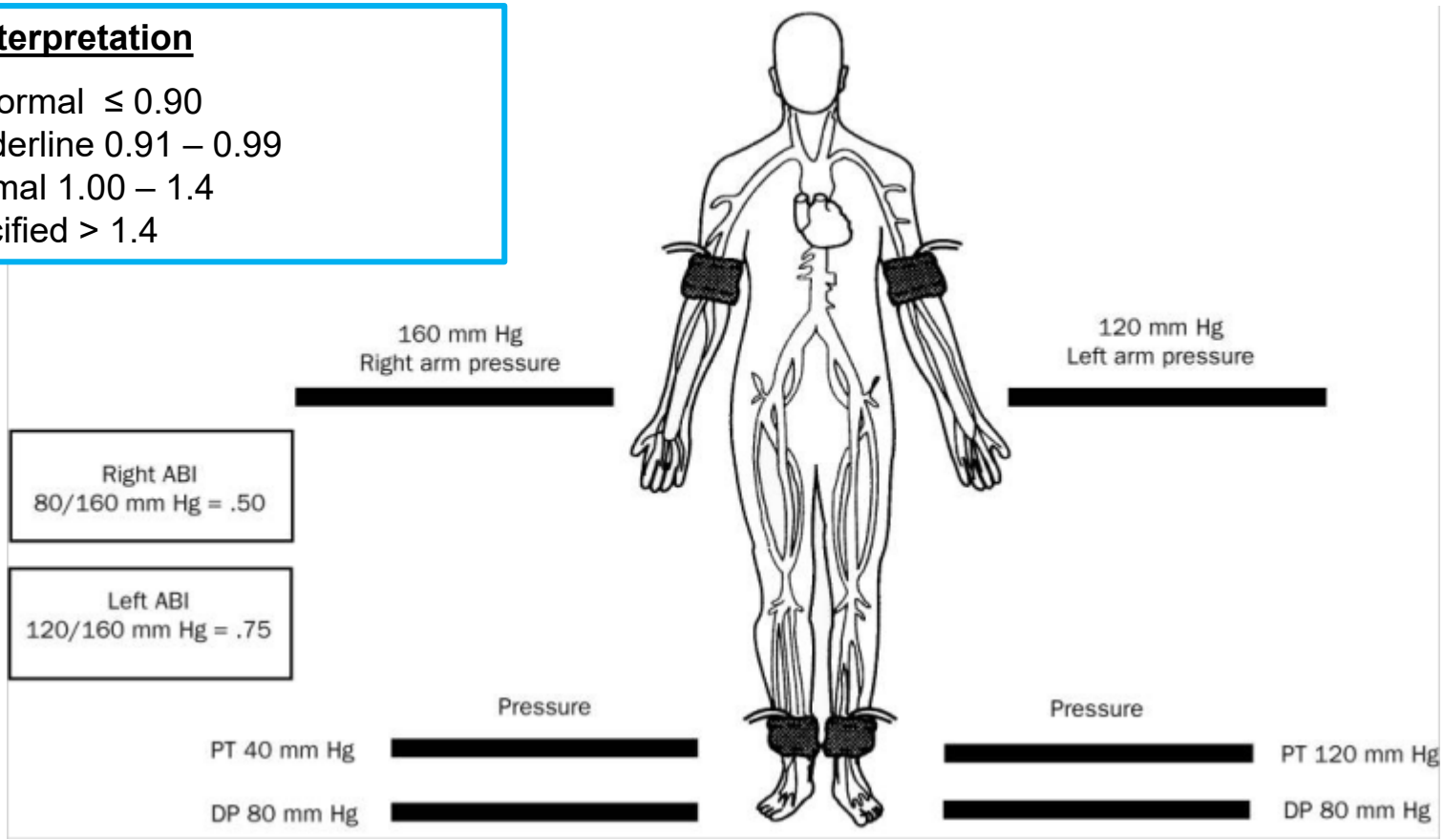




Ankle-Brachial Index

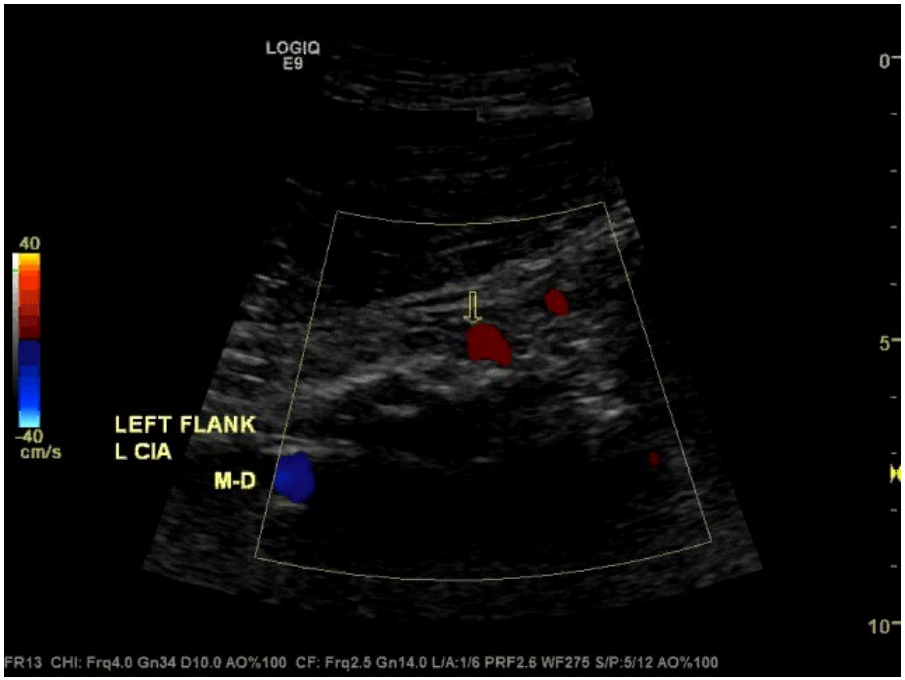
ABI Interpretation

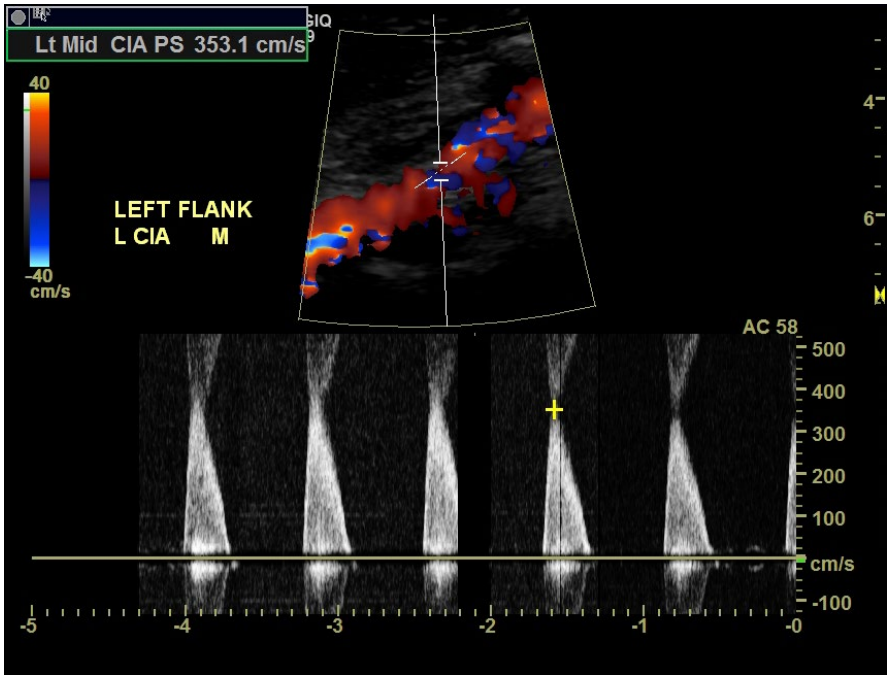
Abnormal ≤ 0.90
Borderline 0.91 – 0.99
Normal 1.00 – 1.4
Calcified > 1.4



$$\text{ABI} = \frac{\text{Highest Ankle (PT/DP) Systolic Blood Pressure of Each Leg}}{\text{Highest Brachial Systolic Blood Pressure (Right or Left)}}$$

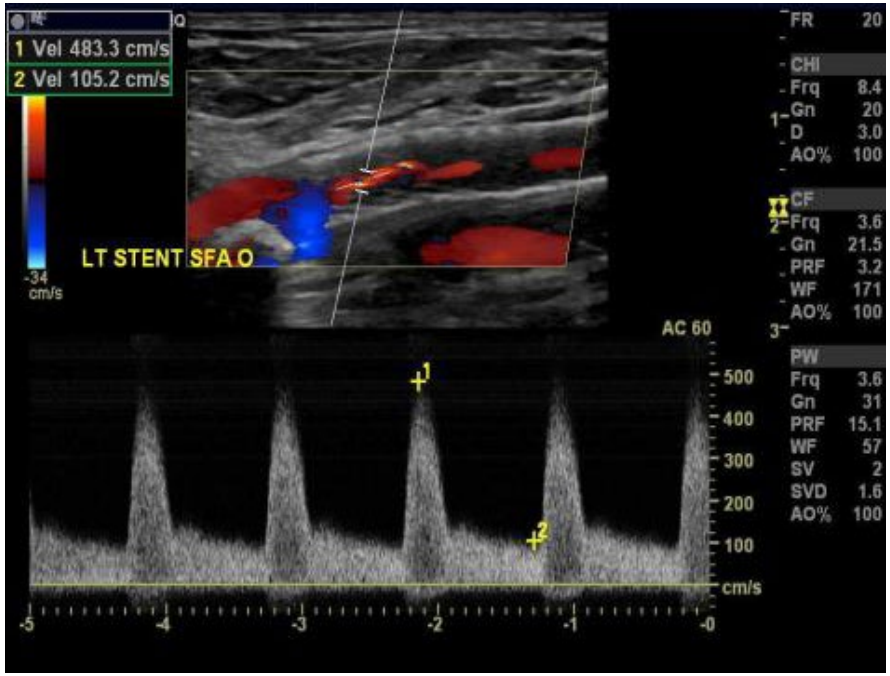
Bilateral Common Iliac Artery Stenosis





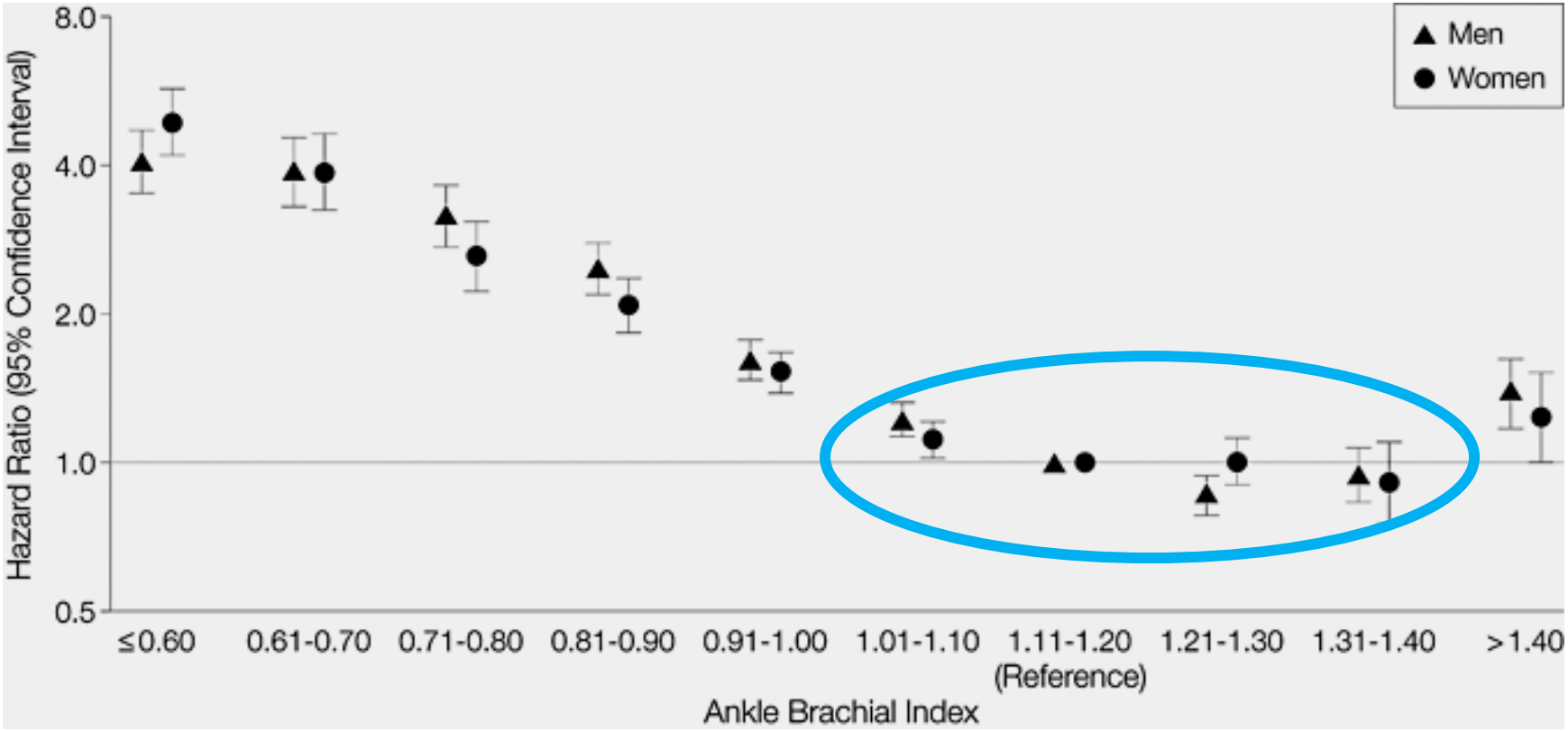
Post-Revascularization Follow-up

- Baseline ABI with exercise and arterial duplex exam
- 3 months, 6 months and Q6 months thereafter up to 2 years, then annual surveillance



ABI and Mortality

Association of ABI with all-cause mortality in a meta-analysis of 16 cohort studies including 48,294 subjects and 480,325 person-years of follow-up.

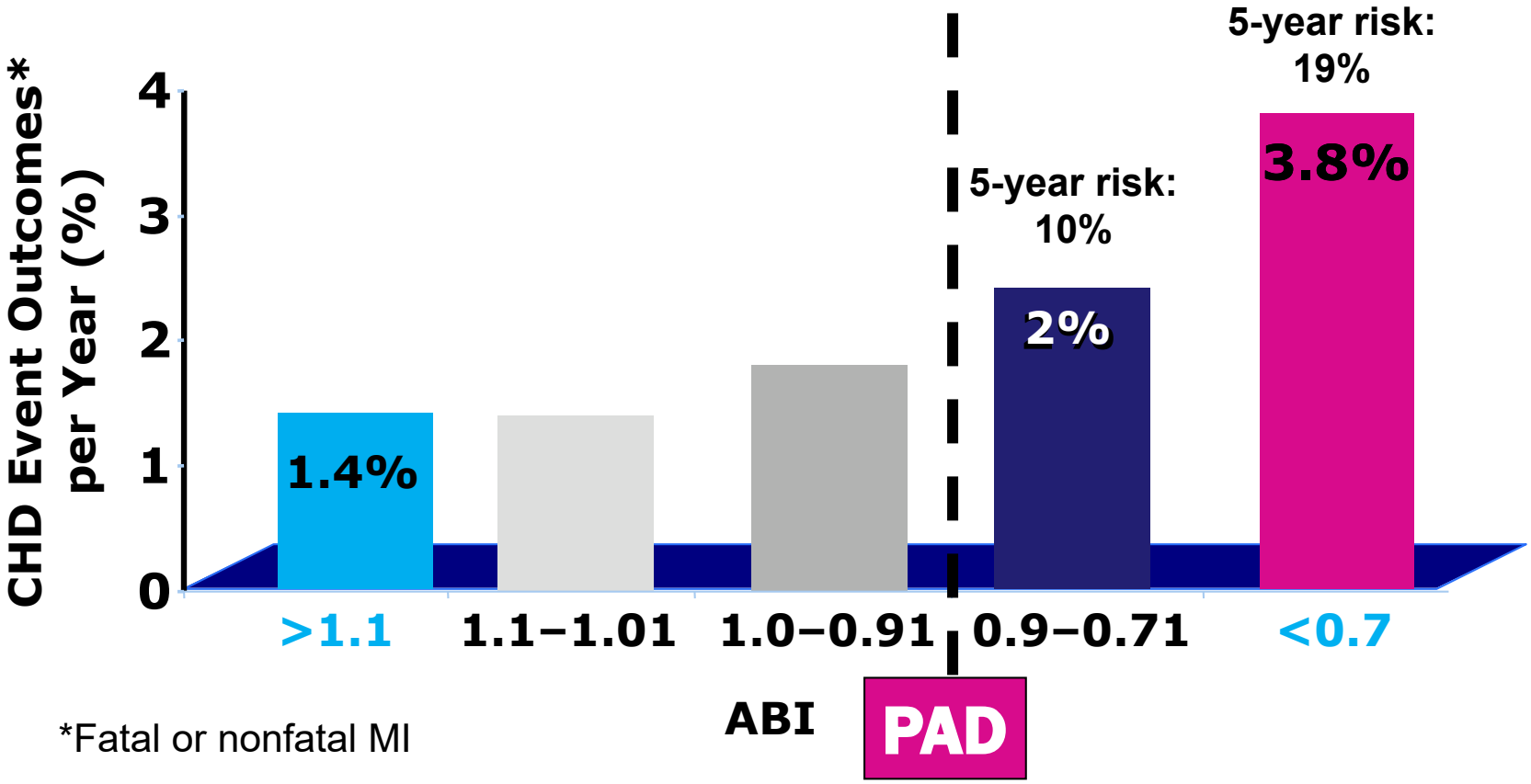


Ankle Brachial Index Collaboration. JAMA 2008.

Cardiovascular Risk Increases With Decreases in ABI

Framingham "High Risk" = 20% at 10 years

Every patient with PAD is at "very high risk"

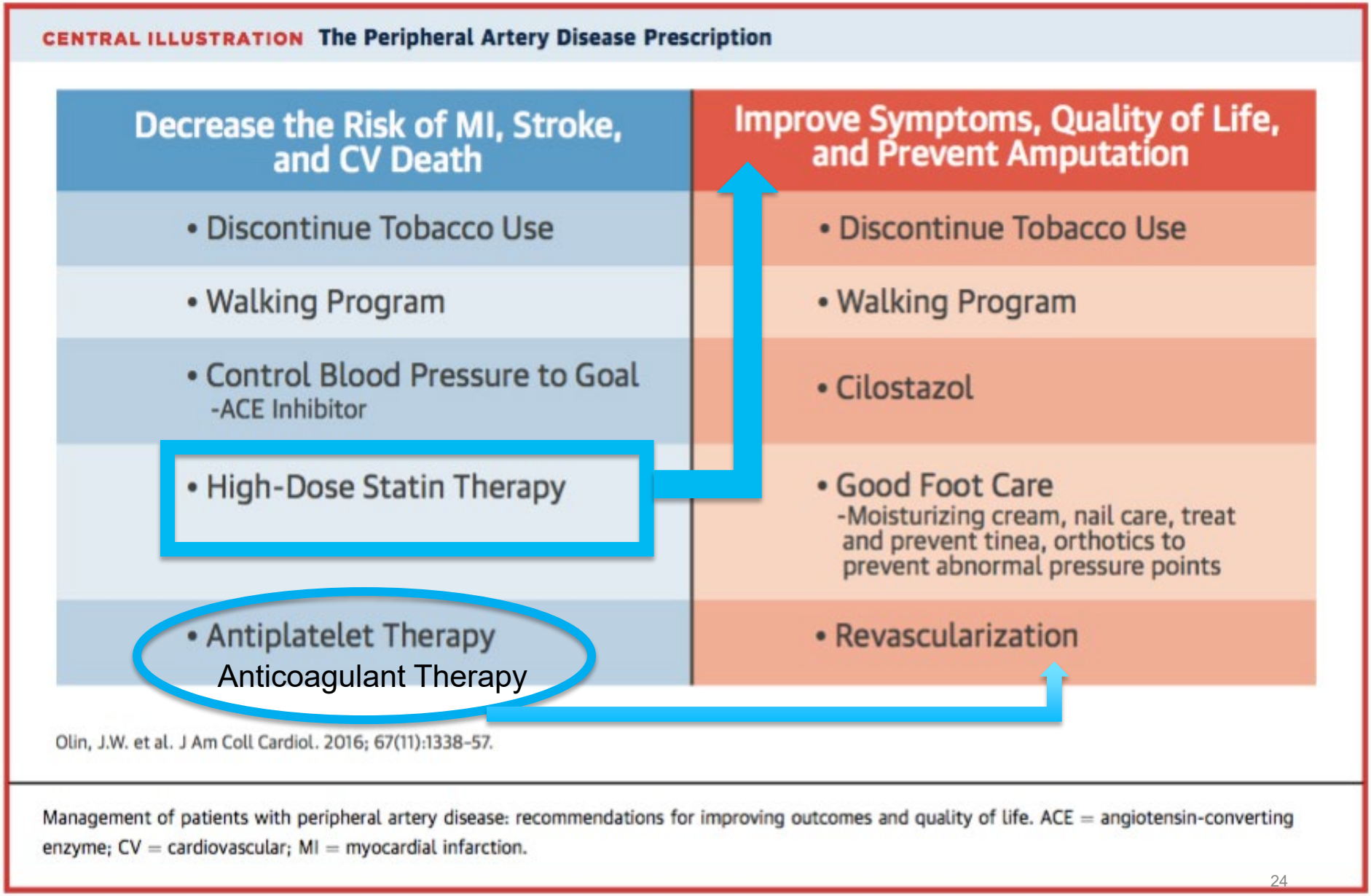


*Fatal or nonfatal MI

Leng GC et al. Brit Med J. 1996;313:1440-1444.

Medical Management

Peripheral Artery Disease Prescription



Smoking Cessation Guidelines

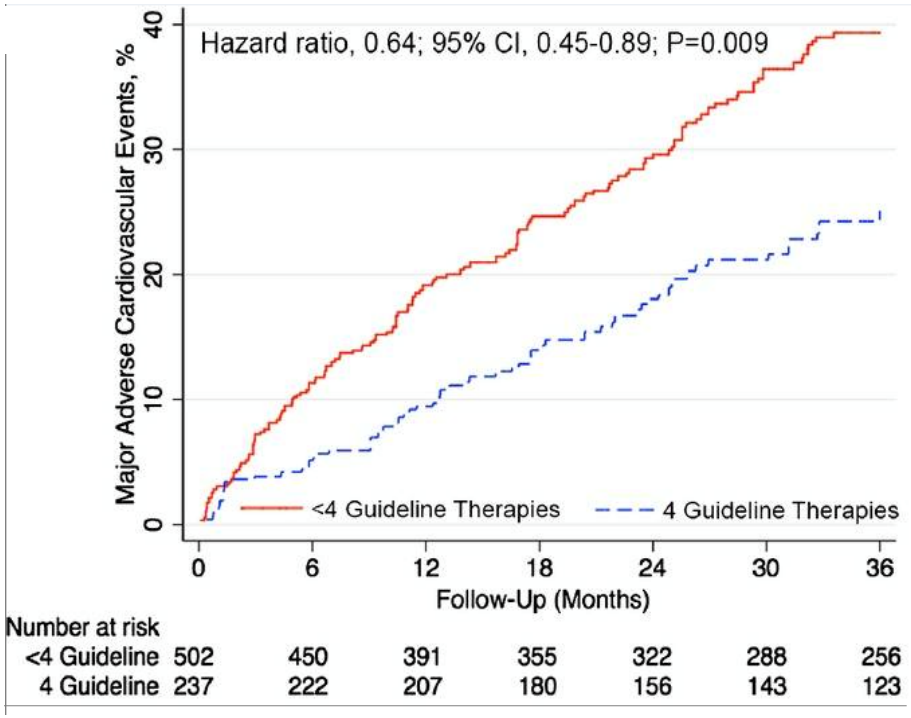
COR	LOE	Recommendations
I	A	Patients with PAD who smoke cigarettes or other forms of tobacco should be advised at every visit to quit
I	A	Patients with PAD who smoke cigarettes should be assisted in developing a plan to quit that involves pharmacotherapy (eg varenicline, bupropion and or nicotine replacement) and/or referral to smoking cessation

J Am Coll Cardiol 2016; 69:e71-126

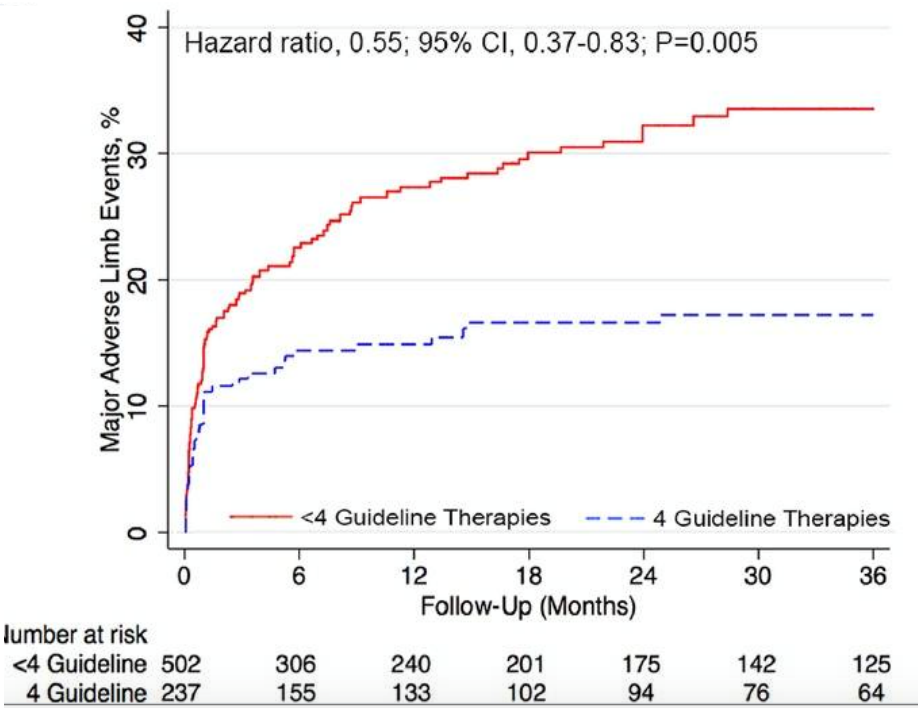
Smoking cessation is associated with decreased mortality and improved amputation-free survival among patients with symptomatic peripheral artery disease

Adherence to Guideline-Recommended Medical Therapies and Outcomes in PAD

Major Adverse CV Events



Major Adverse Limb Events



Armstrong E et al. J Am Heart Assoc 2014;3:e000697.

Effect of Statin Intensity on Mortality and Amputations (N=90,257)

	Mortality	Amputation
Unadjusted model*		
Antiplatelet only, no statin	Ref.	Ref.
Low-to-moderate–intensity statin	0.92 (0.90–0.95)	0.79 (0.75–0.83)
High-intensity statin	0.82 (0.79–0.85)	0.84 (0.78–0.90)
Adjusted model 1†		
Antiplatelet only, no statin	Ref.	Ref.
Low-to-moderate–intensity statin	0.83 (0.81–0.85)	0.76 (0.72–0.80)
High-intensity statin	0.70 (0.67–0.73)	0.61 (0.56– 0.66)
Adjusted model 2‡		
Antiplatelet only, no statin	Ref.	Ref.
Low-to-moderate–intensity statin	0.83 (0.81–0.86)	0.81 (0.75–0.86)
High-intensity statin	0.74 (0.70–0.77)	0.67 (0.61–0.74)

- P value for high versus low-to-moderate statin use is <0.001 in unadjusted, adjusted model 1, and fully adjusted model 2.
- †Model 1 adjusted for age at cohort entry, PAD diagnosis year, and coronary artery disease.
- ‡Model 2 adjusted for age at cohort entry, PAD diagnosis year, race, sex, socioeconomic status, body mass index, comorbidities (diabetes mellitus, hypertension, congestive heart failure, chronic obstructive pulmonary disease, atrial fibrillation, carotid disease, depression, chronic kidney disease, and end-stage renal disease), antiplatelet medications, cilostazol, PAD severity and serum creatinine.

Arya S et al. Circulation 2018;127:1435-1446

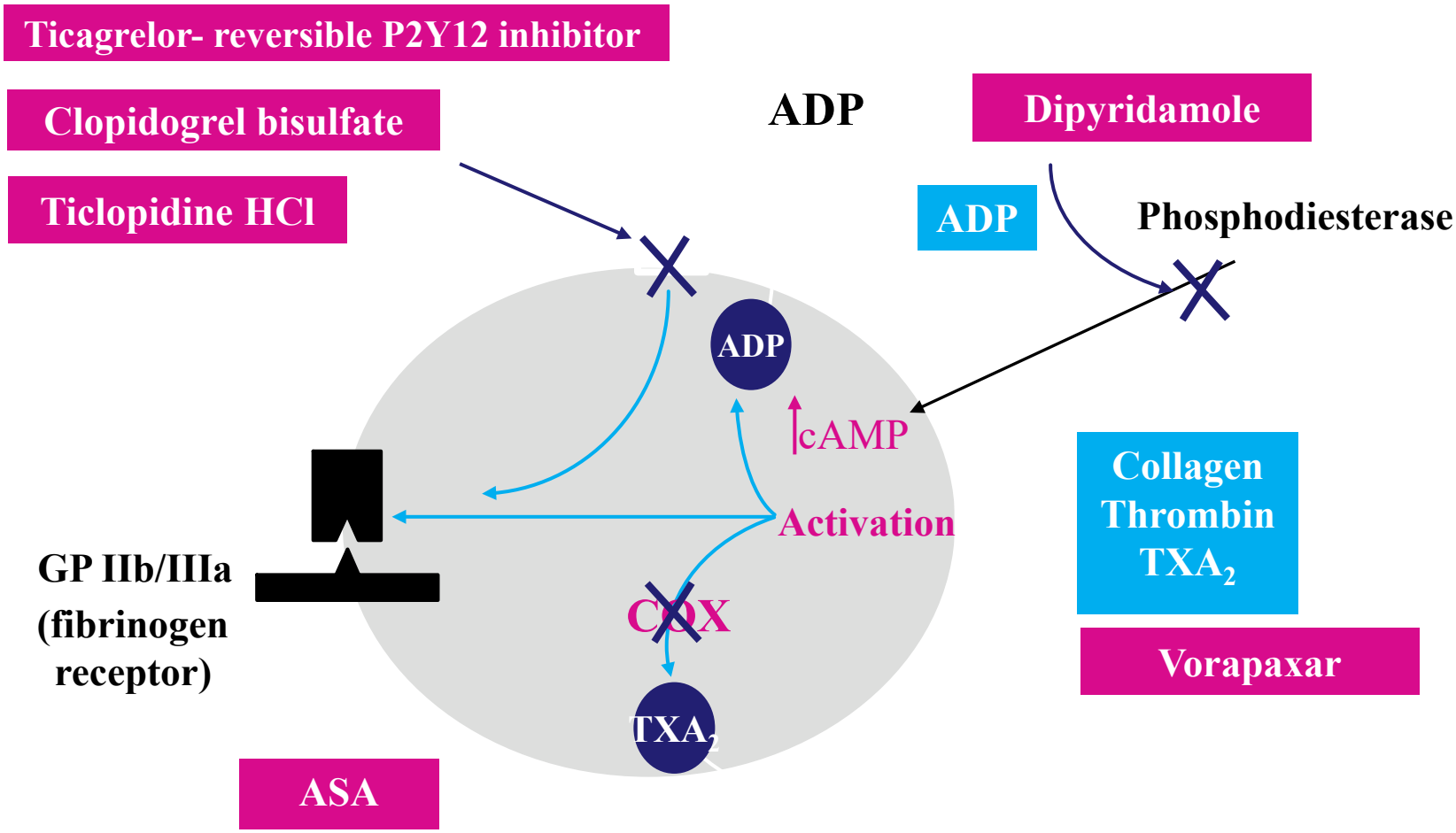
Conclusion

- Statins, especially high-intensity formulations, are **underused in patients with PAD (6.4%).**

- This is the first population-based study to show that high intensity statin use at the time of PAD diagnosis is **associated with a significant reduction in limb loss and mortality** in comparison with low-to-moderate–intensity statin users, and patients treated only with antiplatelet medications but not with statins, as well.

Arya S et al. Circulation 2018;127:1435-1446

Mechanisms of Action of Oral Antiplatelet Therapies



Schafer AI. Am J Med. 1996;101:199

ORIGINAL ARTICLE

Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease

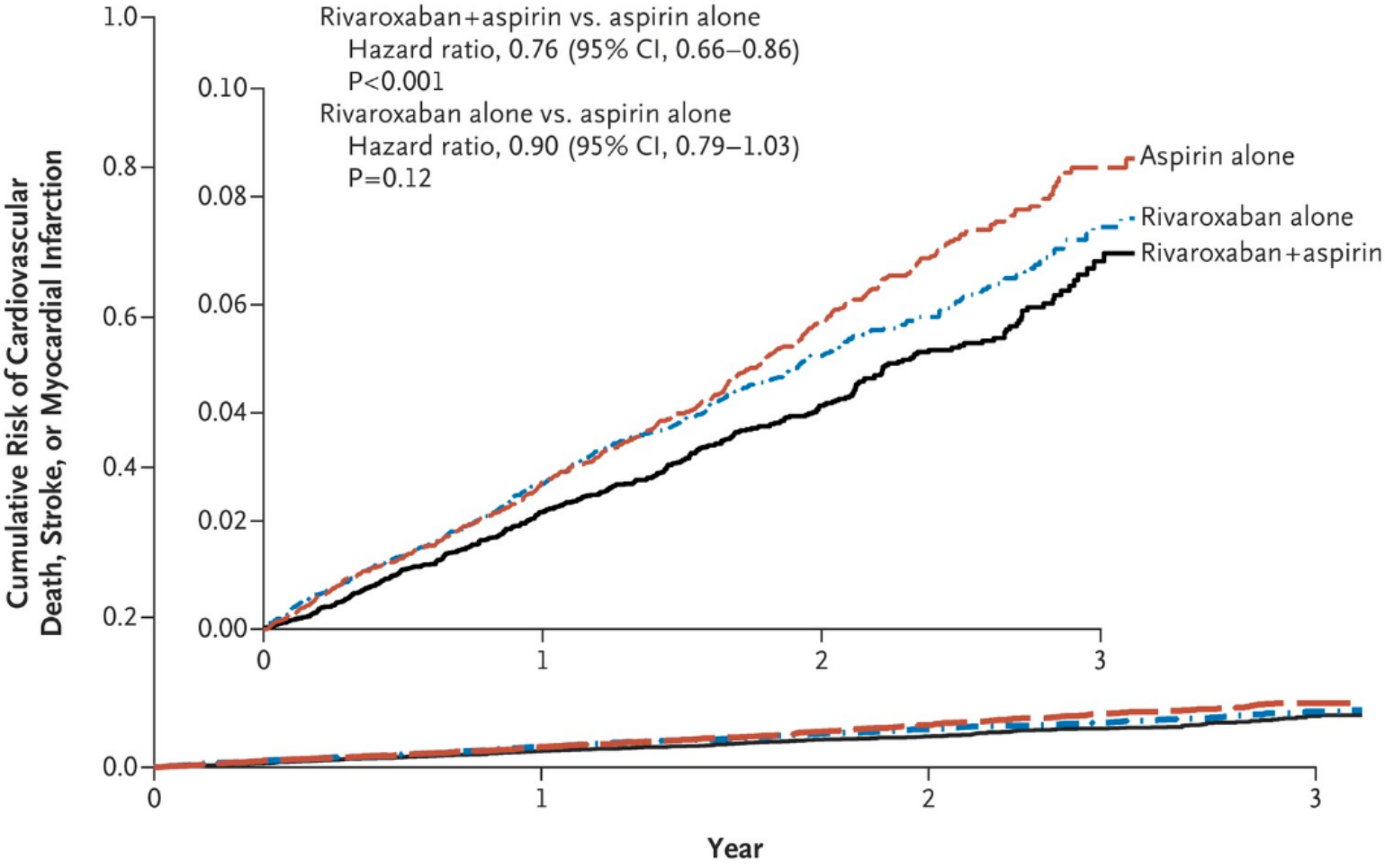
J.W. Eikelboom, S.J. Connolly, J. Bosch, G.R. Dagenais, R.G. Hart, O. Shestakovska, R. Diaz, M. Alings, E.M. Lonn, S.S. Anand, P. Widimsky, M. Hori, A. Avezum, L.S. Piegas, K.R.H. Branch, J. Probstfield, D.L. Bhatt, J. Zhu, Y. Liang, A.P. Maggioni, P. Lopez-Jaramillo, M. O'Donnell, A. Kakkar, K.A.A. Fox, A.N. Parkhomenko, G. Ertl, S. Störk, M. Keltai, L. Ryden, N. Pogosova, A.L. Dans, F. Lanas, P.J. Commerford, C. Torp-Pedersen, T.J. Guzik, P.B. Verhamme, D. Vinereanu, J.-H. Kim, A.M. Tonkin, B.S. Lewis, C. Felix, K. Yusoff, P.G. Steg, K.P. Metsarinne, N. Cook Bruns, F. Misselwitz, E. Chen, D. Leong, and S. Yusuf, for the COMPASS Investigators*

CONCLUSIONS

Among patients with stable atherosclerotic vascular disease, those assigned to rivaroxaban (2.5 mg twice daily) plus aspirin had better cardiovascular outcomes and more major bleeding events than those assigned to aspirin alone. Rivaroxaban (5 mg twice daily) alone did not result in better cardiovascular outcomes than aspirin alone and resulted in more major bleeding events. (Funded by Bayer; COMPASS ClinicalTrials.gov number, NCT01776424.)

N Engl J Med. 2017 Oct 5;377(14):1319-1330

27% of 27,000 patients had PAD



No. at Risk				
Aspirin alone	9126	7808	3860	669
Rivaroxaban alone	9117	7824	3862	670
Rivaroxaban+aspirin	9152	7904	3912	658

COMPASS TRIAL: PAD SUBGROUP

Research in context

Evidence before this study

Patients with peripheral artery disease are at high risk for major cardiovascular and limb events. The mainstay of treatment for patients with peripheral artery disease includes use of a single antiplatelet agent daily to prevent major adverse cardiovascular events. Other antithrombotic regimens have been tested in patients with peripheral artery disease including vitamin K antagonists and newer antiplatelet agents including P2Y12 antagonists used alone or in combination with aspirin, but none have been shown to be superior to antiplatelet therapy alone.

Added value of this study

The peripheral artery disease analysis of the COMPASS trial shows that use of low-dose rivaroxaban twice a day, together with aspirin 100 mg once a day, reduces cardiovascular death, myocardial infarction, stroke, and acute limb ischaemia and amputation, compared with aspirin alone. Although there is an increase in bleeding leading to more hospital admissions, there is no excess of fatal bleeding, intracranial bleeding, or bleeding into critical organs. Thus, the net clinical benefit favours the use of low-dose rivaroxaban plus aspirin.

Implications of all the available evidence

The combination of low dose rivaroxaban twice a day with aspirin could replace aspirin alone as standard of care in patients with stable peripheral artery disease who are not at high risk for bleeding.

Lancet. 2018 Jan 20;391(10117):219-229.

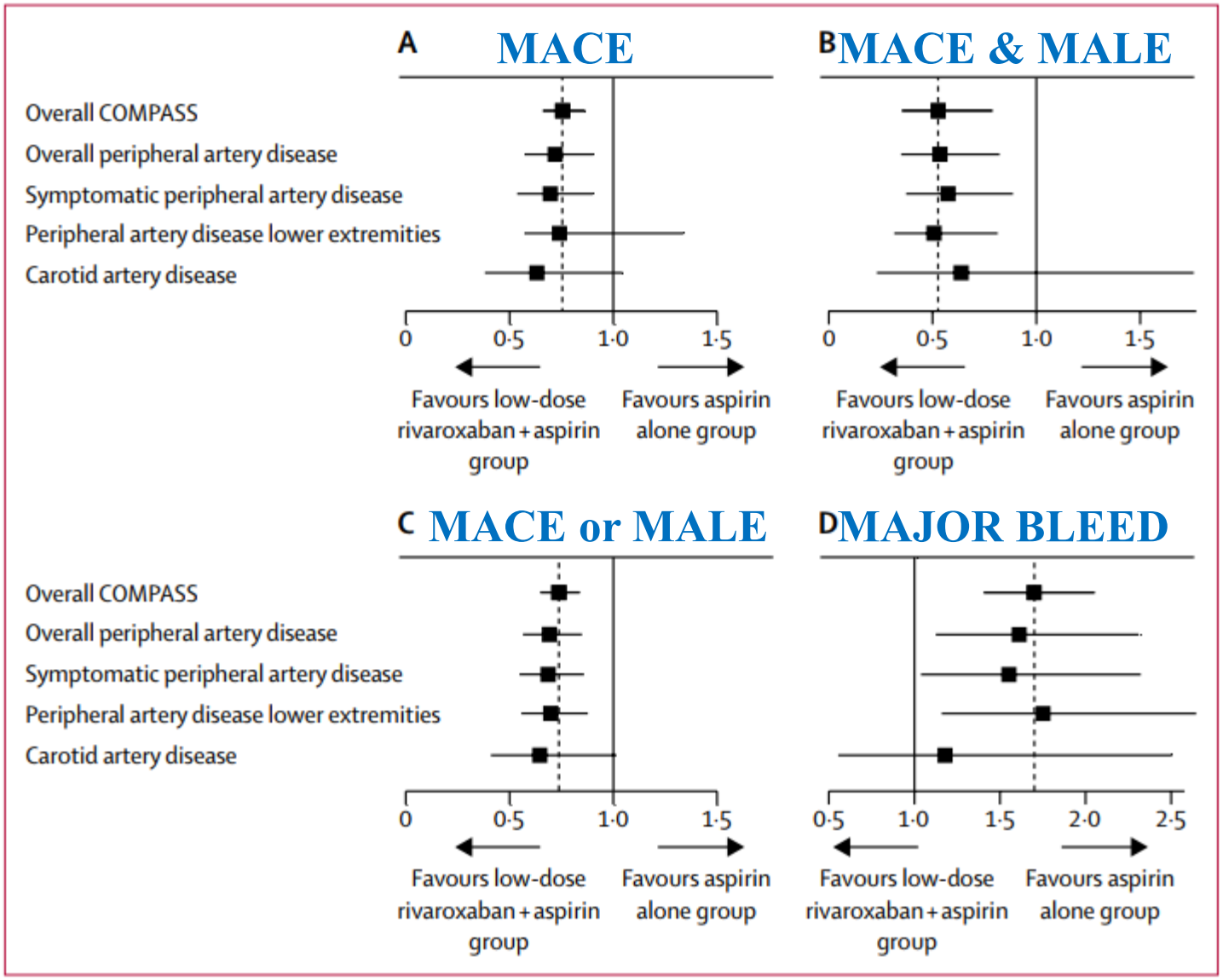


Figure 4: **Analyses of primary and secondary outcomes**

Hazard ratios and 95% CI are shown for all subgroups of patients with peripheral artery disease for major adverse cardiovascular events (A) and major adverse limb events including major amputation (B), major adverse cardiovascular or limb events including major amputation (C) and for major bleeding (D). The dotted line indicates the point estimate for the overall COMPASS trial population (n=27 395).

Home Exercise Program

Frequency: 3–5 days per week

Modality

Treadmill (can be adapted for walking outside)

Method

1. Begin at 2 mph and a gradient of 0 (flat)
2. Stop exercise when pain is 3–4 on claudication pain scale*
3. When the pain has ceased, resume exercise at the same intensity
4. Repeat rest and exercise cycles
5. Progress to a higher work load when the patient can walk for 8 minutes without having to stop for leg symptoms:
    a) Increase speed by 0.2 mph each time the patient can walk for 8 min
    b) Once patients can walk at 3.4 mph, or reach a speed at which they can no longer keep up, begin increasing the grade by 1%–2%

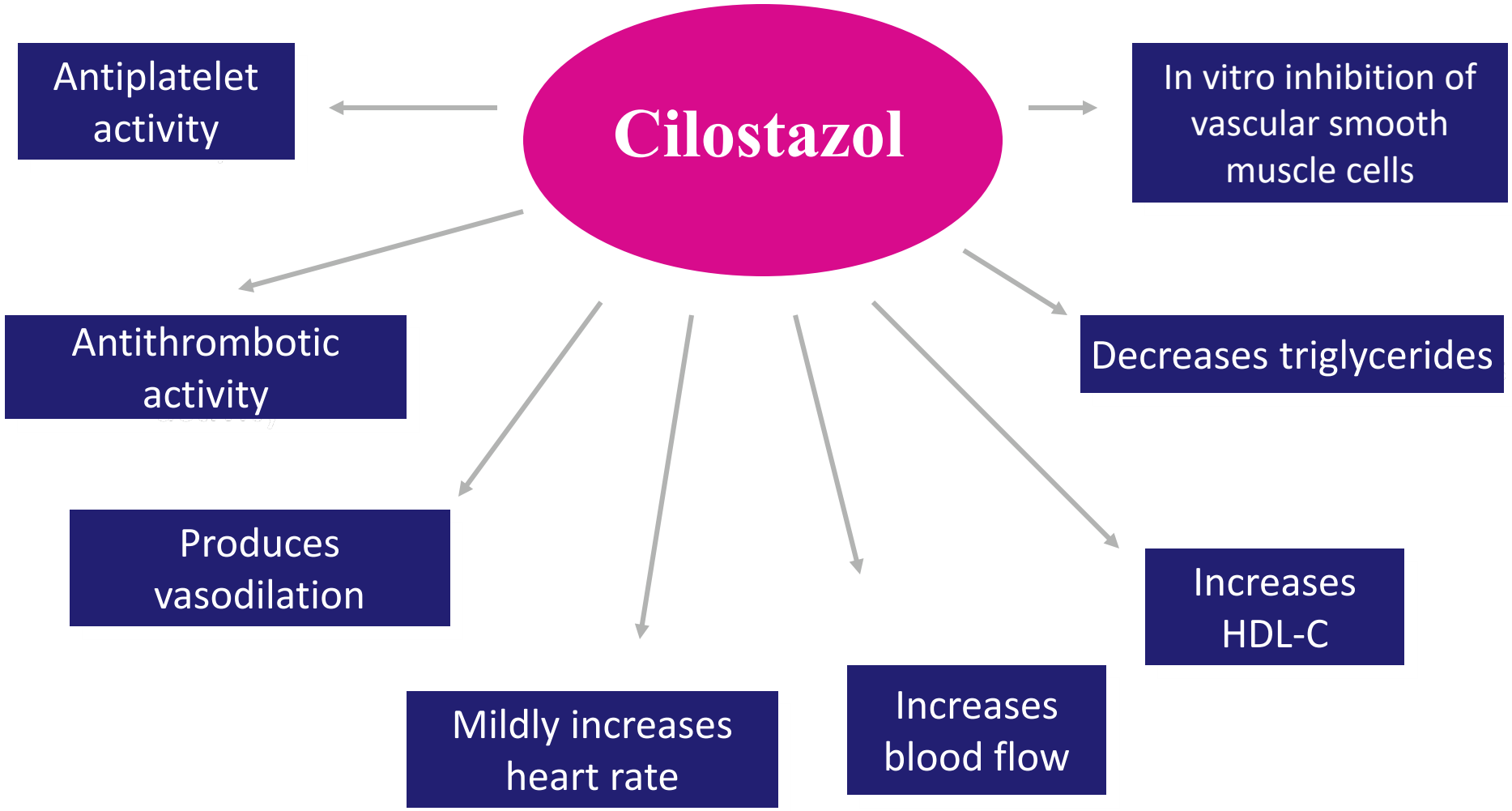
Duration

The total exercise period, including rest periods, should equal 50 minutes per day

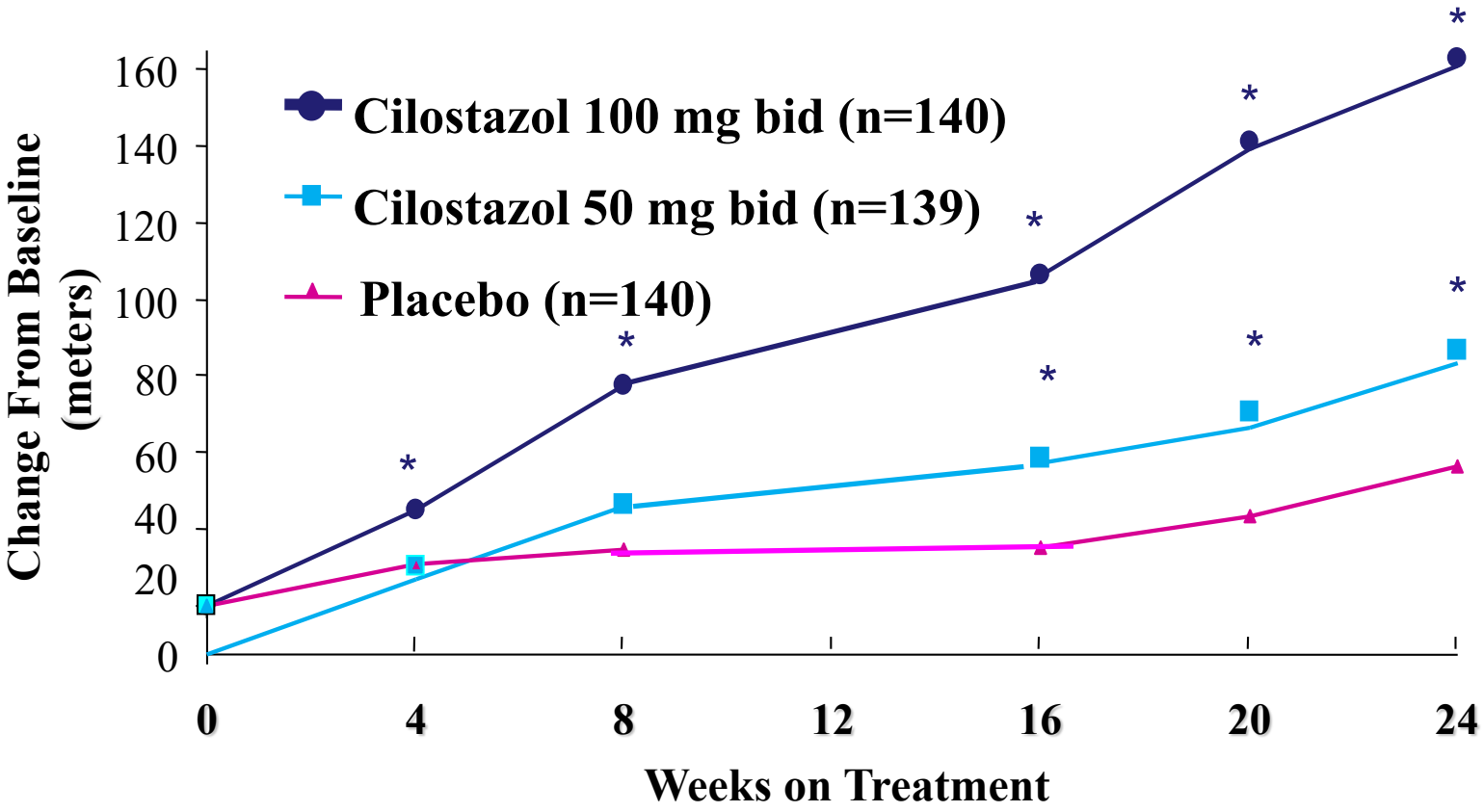
***Claudication pain scale:** 1=no pain; 2=onset of claudication; 3=mild pain or discomfort; 4=moderate pain or discomfort; 5=severe pain or discomfort

Weinberg MD, Lau JF, Olin JW. Nat Rev Cardiol. 2011;8:429-441.

Pharmacologic Effects of Cilostazol



Change in Maximal Walking Distance



* Significantly greater than placebo, $P \leq 0.05$

Strandness DE Jr, et al. Vasc Endovascular Surg. 2002;36:83-91.

6 Things to Remember About Cilostazol

1. It should be used to **treat the symptoms of claudication**, not for cardiovascular risk reduction
2. Use a dose of **100 mg twice a day** (unless the patient is on a medication that requires dose reduction)
3. Take on an **empty stomach** to assure consistent absorption (1/2 hour before breakfast and dinner)
4. Tell the patient it **may take 4 months to get the full effect** of the medication, ie, do not stop the medication too early
5. If **side effects develop**, reduce the dose to 50 mg twice a day for a week and then go back to 100 twice a day
6. This drug **does not CAUSE** heart failure; **however, it should not be used if the patient has had heart failure**

Indications for Revascularization

Iliac Disease

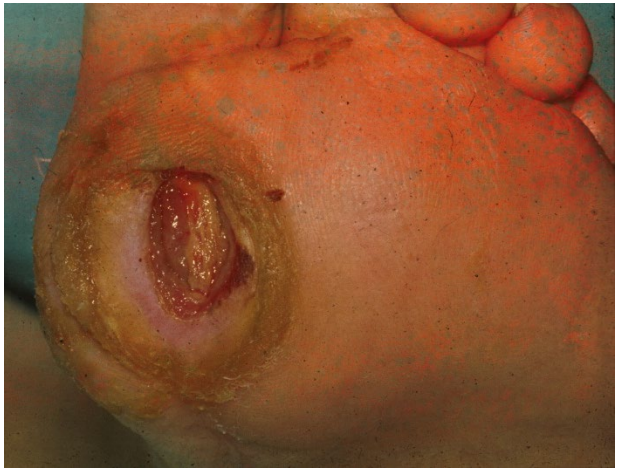
- Hip, thigh, or buttock claudication
- Reduced or absent femoral pulses
- Imaging to identify iliac disease and stenting

Infrainguinal Disease

- Trial of medical therapy for 4–6 months:
  - Structured exercise program
  - Cilostazol
  - ACE Inhibitors?
- If failure, additional imaging to define anatomy and, if feasible, stent placement
- If short segment SFA disease is identified, can proceed directly with stenting

Guiding Principles for Revascularization in Patients With PAD

Patients with PAD should have their feet inspected during every office visit.
This is the single most important thing you can do to prevent amputations.



Olin JW, Sealove B. Mayo Clin Proc. 2010;85(7):678-692

Surgical Interventions for PAD

Management of IC

Treatment Goals:
- Relieve symptoms
- Improve exercise performance
- Improve daily functional abilities

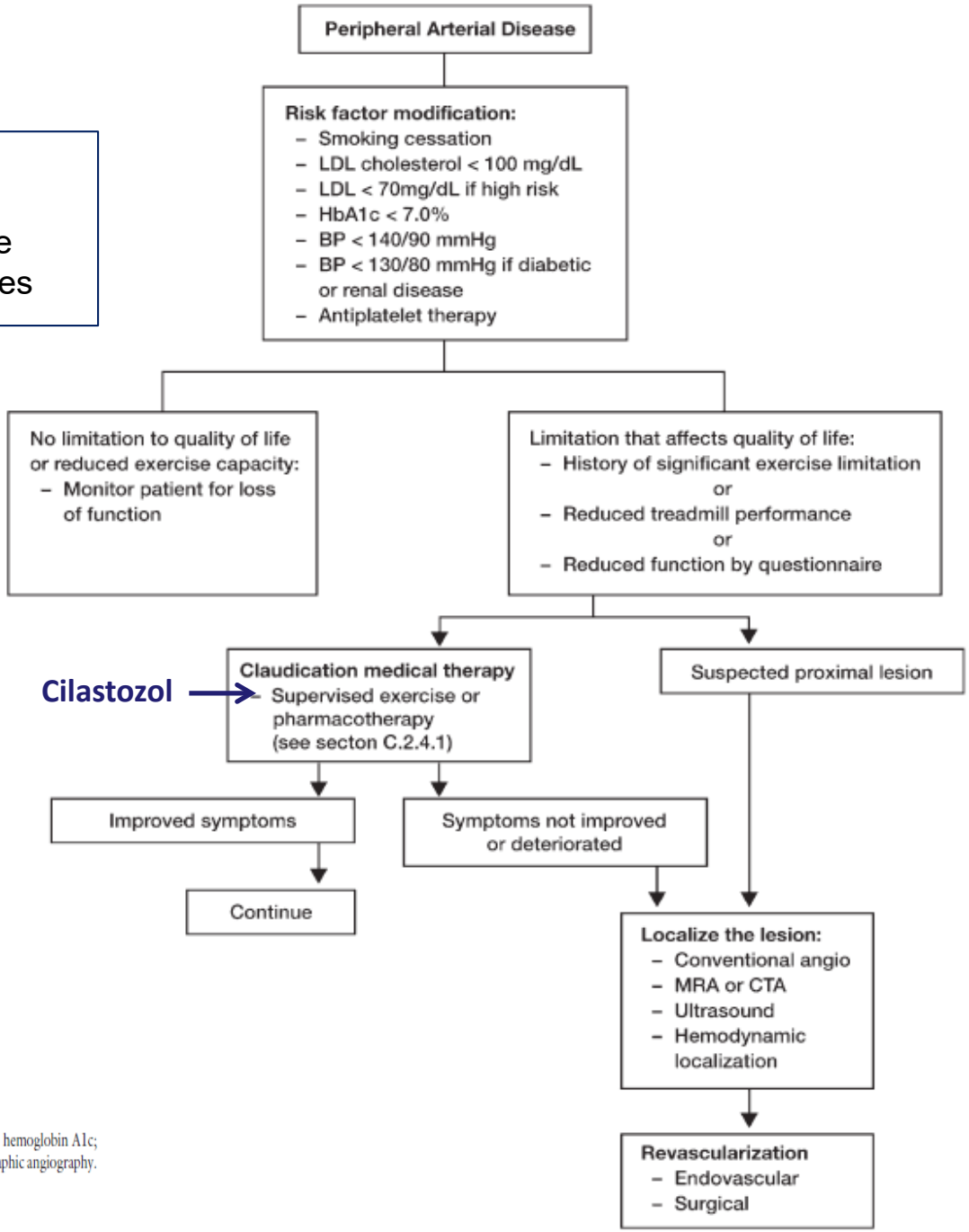
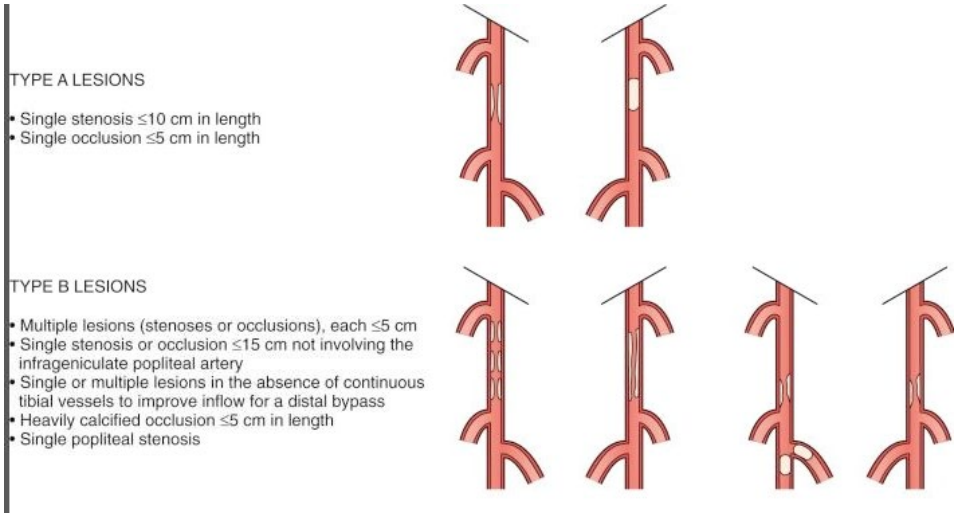


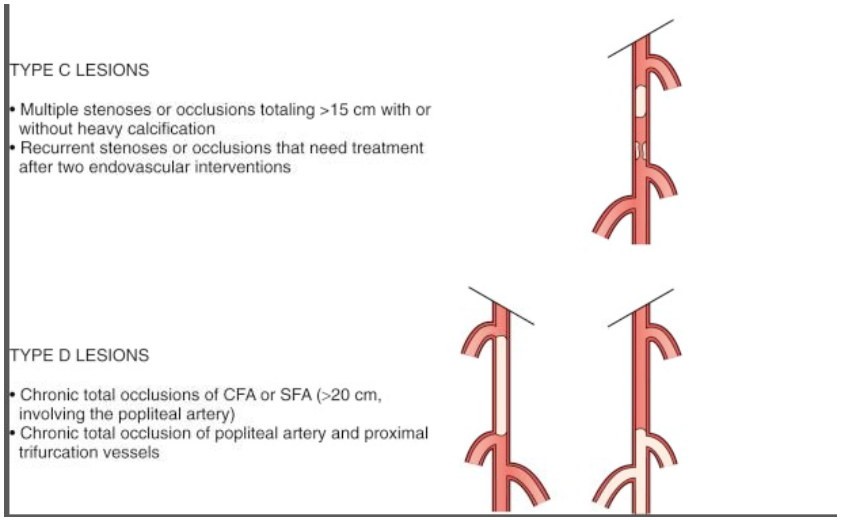
Fig. C3. Overall treatment strategy for peripheral arterial disease. BP – blood pressure; HbA1c – hemoglobin A1c; LDL – low density lipoprotein; MRA – magnetic resonance angiography; CTA – computed tomographic angiography. Reproduced with permission from Hiatt WR. *N Engl J Med* 2001;**344**:1608–1621.

Surgical Treatment for IC

Endovascular

- Classification of Anatomy as defined by TASC 2 (Trans-Atlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease)
  - TASC A: endovascular therapy
  - TASC B: endovascular therapy
  - TASC C: surgery if good-risk patient
  - TASC D: surgery





Outcomes for Surgical Treatment of IC

Table F6. Pooled results of femoral popliteal dilatations

	1-year % patency (range)	*3-year % patency (range)*	*5-year % patency (range)*
PTA: stenosis	77 (78–80)	61 (55–68)	55 (52–62)
PTA: occlusion	65 (55–71)	48 (40–55)	42 (33–51)
PTA+stent: stenosis	75 (73–79)	66 (64–70)	
PTA+stent: occlusion	73 (69–75)	64 (59–67)	

PTA – Percutaneous Transluminal Angioplasty.

Table F7a. 5-year patency following femoral popliteal bypass[191]

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

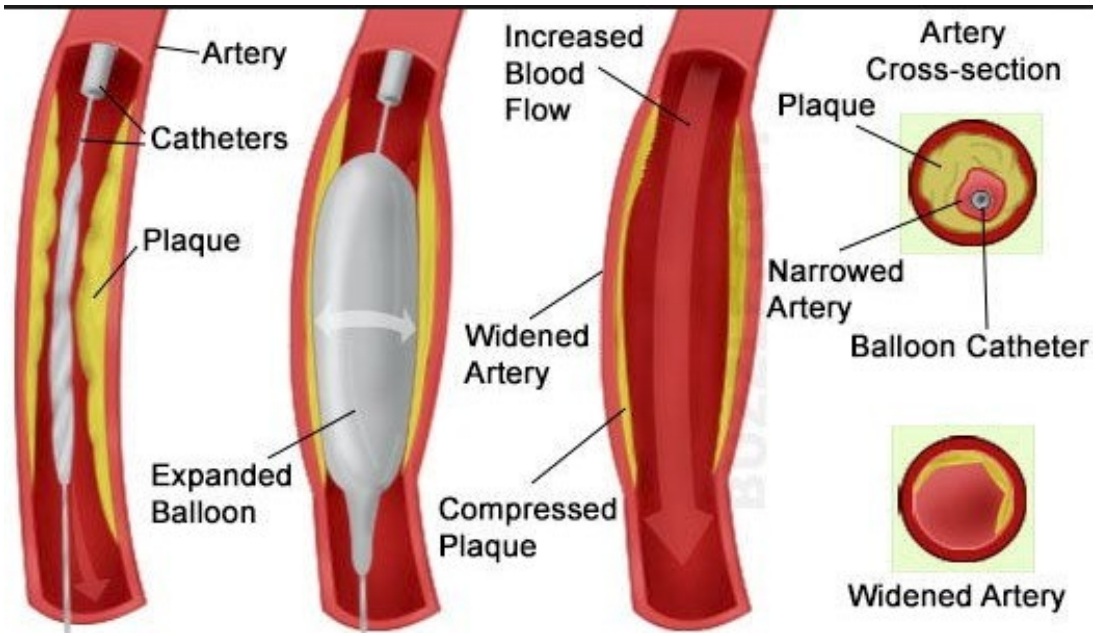
CLI – critical limb ischemia; PTFE – polytetrafluoroethylene graft.

TASC 2 (Trans-Atlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease

Surgical for Treatment for IC

Endovascular Therapy

- Balloon Angioplasty
  - Drug-coated balloon (DCB) vs. Uncoated balloon
    - DCB with statistically significant advantage for: primary vessel patency; binary restenosis rate; target lesion revascularization
    - DCB had no advantage for: amputation; death; change in ABI



Kayssi A, et al. Cochrane Database Syst Rev. Aug 2016:8.

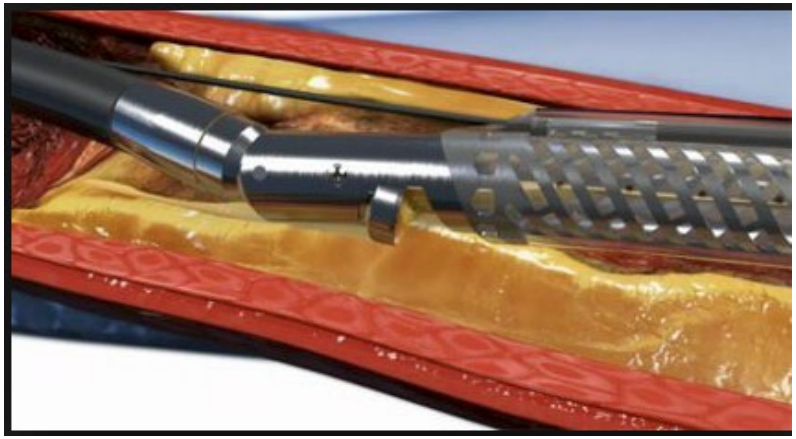
Surgical for Treatment for CLI

Endovascular Therapy

- Atherectomy
  - DEFINITIVE LE trial (800 pts across 47 centers)
  - 12-month primary patency rate in CLI = 71%
  - 12-month freedom from amputation in CLI = 95%
  - 12-month wound healing rates = 72%

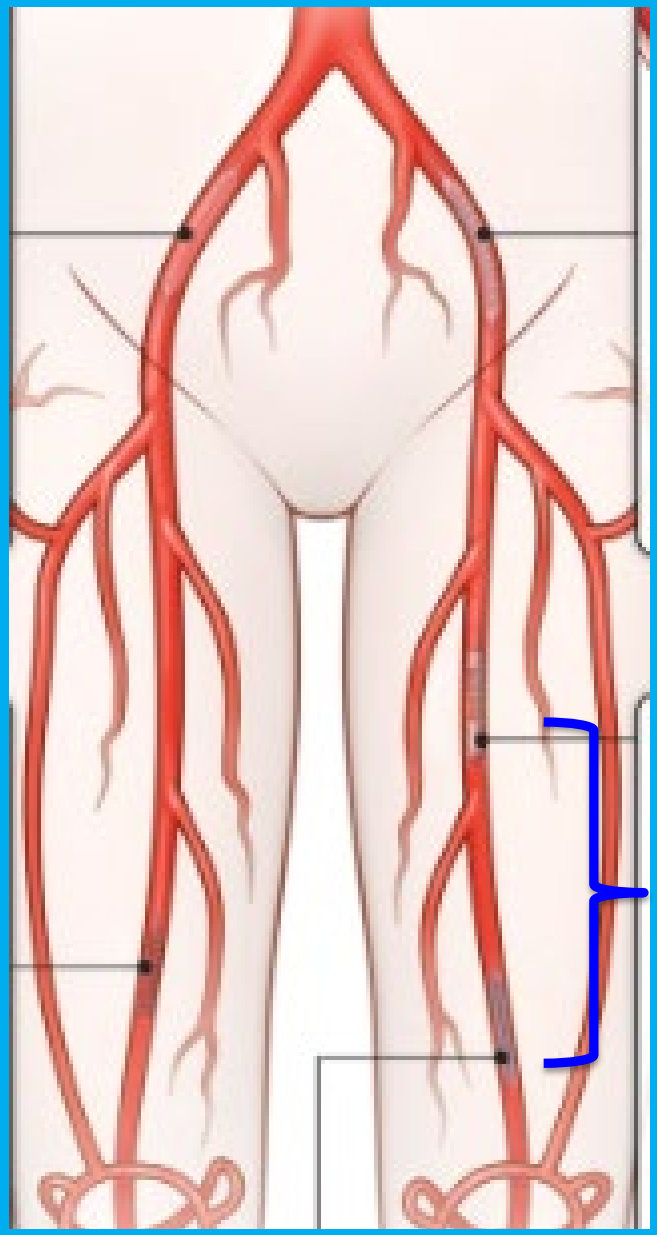
Conclusion

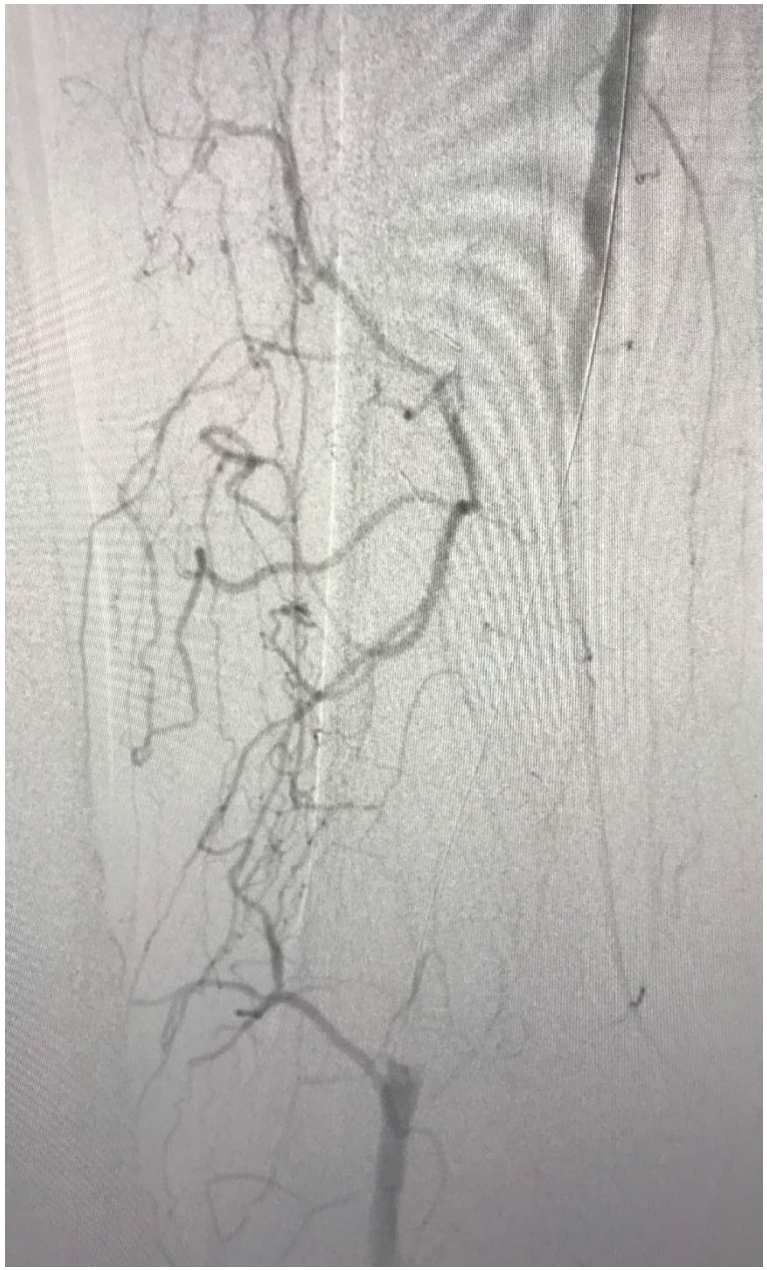
- Safe for multilevel LE disease
- Limb salvage rates and wound healing rates comparable to rates seen in bypass studies
- Does not require permanent endoprothesis

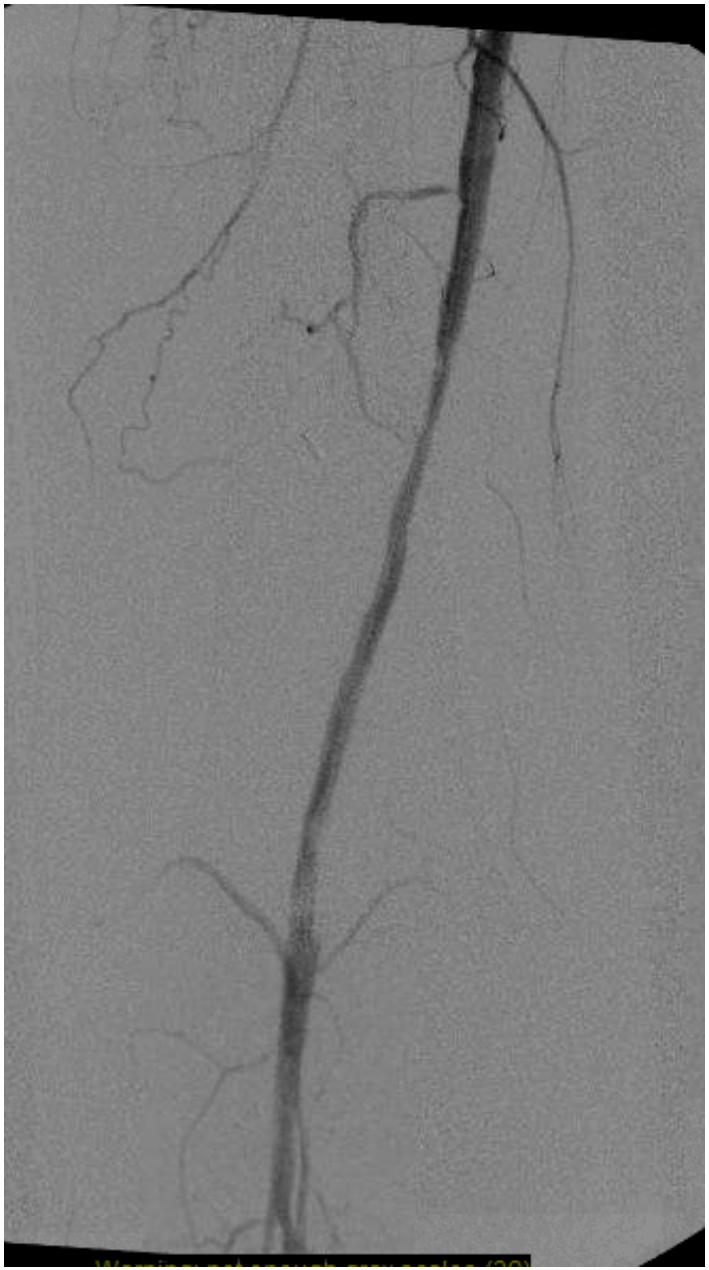


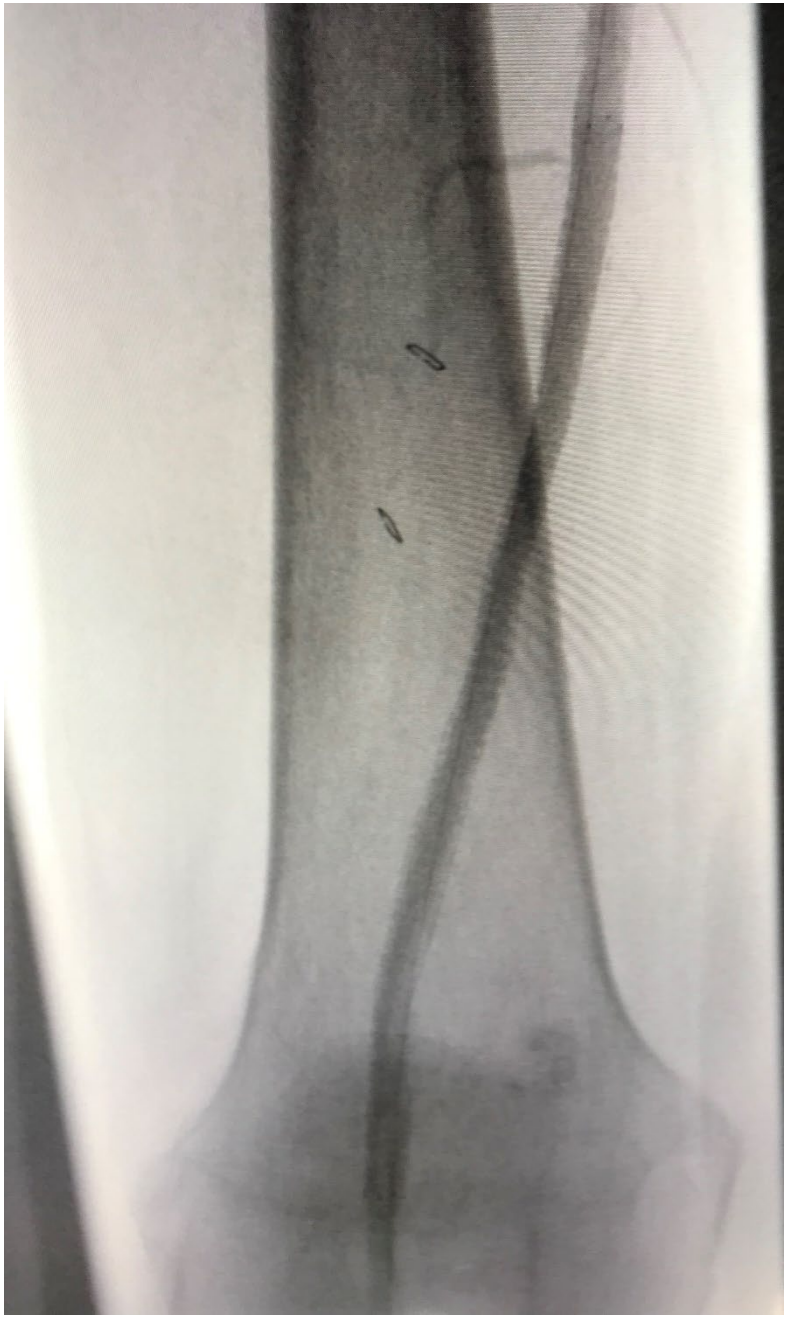
McKinsey J, et al. JACC. Aug 2014:7(8); 922-33.

Treating Mid-SFA Lesion

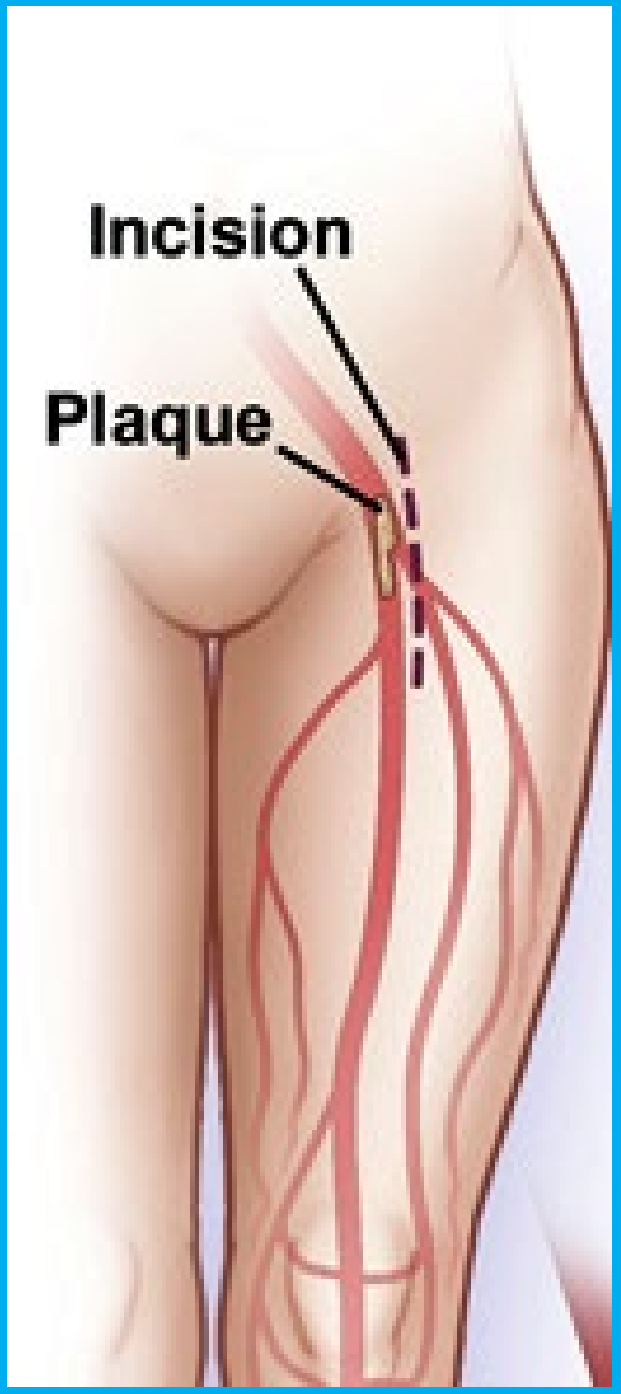


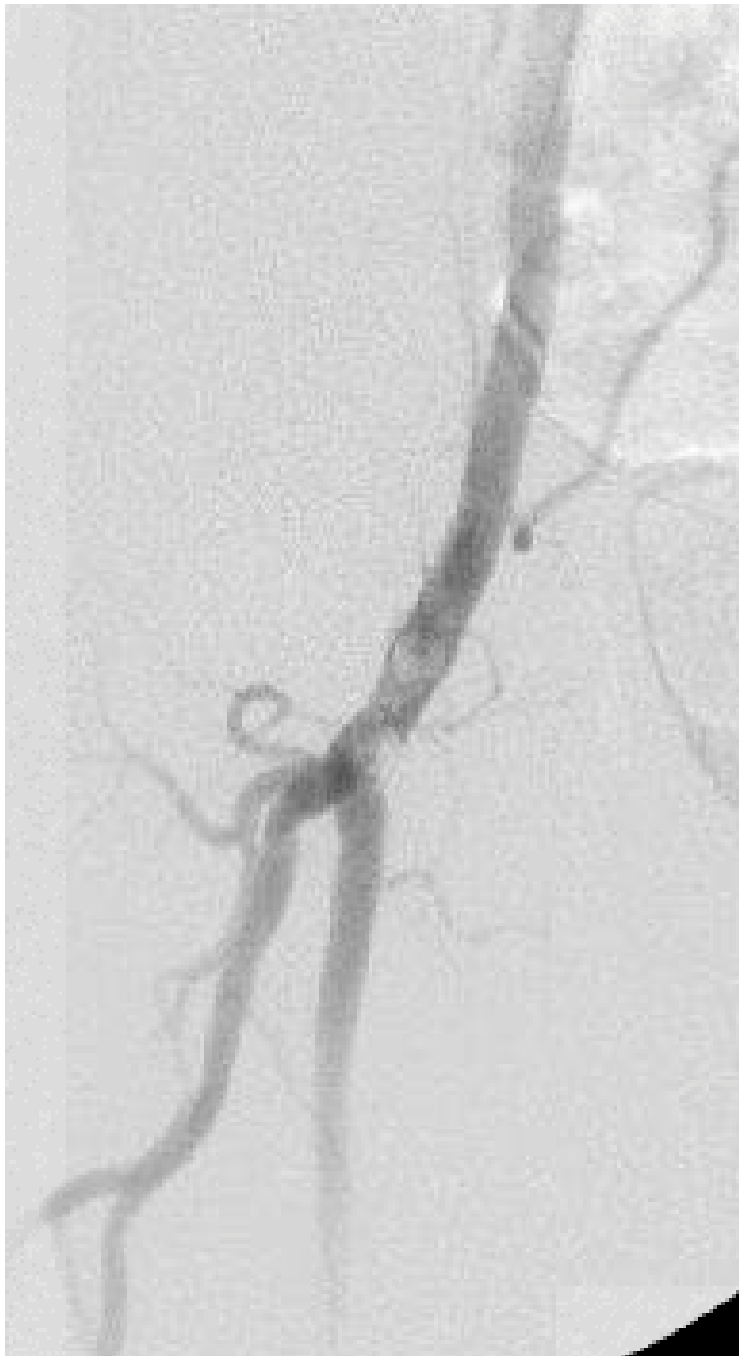




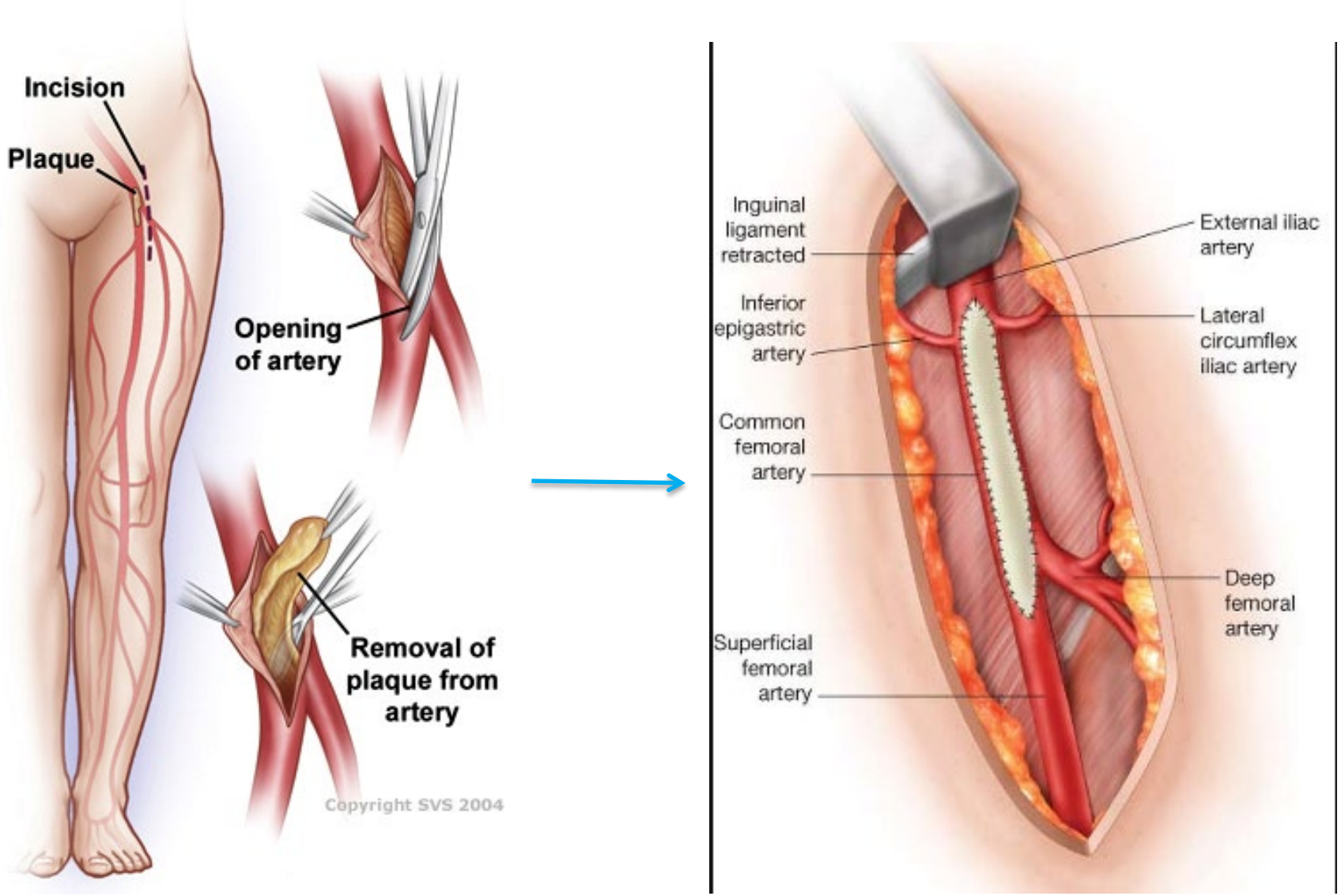


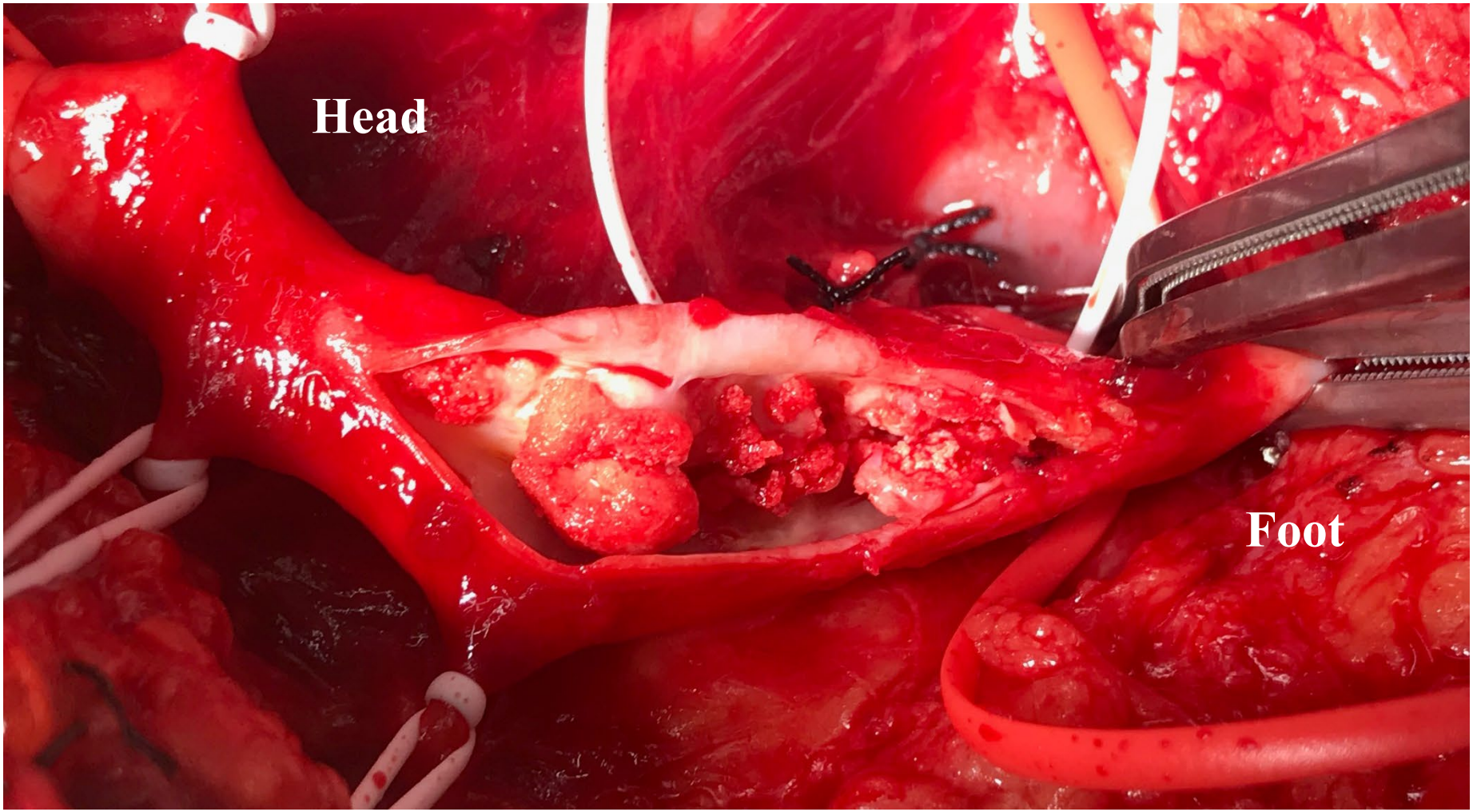
Surgical Treatment of Inflow Lesion





CFA Endarterectomy

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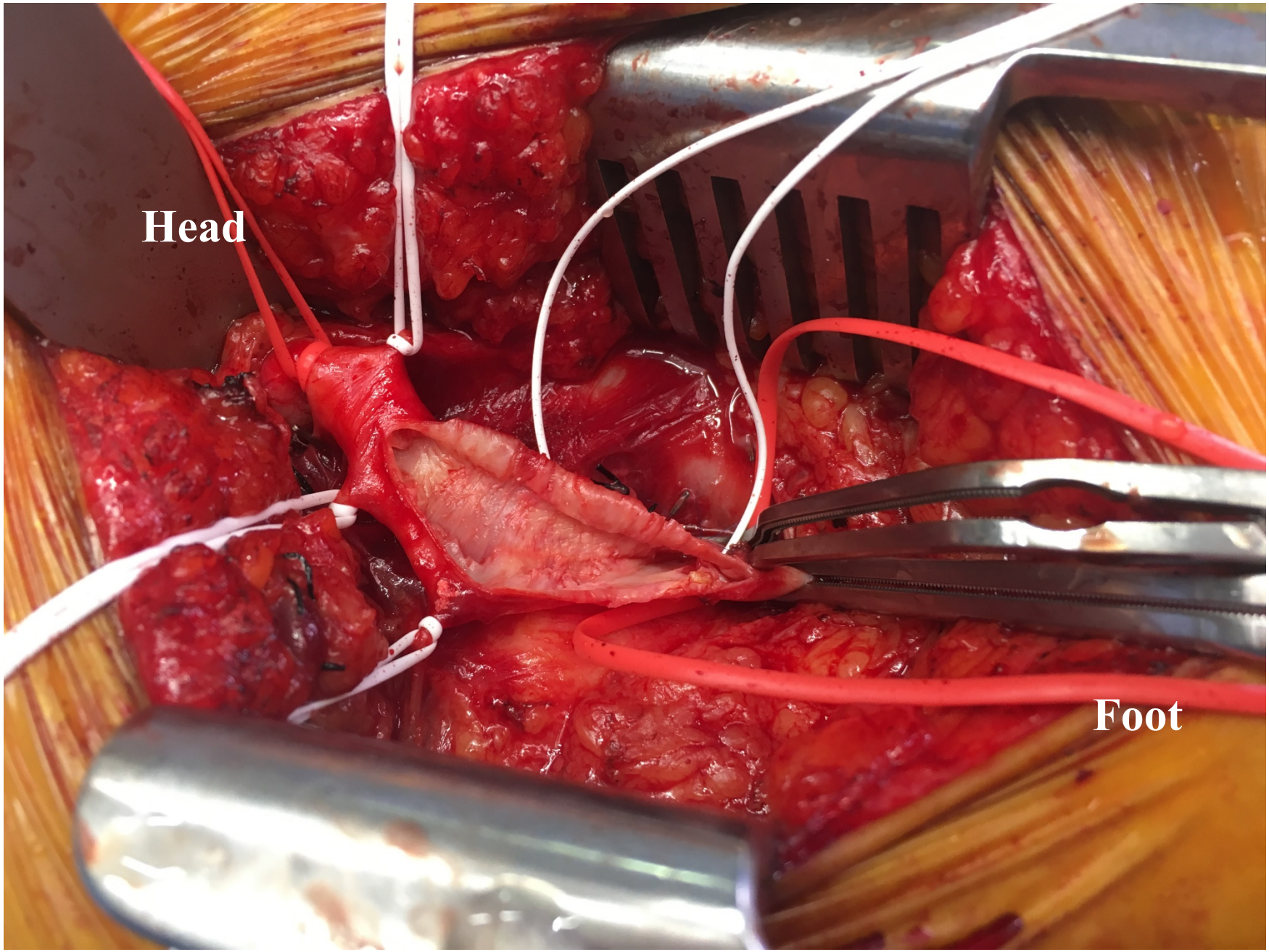
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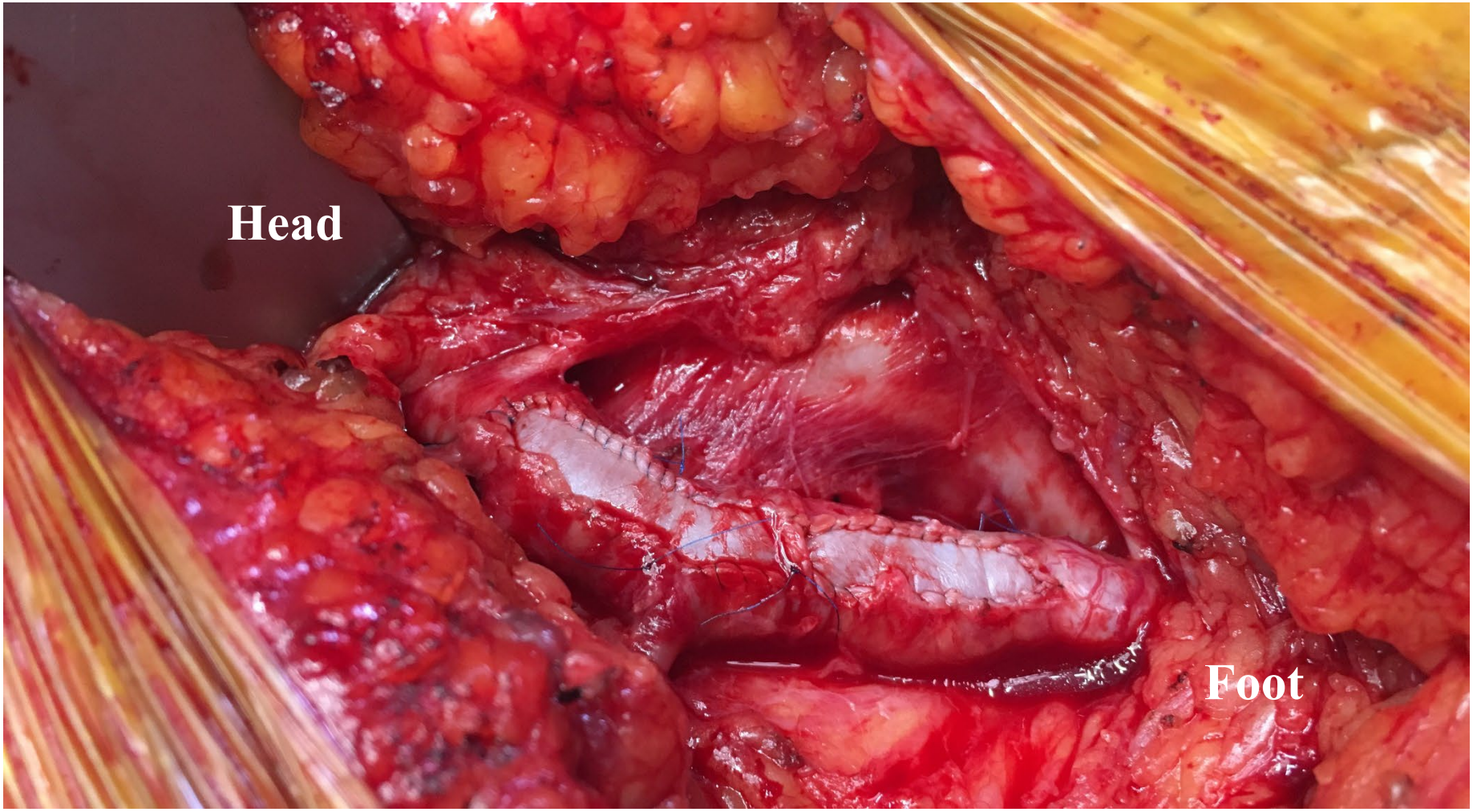
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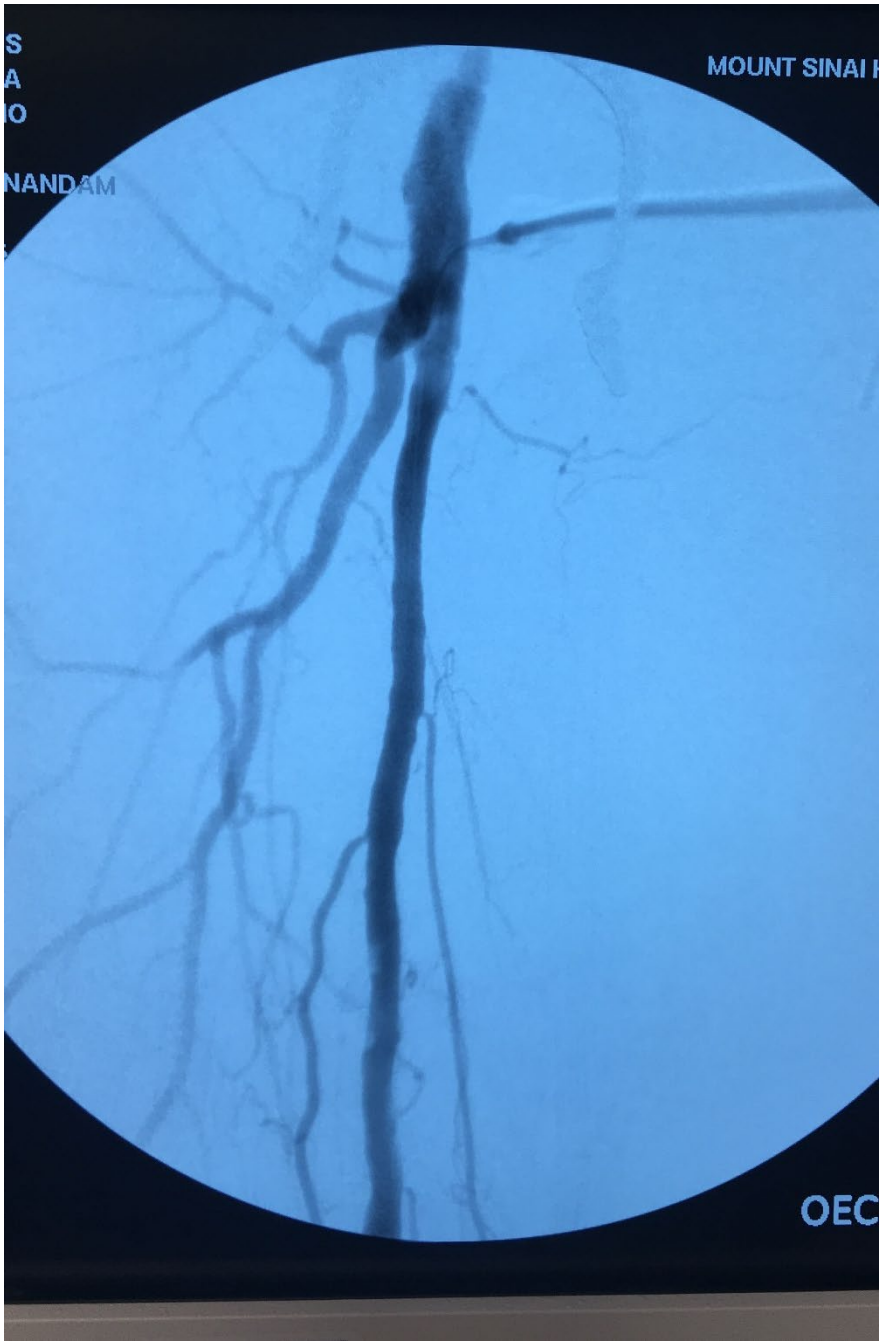
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Natural History of CLI

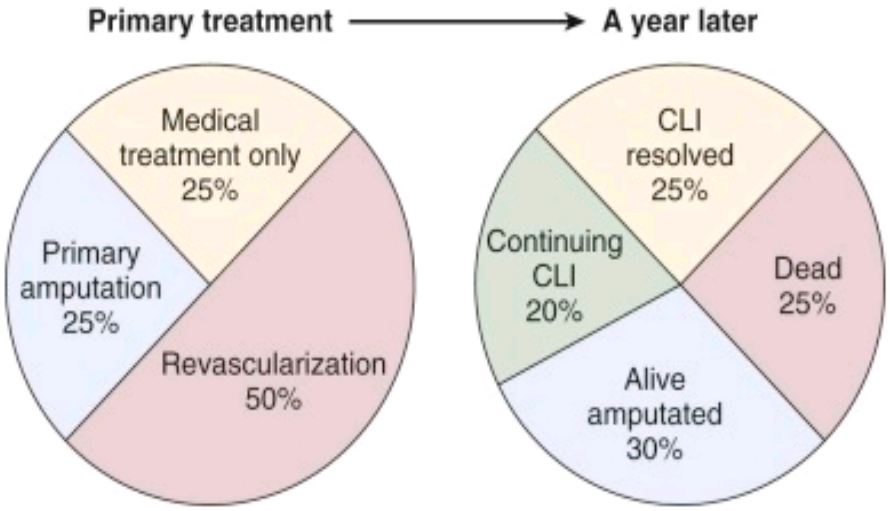


Figure 108-3

The estimate of the initial treatment and status a year later of patients presenting with chronic critical limb ischemia. (Redrawn from Norgren L, et al: TASC II Working Group, Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg* 45:S11, 2007.)

Management of CLI

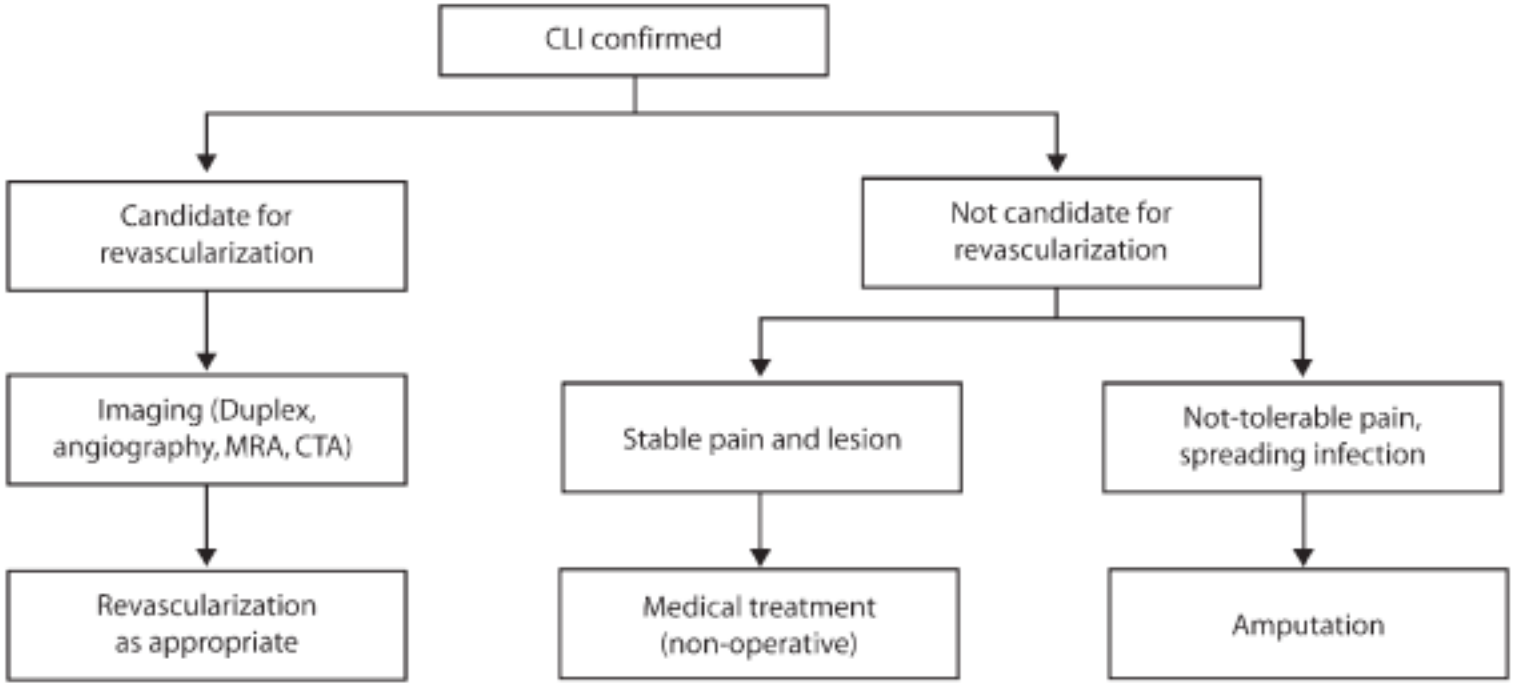


Fig. D4. Algorithm for treatment of the patient with critical limb ischemia. Contraindications are: patients not fit for revascularization; revascularization not technically possible; benefit cannot be expected (i.e. widespread ulceration-gangrene – see also section D7.5). CLI – critical limb ischemia; MRA – magnetic resonance angiography; CTA – computed tomographic angiography.

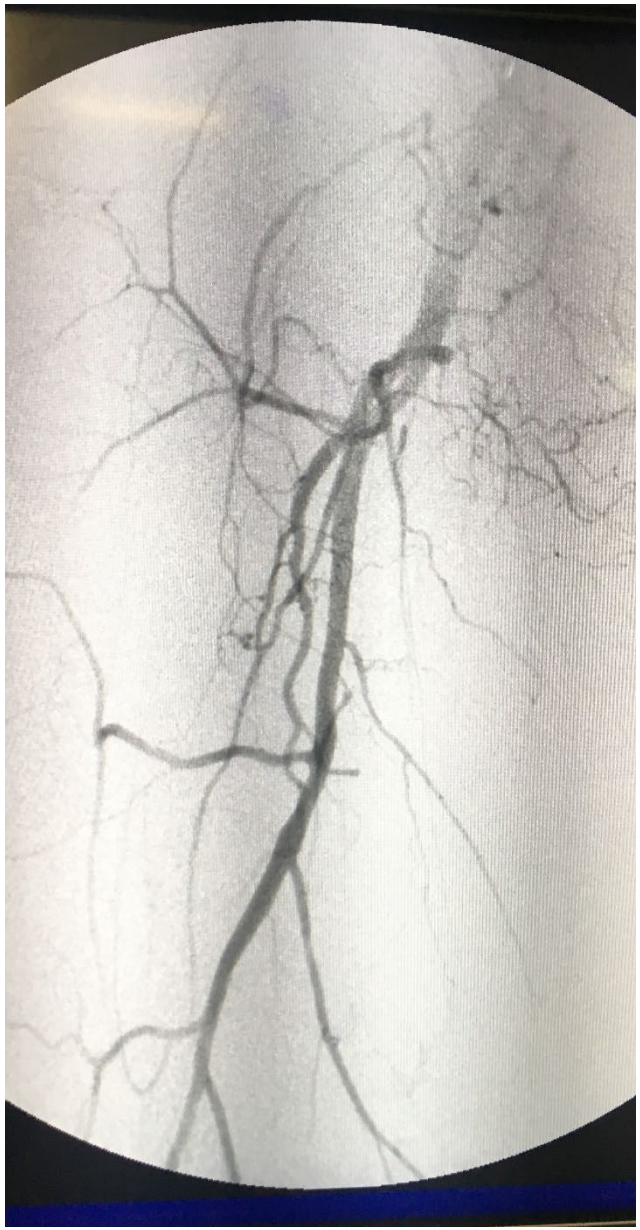
TASC 2 (Trans-Atlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease

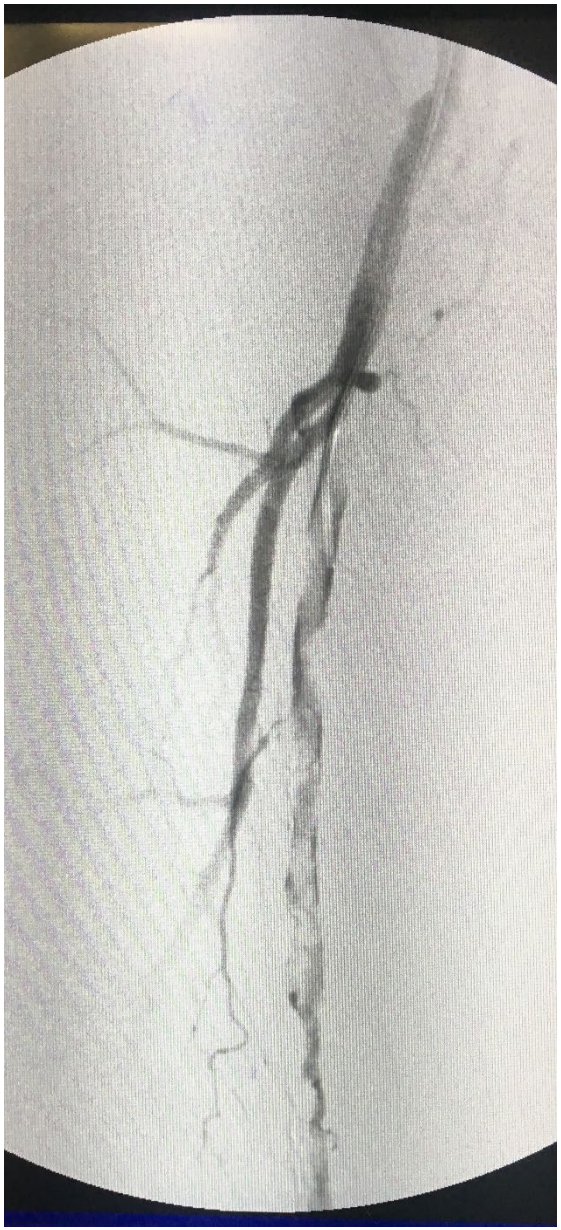
Treatment in CLI

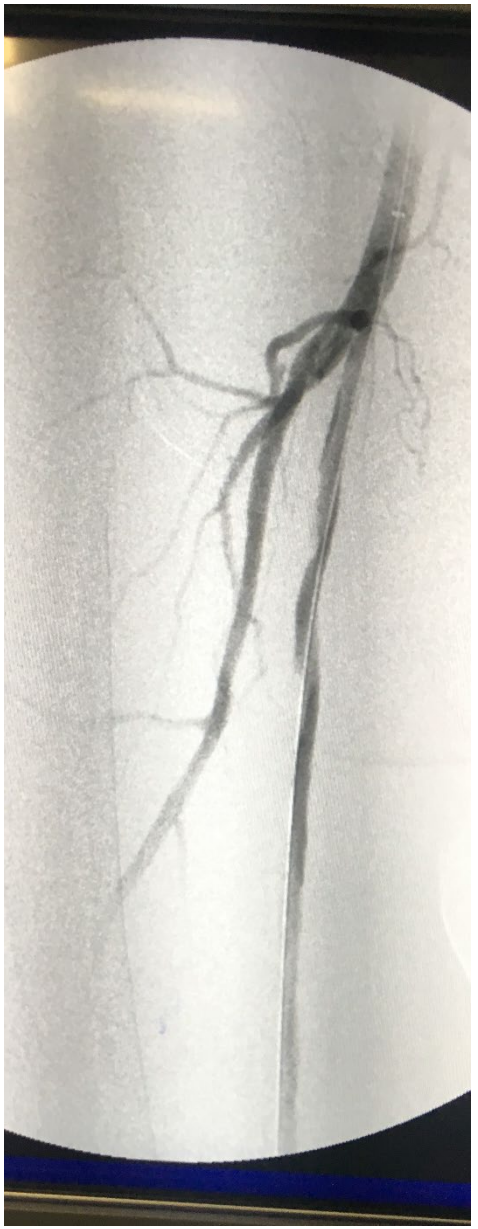
Revascularization Versus Limb Amputation

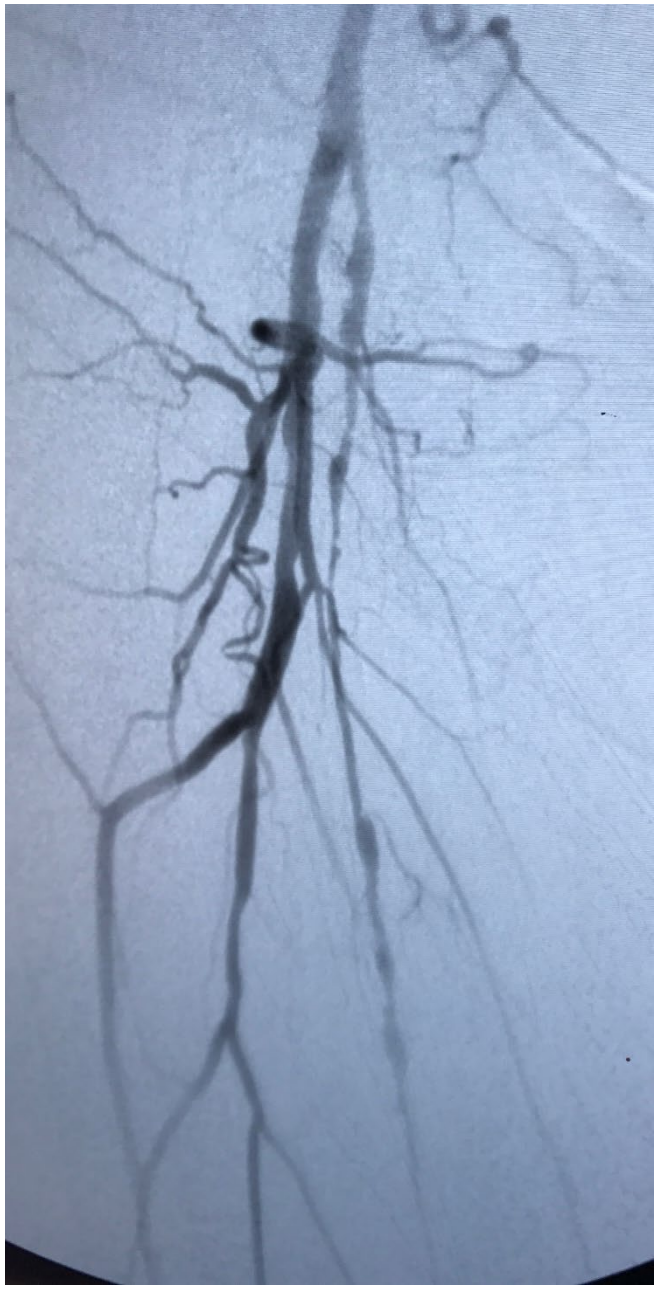
- Revascularization
  - Endovascular
    - Lower morbidity/mortality
    - Basil Trial: Amputation-free survival/overall survival lower after 2 yrs
  - Surgery
    - Superior long-term patency (especially if life expectancy >2 yrs)
    - Higher morbidity/mortality
    - Need vein conduit
    - Postoperative surveillance
- Amputation
  - Improved QoL
  - Useful in high-risk, poor revascularization candidates, extensive tissue loss, or bedridden, elderly, NH bound patients

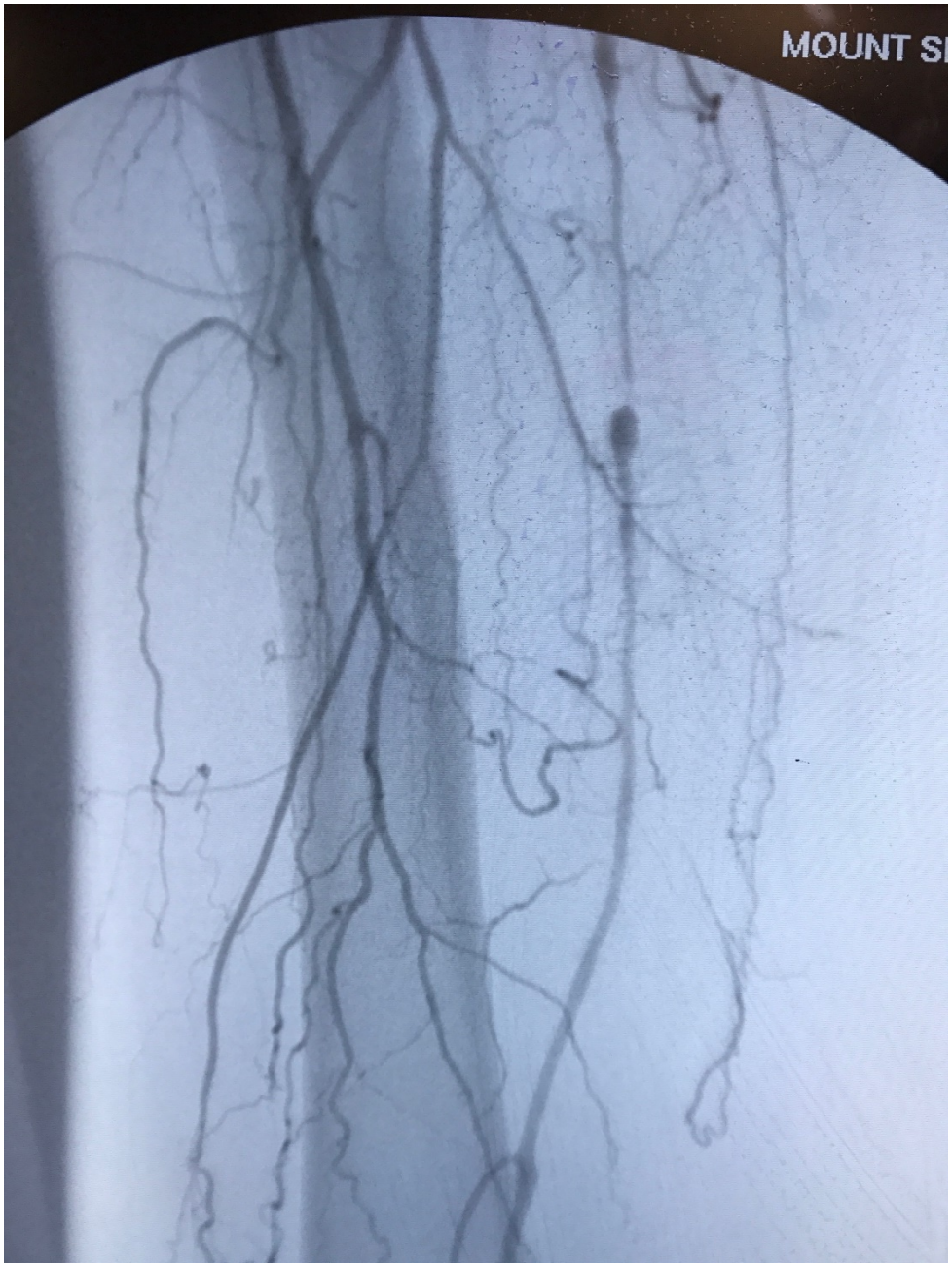
Endovascular Therapy for CLI







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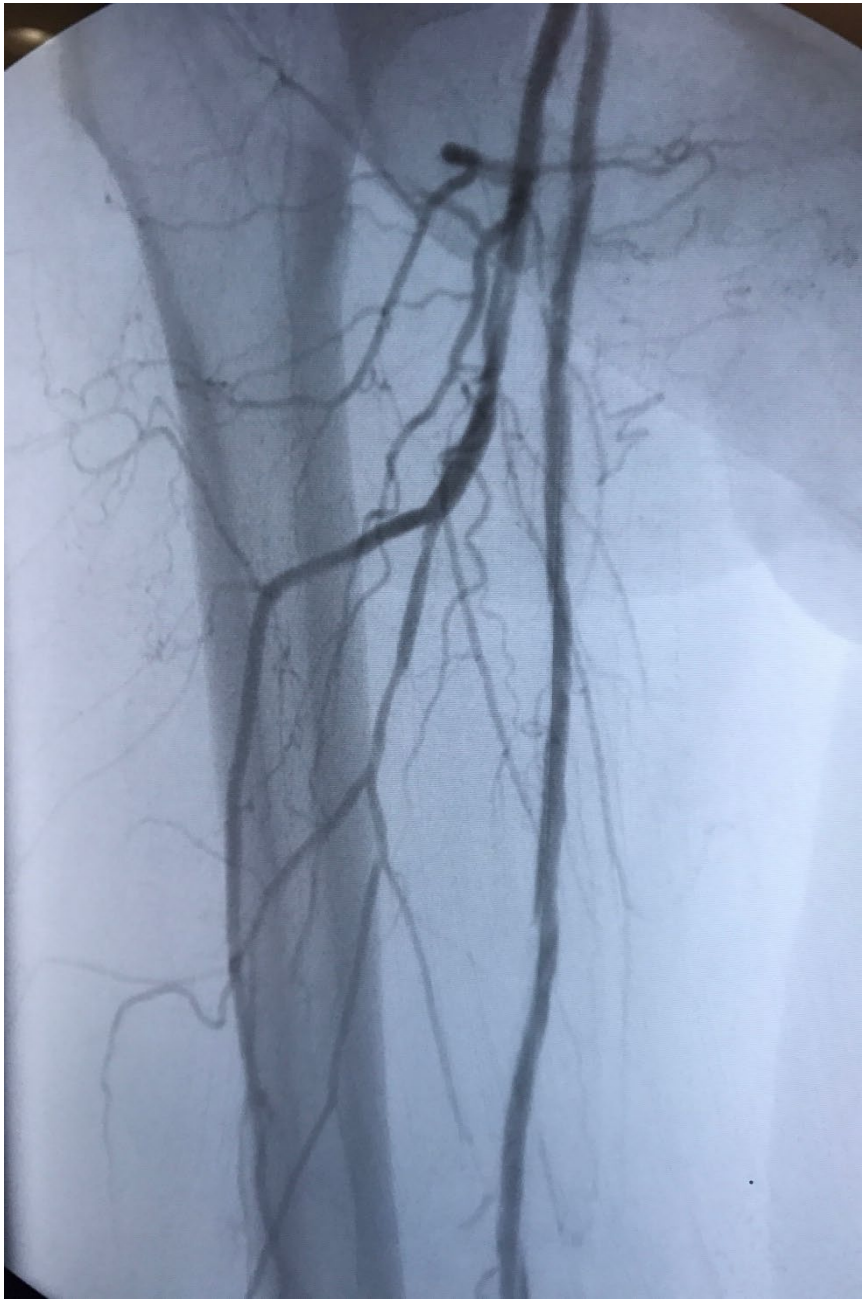
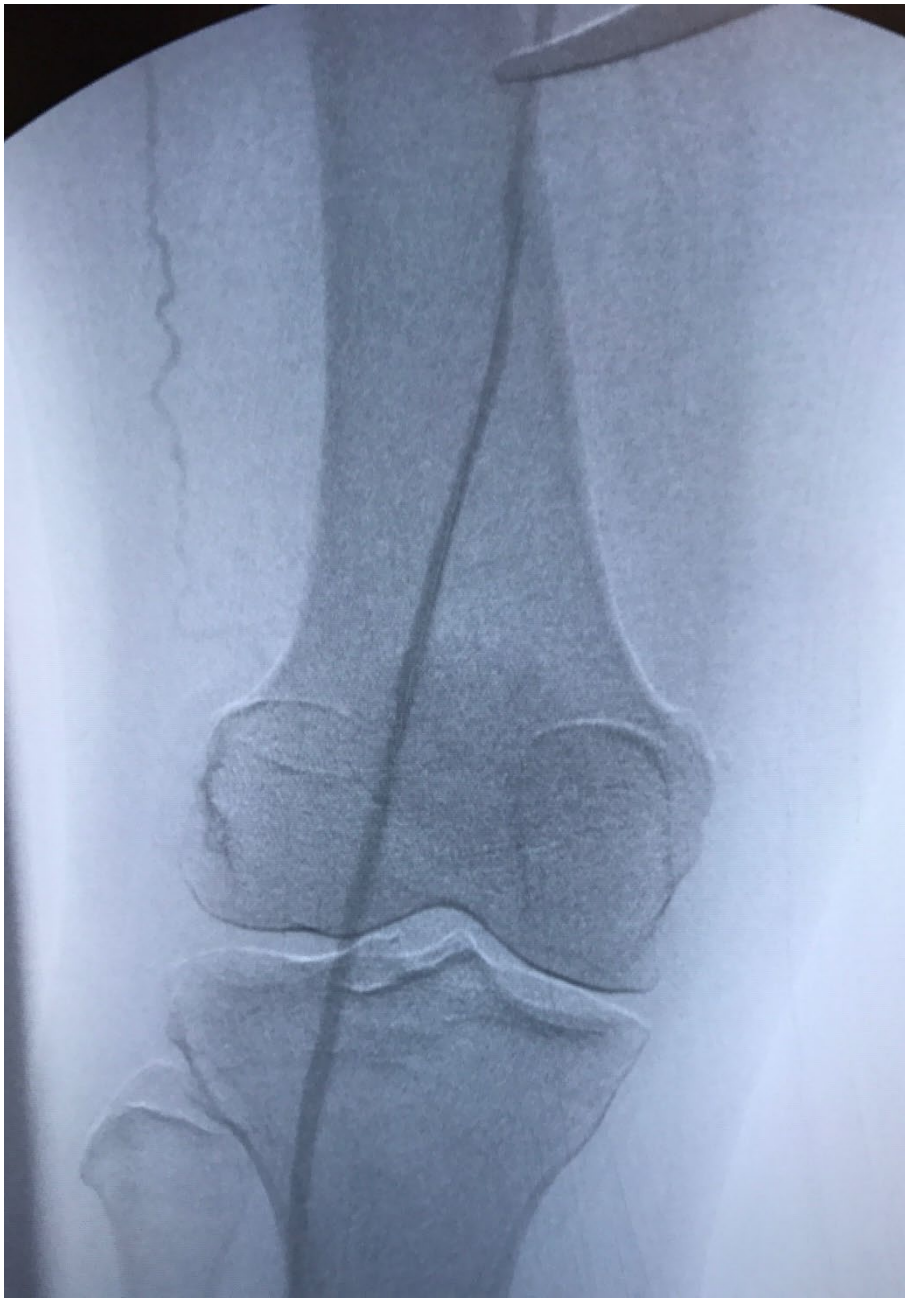
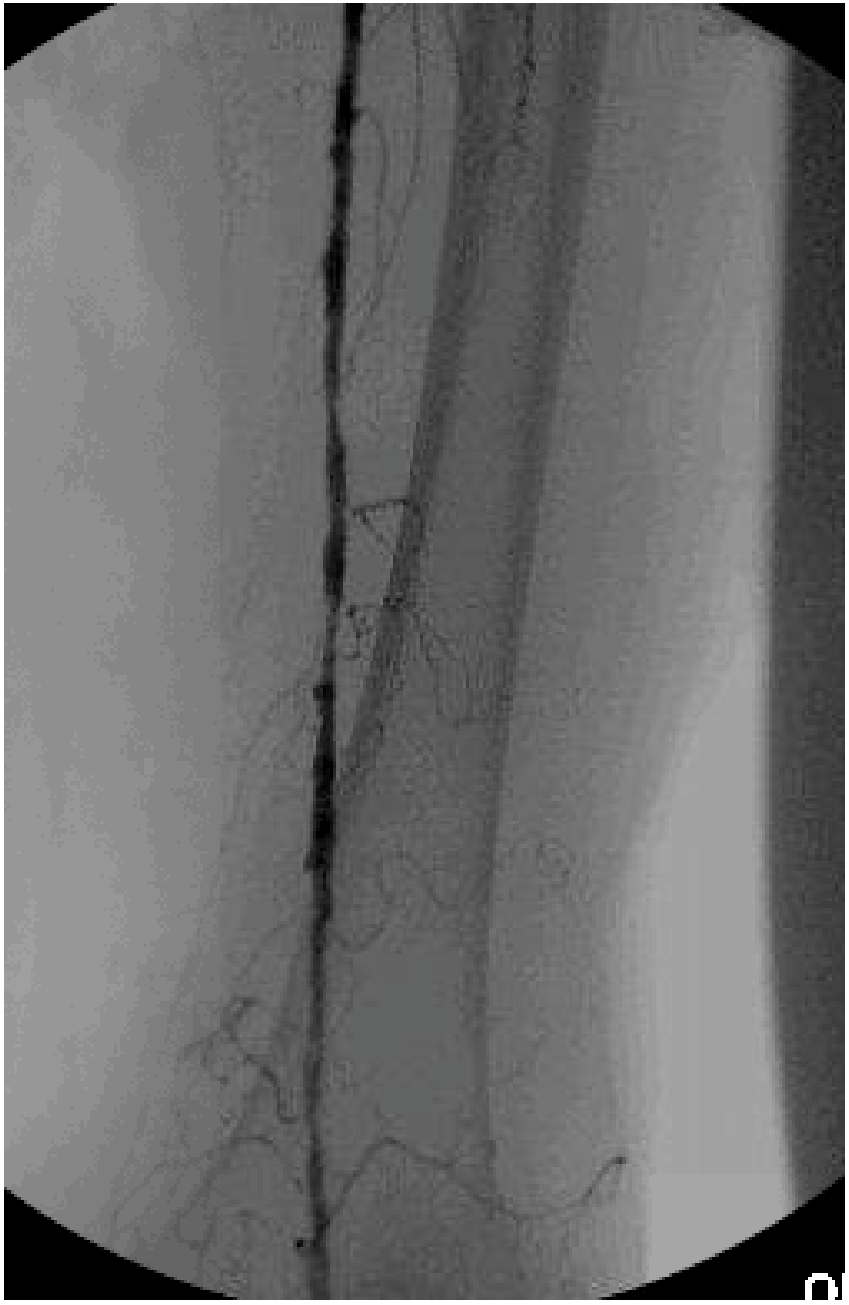
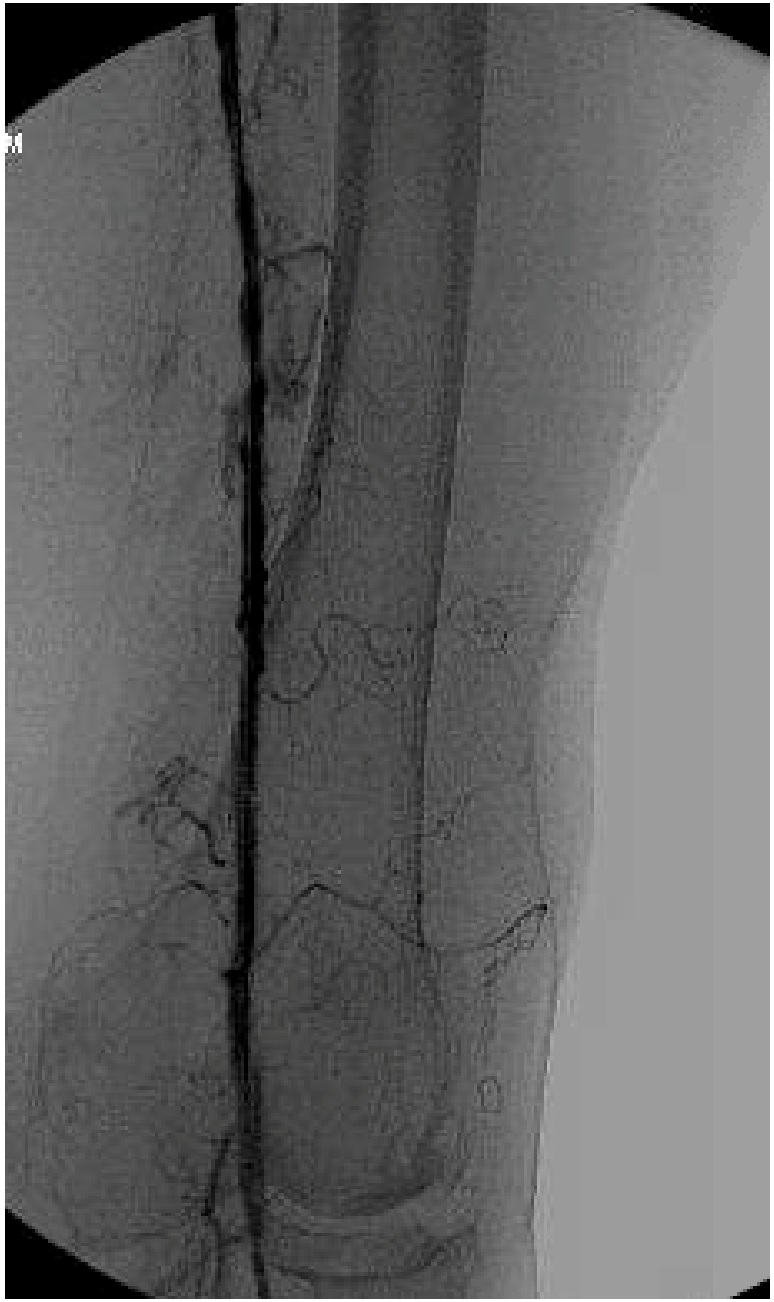
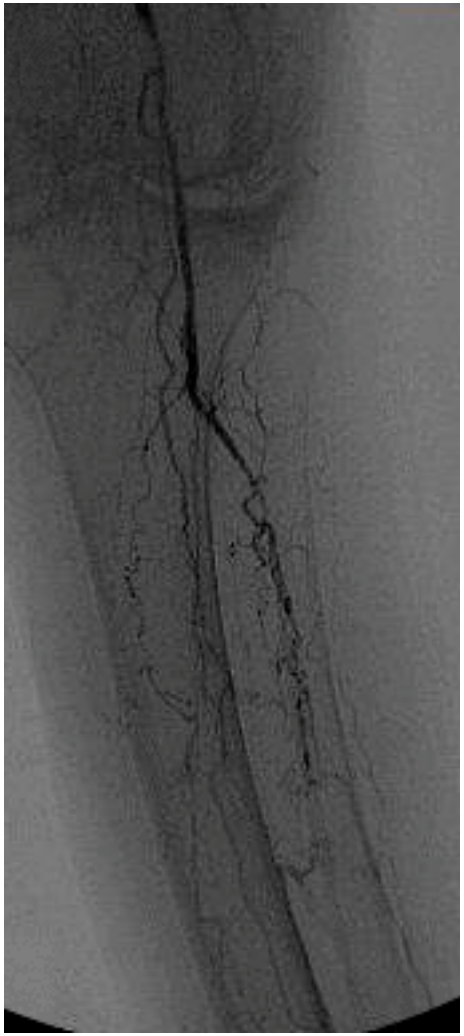


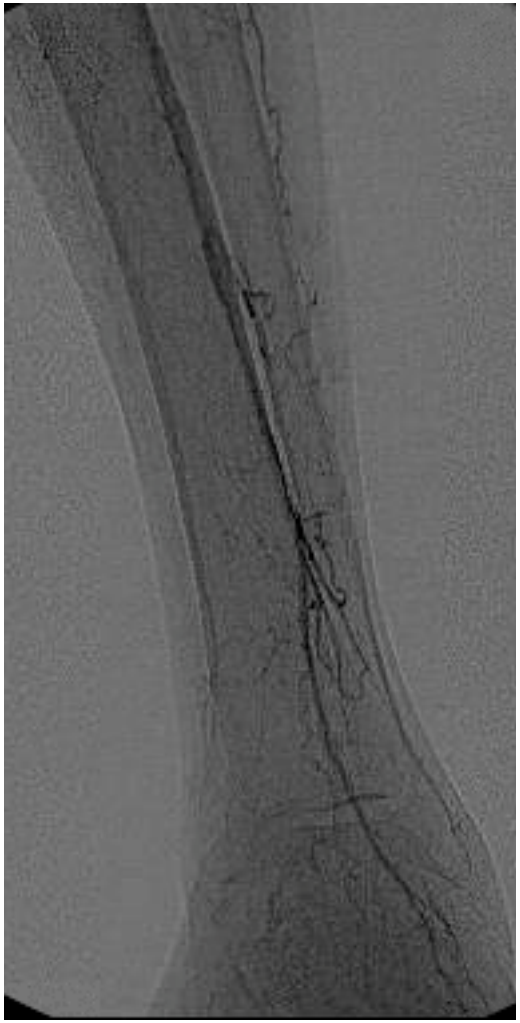


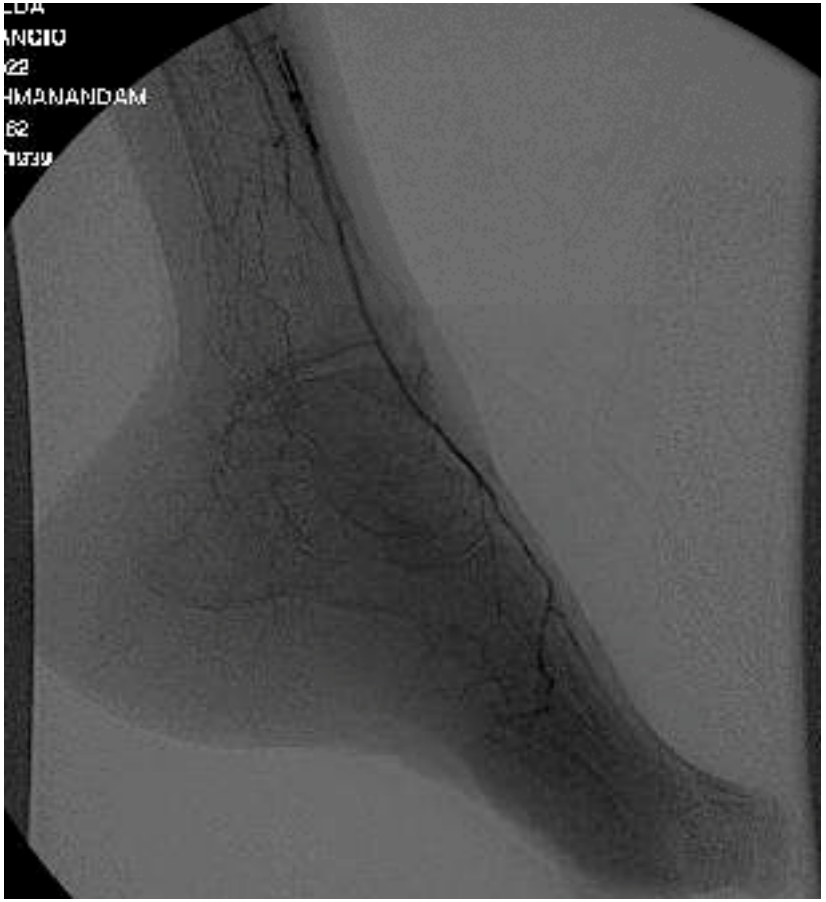
Hybrid Endovascular & Surgical Treatment of CLI







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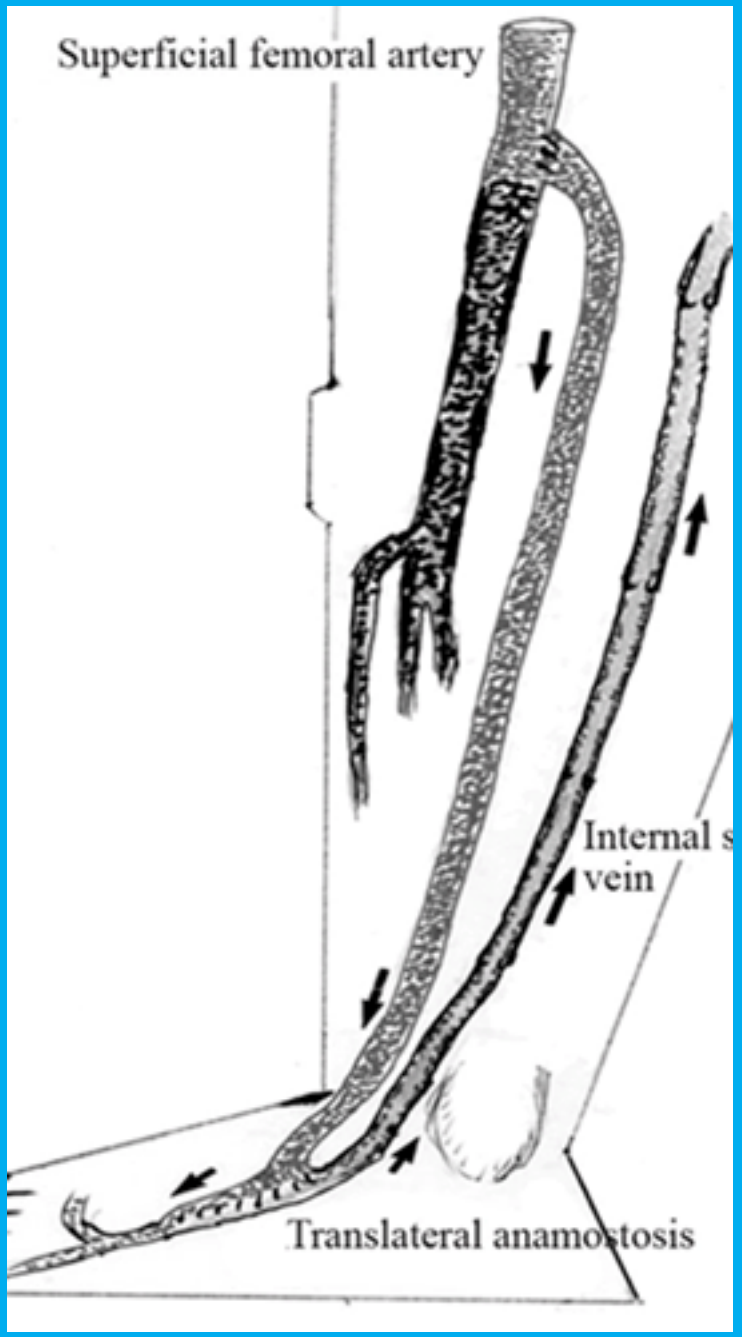
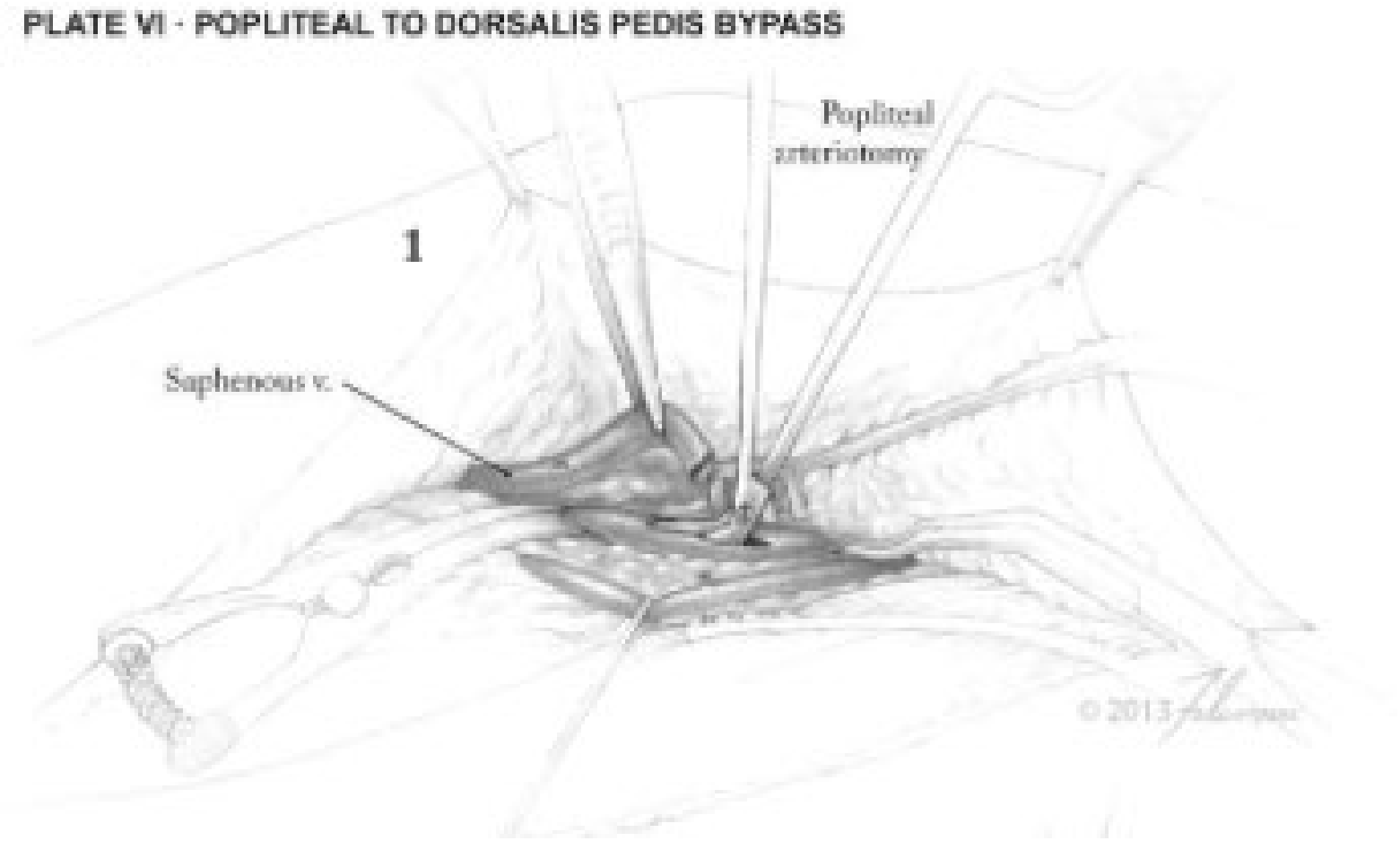
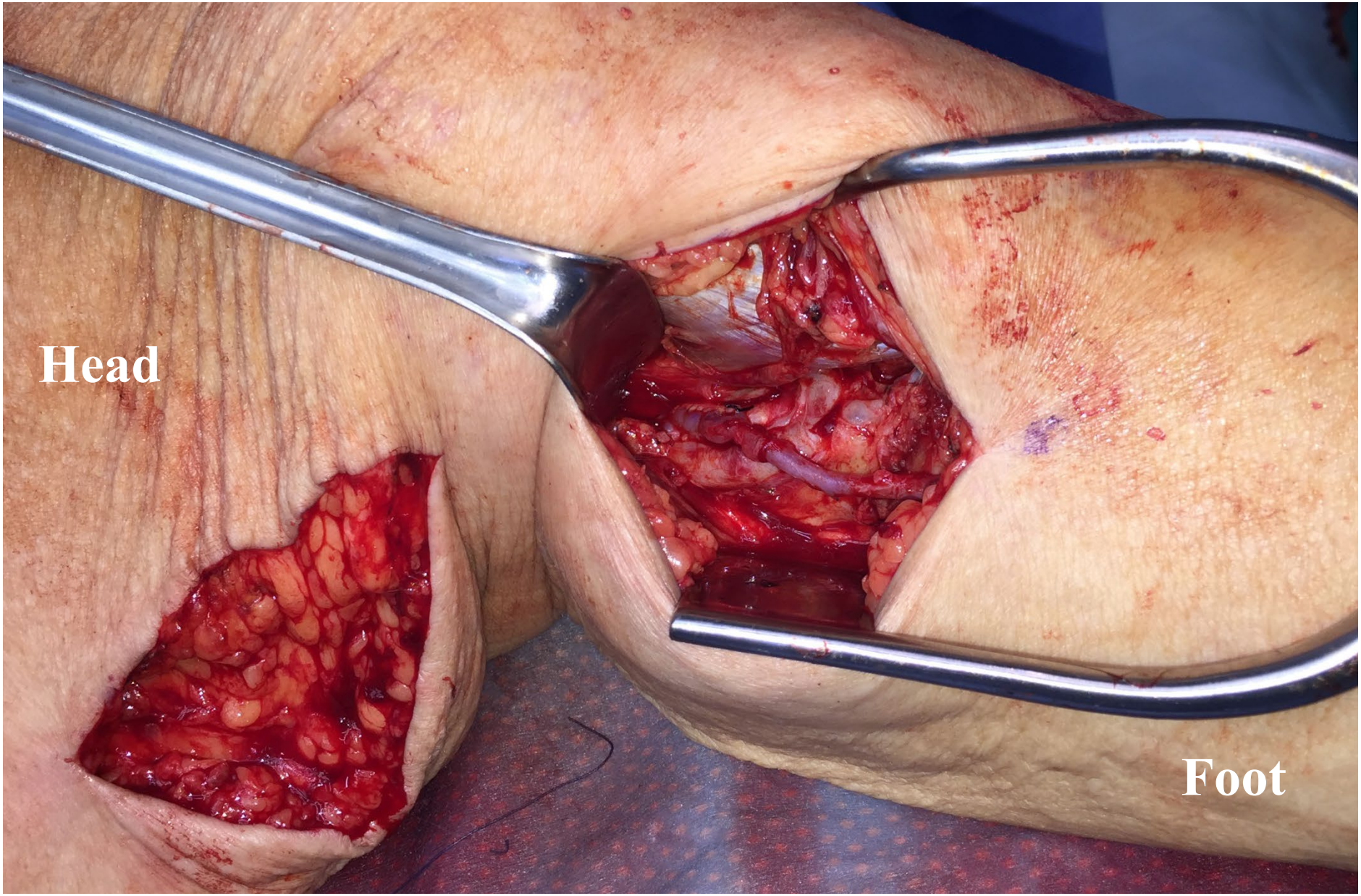
Infra-Popliteal Bypass



Popliteal Anastomosis

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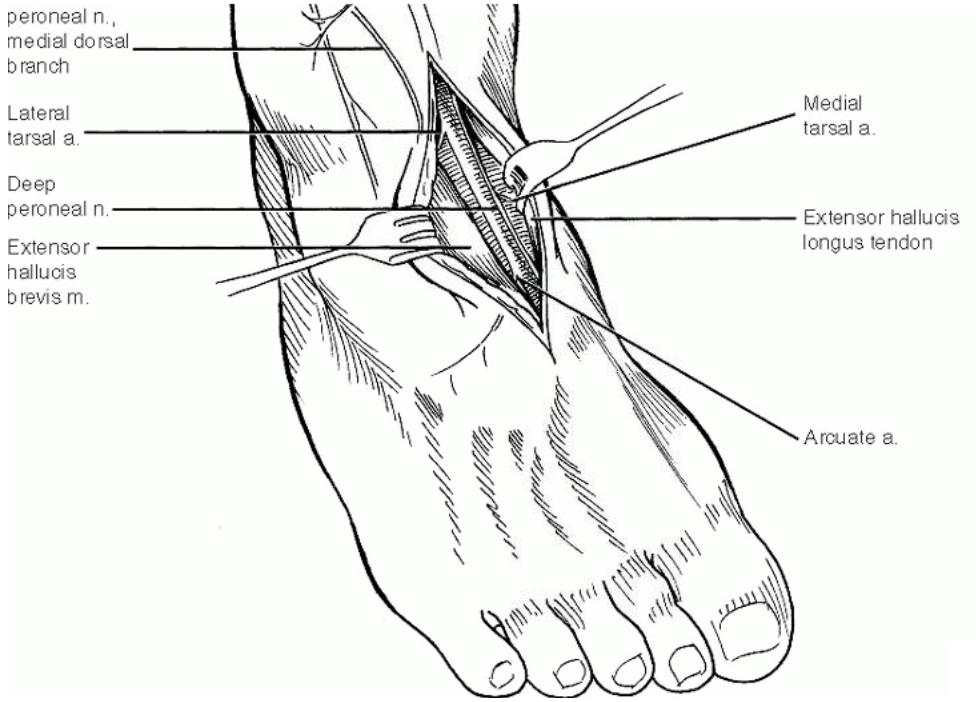
Dorsalis Pedis Anastomosis



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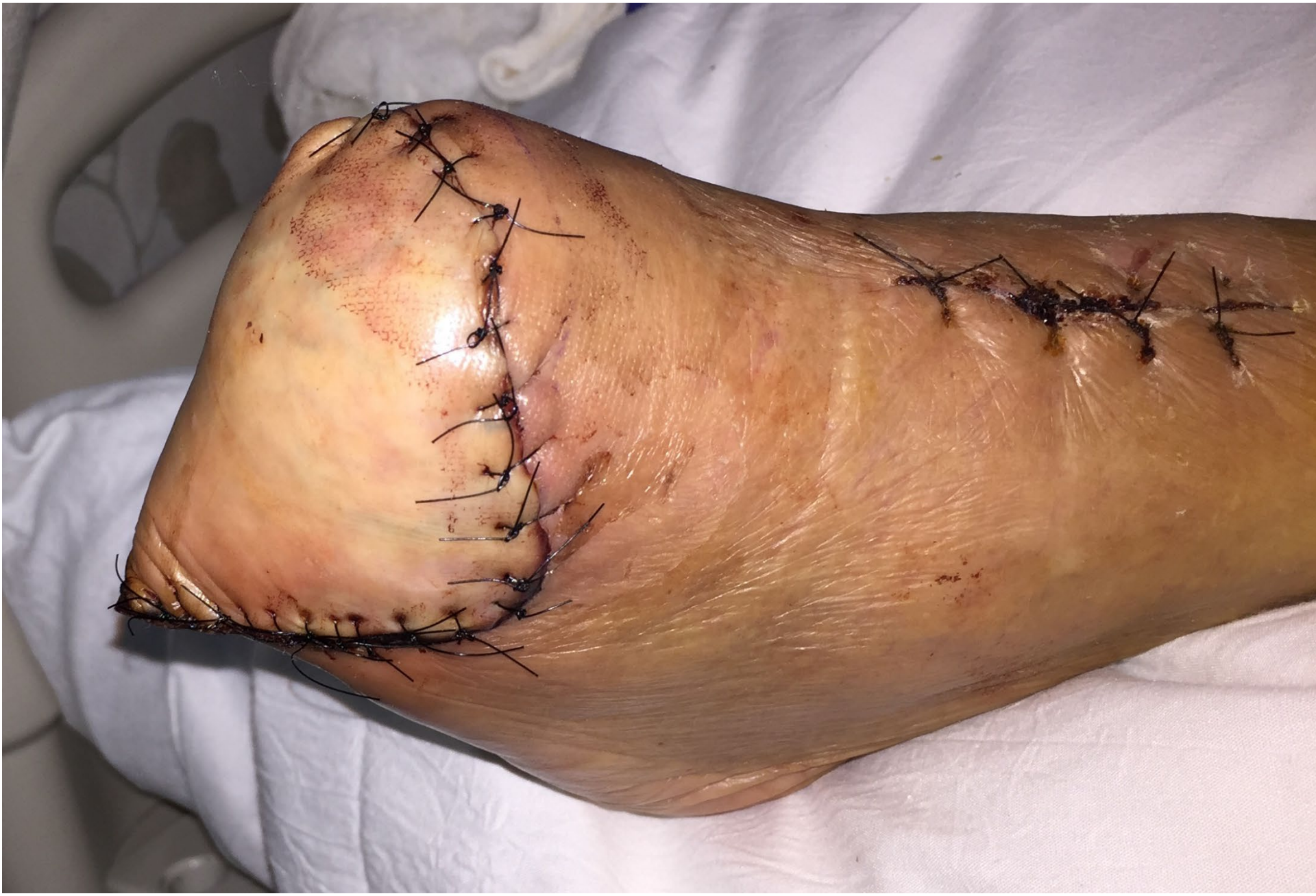
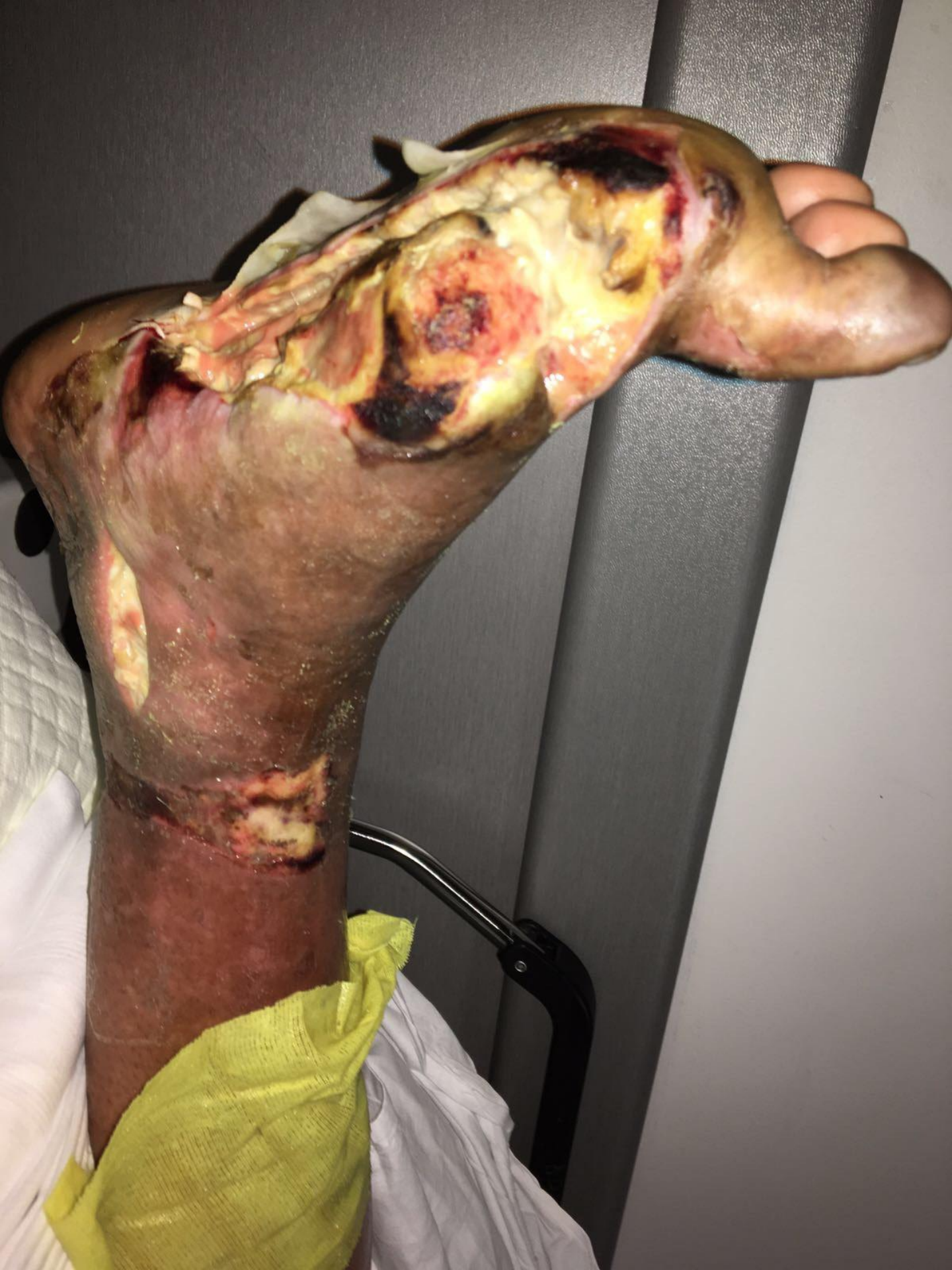
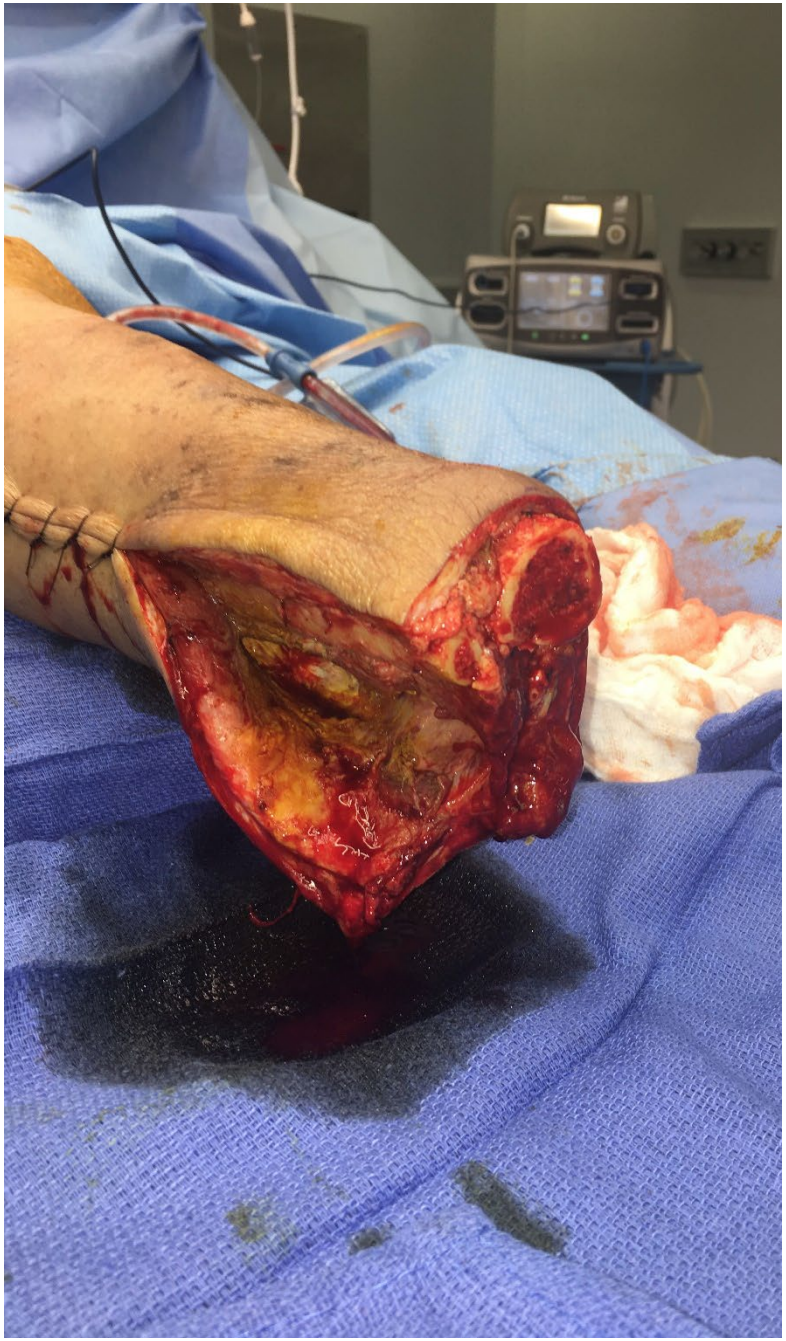
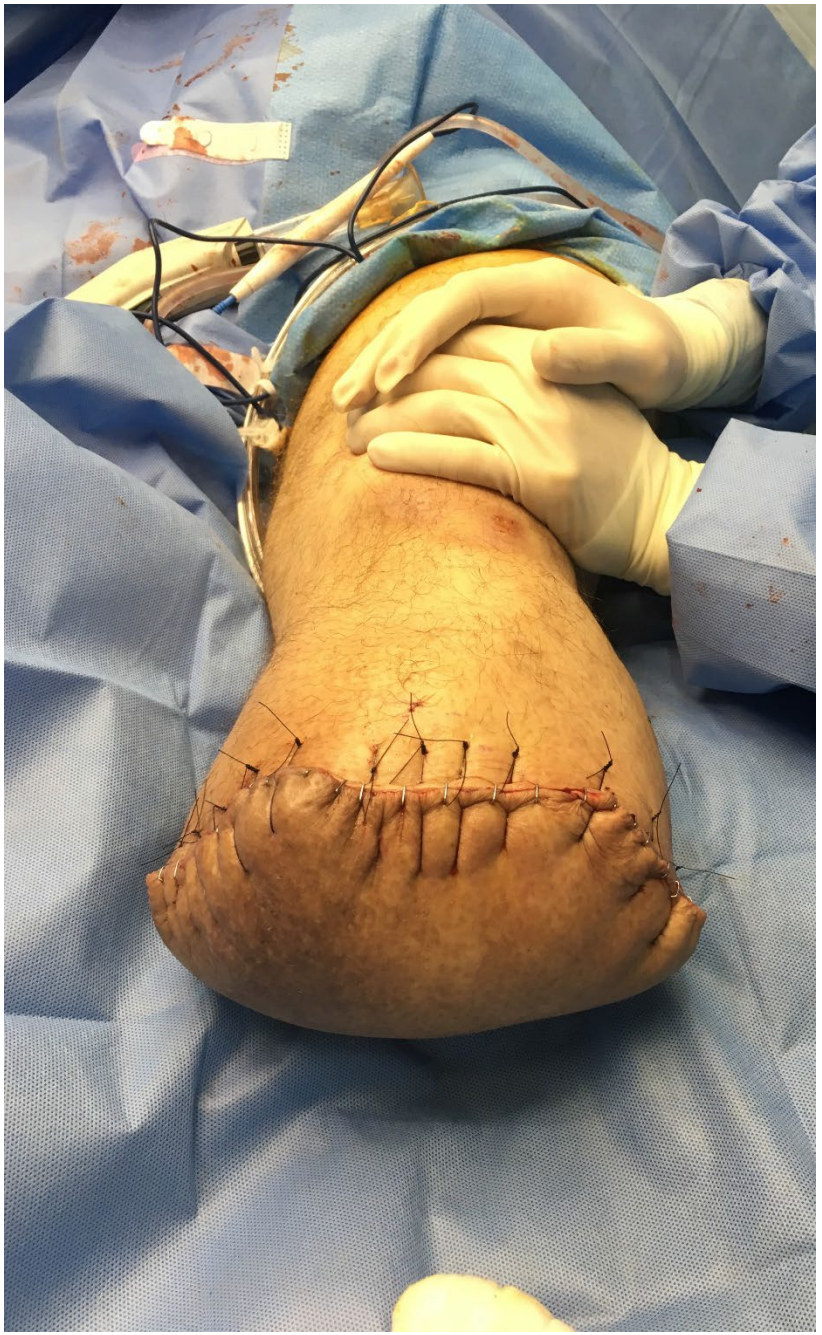


Amputation







Case Study

Case Study Scenario

65 year old male with history of well controlled type 2 diabetes, hypertension, hypercholesterolemia, with a history of non-ischemic cardiomyopathy causing HFrEf.

Has exertional right calf discomfort that only occurs while walking >/= 3 blocks and resolves after a 5 min rest. He does not experience rest pain. He recently recovered from an episode of acute heart failure. He currently smokes 1 ppd cigarettes with a 35 pack-year history. He has no history of excessive bleeding.

Medications include Coreg 25 mg BID, Lisinopril 20 mg daily, Atorvastatin 20 mg daily. He has no medication allergies.

His exam was significant for BP 146/86, P=60, diminished DP/PT pulses bilaterally, no ulcers, edema. Normal sensation and reflexes.
Labs included: Hgb 16, K=4.0, Cr 1.0. LDL 98. HbA1c 6.8%, Ankle Brachial Index is 1.5.

Appendix

Case Study Questions & Answers

1. **What is the recommended next step to confirm the diagnosis?**

   A. No additional testing is necessary as the ABI confirmed the diagnosis.

   B. Toe Brachial Index

   C. MRA of right lower extremity

   D. Angiography of right lower extremity

2. **The Toe Brachial Index was .60 on the right, 0.70 on the left. Which of the following are not appropriate treatment options:**

   A. Increase atorvastatin to 80 mg daily

   B. Titrate antihypertensive medications to achieve BP <130/80

   C. Add aspirin 81 mg daily and Rivaroxaban 2.5 mg twice daily

   D. Add cilostazol 100 mg twice a day

   E. Prescribe treatment to promote smoking cessation

3. **The patient notes that the claudication is significantly limiting his daily functioning and life quality. Which of the following are appropriate?**

   A. Prescribe pentoxifylline 400 mg three times daily
   B. Measure homocysteine levels and if elevated, treat with folic acid (5 mg daily)
   C. Refer patient for exercise therapy
   D. Refer patient to vascular surgery for consideration of revascularization
   E. All of the above
   F. C and D

Frontline Provider Excellence in Ambulatory Chronic Disease Management: COPD

David Steiger, MD

Chief Division of Pulmonary, Critical Care and Sleep Medicine

Mount Sinai Beth Israel and Mount Sinai West

Professor of Medicine

Icahn School of Medicine

September 21, 2021

Mount Sinai Health Partners

Outline

1. Diagnosis and Classification

2. Pharmacologic Management

3. Non-Pharmacologic Therapies and Comorbidities

Definition COPD

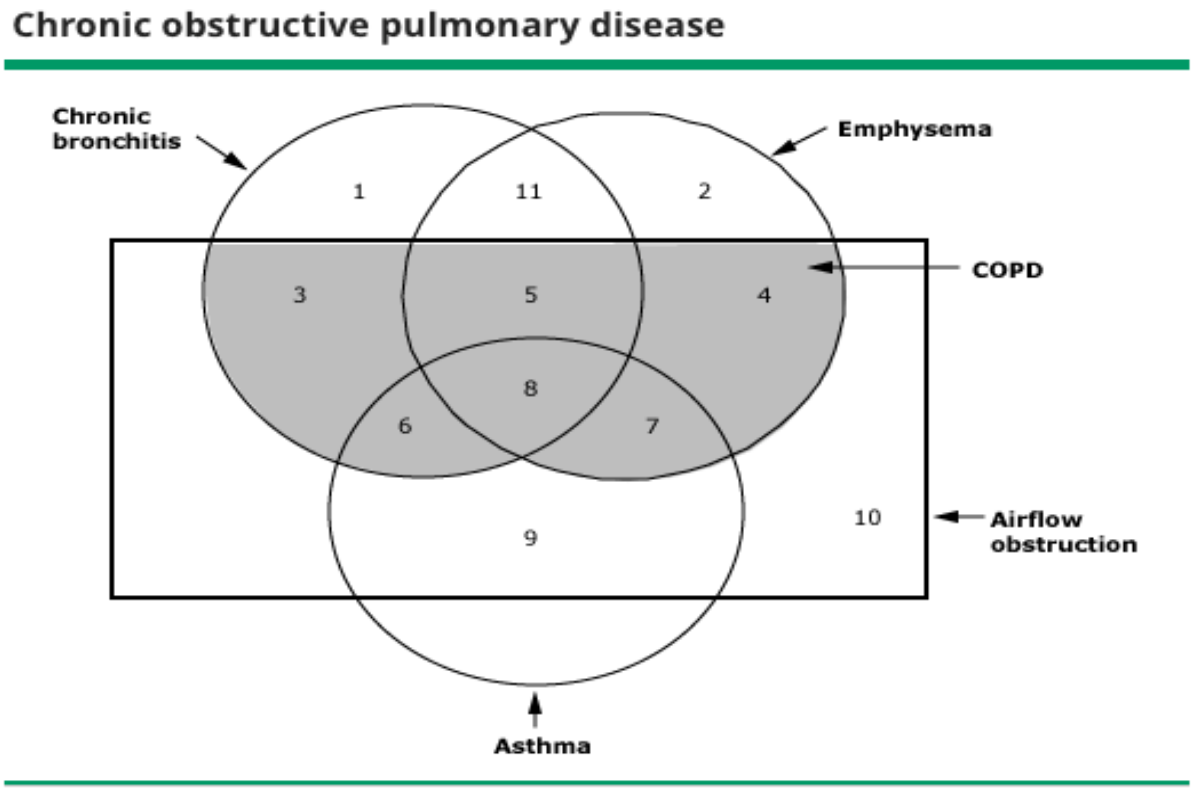
"COPD is a common, preventable and treatable disease that is characterized by ***persistent respiratory symptoms*** and ***airflow limitation*** that is due to airway and/or alveolar abnormalities ***usually caused by significant exposure*** to noxious particles or gases."

GOLD definition

Chronic airflow limitation:

- Small airways disease
- Parenchymal destruction (emphysema) – distal to terminal bronchioles

Interrelationships between Chronic Bronchitis, Emphysema, and Asthma



9	Asthma, reversible OAD
6,7,8	Asthma, partial reversibility
5	CB and emphysema
1,2,11	CB and emphysema without airway obstruction – do not have COPD by definition
10	Airway obstruction, without asthma, COPD, emphysema – e.g. CF

Asthma-COPD Overlap “persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD.”

COPD Epidemiology

- **14 million** patients have COPD in the US, > 5% population U.S. [1]
- **Fourth** leading cause of death in U.S. [2]
- May be underdiagnosed; **24 million** have obstruction on spirometry in a population-based survey [3]
- (20% patients with severe OAD do not report symptoms)

High cost-burden

- 8 million office visits, 1.5 million ED visits
- 715,000 hospitalizations, chronic medication usage
- $50 billion annually in spending [4,5]

1. Ford E et al. Chest, 2013. 144(1): p. 284-305.
2. Hoyert et al. Natl Vital Stat Rep 2011; 61(6): 1-65.
3. Mannino DM et al. MMWR Surveill Summ. 2002; 51(6):1–16.
4. Centers for Disease Control and Prevention; National Center for Health Statistics. 2010
5. Guarascio AJ et al. CEOR 2013; 5: 235-45.

COPD Pathogenesis

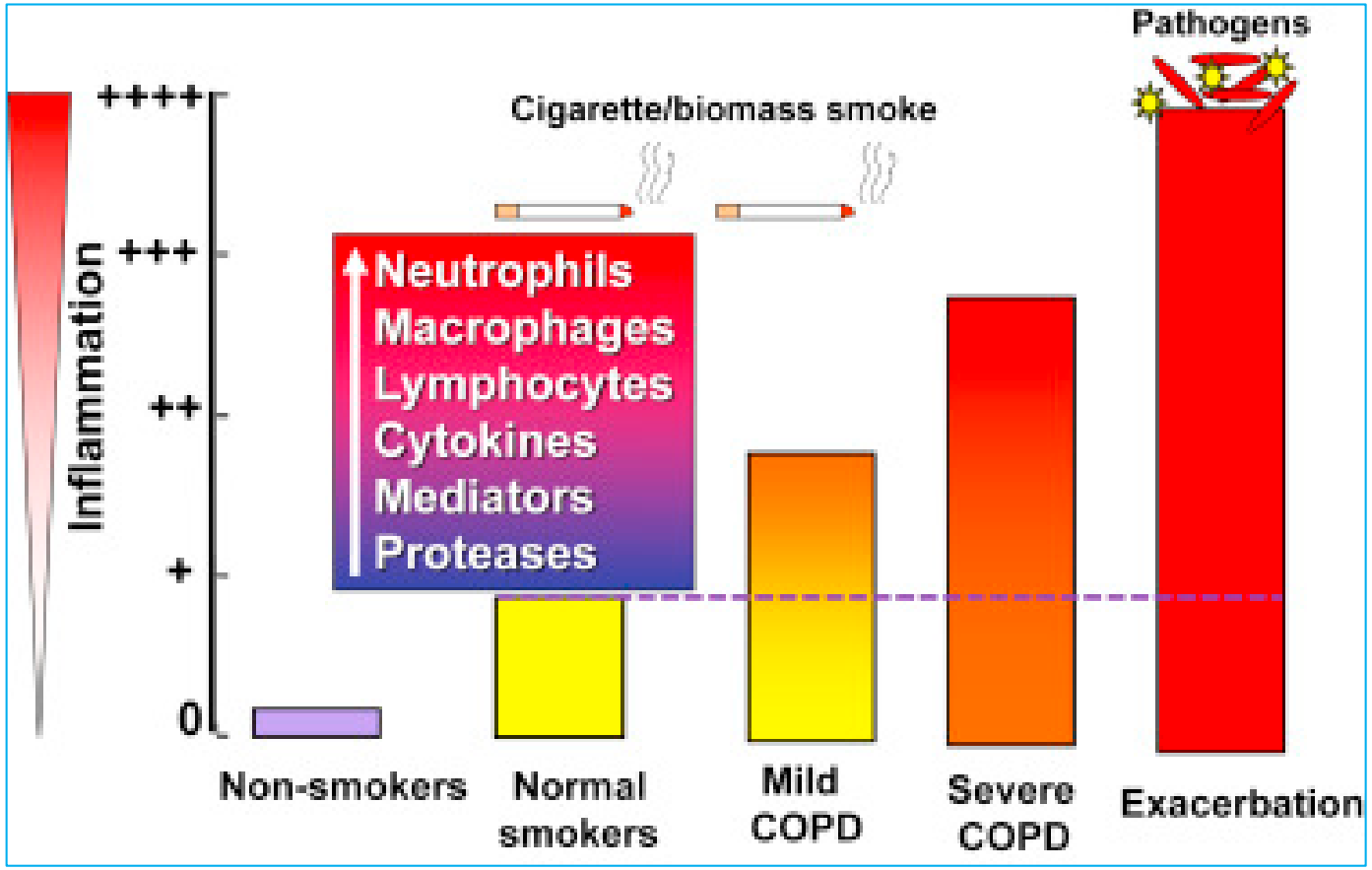
- Tobacco smoke results in airway inflammation involving **innate** (neutrophils, macrophages) and **adaptive** immune responses (Th1 mediated)

- Some patients have eosinophilic inflammation (Th2 mediated) which may lead to increased steroid responsiveness. (Asthma/COPD overlap)

- Pro-inflammatory mediators and oxidative stress in response to cigarette smoke, or released from neutrophils, macrophages, potentiating inflammation:
  - Small airway narrowing:
    - Peribronchiolar fibrosis
    - Mucosal/submucosal thickening from smooth muscle
    - Hypertrophy and mucus gland enlargement
    - Intraluminal exudate/mucus
  - Proteolytic destruction of the lung (emphysema)
    - Neutrophil elastase, MMP's

Small airway disease precedes development of emphysema

Inflammation Secondary to Cigarette Smoke, Biomass, Second Hand Smoke

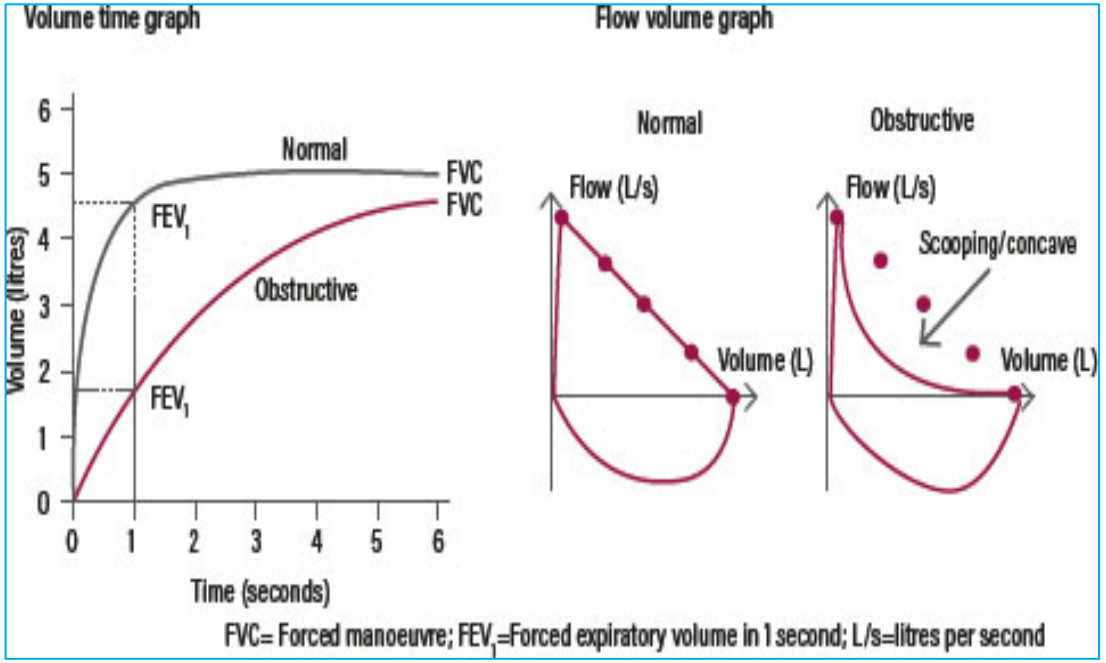


Only 20% smokers develop COPD
Inflammation persists despite smoking cessation

Barnes PJ. J Allergy Clin Immunol. 2016 Jul;138(1):16-27

COPD: Spirometric Assessment: Pre and Post Bronchodilator

- Persistent airflow limitation: post-bronchodilator FEV1/FVC ratio < 70%
- **Not indicated** if no significant exposures,
- Or asymptomatic
- **Indicated:** symptoms/risk factors
- FEV1 and FVC predict all cause mortality
- Predicts increased risk of lung cancer
- Utility of Spirometry
  - Airflow severity
  - Response to medication
  - Follow disease progression



1. National Committee for Quality Assurance. http://www.ncqa.org/ReportCards/HealthPlans/StateofHealthCareQuality.aspx. Accessed February 5, 2020.

Rush. Primary Health Care. 2017 (28)2, 34-41. Imaged Accessed at https://dm3omg1n1n7zx.cloudfront.net/rcni/static/journals/phc/28/2/phc.2018.e1367/graphic/phc_v28_n2_21_0005.jpg Accessed February 5, 2020

COPD: Spirometric Stage

CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV_1)

In patients with FEV1/FVC < 0.70:

GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

TABLE 2.4

COPD: Beyond Spirometry

- COPD severity is an interplay of:
  - Lung function,
  - Symptom burden
  - Exacerbation history

- Lung function correlates weakly with symptom burden [1].

- Dyspnea and high symptom burden are independent risk factor for mortality [2-3]

- Assessment of symptoms:
  - SGRQ, CRQ, COPD Assessment Test (CAT)

1. Mahler DA. Chest 1984;85:751-758
2. Nishimura K. Chest 2002;121:1434-1440
3. Domingo-Salvany A. Am J Respir Crit Care Med 2002;166:680-685

MODIFIED MRC DYSPNEA SCALE[a]

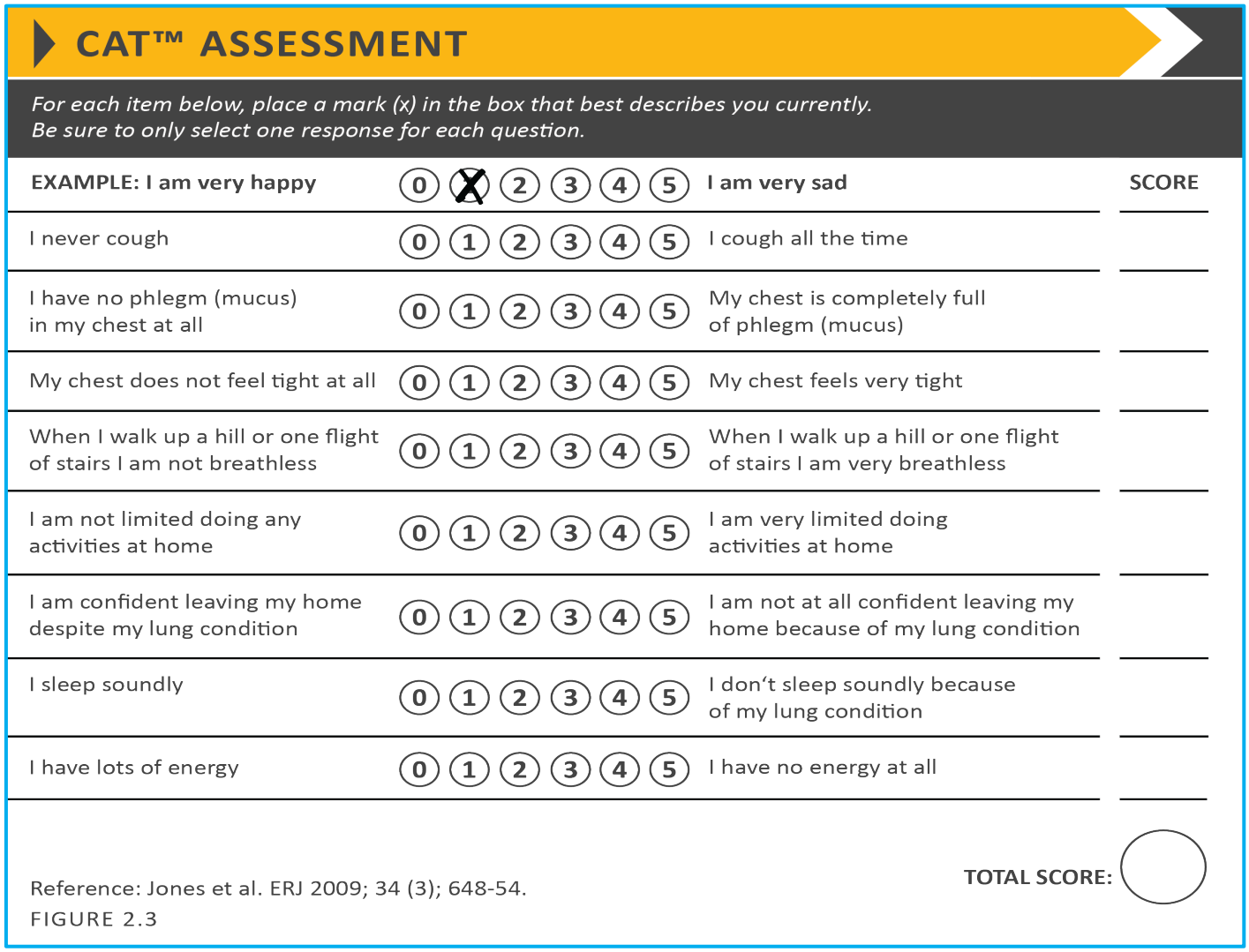
PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

MMRC correlates with health status, predicts future mortality



CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 **X** 2 3 4 5	**I am very sad**	**SCORE**
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don‘t sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

TOTAL SCORE:

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

FIGURE 2.3

CAT is a validated test for evaluation of impact of COPD on health status
Higher scores correlate with FEV1

COPD: Exacerbations

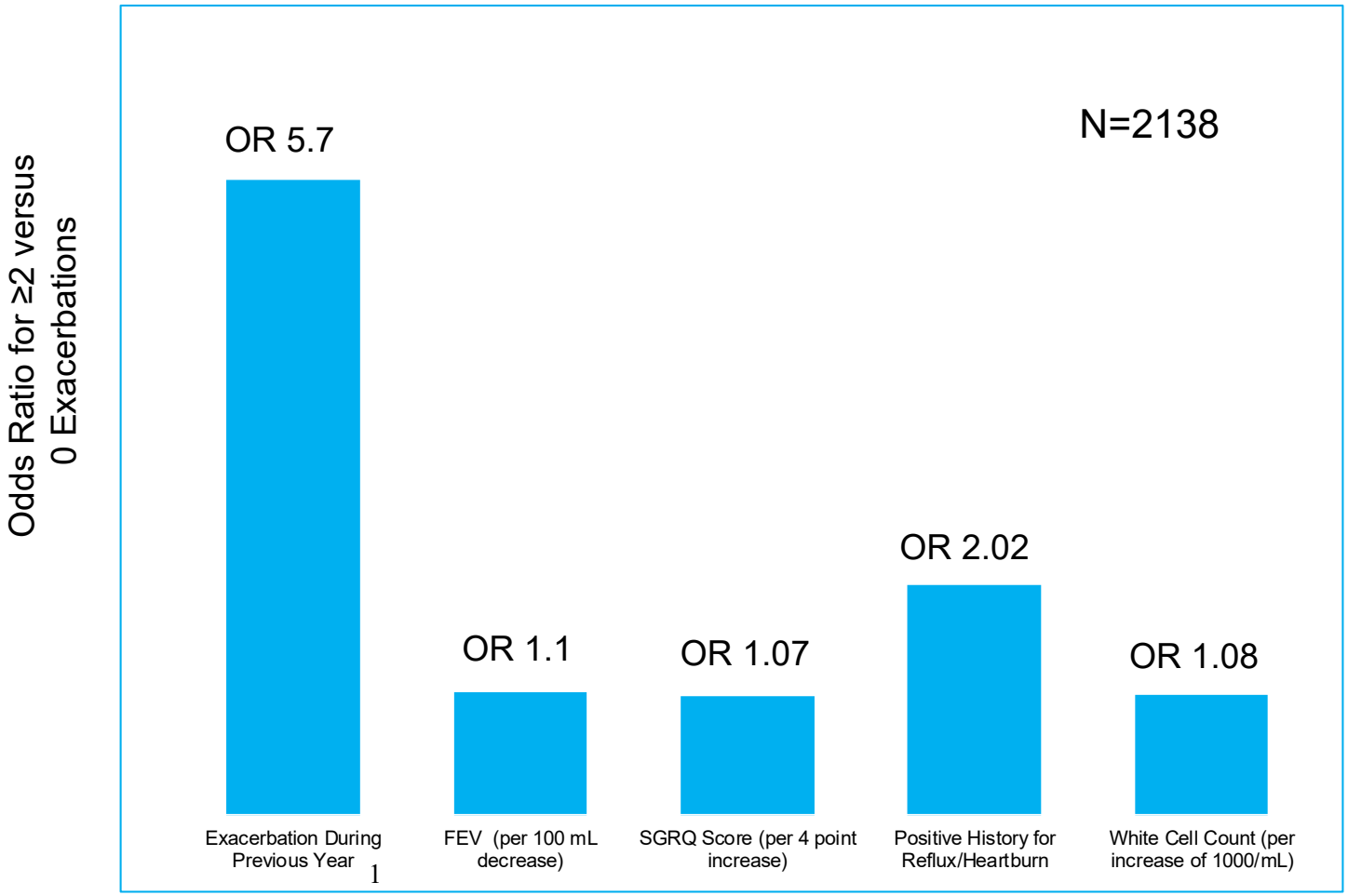
- Defined as any change in symptoms requiring additional therapy [1]

- At least 2 consecutive days of at least 2 major criteria, or 1 major and 1 minor criteria [2]
  - **Mild exacerbation**: treated with bronchodilators only
  - **Moderate exacerbation**: treated with steroids and antibiotics
  - **Severe exacerbation**: any exacerbation requiring ED visit or hospitalization

Major Criteria	Minor Criteria
Increased sputum volume	Wheezing
Sputum purulence	Sore throat
Dyspnea	Nasal congestion
	Cough

1. Global Initiative for Chronic Obstructive Lung Diseases. 2020.
2. Seemungal TA et al. Am J Respir Crit Care Med, 2000.161(5): 1608-13.

Factors Associated With Increased Exacerbation Frequency (ECLIPSE)



Hurst JR, et al. N Engl J Med. 2010;363:1128-1138.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 12, 2016 VOL. 374 NO. 19

Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function

- Many smokers have nl FEV1/FVC but are symptomatic
- Observational study 2736 current/former smokers
- Symptoms: CAT score, 0-40

Results

Respiratory symptoms present 50% patients with nl spirometry

In patients with nl spirometry:

- Respiratory symptoms associated with increased risk of:
  - Exacerbations VS patients without symptoms
  - Emphysema

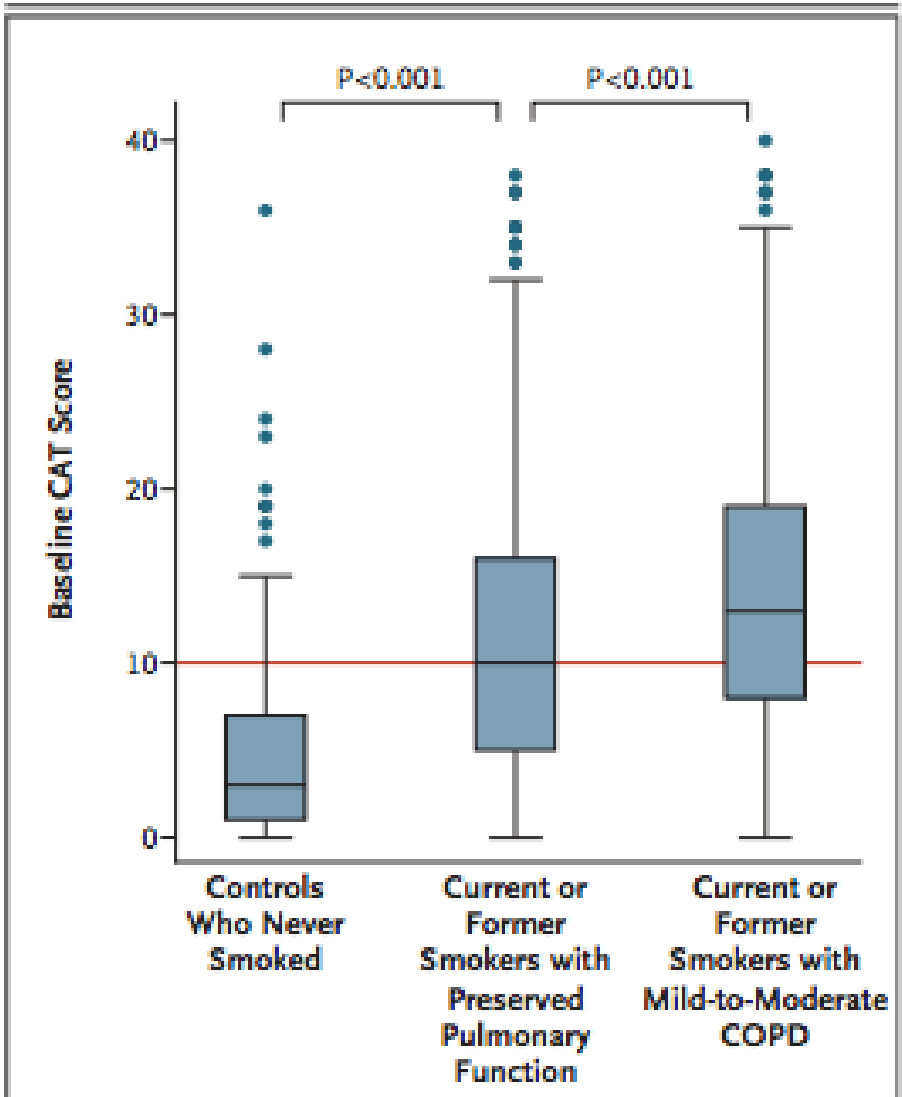


Figure 1. Prevalence of Respiratory Symptoms, According to Study Group.

The New England Journal of Medicine, May 12, 2016

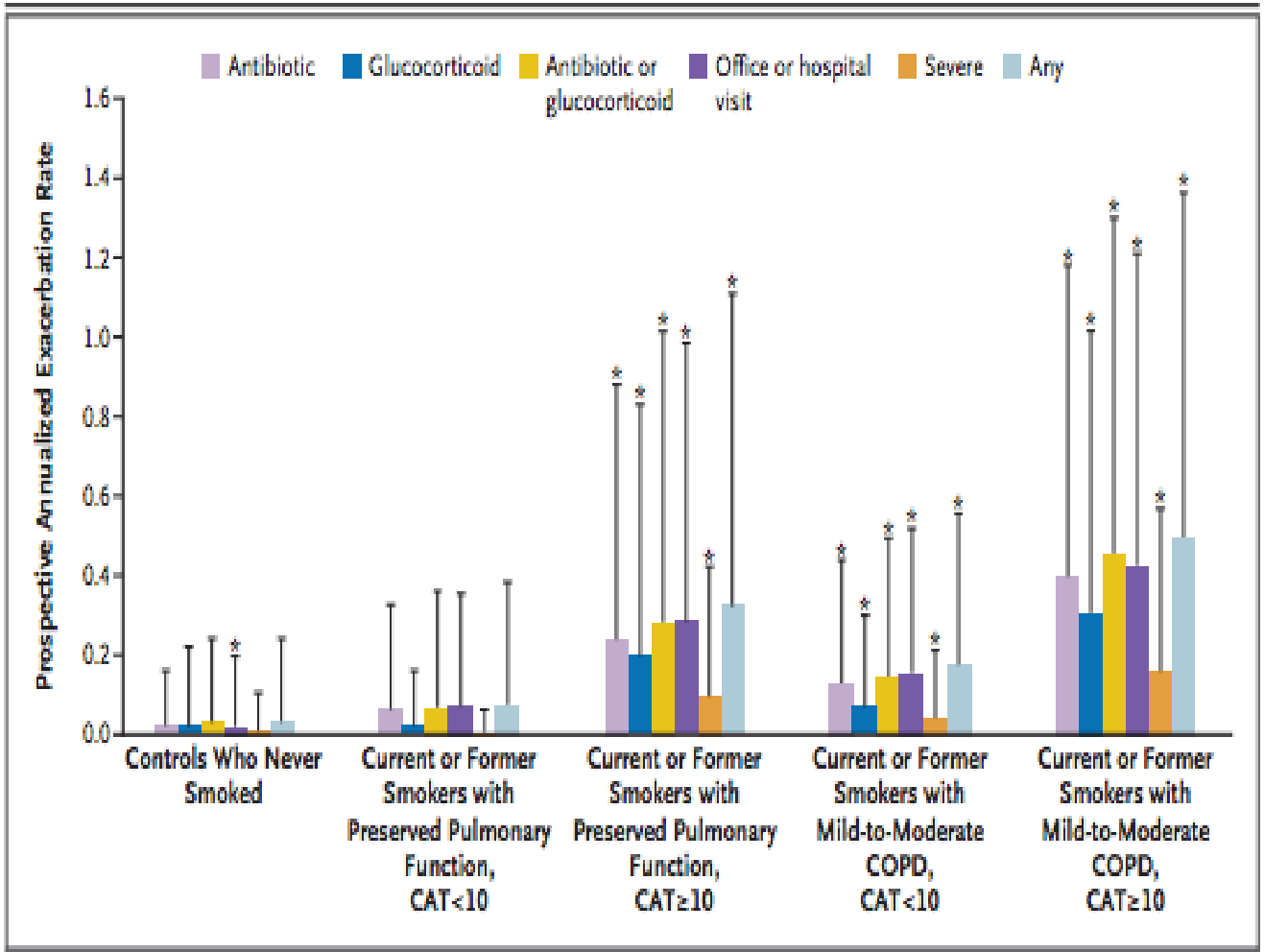


Figure 2. Prevalence of Symptoms and Risk of Respiratory Exacerbations, According to Study Group.

The New England Journal of Medicine, May 12, 2016

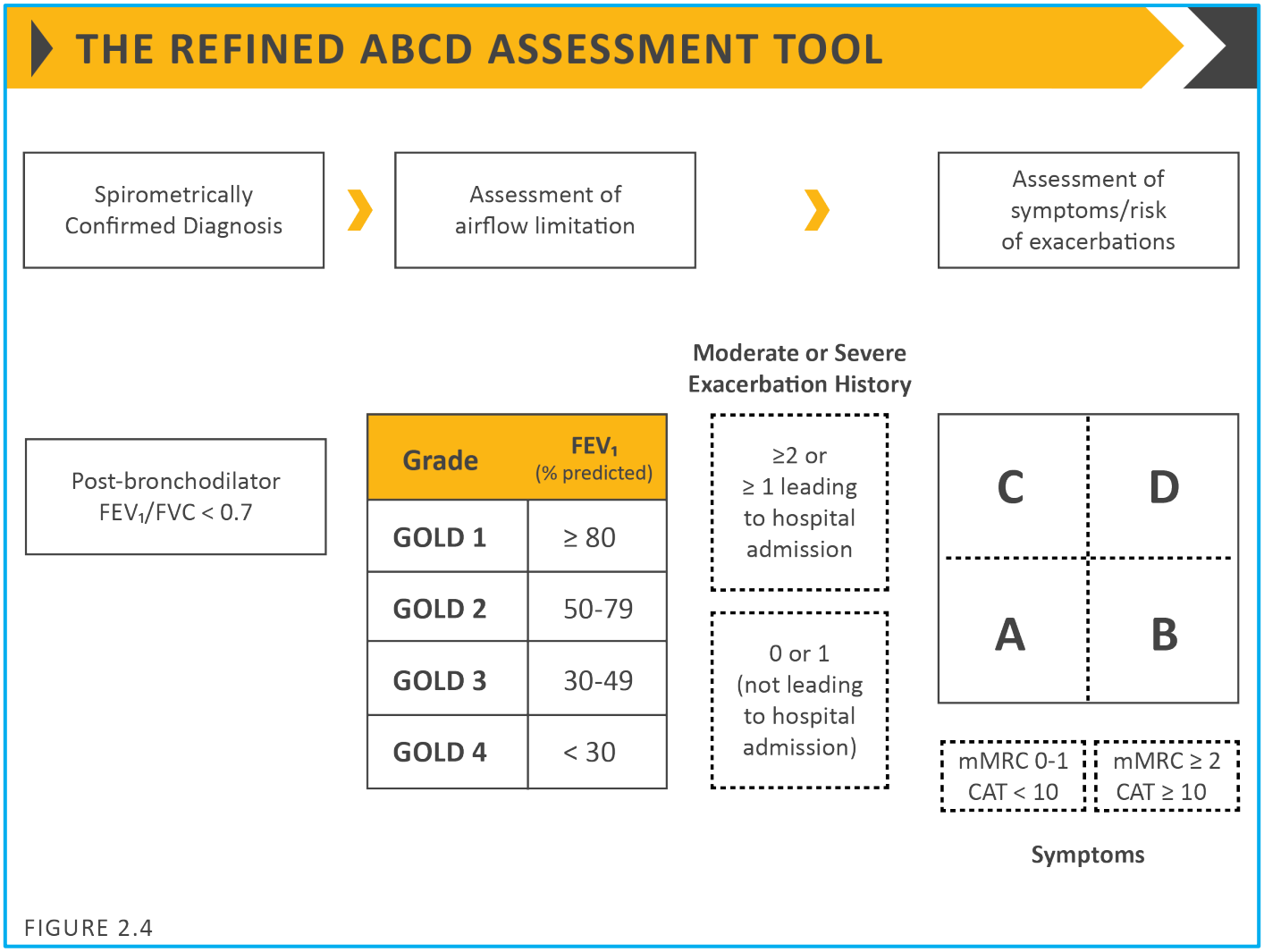


FIGURE 2.4

Impact of COPD combining symptomatology, spirometry, risk of exacerbations

Although FEV1 predicts mortality and hospitalization risk at population level
At individual level, FEV1 predictive power less precise

A Personalized Approach to Diagnosing COPD

- Management is determined by ABCD group, not spirometric stage
- If discordance between FEV1 and symptoms, assess with full set PFT's, CT, comorbidities (eg CHF)
- Patients may have near nl FEV1 but severe symptoms (eg. CVS disease, CHF, PH)
- Patients may have very low FEV1 but minimal symptoms

DIFFERENTIAL DIAGNOSIS OF COPD

Diagnosis	Suggestive Features
COPD	Onset in mid-life. Symptoms slowly progressive. History of tobacco smoking or exposure to other types of smoke.
Asthma	Onset early in life (often childhood). Symptoms vary widely from day to day. Symptoms worse at night/early morning. Allergy, rhinitis, and/or eczema also present. Family history of asthma. Obesity coexistence.
Congestive Heart Failure	Chest X-ray shows dilated heart, pulmonary edema. Pulmonary function tests indicate volume restriction, not airflow limitation.
Bronchiectasis	Large volumes of purulent sputum. Commonly associated with bacterial infection. Chest X-ray/CT shows bronchial dilation, bronchial wall thickening.
Tuberculosis	Onset all ages. Chest X-ray shows lung infiltrate. Microbiological confirmation. High local prevalence of tuberculosis.
Obliterative Bronchiolitis	Onset at younger age, nonsmokers. May have history of rheumatoid arthritis or acute fume exposure. Seen after lung or bone marrow transplantation. CT on expiration shows hypodense areas.
Diffuse Panbronchiolitis	Predominantly seen in patients of Asian descent. Most patients are male and nonsmokers. Almost all have chronic sinusitis. Chest X-ray and HRCT show diffuse small centrilobular nodular opacities and hyperinflation.

COPD: Pharmacologic Management

Key Principles

1. Modes of Delivery of Inhaled Devices
2. Initial Pharmacologic Delivery
3. Dose Escalation
4. De-escalating Therapy if Appropriate
5. Oral Medications

Pharmacologic Therapy

- **4 Types of Inhaled Devices**
  - Pressurized Metered Dose Inhaler (MDI)
  - Soft Mist Inhaler (SMI)
  - Dry Powder Inhaler (DPI)
  - Nebulizer

- **3 Classes of Drugs**
  - Beta-Agonists
  - Muscarinic Antagonists
  - Inhaled corticosteroids

Types of Inhaler Devices

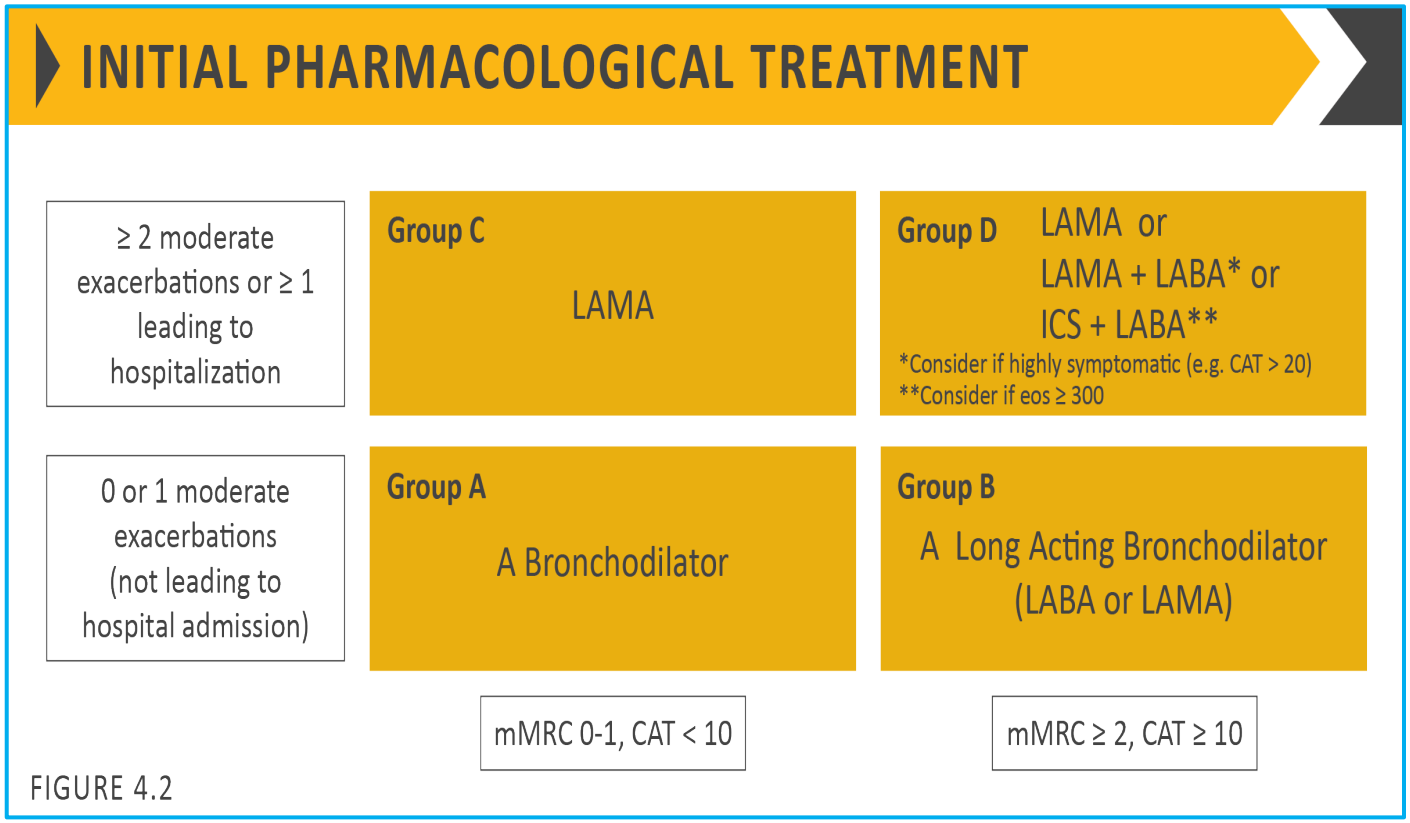
- Metered Dose Inhaler (MDI)
  - **Advantages:** Multiple doses (≥100/inhaler), compact, portable, available for most inhaled medicines, short administration time, low cost, and can be used with a “spacer”
  - **Disadvantages:** Requires coordination and hits the back of the throat (**the “cold freon” effect**), needs to bsufficient hand strength, propellant causes some patients to stop inhaling when the medicine e shaken prior use

- Dry-Powder Inhaler (DPI)
  - **Advantages:** Does not require coordination of inhalation and actuation, do not contain propellant, compact, and portable
  - **Disadvantages:** Requires patient to generate sufficient inspiratory force (PIF rate >30 mL/min), generally not suitable for young children or elderly

Types of Inhaler Devices (Continued)

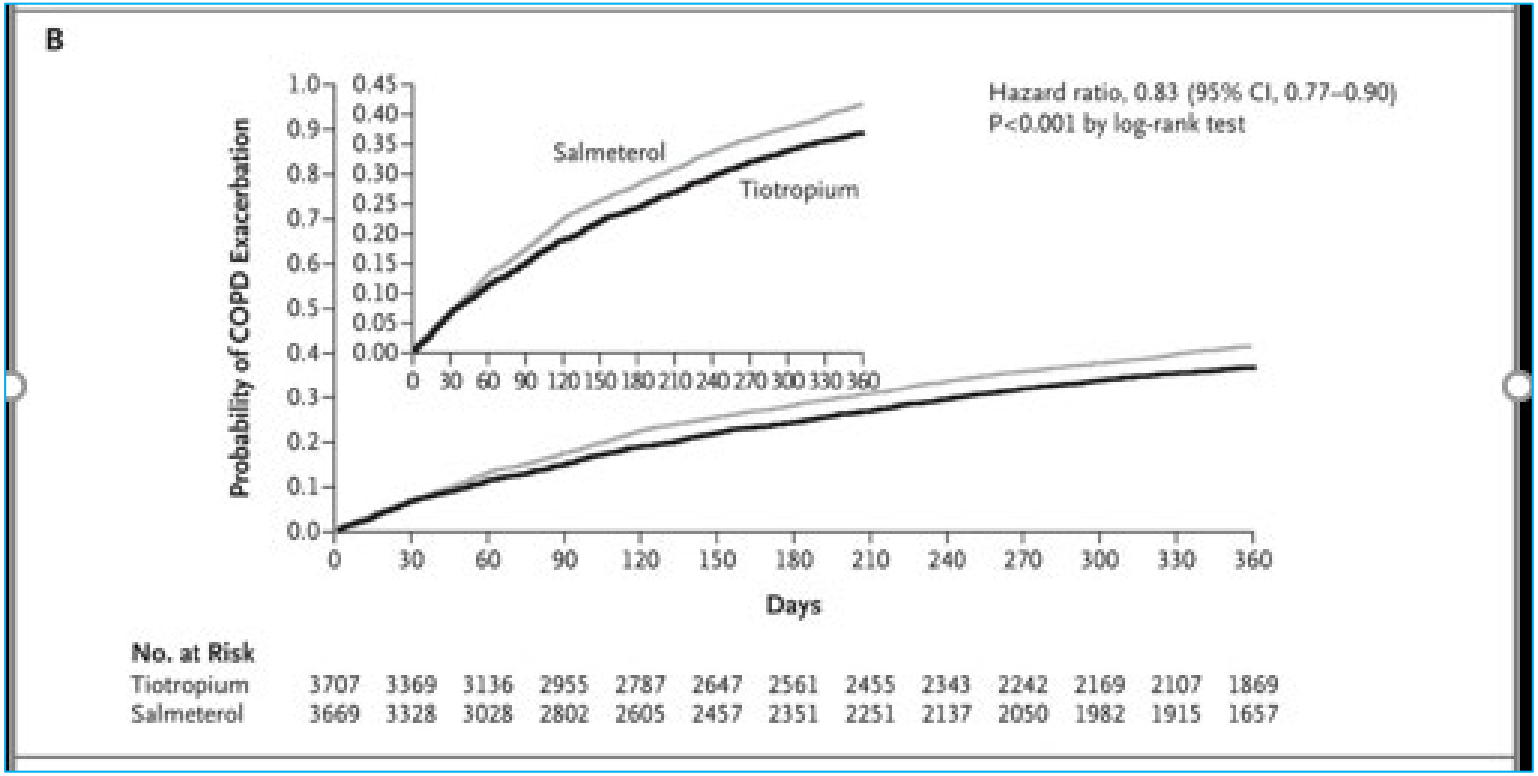
- Soft Mist Inhaler (SMI)
  - **Advantages:** No propellant, easy to use for patients with impaired dexterity, high lung deposition, long plume duration, and does not require coordination
  - **Disadvantages:** Requires dose loading into device and priming

- Nebulizer
  - **Advantages:** No coordination, propellant free, and high patient adherence
  - **Disadvantages:** Long administration time, bulky, much less portable compared to all other inhalers, needs power source, and requires daily cleaning



All patients: SABA, or SAMA, PRN
Group A: SABA +/- SAMA – improvement symptoms, airflow limitation, effect additive
Group B: LAMA, or LABA depending on comorbidities, adverse effects
Both decrease exacerbations, improve lung function
Tiotropium may slow rate of decline FEV1
(Lancet 2009; 374 (9696): 1171)
Group C: LAMA – reduced risk of exacerbations
Group D: (above)

Efficacy of LAMA vs. LABA in Reducing Exacerbations (Groups C-D)



LAMA more efficacious than LABA in reducing exacerbations in 2 large RCTs
Upper any exacerbation
Lower serious exacerbation

Vogelmeier C et al. N Engl J Med 2011;364:1093-1103.

Use of Combined LAMA/LABA for Symptomatic COPD Patients: FLIGHT 1 and 2

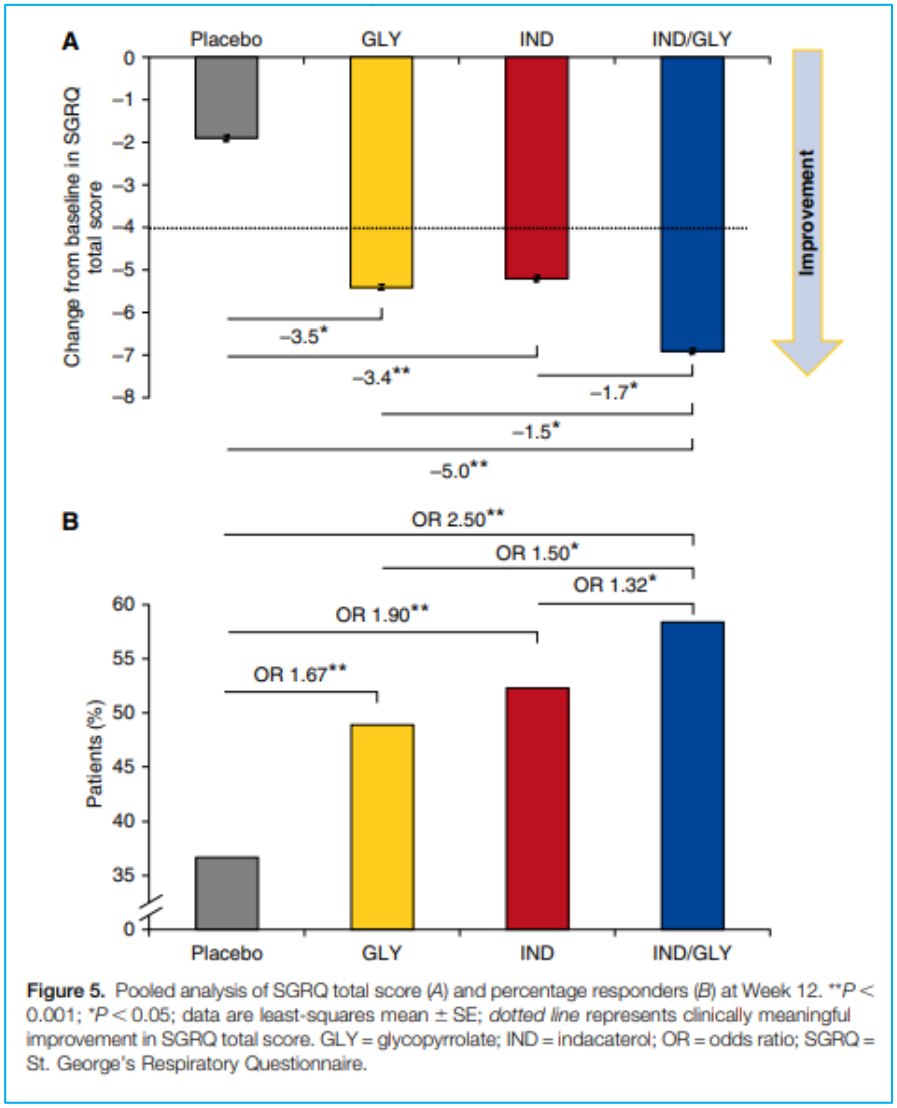
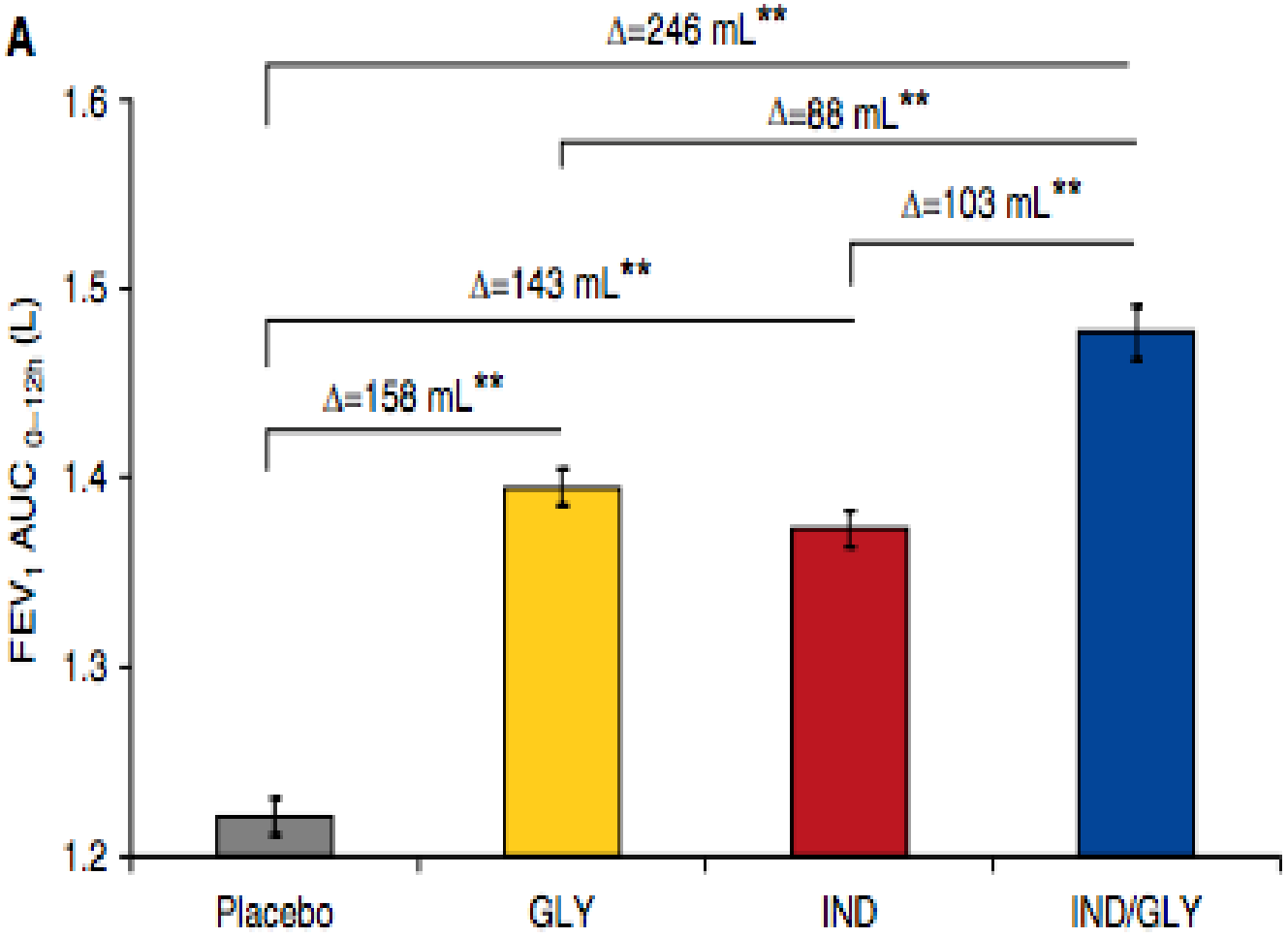


Figure 5. Pooled analysis of SGRQ total score (*A*) and percentage responders (*B*) at Week 12. $^{**}P < 0.001$; $^{*}P < 0.05$; data are least-squares mean ± SE; *dotted line* represents clinically meaningful improvement in SGRQ total score. GLY = glycopyrrolate; IND = indacaterol; OR = odds ratio; SGRQ = St. George's Respiratory Questionnaire.

SGRQ total score

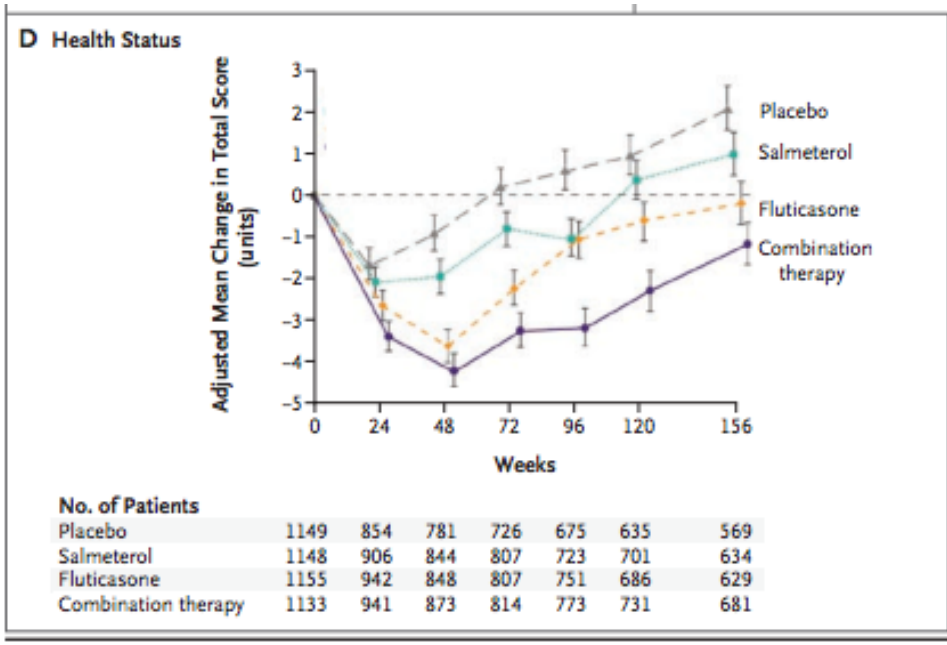
Week 12
Combination:
Improved QoL
Less inhaler use

Mahler et al. *Am J Respir Crit Care Med* 2015, 192, 91068-1079.

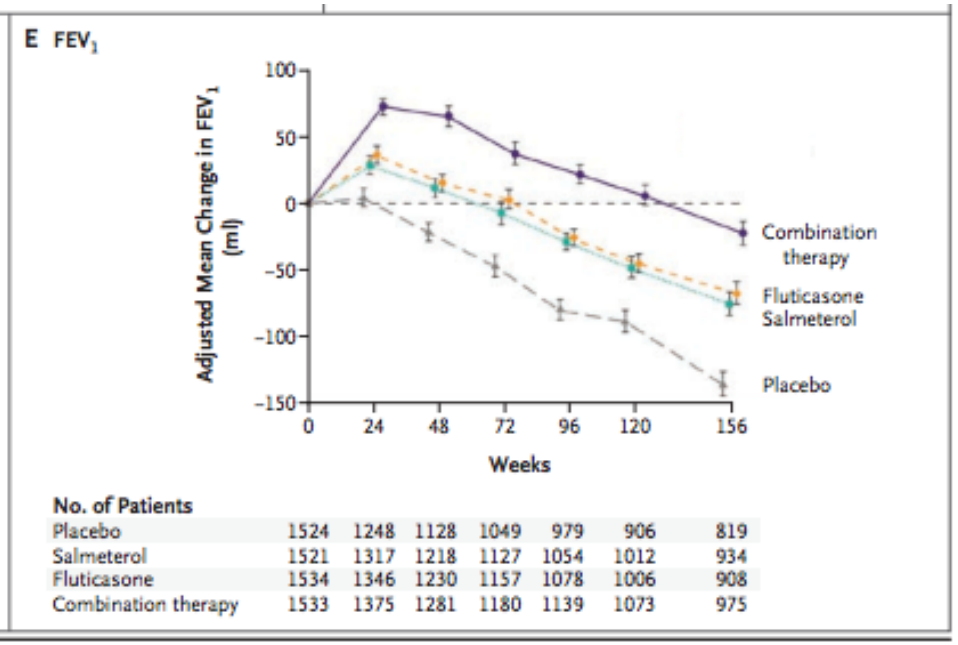


Mahler et al. *Am J Respir Crit Care Med* 2015, 192, 91068-1079

Use of Inhaled Corticosteroids in Severe COPD (TORCH)
LABA/ICS Improves Outcomes Vs LABA, or ICS alone or placebo



No. of Patients							
Placebo	1149	854	781	726	675	635	569
Salmeterol	1148	906	844	807	723	701	634
Fluticasone	1155	942	848	807	751	686	629
Combination therapy	1133	941	873	814	773	731	681



No. of Patients							
Placebo	1524	1248	1128	1049	979	906	819
Salmeterol	1521	1317	1218	1127	1054	1012	934
Fluticasone	1534	1346	1230	1157	1078	1006	908
Combination therapy	1533	1375	1281	1180	1139	1073	975

Moderate to Severe Exacerbations

	Rate Ratio (95% CI)
Combination therapy vs. placebo	0.75 (0.69-0.81)
Combination therapy vs. salmeterol	0.88 (0.81-0.95)
Combination therapy vs. fluticasone	0.91 (0.84-0.99)

No statistically reduced mortality in ICS/LABA patients

Calverley PM. N Engl J Med. 2007 Feb 22;356(8):775-89.

ORIGINAL ARTICLE

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

N Engl J Med 2018 April 18

Method

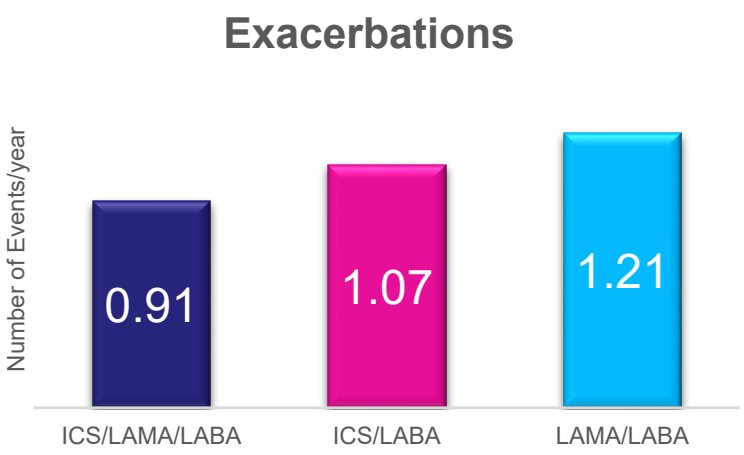
10, 355 patients with moderate to very severe COPD,
Patients randomized to once daily:
ICS/LABA/LAMA, Vs ICS/LABA, Vs LABA/LAMA over 52 weeks

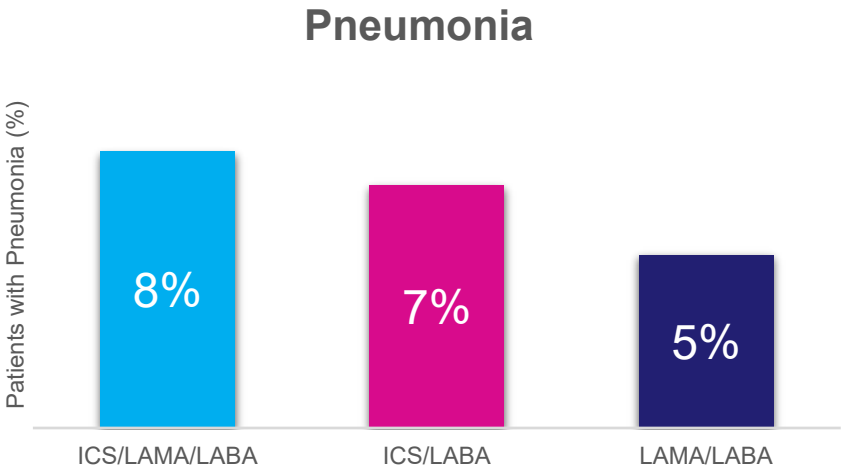
Patients > 40 years, CAT≥ 10, FEV1≤ 50% and ≥ 1 AECOPD previous year, or
FEV1 ≥ 50 % ≤ 80%, with ≥2 AECOPD, or x 1 severe AECOPD

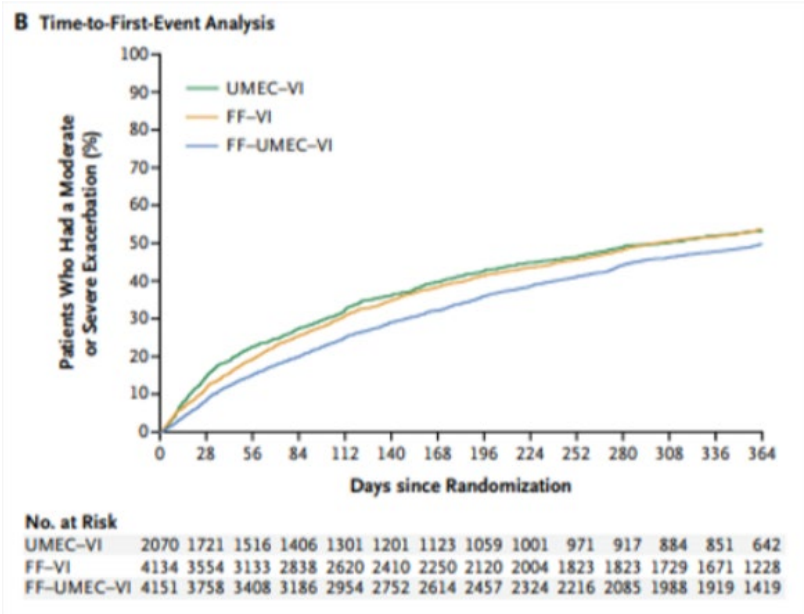
Results

Triple therapy – fewer moderate/severe AECOPD
ICS/LABA superior to LAMA/LABA

IMPACT Trial (Group D)







Inhaled corticosteroids (ICS) increased the risk
of pneumonia relative to LAMA/LABA
(HR, 1.53; 95% CI, 1.22 to 1.92)
Consistent with a Cochrane meta-analysis of ICS in
COPD (OR 1.62-1.78) [1].

1. Kew KM et al. Cochrane Database Syst Rev, 2014 (3): p.Cd010115

Lipson DA, et al. N Engl J Med 2018; 378:1671-1680

THE LANCET
Respiratory Medicine

ARTICLES | VOLUME 7, ISSUE 9, P745-756, SEPTEMBER 01, 2019

Blood eosinophils and treatment response with triple and dual combination therapy in chronic obstructive pulmonary disease: analysis of the IMPACT trial

Steven Pascoe, MBBS • Neil Barnes, FRCP • Prof Guy Brusselle, MD • Chris Compton, MD • Gerard J Criner, MD • Prof Mark T Dransfield, MD • et al. Show all authors

Published: July 04, 2019 • DOI: https://doi.org/10.1016/S2213-2600(19)30190-0 • Check for updates

Rates of moderate and severe exacerbations

	Eos < 90 cells/uL	Eos > 310 cells/uL
Triple Therapy vs LAMA/LABA	0.88	0.56
ICS-LABA vs LAMA/LABA	1.09	0.56

- Former smokers were more responsive to ICS at any eosinophil count than current smokers
- Post-hoc analysis demonstrated efficacy of ICS-LABA at an eosinophilic cutoff of 100 cells/µL [1]

[1] Pascoe, S., et al. The Lancet 2019. Respiratory Medicine, 7(9), 745–756.

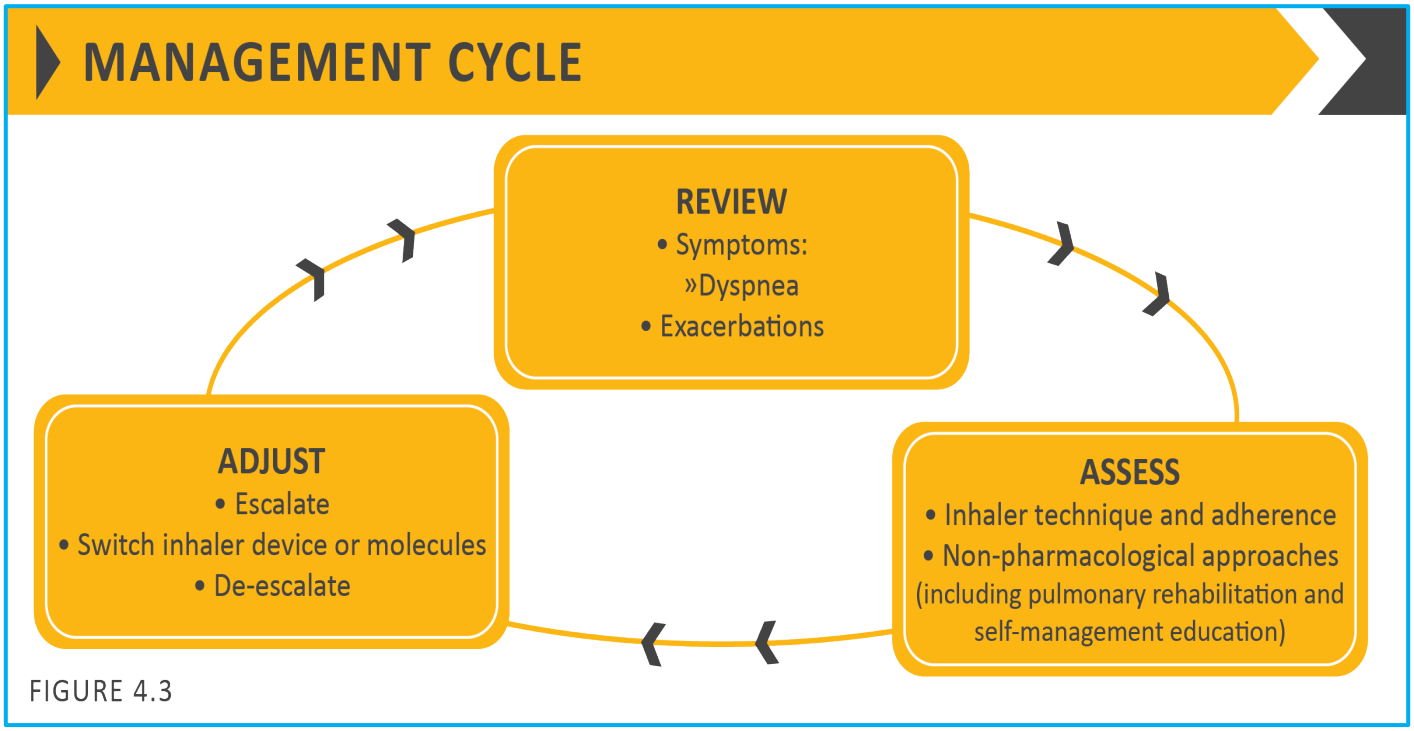
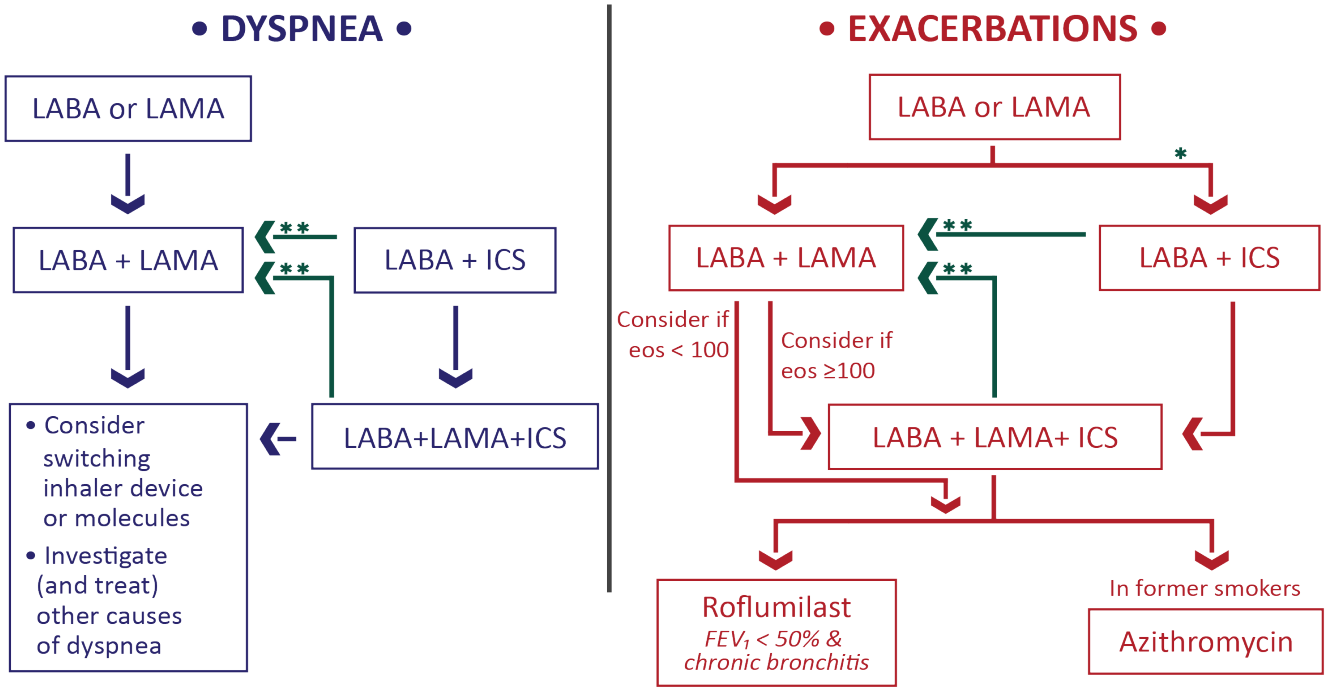

MANAGEMENT CYCLE
REVIEW
• Symptoms:
»Dyspnea
• Exacerbations
ASSESS
• Inhaler technique and adherence
• Non-pharmacological approaches
(including pulmonary rehabilitation and
self-management education)
ADJUST
• Escalate
• Switch inhaler device or molecules
• De-escalate

FIGURE 4.3

FOLLOW-UP PHARMACOLOGICAL TREATMENT

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

FIGURE 4.4

Oral Therapies for COPD

- **Systemic corticosteroids** are not recommended and may be associated with an increased risk of death, HR 1.73 (p=0.0001) [1].

- **Azithromycin** is associated with reduced exacerbations in frequent exacerbators (HR=0.73; 95%CI 0.63-0.84) [2].
  - Azithromycin also resulted in better symptom burden as assessed by the SGRQ.
  - There was a small increase in hearing loss (25% vs. 20%, p=0.04)
  - Post hoc analysis showed the benefit was shown in non-smokers only [3].
  - The long-term effects, cardiovascular events and bacterial resistance are unknown.

1. Horita, N. Respir Res, 2014. 15: 37.
2. Albert RK et al. N Engl J Med, 2011. 365(8):689-98.
3. Han MK et al. Am J Respir Crit Care Med, 2014. 189(12):1503-8

Oral Therapies for COPD

- **Roflumilast** is a phosphodiesterase-4 inhibitor which reduces airway inflammation.
  - Reduces exacerbations and improves lung function in patients with an FEV1<50% and history of chronic bronchitis [1,2].
  - Side effects include weight loss and diarrhea
  - Caution should be employed in patients with depression or suicidality.

- **Theophylline** is a methylxanthine that results in bronchodilator through unclear mechanisms.
  - Improves lung function and symptoms when added to long-acting bronchodilators [3].
  - No benefit when added to inhaled corticosteroids in reducing exacerbations [4].
  - Given toxicity and narrow therapeutic window, theophylline is no longer first line for adjunctive therapy.

1. Fabbri LM et al. Lancet, 2009. 374(9691):695-703.
2. Martinez FJ et al. Lancet, 2015. 385(9971):857-66.
3. ZuWallack RL et al. Chest. 2001;119(6):1661-70.
4. Devereux G et al. JAMA. 2018 320(15):1548-1559.

THE LANCET
Volume 385, Issue 9971, 7–13 March 2015, Pages 857-866

Articles

Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a multicentre randomised controlled trial

Prof Fernando J Martinez MD [a, b, *], Prof Peter M A Calverley MD [c, *], Udo-Michael Goehring MD [d], Manja Brose MSc [e], Prof Leonardo M Fabbri MD [f, †], Prof Klaus F Rabe MD [g, h, †]

1 year – double-blind, placebo-controlled, parallel group, multicenter, phase 3-4 trial

Eligible patients:

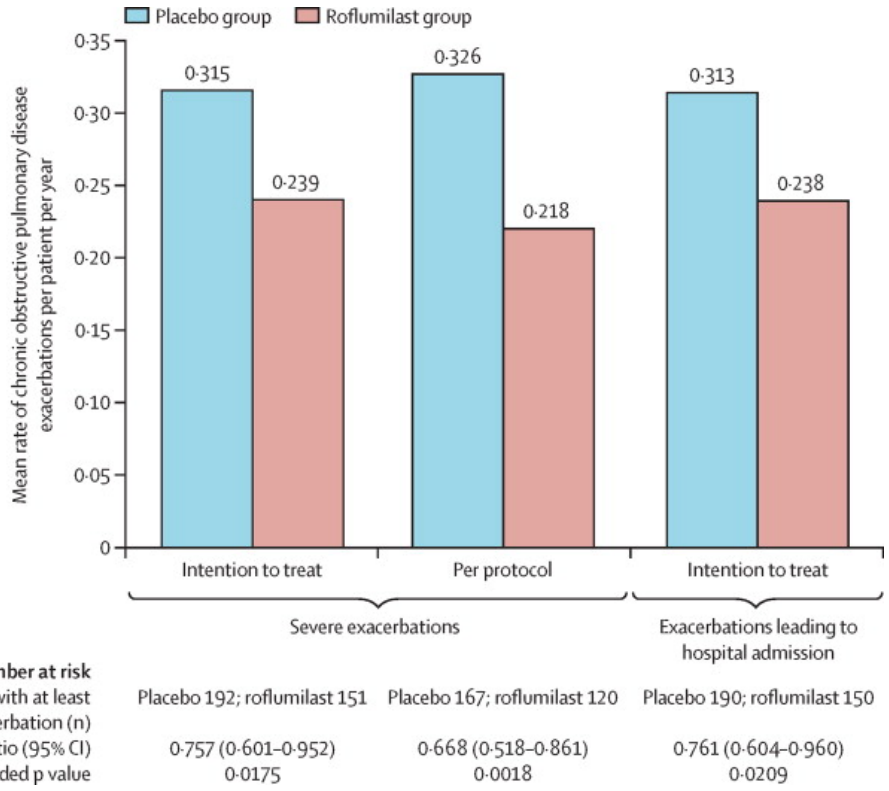
≥ 40 years, ≥ 20 pack years, COPD w/severe airflow limitation,
Symptoms of chronic bronchitis, ≥ 2 exacerbations in past year

Roflumilast 500 ug OR placebo

All patients given fixed inhaled corticosteroid and long acting Beta agonist.

REACT Trial

- 24.3% reduction in severe events
- 23.9% reduction in exacerbations necessitating hospital admissions



COPD: Non-Pharmacologic Management

Key Principles

1. Vaccination
2. Smoking Cessation
3. Pulmonary Rehabilitation
4. Self-Management Strategies
5. Supplemental Oxygen
6. Non-Invasive Positive Pressure Ventilation
7. Comorbidities

GOLD guidelines for Non-Pharmacologic Management by Gold Group

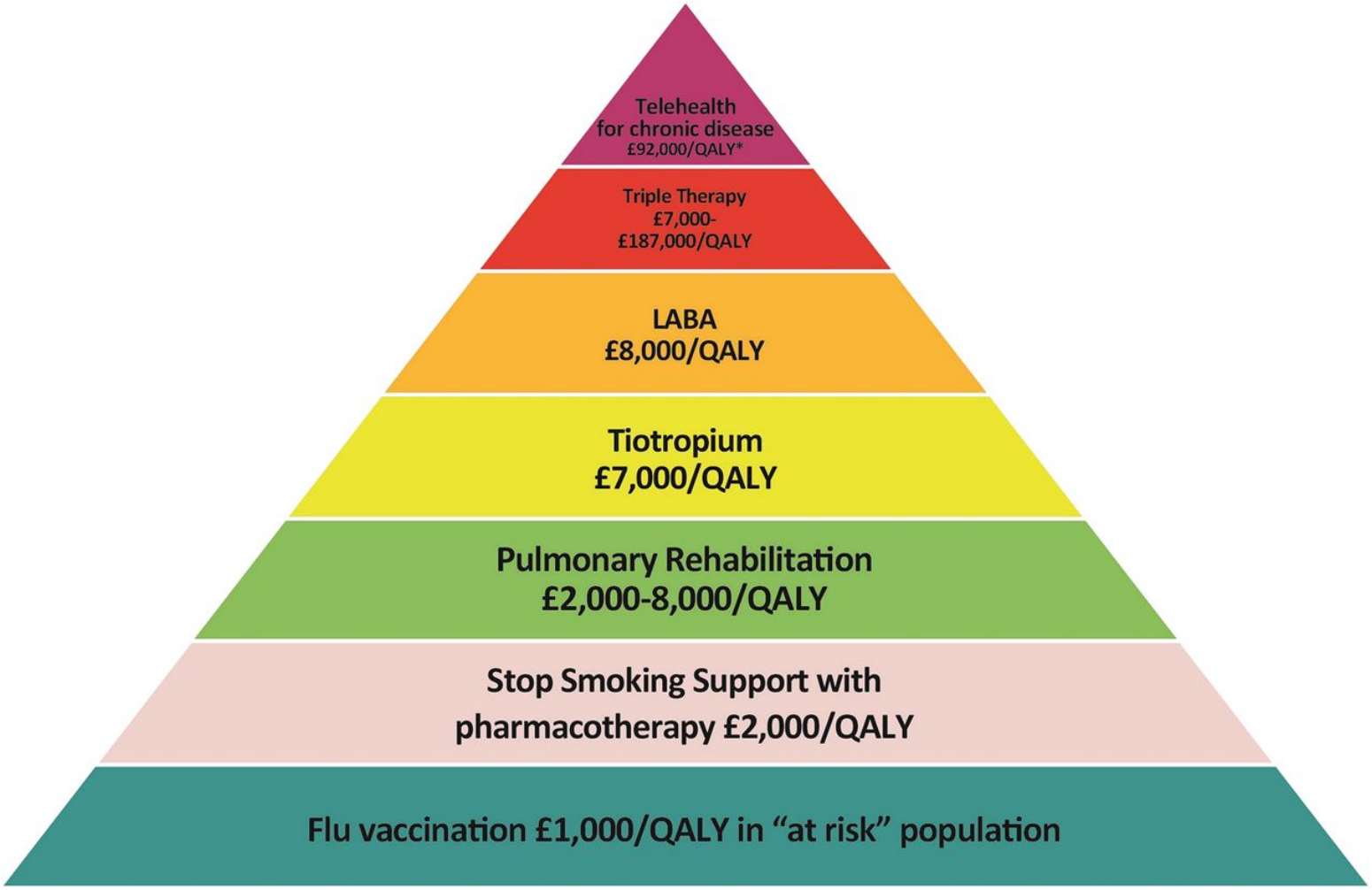
NON-PHARMACOLOGIC MANAGEMENT OF COPD*

PATIENT GROUP	ESSENTIAL	RECOMMENDED	DEPENDING ON LOCAL GUIDELINES
A	Smoking Cessation (can include pharmacologic treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination
B, C and D	Smoking Cessation (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination

*Can include pharmacologic treatment.

TABLE 4.8

COPD Pyramid of Value
Improving Longevity and QoL

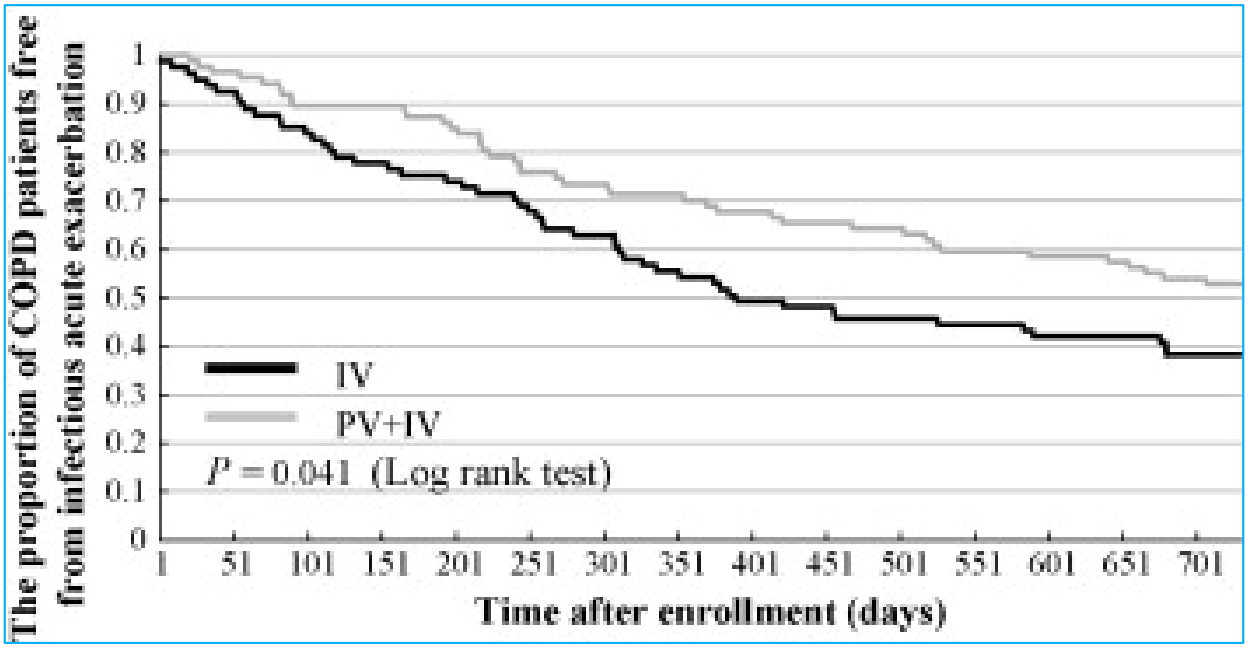


Role of Vaccinations

- Influenza vaccination has been shown to reduce COPD exacerbations on meta-analysis of 11 studies (MD -0.37, 95% CI: -0.64 to -0.11)[1].
- Influenza vaccination also results in a reduction in all cause mortality in patients with COPD (HR=0.55) [2].
- Data is less robust for pneumococcal vaccination
  - No benefit on pneumonia incidence, acute exacerbations, hospital admissions or ED visits on meta-analysis [3].

1. Kopsaftis, Z., et al. Cochrane Database Syst Rev, 2018. **6**: p. Cd002733.
2. Wang, C.S., et al. Vaccine, 2007. **25**(7): p. 1196-203.
3. Walters, J.A., et al. Cochrane Database Syst Rev, 2010(11): p. Cd001390.

Additive Effect of Influenza and Pneumococcal Vaccination



- Given the additive effective in reducing exacerbations and the clear pathogenic role that *Strep pneumonaie* plays, pneumococcal vaccination is also recommended for all patients with COPD.

1. Furumoto, A., et al., Vaccine, 2008. **26**(33): p. 4284-9.

Smoking Cessation

- One of the most cost-effective interventions in COPD, and reduces [1-2]:
  - Symptom burden
  - Mortality
  - Exacerbation rate
  - Lung function decline

- Active smoking is independently associated with increased mortality (HR 2.5, 95% CI 1.03-6.05) [2].

1. Wedzicha J.A., et al. Eur Respir J, 2017. 50(3).
2. Hersh C.P., et al., Chest, 2004. 126(5): p. 1443-51.

Smoking Cessation

- US Public Health Service Clinical Practice Guidelines recommend 5 A's:
  - **Ask** every patient about active smoking
  - **Advise** against smoking, to quit
  - **Assess** readiness to quit
  - **Assist** with counselling, consider pharmacologic aids unless contraindications exist)
  - **Arrange** schedule follow-up visits.

- For the busy practitioner
  - **AAR** (ask, advise, refer to smoking cessation) and **AAC** (ask, advise, connect to smoking cessation electronic resources/quitlines) is reasonable

Pharmacologic Smoking Cessation Aids

- Combination of pharmacologic aids and behavioral therapy is more effective [1].
- First line therapies include: combination NRT or varenicline
  - Varenicline is superior to bupropion (OR 1.59; 95% CI 1.29–1.96) and single forms of NRT (OR 1.57; 95%CI 1.29–1.91) [2]
  - Not more effective than combination NRT (OR1.06; 95% CI 0.75–1.48) [2]
- E-cigarettes are not recommended at this time given safety concerns, though a recent RCT demonstrated superiority compared to other NRT (RR 1.83; 95%CI 1.30-2.58) [3].

1. Patel, M. et al. *Ann Intern Med.* 2016;164(5):ITC33-ITC48.
2. Cahill,K. et al.Cochrane Database Syst Rev 2013;5:Cd009329
3. Hajek, P et al. N Engl J Med. 2019 Feb 14;380(7):629-637

Tobacco Cessation Resources

New York State Smokers' Quitline
1-866-697-8487
nysmokefree.com

National Cancer Institute Quitline
877-448-7848

American Cancer Institute Quitline
800-227-2345

American Lung Association (online/phone advice)
www.lung.org/stop-smoking/join-freedom-from-smoking

Pulmonary Rehabilitation

Pulmonary Rehabilitation (PR)

Comprehensive intervention based on a thorough patient assessment followed by patient – tailored therapies:

- Exercise training
- Education
- Behavior change

Designed to improve physical and psychological condition people with chronic respiratory disease promote long term adherence to health-enhancing behaviors.

Am J Respir Crit Care Med Vol 192, Iss 11, pp 1373–1386, Dec 1, 2015
ATS/ERS Policy Statement

Pulmonary Rehabilitation

- Benefits include improved exercise capacity and health-related QoL [1].
  - Improved 6MWD (MD 43.93; 95%CI 32.64-55.21)
  - Improved symptom burden assessed by SGRQ (MD -6.89; 95%CI -9.26 to -4.52)
- When initiated within 3 weeks of discharge after a COPD exacerbation, readmissions were reduced by 66% (OR 0.44, 95%CI 0.21-0.91)[2].

1. McCarthy B. et al. Cochrane Database Syst Rev. 2015 Feb 23;(2):CD003793
2. Puhan MA, Cochrane Database Syst Rev. 2016 Dec 8;12:CD005305.

Pulmonary Rehabilitation - Challenges

Challenges - Global
Impaired access to Pulmonary Rehabilitation (PR)

PR underutilized despite recognized value PR

- Poor funding, inadequate reimbursement
- Lack of insurance coverage
- Insufficient awareness/knowledge
  - Professional, payer, patient, caregiver regarding potential benefits/process
- Excess of eligible patients with respect to number of existing programs

Infrastructural needs

- Space for exercise training, monitoring equipment
- Space to evaluate patients, and provide education
- Staffing

Geographic

- Fewer sites in non-urban areas, lack of transportation

Pulmonary Rehabilitation: Conventional Versus Telehealth

- Global COVID-19 pandemic responsible for closure traditional PR programs

- Need for PR remains/increased

- Preliminary studies comparing conventional Vs PR Telehealth (PRT) benefits PRT comparable to traditional PR, or inferior

  BMJ Open 2017;7:e014580.
  Thorax 2017;72:57–65.
  Thorax 2018;73:29–36.

RCT PRT Vs PR in severe COPD (*Thorax* 2020;75:421)

- Short and midterm improvement FC, symptoms, not superior to PR
- Subjects reluctant to enroll in PRT, high drop out rate, patients have different needs

Methods

- PRT – supervised via videoconference, 8-10 participants
- 35 minute session
- Use of dumbells and one step box, resistance bands

Advantage: extend choices available for participant

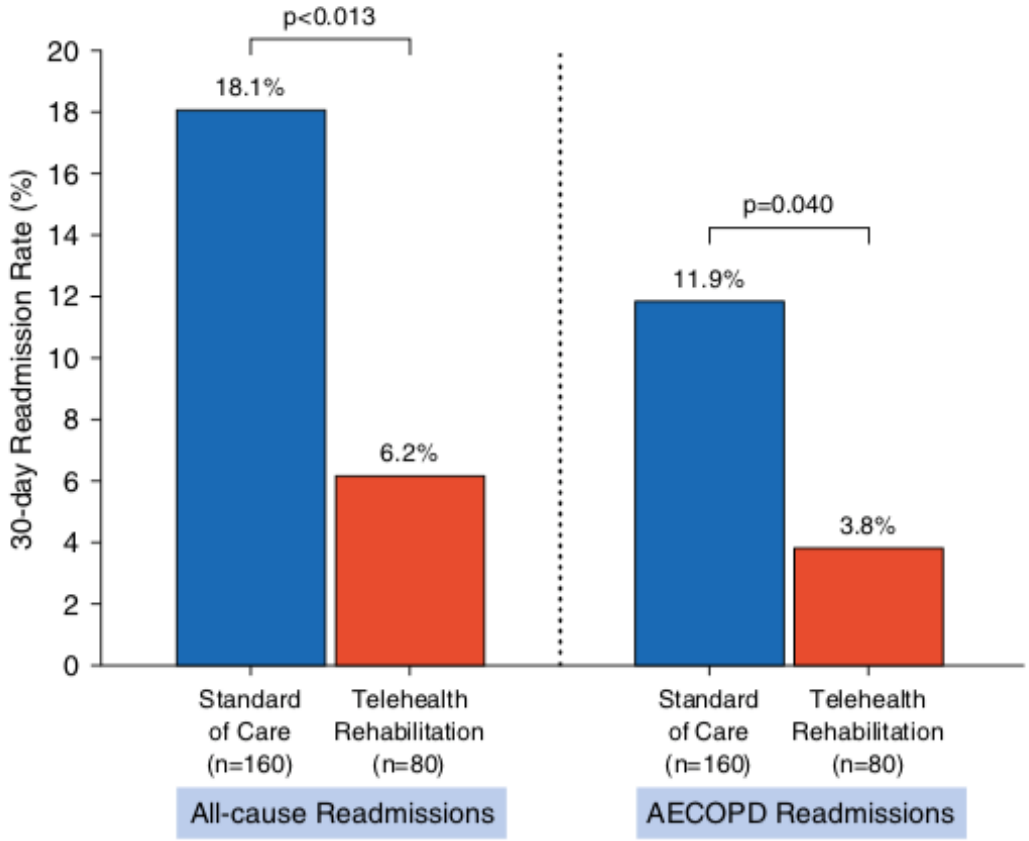


Figure 1. Comparison of 30-day readmission rates for all causes and for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) after an index admission for AECOPD.

Am J Resp Crit Care Med 200, 4, August 15, 2019

Self Management Strategies

- "A COPD self-management intervention is structured but personalized and often multi-component, with goals of motivating, engaging and supporting the patients to positively adapt their health behavior(s) and develop skills to better manage their disease." [1]
- What it is not: a blank script for prednisone and antibiotics when symptoms worsen.
- Meta-analysis demonstrated reduction in respiratory hospitalizations (OR 0.69, 95%CI 0.51-0.94) and improvement in dyspnea. [2]
- Very small, statistically significant increase in respiratory deaths (RD 0.028, 95% CI 0.0049-0.0511)

1. Effing TW et al. Eur Respir J. 2016 Jul;48(1):46-54.
2. Lenferink, A., et al. Cochrane Database Syst Rev, 2017. **8**: p. Cd011682.

FOLLOW-UP OF NON-PHARMACOLOGICAL TREATMENT

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT AND OFFER:

- Flu vaccination every year and other recommended vaccinations according to guidelines
- Self-management education
- Assessment of behavioral risk factors such as smoking cessation (if applicable) and environmental exposures

Ensure

- Maintenance of exercise program and physical activity
- Adequate sleep and a healthy diet

2. IF NOT, CONSIDER THE PREDOMINANT TREATABLE TRAIT TO TARGET

• DYSPNEA •

- Self-management education (written action plan) with integrated self-management regarding:
  - Breathlessness and energy conservation techniques, and stress management strategies
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program post PR

• EXACERBATIONS •

- Self-management education (written action plan) that is personalized with respect to:
  - Avoidance of aggravating factors
  - How to monitor/manage worsening of symptoms
  - Contact information in the event of an exacerbation

All patients with advanced COPD should be considered for end of life and palliative care support to optimize symptom control and allow patients and their families to make informed choices about future management

TABLE 4.9

Supplemental Oxygen

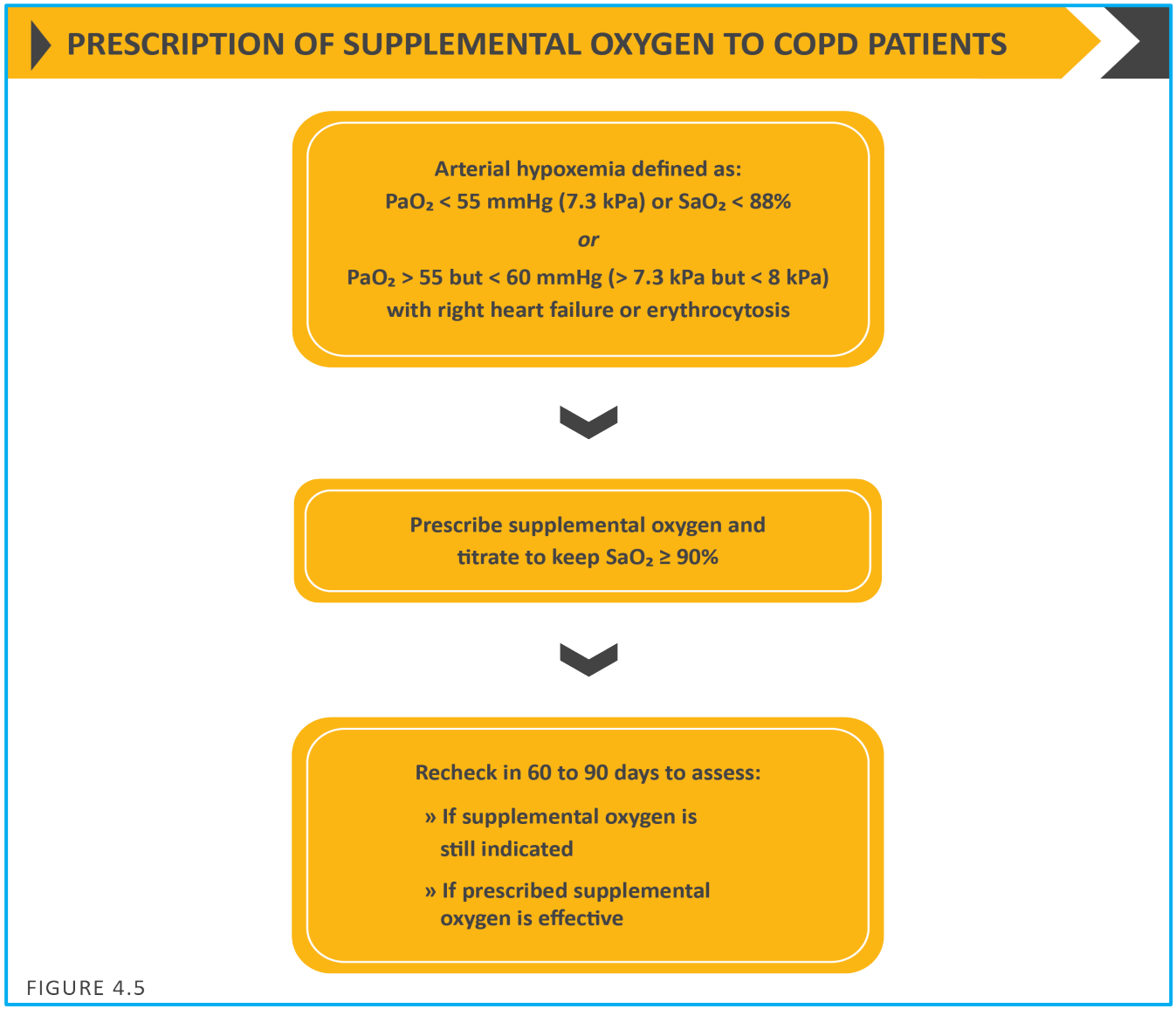
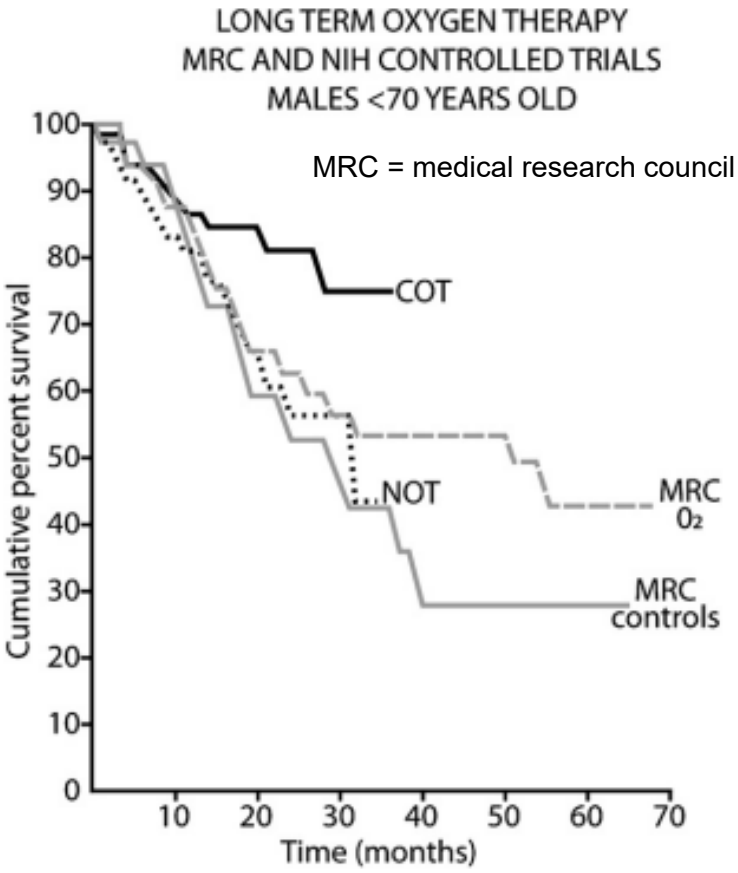


FIGURE 4.5

Home Oxygen

Long-term administration (> 15 hours/day) - **increases survival** in patients with severe resting hypoxemia

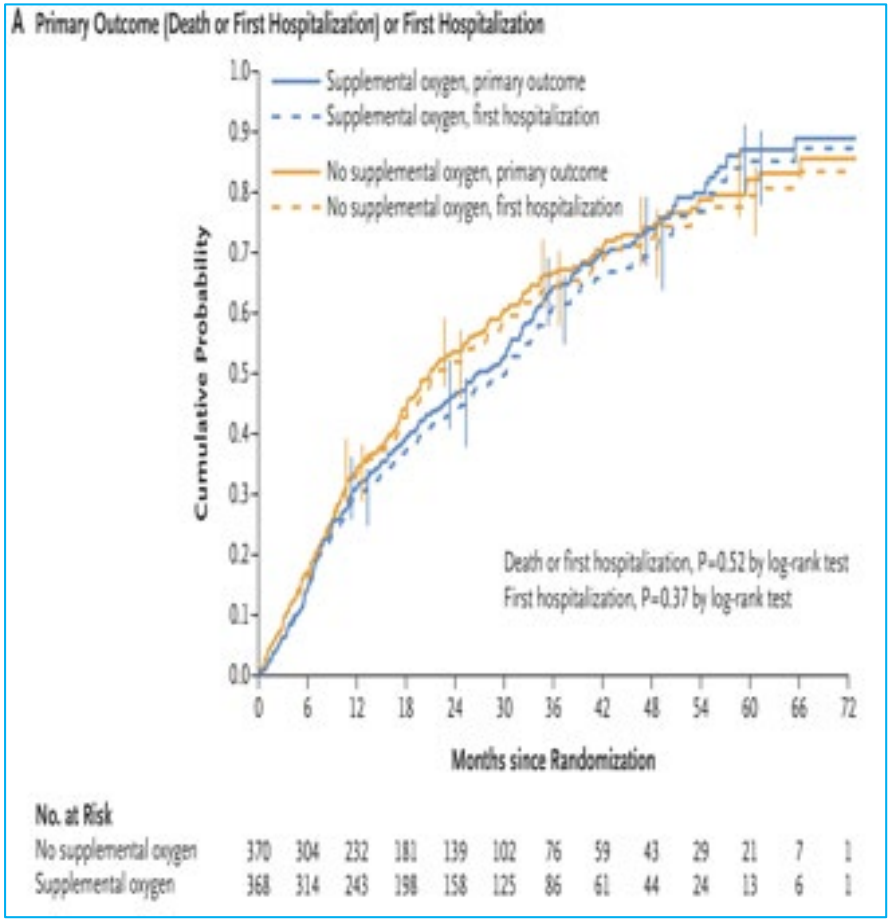
PaO2 ≤ 55mmHg or SaO2 < 88%



Stoller JK, et al. *Chest* 2010;138:179-87.

Oxygen Supplementation for Mild Exertional Hypoxemia

- LTOT is not beneficial in those with mild to moderate exertional hypoxemia:
  - Resting saturation between 89-93% and moderate desaturation to 80% with exertion.



Albert, R.K., et al. N Engl J Med, 2016. **375**(17): p. 1617-1627.

JAMA | Original Investigation

Effect of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on Hospital Readmission or Death After an Acute COPD Exacerbation

A Randomized Clinical Trial

JAMA 2017;317:2177-2186

Method

116 patients, severe COPD, mean FEV1 23%, $PaCO_2$ > 53 mmHg 2-4 weeks after AECOPD discharge
Home NPPV plus HO, Vs HO alone for one year

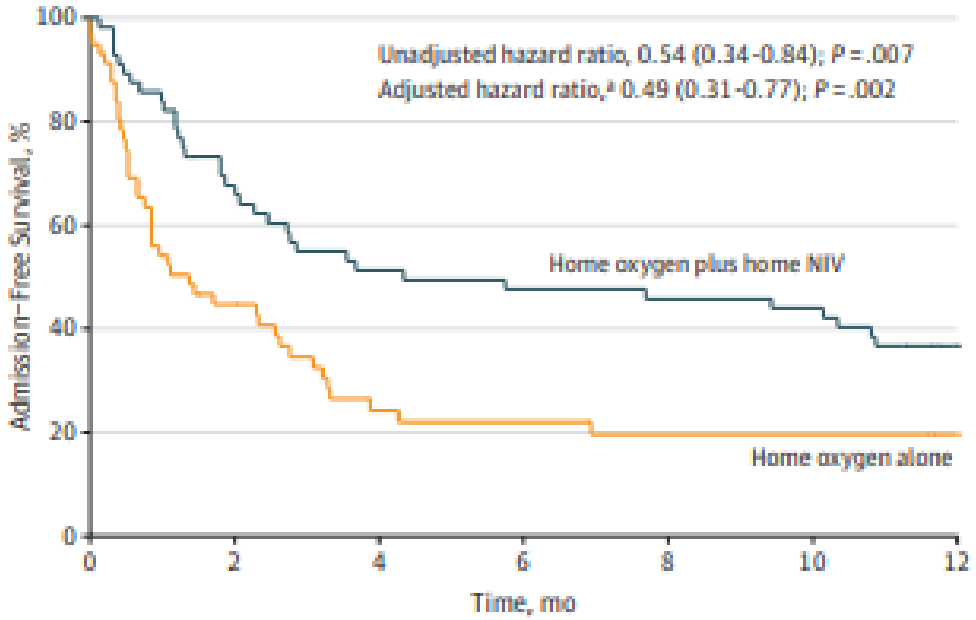
NPPV IPAP 24 cm, EPAP 4 cm H_2O

Results

12 month risk of readmission/death 63% Vs 80% in study Vs control respectively (No mortality benefit)
AECOPD rates/year NPPV+HO 3.8 Vs 5.1 HO

Non-Invasive Positive Pressure Ventilation following a Hospitalization for COPD exacerbation

Figure 2. Kaplan-Meier Survival Plot of Time to Readmission or Death From Randomization to the End of Trial Follow-up at 1 Year



No. at risk							
Home oxygen plus home NIV	57	37	28	26	25	24	16
Home oxygen alone	59	23	11	10	8	8	6

Murphy, P.B., et al. JAMA 2017. 317(21): 2177-2186.

CMS criteria for BiPAP

- The Centers for Medicare and Medicaid Services criteria for initiation of NIPPV for chronic respiratory failure without a back-up rate include:
  - Arterial blood gas while awake and on prescribed O2 with pCO2>52 mmHg and
  - Overnight oximetry <88% for over 5 minutes with a minimum of 2 hours of nocturnal recording on 2L via nasal cannula or the patient's prescribed oxygen rate (whichever is higher)

- Of note, this excludes patients with OSA/OHS

- To qualify for a back-up rate, patients must have evidence of persistent hypercapnia 60 days after bi-level initiation with demonstrated compliance

Comorbidities in COPD

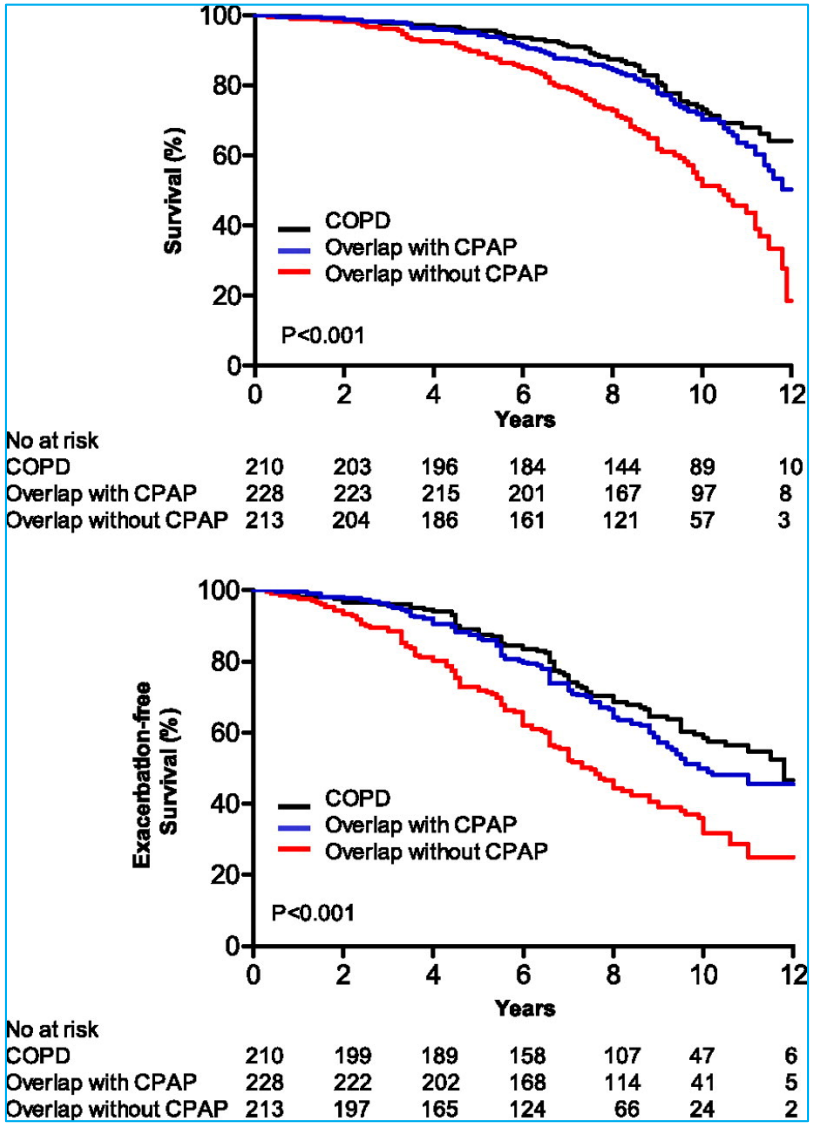
- Important comorbidities include
  - Asthma-COPD overlap
  - COPD-OSA overlap
  - Lung Cancer
  - Skeletal Muscle Dysfunction and Frailty
  - Anxiety and Depression

Comorbidities: Asthma

- Assess for environmental factors/allergens which may be triggering symptoms.
- Ensure on inhaled corticosteroids regardless of COPD Group.
- Currently no clearly defined role for biologic therapy in eosinophilic COPD.
- Ensure not chronic obstructive asthma (in which there is a clearly defined role for biologic therapy).

Comorbidities: OSA

- Patients tend to have more severe hypercapnia (out of proportion to lung function) and increased risk of pulmonary hypertension [1].
- Untreated COPD-OSA overlap have higher mortality relative to COPD alone (RR 1.79; 95% CI, 1.16-2.77) [2].
- Screen patients with the Stop-Bang questionnaire
- Refer for sleep study with titration.



1. McNicholas WT et al. Chest. 2017 Dec;152(6):1318-1326
2. Marin, JM et al. Am J Respir Crit Care Med, 182 (2010), pp. 325-331

Comorbidities: Lung Cancer

- Lung cancer accounts for nearly 25% of all deaths in patients with COPD [1].
- Experimental tools designed to assess the risk of lung cancer in COPD include the COPD-LUCCS score [2].
- Currently, LDCT is reimbursed according to the following CMS criteria based on the National Lung Screening Trial [3]:
  - Age 55-77
  - At least 30 pack-year smoking
  - Current smoker or quit within 15 years.

1. McGarvey LP et al. *Respiratory medicine* 2012; 106: 515-521.
2. de-Torres JP et al. *Chest* 2016; 149: 936-942.
3. Aberle DR et al. N Engl J Med. 2011 Aug 4;365(5):395-409

Comorbidities: Frailty and Mood Disturbances

- Patients with COPD should be assessed for frailty and low BMI is independently associated with mortality [1].
  - Referral to nutrition services and pulmonary rehabilitation is essential.

- Patients with COPD should be screened for anxiety and depression using validated questionnaires:
    - Generalized Anxiety Disorder (GAD)-7 and
    - Patient Health Questionnaire (PHQ)-9 depression scale [2,3].

  - Those with positive screens for anxiety (GAD-7 score>10) and depression (PHQ-9>15) should have a palliative care and pulmonary rehabilitation referral for symptom management.

1. Celli BR et al. N Engl J Med. 2004 Mar 4; 350(10):1005-12
2. Lowe B et al. *Medical care* 2008; 46: 266-274.
3. Kroenke K *Journal of general internal medicine* 2001; 16: 606-613.

Discussing End of Life Care

Guidelines

Disabling dyspnea at rest, poorly responsive to bronchodilators

Progression of advanced disease (increased hospitalizations/ER visits)

Gradual decline in health status and increasing symptoms punctuated by acute exacerbations

Mortality after hospitalization: 23% - 80%

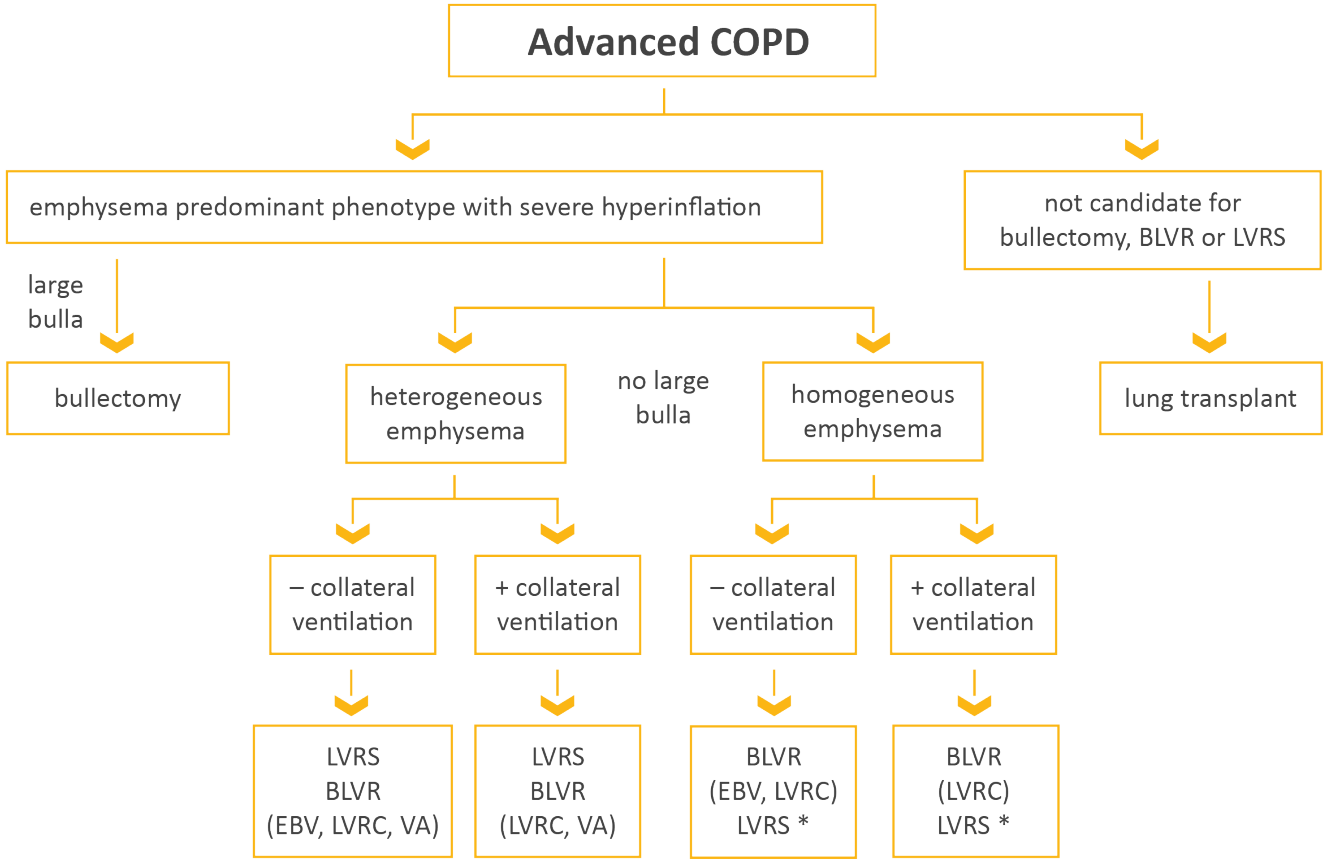
Studies comparing severe COPD vs non-operable lung cancer in last 6 months of life

Worse health-related quality of life, depression and anxiety, received fewer palliative care services, and, despite having similar preferences for indefinite mechanical ventilation, were more likely to receive invasive therapy

Au DH et al. Differences in health care utilization at the end of life among patients with chronic obstructive pulmonary disease and patients with lung cancer. Arch Intern Med 2006;166(3):326-31.

INTERVENTIONAL BRONCHOSCOPIC AND SURGICAL TREATMENTS FOR COPD

Overview of various therapies used to treat patients with COPD and emphysema worldwide. Note that all therapies are not approved for clinical care in all countries. Additionally, the effects of BLVR on survival or other long term outcomes or comparison to LVRS are unknown.



Definition of Abbreviations: BLVR, Bronchoscopic Lung Volume Reduction, EBV, endobronchial Valve, LVRS, Lung volume reduction surgery, LVRC, Lung volume reduction coil, VA, Vapor ablation

*at some but not all centers

FIGURE 4.6

Summary

- Management of COPD involves a personalized approach of characterizing exacerbation history, symptom burden and eosinophilic phenotype.
- Pharmacologic interventions can improve quality of life, lung function and exacerbations.
- The most cost-effective interventions are none-pharmacologic: vaccination, smoking cessation and pulmonary rehabilitation.
- Assess for common and lethal comorbidities.
- Ensure patients have undergone a complete evaluation, including pulmonary rehabilitation and advanced therapies, before prognosticating if COPD is the main life-limiting disease.

Proposed Role of Primary Care in Condition Management

Primarily management of Chronic Stable Disease

Directional plan in alignment with Specialist Champion(s)

Patient Self-management Education

General Health Maintenance Screenings and Preventative Care

Care Coordination (as needed)
Care Management (as needed)

Case Study Scenario

56 year old female with gradual onset of dyspnea when walking quickly on flat terrain or climbing a street with modest incline.

(+) infrequent cough, productive of grey mucus and accompanied by chest tightness.

Activities are not limited at home or at work.

S/P ED visit 5 months ago for acute bronchitis.

Medications
Albuterol 2 puffs twice a day, PRN.

SH/FH 1 PPD for 35 years
Exam normal except for faint diffuse wheezes.
PFTs: FEV 1: 60% predicted, FEV1/FVC ratio is 0.65. CAT Score is 9.

Case Study Questions

Question #1: Which is the following is not correct?

1. MMRC score is: 1
2. Gold Stage (based on PFTs): Grade 2 Moderate COPD
3. She has Restrictive Lung Disease,
4. Gold Grade: B
5. #1, 2, and 4

Question #2: Which of the following would not be appropriate?

1. Chest X-ray: PA and Lat.
2. Smoking cessation counseling, including a prescription for medication, if amenable
3. Long Acting Beta Agonist (LABA): salmeterol
4. Long Acting Muscarinic Antagonist (LAMA) such as tiotropium, umeclidium
5. Combined LABA and inhaled corticosteroid

Case Study Scenario (continued)

5 years later

Chronic productive cough throughout the day,
S/P hospitalization for severe bronchitis 4 months ago.
S/P recent ED visit for bronchitis.

Difficulty climbing one flight of steps, limited by dyspnea and chest tightness.
Difficult to clean her house and carry groceries.
(+) insomnia due to coughing spells and stress.
She smokes ½ PPD cigarettes.

Meds: Tiotropium 1.25 mcg daily, Albuterol 2 puffs QID prn (using improper technique).

Exam: BMI 19, increased AP diameter of chest, distant breath and heart sounds, faint wheezing.
No clubbing

Data:
WBC 8.0 with 200 eosinophils,
02 sat 91%,
PFTs: FEV1/FVC Ratio 0.60, FEV1 40% predicted,
Chest X-ray: radiolucent lungs, flattened diaphragms, increased retrosternal airspace,
ECG: HR 98, right axis deviation, p-pulmonale. S/P nl dobutamine stress echo

Case Study Questions (continued)

Question #3 - Which of the following is not indicated?

1. Smoking Cessation Counseling including prescription of anti-smoking medication
2. Prescribe spacer for use with albuterol inhaler
3. Increase tiotropium to 2.5 mg daily
4. Addition of Salmeterol 50 mcg twice a day
5. Addition of Salmeterol and flucticasone 500 mcg/50 mcg twice a day
6. Screen for depression and treat or refer if present
7. Referral to pulmonary medicine