

# PAOD

**Suk-Won Song, MD, PhD**

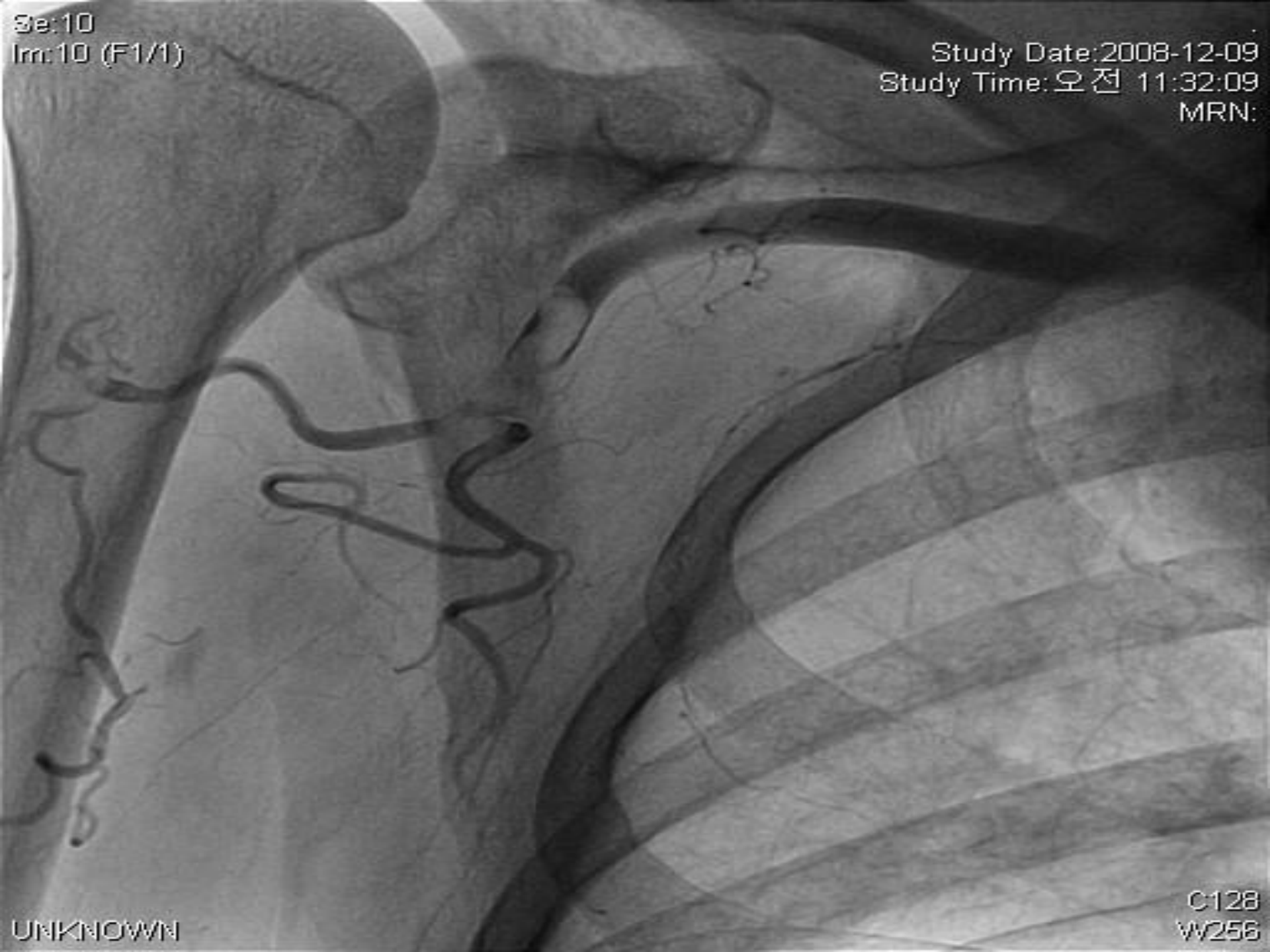
**Gangnam Severance Hospital,  
Yonsei University Health System, Seoul, Korea**



***Pain***  
***Color change***  
***Motor weakness***

Se:10  
Imm:10 (F1/1)

Study Date:2008-12-09  
Study Time:오전 11:32:09  
MRN:



UNKNOWN

C128  
W256

Se:602  
Im:1

MEDCOM RESAMPLED

[H]

Study Date:2008-12-16  
Study Time:오전 9:45:58  
MRN:



[R]

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A

[F]

C78  
W369



Se:602  
Im:1

MEDCOM RESAMPLED  
[H]

Study Date:2009-02-09  
Study Time:오전 10:55:27  
MRN:

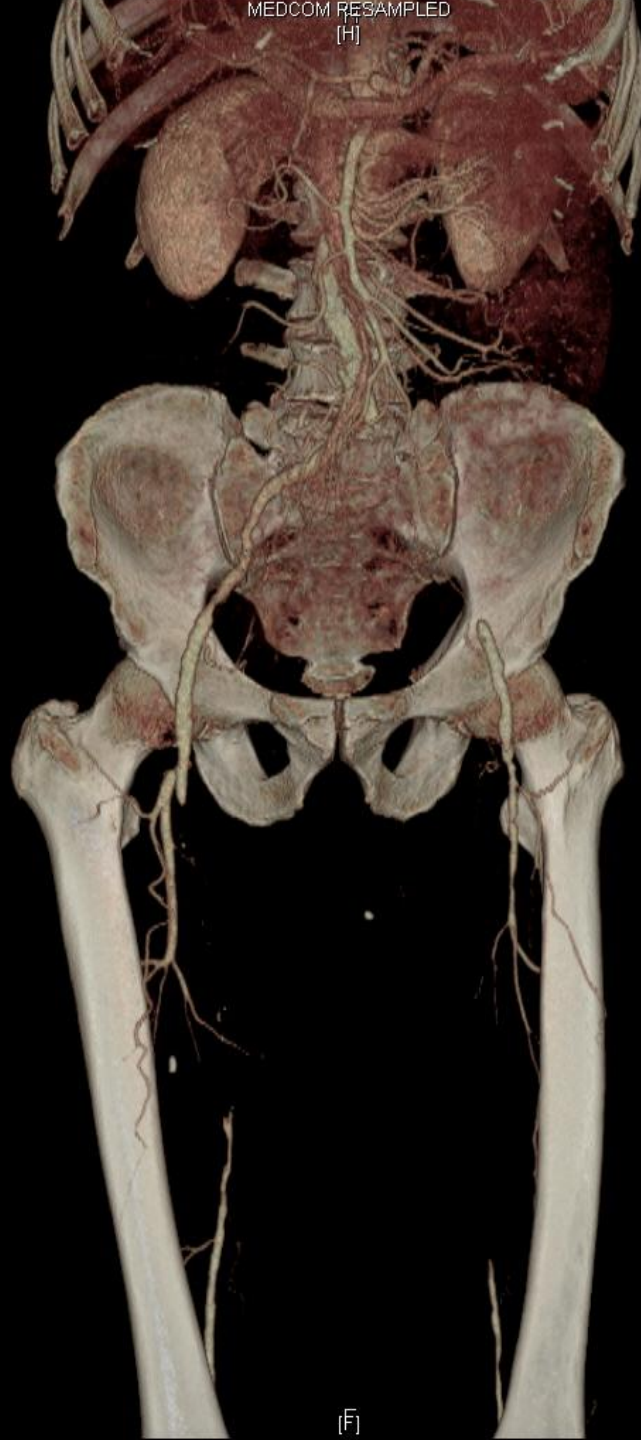
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C155  
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# By whom PAOD should be Treated ?

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- IC            Interventional Cardiologist ?
- IR            Interventional Radiologist ?
- VS            Vascular Surgeon ?
- CS            Cardiovascular Surgeon ?

# **PAD: A Call to Action**

- Section 1**      What is peripheral arterial disease (PAD) and why is it so dangerous?
- Section 2**      Diagnosing PAD in the primary care setting
- Section 3**      The importance of aggressive risk management of PAD
- Section 4**      Evidence base for protecting patients with PAD

# Section 1: What is peripheral arterial disease (PAD) and why is it so dangerous?

## ➤ Case Study

## ➤ Key Learning Objectives

- What is PAD?
- Which patients are most at risk of developing PAD?
- Why is PAD so dangerous?



# Case Study

## Man with calf cramping

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### Presentation

At 59 years old, patient described exercise-induced pain in left calf

- Onset after walking ~200m
- Symptom relieved by stopping and standing for 30-60 seconds

### Risk assessment

Former smoker

- 20 cigarettes/day

No diabetes

BMI = 23

- Height: 6ft /1.83m, Weight 12st 3lb/78kg

Hypertension

- BP: 158/92 mm Hg
- Treated with hydrochlorothiazide and atenolol

Hyperlipidemia – untreated

- TC: 6.2mmol/L / 240mg/dL
- HDL: 1.5mmol/L / 60mg/dL
- LDL: 4.1mmol/L / 159mg/dL
- TG: 1.8mmol/L / 160mg/dL

## *Case Study*

### **Man with calf cramping**

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- Outcome**
- 5 years after first symptoms seen, at 64 years old, patient had an inferior myocardial infarction
  - 1 year later, at 65 years old, he had a large left cerebral hemisphere stroke and died

# What is PAD?

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**PAD is an atherothrombotic disorder affecting the peripheral arteries and it is associated with a high risk of MI, stroke and vascular death<sup>1</sup>**

**The major risk factors for PAD are:<sup>2</sup>**

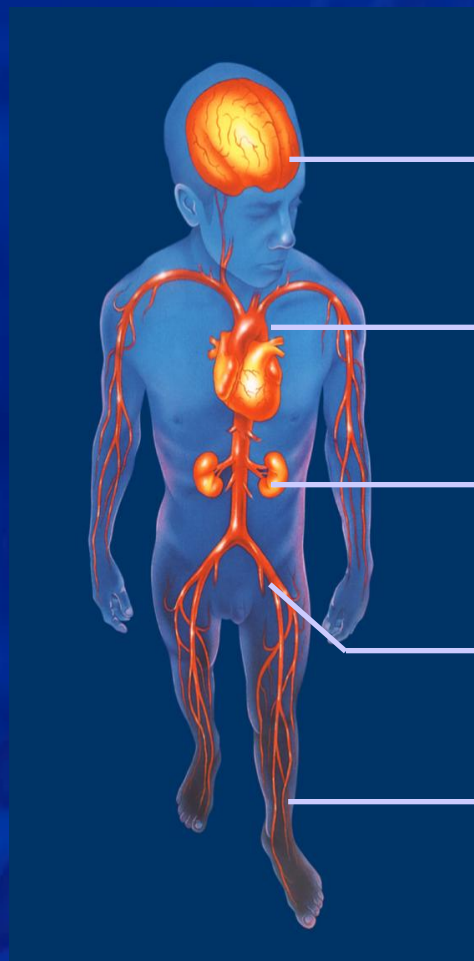
- **smoking**
- **diabetes**
- **age >55 years (men) or >65 years (women)**
- **hyperlipidemia**
- **hypertension**
- **history of cardiovascular disease**

1. Hiatt WR. *J Vasc Surg.* 2002; **36**:1283-1291.

2. Belch JJ et al. *Arch Intern Med* 2003; **163**: 884- 892.

# Major manifestations of atherothrombosis

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**Cerebrovascular disease**

**Coronary artery disease**

**Renal artery stenosis**

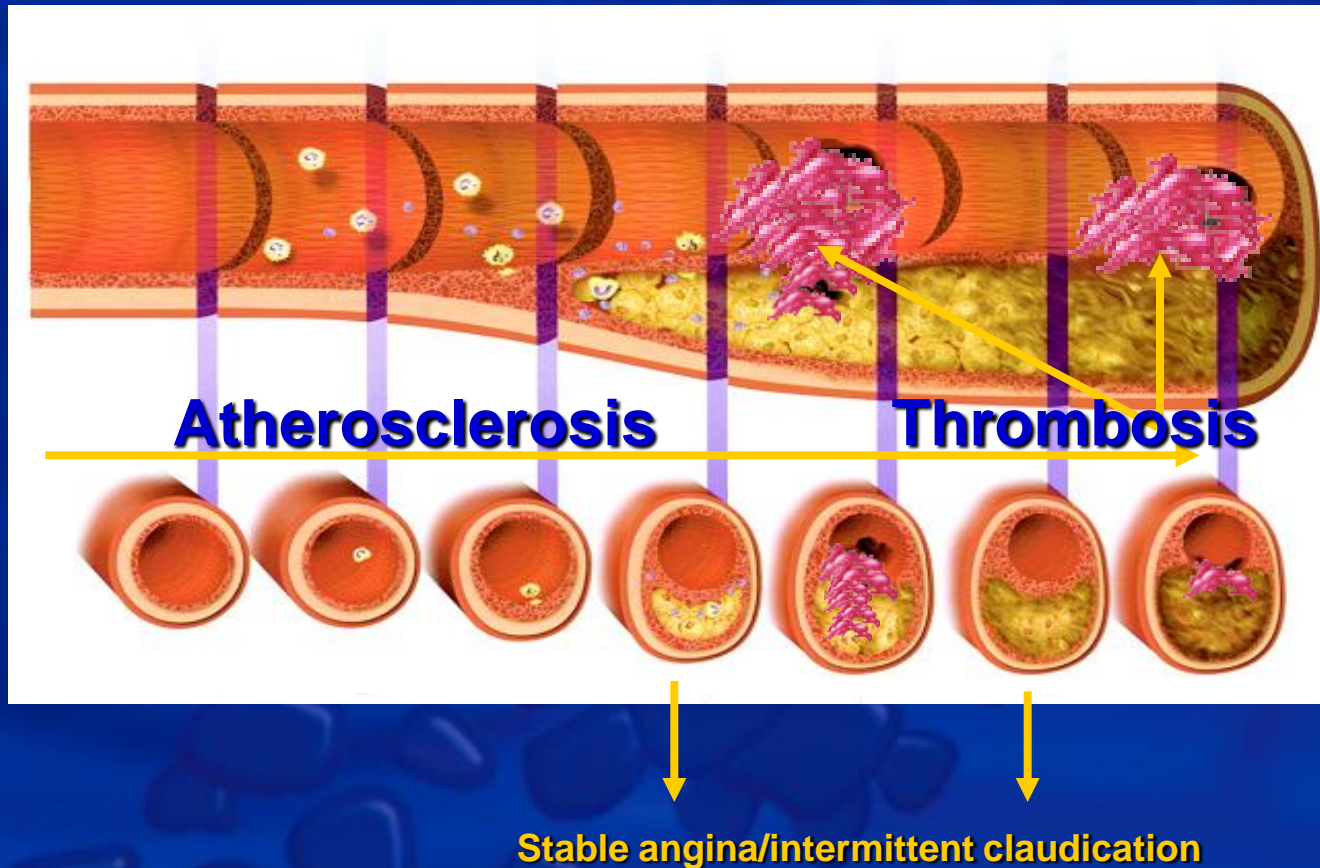
**Visceral arterial disease**

**Peripheral arterial disease**

- Intermittent claudication
- Critical limb ischemia



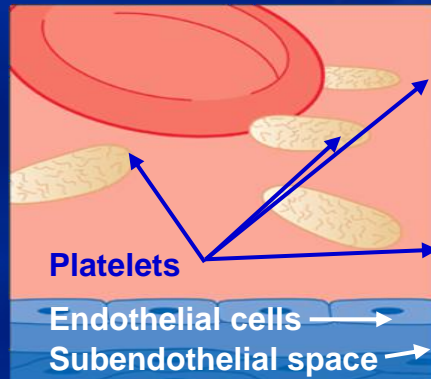
# Pathologic progression to atherothrombosis



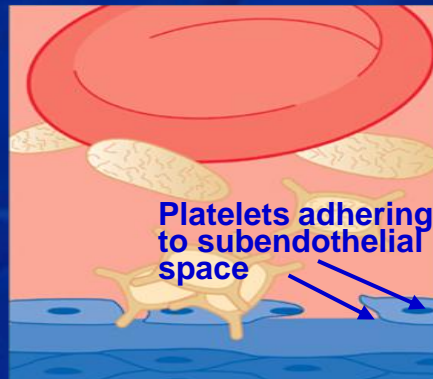
- unstable angina
- MI
- ischemic stroke/TIA
- critical limb ischemia
- CV death

# Platelets are activated following the rupture of an atherosclerotic plaque

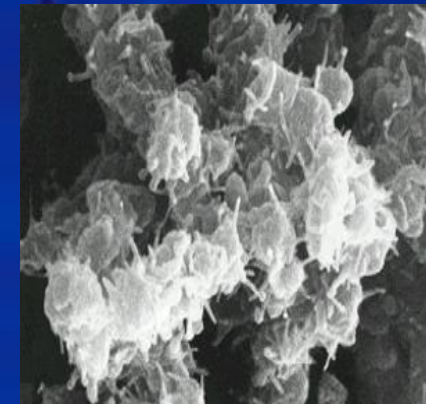
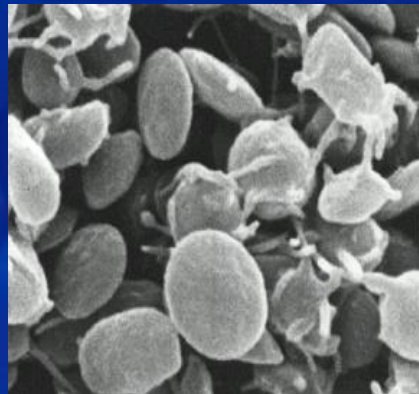
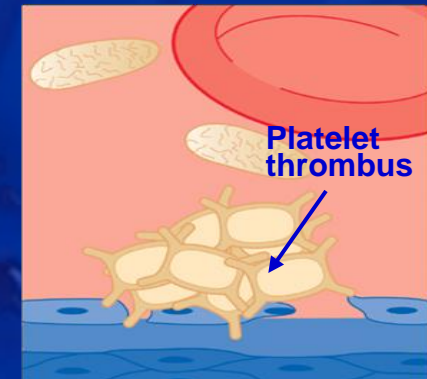
Normal platelets



Activated platelets



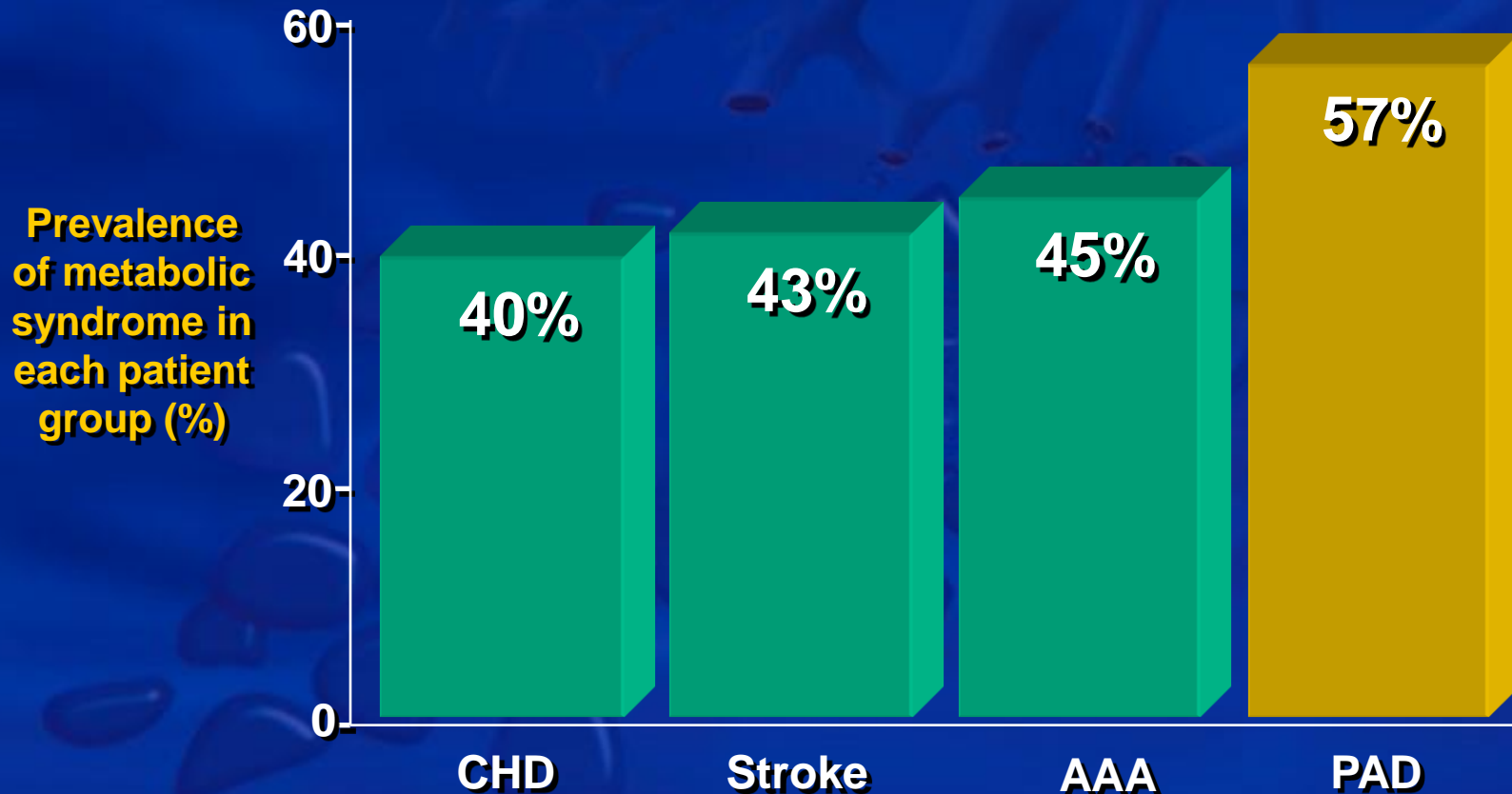
Platelet aggregation



# Metabolic syndrome is more common in PAD than in CHD or stroke

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Cross-Sectional survey of 1,045 vascular disease patients



AAA = Abdominal Aortic Aneurysm

# Prevalence of PAD increases with age

■ Rotterdam Study (ABI Test  $<0.9$ )<sup>1</sup> ■ San Diego Study (PAD by noninvasive tests)<sup>2</sup>

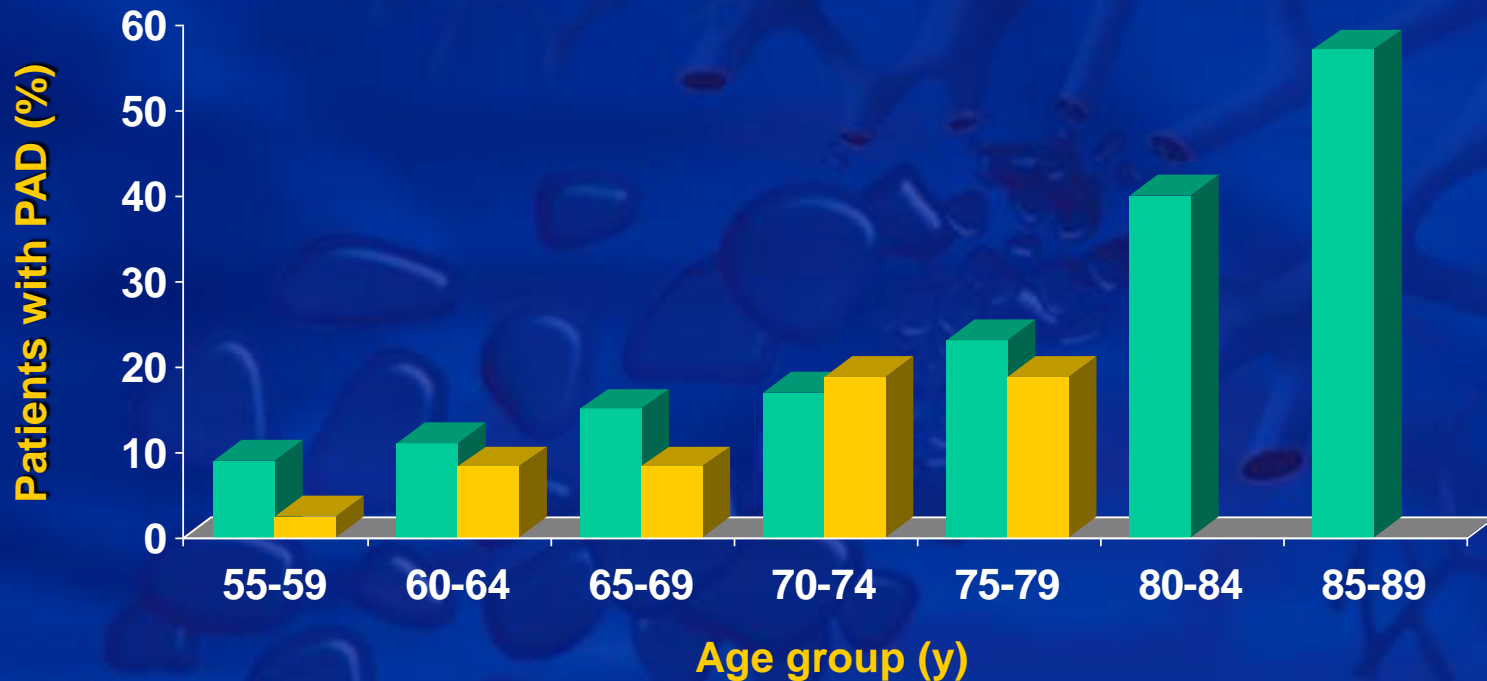


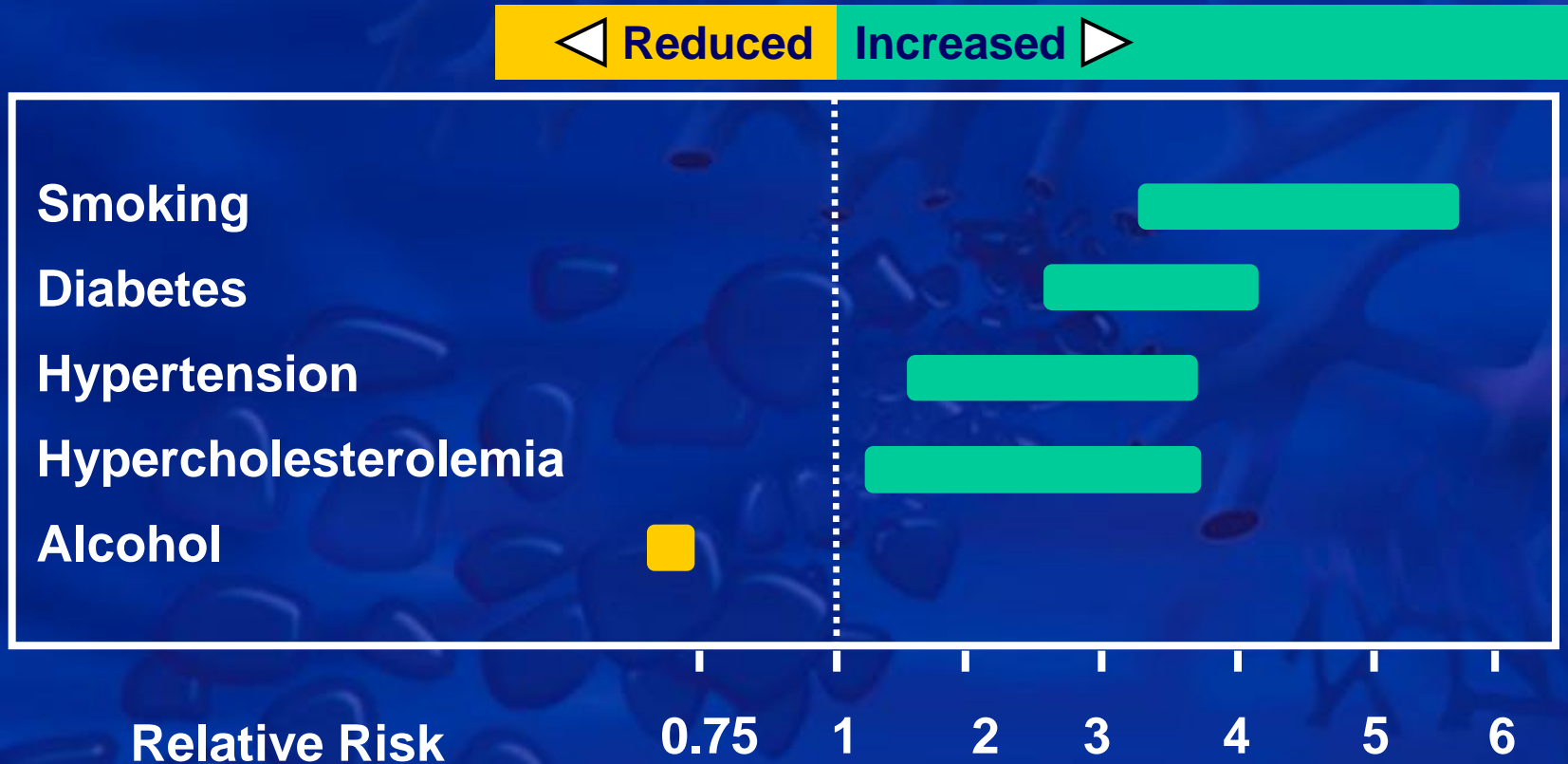
Figure adapted from Creager M, ed. *Management of Peripheral Arterial Disease. Medical, Surgical and Interventional Aspects*. 2000.

1 Meijer WT et al. *Arterioscler Thromb Vasc Biol* 1998; **18**: 185-192.

2. Criqui MH et al. *Circulation* 1985; **71**: 510-515.

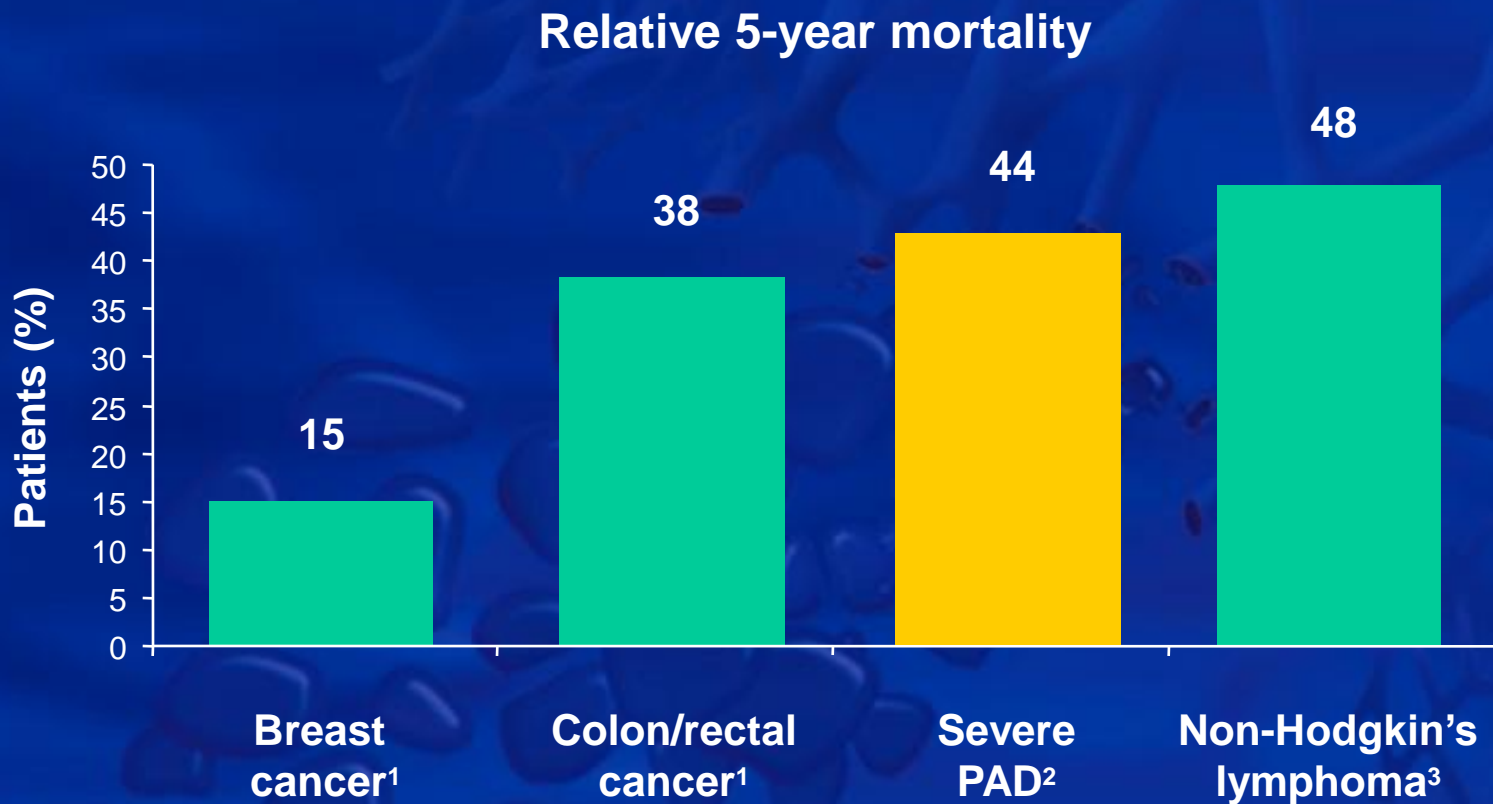


# Risk factors for PAD



Newman AB *et al.* *Circulation* 1993; **88**: 837-845.  
TASC Working Group. *J Vasc Surg* 2000; **31** (1, pt 2): S1-S288.  
Djousse PM *et al.* *Circulation* 2000; **102**: 3092-3097.

# Mortality is very high in patients with severe PAD

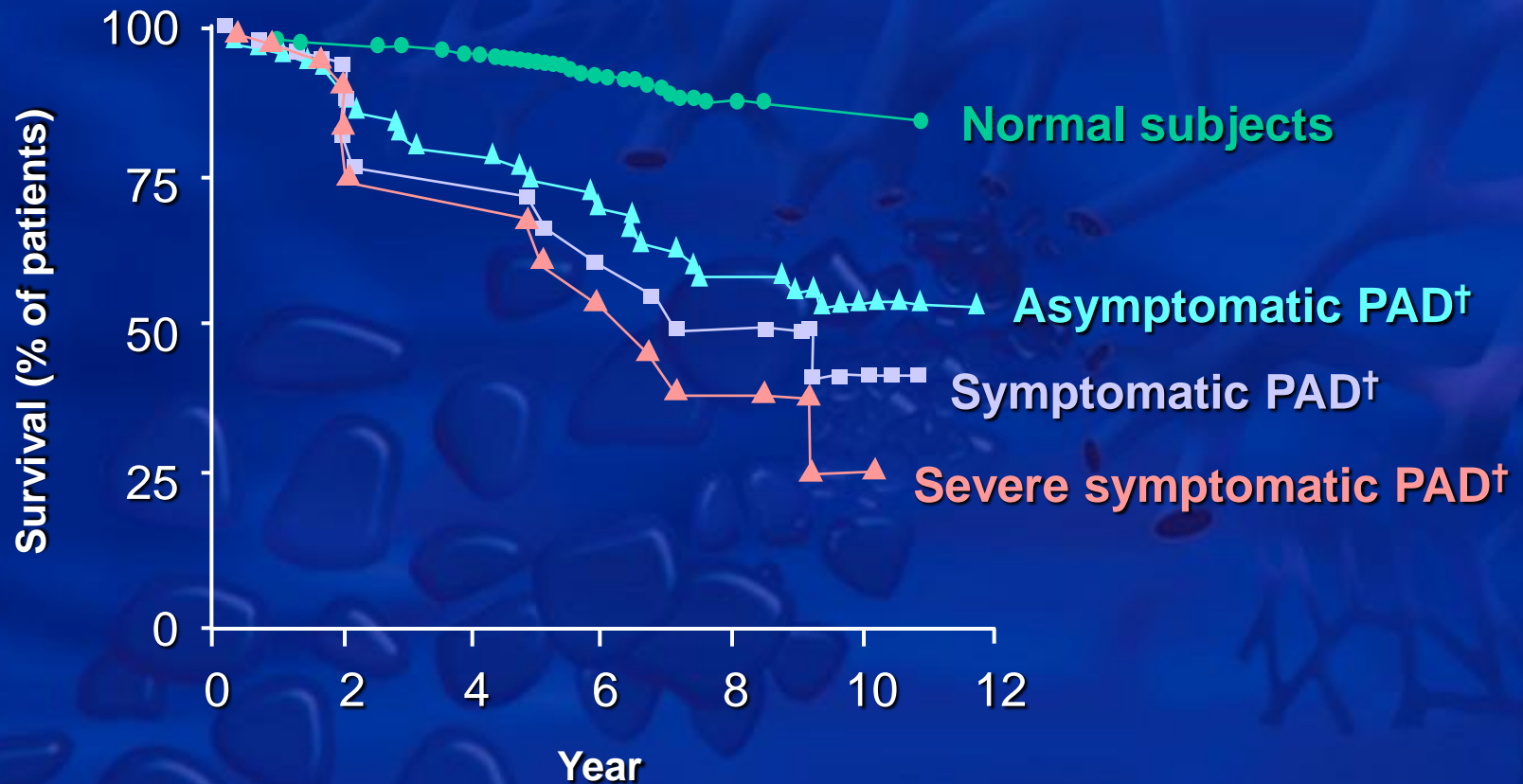


1. Criqui MH. *Vasc Med* 2001; **6** (suppl 1): 3–7.

2. McKenna M *et al. Atherosclerosis* 1991; **87**: 119–28.

3. Ries LAG *et al. (eds). SEER Cancer Statistics Review, 1973–1997*. US: National Cancer Institute; 2000.

# Risk of death is increased in patients with both symptomatic and asymptomatic PAD



\*Kaplan-Meier survival curves based on mortality from all causes.

†Large-vessel PAD.

# Section 1: Key learning points

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## **REMEMBER**

PAD is...

- a commonly occurring atherothrombotic disorder
- associated with a high prevalence of cardiovascular morbidity and mortality

Patients with a history of cardiovascular disease have a higher risk for PAD

## **ACTION**

Check for PAD in patients with risk factors which include:

- smoking
- diabetes
- age >55 years (men)  
>65 years (women)
- hyperlipidemia
- hypertension



## **Section 2: Diagnosing PAD in the primary care setting**

- **Case Study**
- **Key Learning Objectives**
  - PAD symptoms
  - Diagnostic tools useful in identifying PAD

# Case Study

## 55-year-old man with vascular risk factors

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### Presentation

- Experiences right calf discomfort while walking
- Discomfort has been worsening over the past two months

### Risk Assessment

Smoker (25 cigarettes/day)

No diabetes

BMI: 25

- Height: 5ft 11/1.75m, Weight 11st 12/75kg

Hypertension diagnosed 20 years ago

- BP: 160/92 mm Hg

Dyslipidemia

- TC: 5.2mmol/L / 200mg/dL
- HDL: 1.0mmol/L / 40mg/dL
- LDL: 4.2mmol/L / 162mg/dL
- TG: 1.7mmol/L / 150mg/dL

Current medical therapy

- ASA, diltiazem, metoprolol

# PAD can be silent or cause symptoms ranging from exertional pain to critical limb ischemia

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Typical <sup>1</sup>	Atypical <sup>1</sup>
<p><b>Intermittent claudication:</b> pain, ache, cramp, numbness, muscle fatigue in calves, thighs or buttocks; exacerbated by exercise and relieved by rest</p> <p><b>Critical limb ischemia:</b> rest pain, ulcers, gangrene</p>	<p><b>Decreased walking ability:</b> (speed or distance) for reasons other than classical symptoms of intermittent claudication</p> <p><b>Pain in other areas:</b> e.g. general aching</p>

# Guidance for PAD diagnosis

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## STEP 1

- **Assess patient for risk factors**
  - smoking
  - diabetes
  - age: men >55 years and women >65 years
  - hypertension
  - hyperlipidemia
  - history of cardiovascular disease
- **Assess patient for leg symptoms**
  - intermittent claudication
  - critical limb ischemia
- **Tools: PAD checklist, Rose questionnaire, Edinburgh questionnaire**

## STEP 2

- **If suspicion of PAD, perform an ABI to confirm diagnosis**
- **Tool: Doppler**



# How is Ankle-Brachial Index (ABI) measured?

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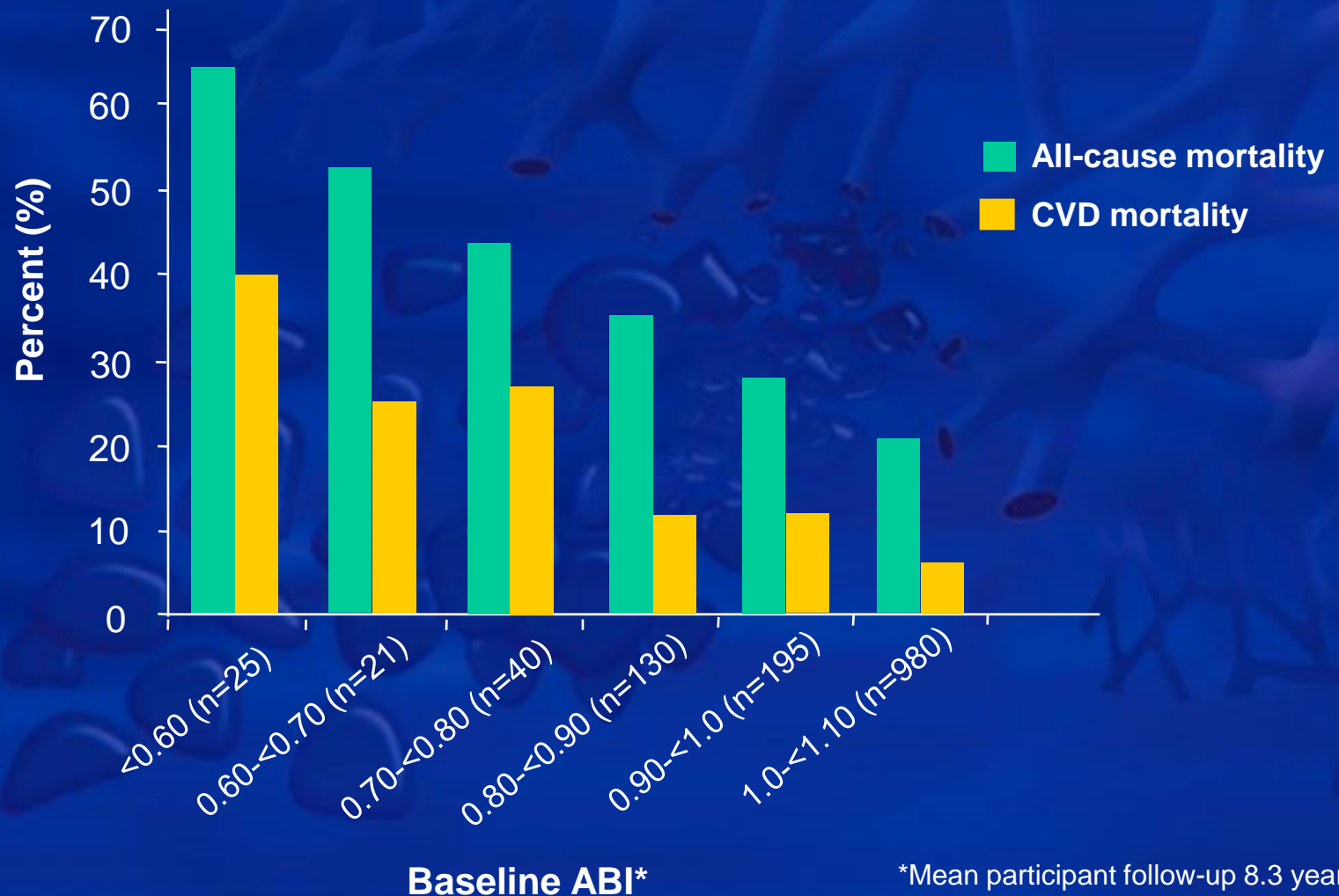
$$\text{ABI} = \frac{\text{Ankle systolic pressure}}{\text{Brachial systolic pressure}}$$

- Measure ankle and brachial systolic pressures with Doppler<sup>1,2</sup>
- Use highest arm and each ankle pressures<sup>1,2</sup>

## ABI Interpretation<sup>3</sup>

<b>&gt; 0.90</b>	<b>Normal</b>
<b>0.41 – 0.90</b>	<b>Mild-to-moderate peripheral arterial disease</b>
<b>0.00 – 0.40</b>	<b>Severe peripheral arterial disease</b>

# There is a strong two way association between decreased ABI and increased risk for cardiovascular death<sup>1</sup>



## Case Study

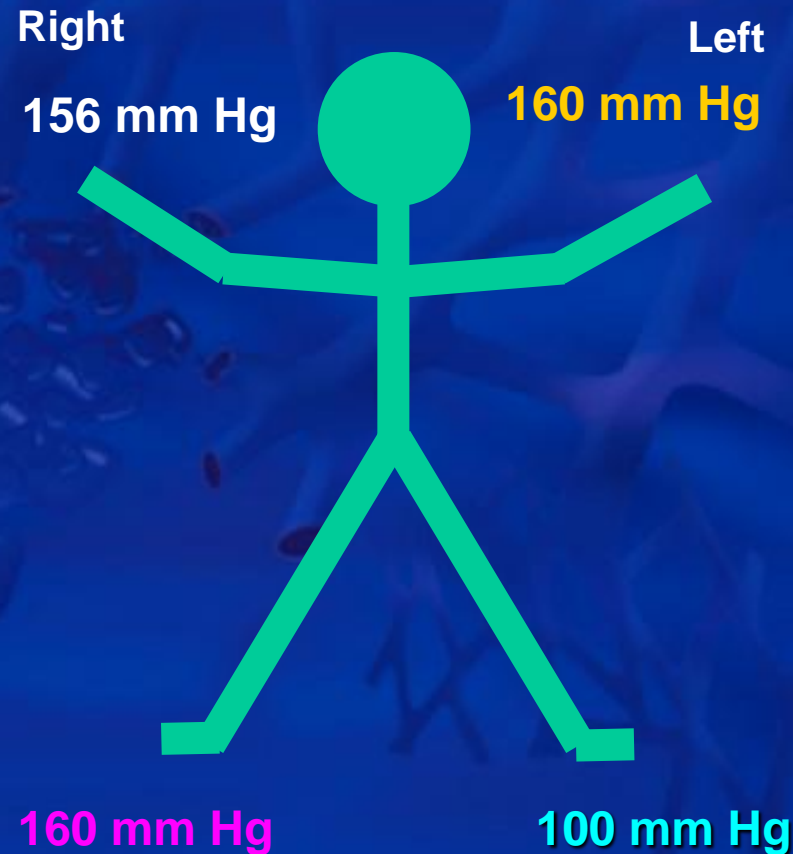
### 55-year-old man with vascular risk factors: ABI measurement

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#### Physical Examination

- Brachial blood pressure
  - Right: 156/88 mm Hg
  - Left: 160/92 mm Hg
- ABI performed in office
  - Take the higher of the two arm pressures
  - Right:  
 $160/160 = 1.00$
  - Left:  
 $100/160 = 0.63$

**Diagnosis:**  
moderate PAD in left leg



## *Case Study*

### **55-year-old man with vascular risk factors**

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**What management approach would you recommend?**

- **Lifestyle modification**
  - smoking cessation
  - weight reduction (Target BMI = 18.5–24.9)
  - walking exercise
- **Control of lipids**
- **Control of blood pressure (BP <140/90)**
- **Platelet inhibition**
- **Leg pain symptom relief**



## Section 2: Key learning points

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### **REMEMBER**

Many high risk patients could be easily diagnosed in the primary care setting

### **ACTION**

- Make a physical examination for PAD in patients with associated risk factors and/or atypical symptoms
- Assess patients for leg pain on exertion and reduced walking
- Use a diagnostic check-list to assist with PAD detection
- Confirm diagnosis with an ABI

## **Section 3: The importance of aggressive risk management of PAD**

- **Case Study**
- **Key Learning Objectives**
  - **Asymptomatic PAD**
  - **Early detection of PAD in patients at high risk of vascular disease (e.g. with diabetes)**

# Case Study

## 65 year-old woman with diabetes

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### Presentation

Annual physical examination

### Risk assessment

Non-smoker

Diabetic

Hypertensive

- BP: 150/90 mm Hg

**BMI: 35**

- Height: 5' 6" / 1.67m, Weight: 215 lbs / 97.5 kg

**Overweight, with central obesity**

**Sedentary lifestyle**

**Reports no symptoms of claudication**

**Abdominal exam: no bruits detected**

**Medications**

- Glyburide
- Metformin
- Lisinopril

# *Case Study*

## **Case study discussion points**

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- 1. What examination/investigation would you carry out?**
- 2. What would be the considerations for treatment and risk reduction?**



## Case Study

### 65-year-old woman with diabetes

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#### Laboratory findings

- Lipid profile

- TC
- LDL-C
- HDL-C
- TG

mg/dL	mmol/L
204	5.27
130	3.36
30	0.77
200	2.48
130	7.45

- Fasting glucose

- HbA1c (%)

9.2

# Only 1 in 10 patients with PAD has classical symptoms of intermittent claudication

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1 in 5 people over 65  
has PAD<sup>†</sup>



Only 1 in 10 of these  
patients has classical  
symptoms of intermittent  
claudication (IC)



<sup>†</sup> ABI < 0.9

# Case Study

## 65-year-old woman with diabetes: ABI measurement

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### ABI Measurement

- Brachial blood pressure
  - Highest of the two is **152/86**
- ABI measured
  - Right  
 $\frac{152}{152} = 1.00$
  - Left  
 $\frac{100}{152} = 0.66$

**Diagnosis:**  
**mild-to-moderate PAD in both legs**

False high readings occur in some patients with diabetes due to non-compressible arteries



# The American Diabetes Association recommends screening for PAD in patients with diabetes

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A screening ABI should be performed in patients with diabetes

Those >50 years of age

- If normal an exercise test should be carried out
- The ABI test should be repeated every 5 years

Those <50 years of age who have other risk factors associated with PAD

- Smoking
- Hypertension
- Hyperlipidemia
- Duration of diabetes >10 years

- Foot care is also important in diabetic patients as PAD is a major contributor to diabetic foot problems<sup>2</sup>

1. American Diabetes Association. *Diabetes Care* 2003; **26**: 3333–3341.

2. Estes JM, Pomposelli FB Jr. *Diabet Med* 1996; **13**: S43–S57.



# Risk factor management approach

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- **Smoking cessation**
- **Weight reduction**
- **Total cholesterol  $<175$  mg/dL /  $<4.5$  mmol/L**
- **LDL cholesterol  $<100$  mg/dL /  $<2.6$  mmol/L**
- **Glycosylated hemoglobin  $<7.0\%$**
- **Blood pressure (BP)  $<140/90$  mm Hg**
  - For patients with diabetes BP  $< 130/80$ mm Hg
- **Platelet inhibition**

## Section 3: Key learning points

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### **REMEMBER**

Only 1 in 10 patients with PAD have typical claudication<sup>1</sup>

Patients with diabetes are at high risk of PAD

It is important to improve the management of PAD to protect patients from an increased risk of ischemic events

### **ACTION**

- Ensure aggressive and early risk management of patients who are at high risk but may be asymptomatic
- Screen patients with diabetes >50 years of age, and those <50 years of age who have additional risk factors associated with PAD

## **Section 4: Evidence base for protecting patients with PAD**

### **➤ Key Learning Objectives**

- Objectives of therapy for PAD
- Guidelines for PAD treatment

# Two complementary objectives for PAD management

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## Risk Reduction of Ischemic Events<sup>3</sup>

- Smoking
- Hyperlipidemia
- Hypertension
- Diabetes
- Antiplatelet therapy<sup>2</sup>

## Symptomatic Treatment

- Exercise<sup>1</sup>
- Smoking cessation<sup>2</sup>
- Pharmacologic therapy
- Selective use of interventional therapy<sup>3</sup>

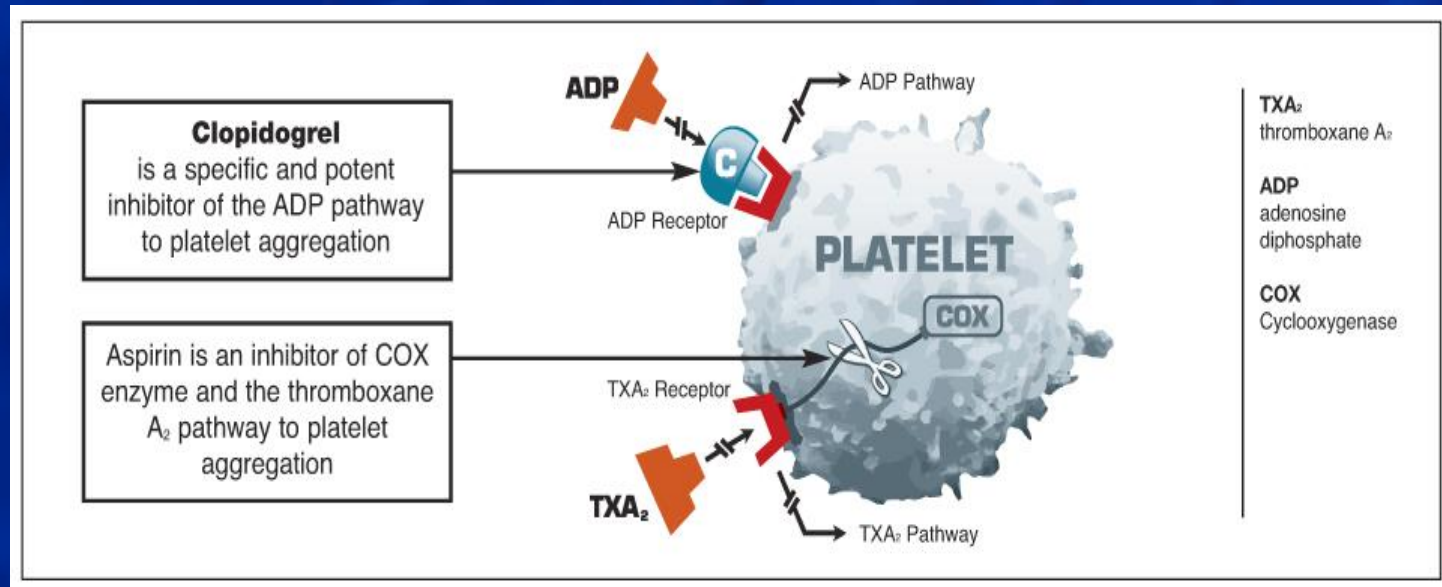
1. McDermott MM, McCarthy W. *Surg Clin North Am* 1995; **75**: 581–591.

2. Clagett GP, Krupski WC. *Chest* 1995; **108** (4 suppl): 431S–443S.

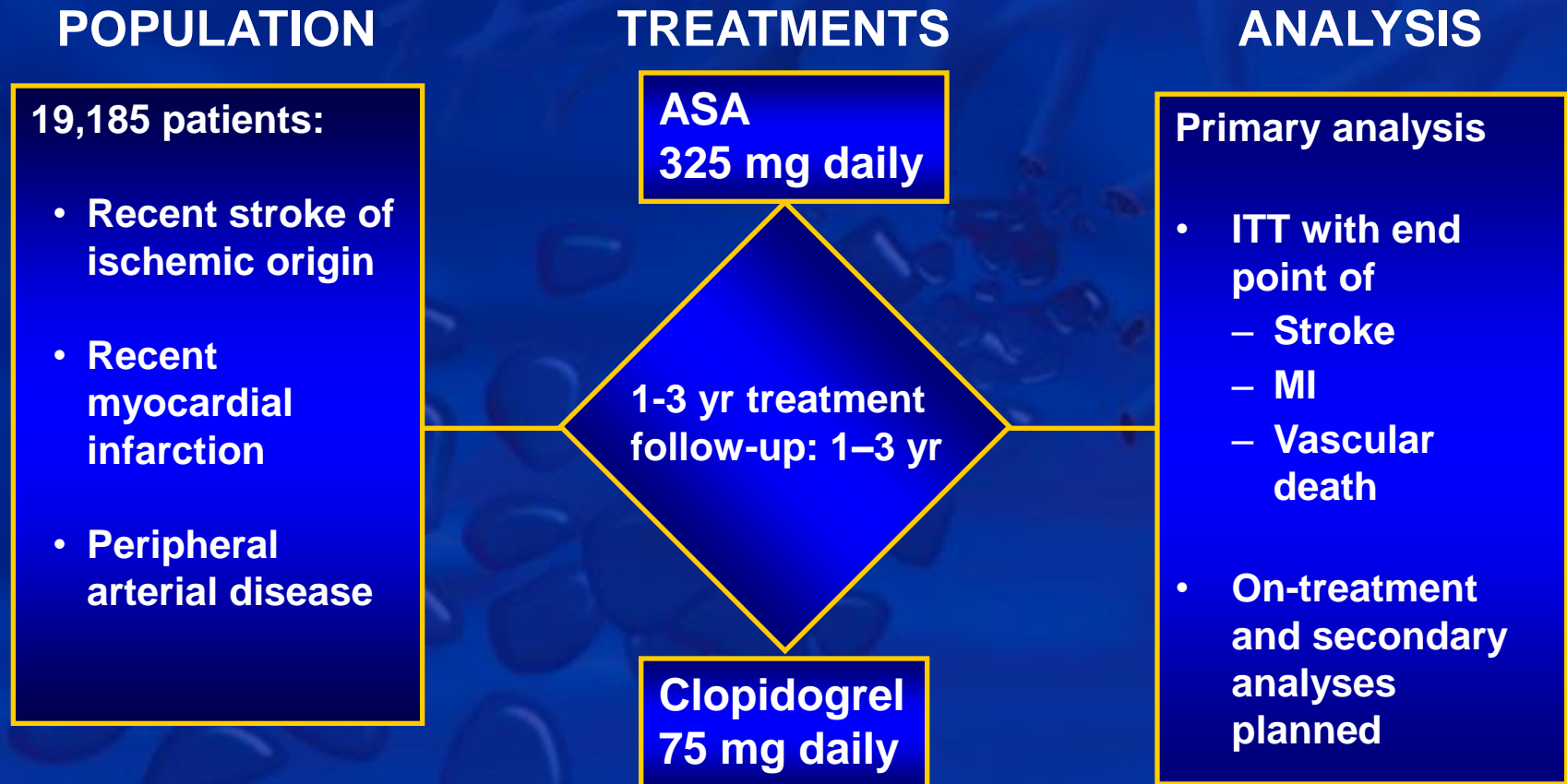
3. Kempczinski RF, Bernhard VM. In: Rutherford RB, ed. *Vascular Surgery*. 1989: chapt 53.



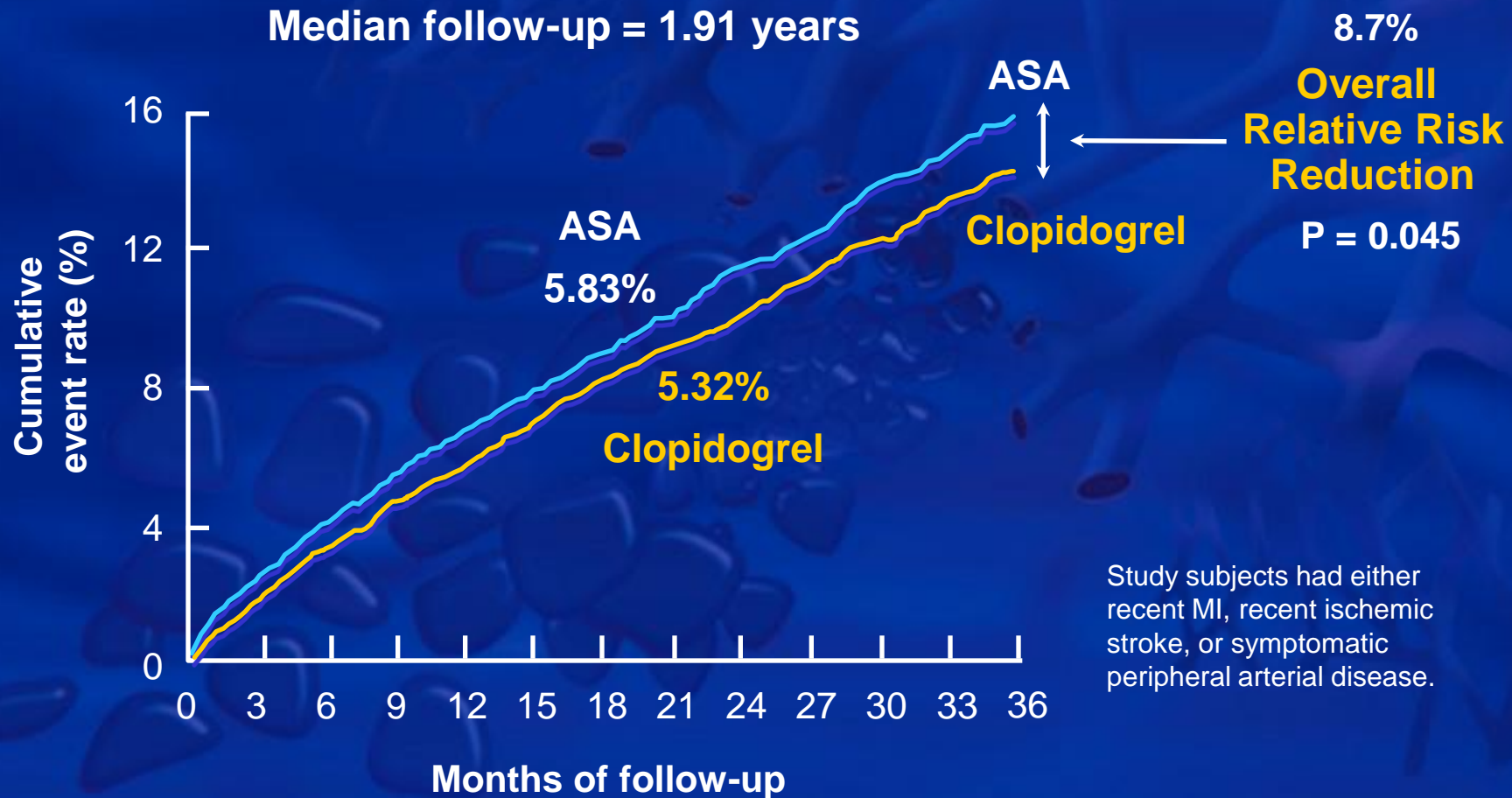
# Antiplatelet therapies: ASA and clopidogrel have different mechanisms of action



## Clopidogrel vs ASA: Clinical Study Design



## Efficacy of clopidogrel vs ASA in MI, ischemic stroke, or vascular death (N=19,185)



## Proven safety profile

### Safety of clopidogrel

	% of patients	
	Clopidogrel (n = 9599)	ASA* (n = 9586)
<b>GI hemorrhage</b>	<b>2.0</b>	<b>2.7</b>
<b>Hospitalization due to GI hemorrhage</b>	<b>0.7</b>	<b>1.1</b>
<b>GI ulcers</b>	<b>0.7</b>	<b>1.2</b>
<b>Intracranial hemorrhage</b>	<b>0.4</b>	<b>0.5</b>
<b>Severe neutropenia</b>	<b>0.04</b>	<b>0.02</b>

Although the risk of myelotoxicity appears to be quite low, this possibility should be considered when a patient receiving clopidogrel demonstrates fever or other sign of infection.

\* Patients with a history of ASA intolerance were excluded from CAPRIE.



# **American Diabetes Association Consensus Statement 2003: PAD in people with diabetes**

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- **“It is recommended that patients with diabetes who are >50 years of age have an ABI performed. An ABI is also useful in patients with other PAD risk factors and in those with symptoms.”**
- **“Patients with diabetes and PAD may benefit more by taking clopidogrel [than ASA].”**

# The Call to Action Paper highlighted 5 key action items

**Increase awareness of PAD and its consequences**

**Improve the identification of patients with symptomatic PAD**

**Initiate a screening protocol for patients at high risk for PAD**

## COMMENTARY

### Critical Issues in Peripheral Arterial Disease Detection and Management

#### A Call to Action

Jill J. F. Belch, MD; Eric J. Topol, MD; Giancarlo Agnelli, MD; Michel Bertrand, MD; Robert M. Califf, MD; Denis L. Clement, MD; Mark A. Creager, MD; J. Donald Easton, MD; James R. Gavin III, MD, PhD; Philip Greenland, MD; Graeme Hankey, MD; Peter Hansch, MD; Alan T. Hirsch, MD; Jürgen Meyer, MD; Sidney C. Smith, MD; Frank Sullivan, PhD; Michael A. Weber, MD; for the Prevention of Atherosclerotic Disease Network

**T**HIS CALL-TO-ACTION document is an initiative of the Prevention of Atherosclerotic Disease Network, an international, multidisciplinary network, joined by the mutual goal of increasing awareness, detection, and treatment rates of peripheral arterial disease (PAD) and increasing awareness of the interrelationship between PAD and the risk of ischemic events. Although the prevalence of PAD in Europe and North America is estimated at approximately 27 million people, PAD remains a largely underdiagnosed and

#### For editorial comment see page 877

undertreated disease. Several recent epidemiologic studies have revealed PAD detection rates of 20% to 30% when specific at-risk populations were screened. In an effort to guide diagnostic and treatment protocols, the Prevention of Atherosclerotic Disease Network has recommended 5 action items. These are to (1) increase awareness of PAD and its consequences; (2) improve the identification of patients with symptomatic PAD; (3) initiate a screening protocol for patients at high risk for PAD; (4) improve treatment rates among patients who have been di-

agnosed with symptomatic PAD; and (5) increase the rates of early detection among the asymptomatic population.

#### INTRODUCTION

Peripheral arterial disease is a distinct atherosclerotic syndrome that is associated with an elevated risk of cardiovascular and cerebrovascular events, including death, myocardial infarction (MI), and stroke. With the prevalence of PAD in Europe and North America estimated at approximately 27 million people, PAD is a critical public health issue.<sup>1</sup>

The deleterious nature of PAD is compounded by its status as an underdiagnosed and undertreated disease. However, several recent developments suggest that this may be an opportune time to reexamine traditional assumptions regarding methods used to diagnose and manage PAD. These developments include (1) data from recent community surveys of PAD prevalence, treatment, and outcomes, which have shed new light on the magnitude of the burden of PAD and its undertreatment<sup>2,3</sup>; (2) a large body of epidemiologic evidence supporting the efficacy of the ankle-brachial index (ABI) [also known as the ankle-brachial pulse index or the ankle/arm index<sup>4</sup>] as an effective diagnostic and risk-assessment tool<sup>5</sup>; (3) increasing awareness of the cost-effective benefit associated with the management of cardiovascular risk<sup>6</sup>; and (4) clinical study results showing that substantial risk reduction

can be achieved with pharmacologic intervention in PAD.<sup>7-9</sup>

This call-to-action document is an initiative of the Prevention of Atherosclerotic Disease Network, an international, independent group comprising specialists in the fields of vascular medicine, neurology, dermatology, nephrology, cardiology, and primary care. The mission of this network is to evaluate current data regarding the prevalence of PAD and thereby to (1) advocate for increased international awareness that PAD is a manifestation of disseminated atherosclerosis and (2) promote effective identification and treatment of patients with PAD to prevent ischemic events. The Prevention of Atherosclerotic Disease Network has achieved consensus that improvement in the detection of symptomatic PAD is of primary importance, since those with symptomatic PAD are at very high risk for an ischemic event and are likely to experience the greatest degree of risk reduction from pharmacologic therapy.

#### PAD EPIDEMIOLOGY, PREVALENCE, AND RISK FACTORS

Peripheral arterial disease is a progressive condition characterized by arterial stenosis and occlusions in the peripheral arterial bed; it can be symptomatic or asymptomatic. Symptomatic PAD ranges in severity from intermittent claudication to critical limb ischemia. Critical limb ischemia exists in part due to the late recognition of PAD, and if

**Improve treatment rates among patients who have been diagnosed with symptomatic PAD**

**Increase the rates of early detection among the asymptomatic population**

## Section 4: Key learning points

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### **REMEMBER**

Early, aggressive management of PAD is important to reduce risk of cardiovascular and cerebrovascular events

### **ACTION**

Manage risk factors aggressively, as per the guidelines, including...

- diabetes
- hypertension
- high cholesterol
- smoking cessation

Don't forget...

- lifestyle modification
- antiplatelet therapy to lower the risk of MI or stroke associated with PAD

## Overall learning points

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**PAD is a reliable warning sign that a patient is at high risk for life threatening cardiovascular and cerebrovascular events**

**PAD is easily overlooked by both patients and physicians – assess whether patients presenting with symptoms or associated risk factors have PAD**

**Treatments are available to protect the patients with PAD from future MI or stroke**



# By whom PAOD should be Treated ?

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- IC            Interventional Cardiologist ?
- IR            Interventional Radiologist ?
- VS            Vascular Surgeon ?
- CS            Cardiovascular Surgeon ?



**Help protect patients with PAD  
from their increased risk of MI or stroke**