The burden of PAD & CAD in patients with diabetes

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Agenda

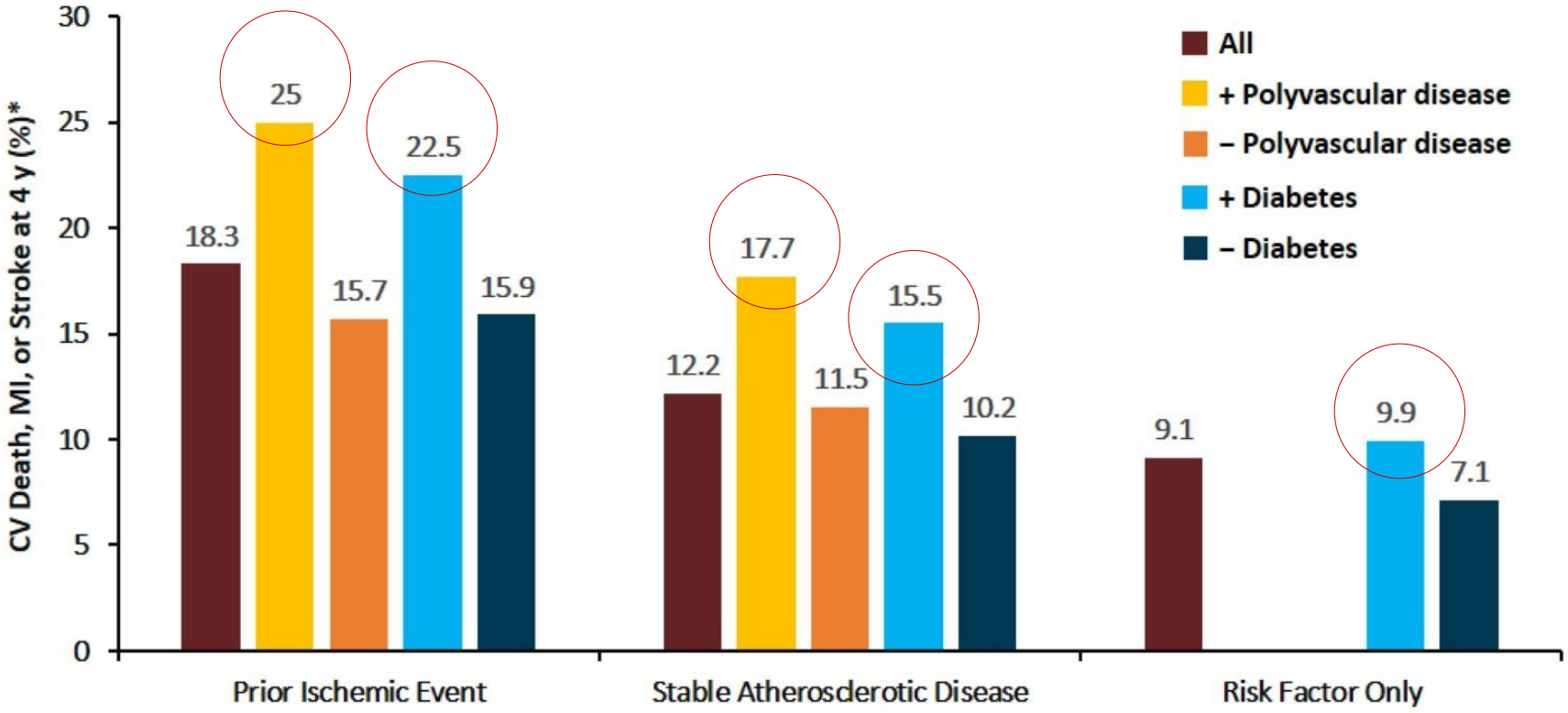
- Introduction
- Burden of CVD and PAD
- Definition of vascular disease
- Peripheral vascular disease
- Screening of PAD
- Prognosis of PAD
- Medical treatment of PAD

Global estimate of association and impact of diabetes on CVD

Outcome	Impact	Data systems / study	Reference
Prevalence of cardiovascular diseases	Any cardiovascular disease: 32% Coronary heart disease: 21% Myocardial infarction: 10% Stroke: 7.6%	57 cross-sectional studies	Einarson et al., 2018[14]
Coronary heart disease	160% increased risk	102 prospective studies	Emerging Risk Factors Collaboration, 2010[12]
Ischaemic heart disease	127% increased risk	102 prospective studies	Emerging Risk Factors Collaboration, 2011[13]
Haemorrhagic stroke	56% increases risk	102 prospective studies	
Cardiovascular diseases death	132% increased risk	97 prospective studies	
Years of life lost	5.8 years for men age 50 6.4 years for women age 50	97 prospective studies	

International Diabetes Federation

Effect of Prior Ischemic Events or Stable Atherosclerosis on CV Events at 4 Years (cont)



Bhatt DL, et al. *JAMA*. 2010;304:1350-1357.

Coronary artery disease

- Coronary artery disease (CAD) is a major cause of morbidity and mortality among patients with diabetes mellitus
- Compared to nondiabetic patients, patients with diabetes are more likely to have CAD, which is most often multivessel, and to have episodes of silent ischemia
- Diabetic patients with CAD have a lower ongterm survival rate than nondiabetic patients with CAD

ADA Guidelines before 2019

Glucose Centric

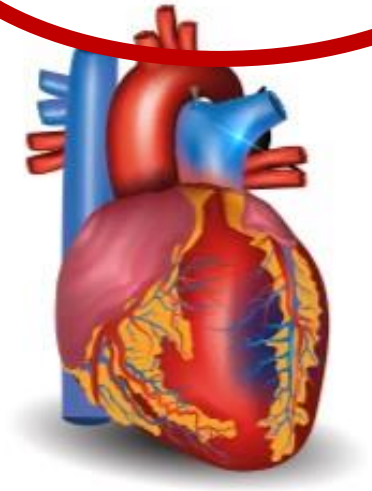
ADA 2019 & 2020

STROKE

AFFECTS THE BLOOD VESSELS SUPPLYING BLOOD TO THE BRAIN

includes:
cerebrovascular disease,
cerebral arterial disease,
intracerebral hemorrhage,
cerebral infarction

CORONARY ARTERY DISEASE



AFFECTS THE BLOOD VESSELS SUPPLYING BLOOD TO THE HEART

includes:
ischaemic heart disease,
atherosclerotic heart disease,
coronary heart disease,
angina pectoris, heart attack
(myocardial infarction),
sudden coronary death

PERIPHERAL ARTERY DISEASE

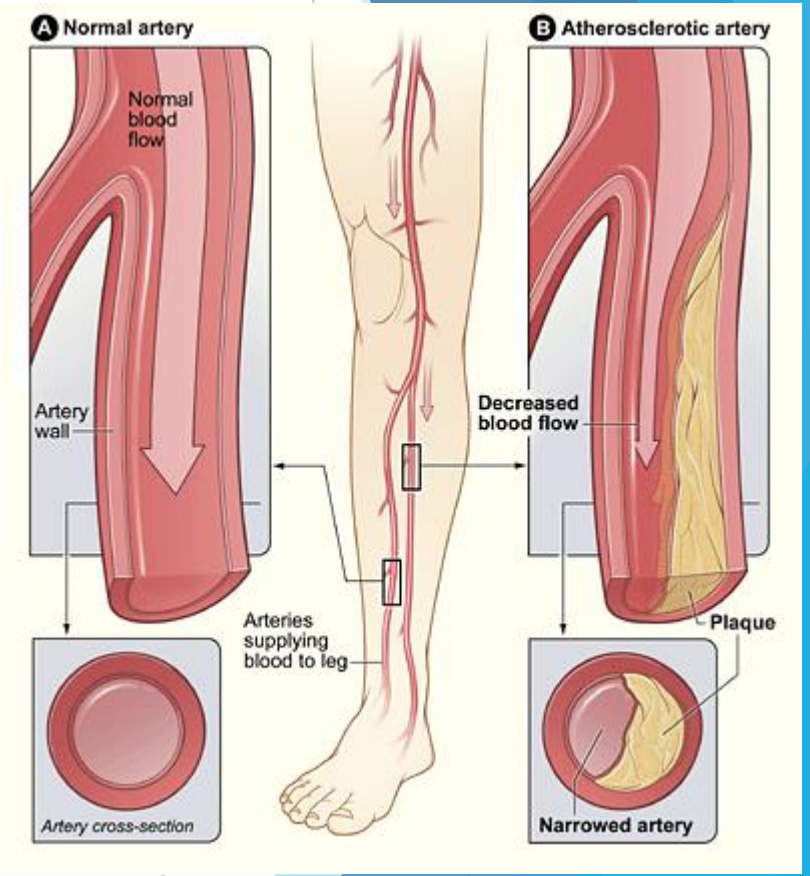
AFFECTS THE BLOOD VESSELS SUPPLYING BLOOD TO THE LEGS AND FEET

includes:
lower-extremity arterial disease,
limb threatening ischaemia,
intermittent claudication,
critical limb ischaemia

Peripheral Arterial Disease (PAD)

- Peripheral Arterial disease, which includes lower-extremity arterial disease, is a narrowing of the arteries other than those that supply blood to the brain or the heart.
  - **Symptoms can include**

  1. Intermittent Claudication
  2. Critical Limb Ischemia



Intermittent claudication

- This term describes pain, usually in the calves when walking, and is due to an impaired blood supply to the calf muscles.

Critical Limb Ischemia (CLI)

- Critical limb ischemia, also known as limb threatening ischemia, is an advanced stage of peripheral artery disease.

- It includes ischemic rest pain, arterial insufficiency ulcers and gangrene.

Figure 2. Photograph of the patient's feet demonstrating early ischemic changes of the left foot. The left foot was cool to the touch, had a slightly mottled appearance, and revealed red discoloration of the toes. All toes showed nail and skin changes, as well as hair loss. No ulcers or gangrene were identified. Note how there was no mark on the dorsum of the left foot, since arterial doppler pulses could not be identified.

Gangrene

- **Gangrene** is used to describe the **death of tissue** due to a loss of blood supply

- **Severe gangrene can occur as a result of:**
  - The blockage of a **large blood vessel**
  - Disease of the smaller blood vessels

Characteristics of PAD in people with diabetes (compared to people without diabetes)
More common
Affects younger individuals
Multi-segmental and bilateral
More distal
More medial calcification
Impaired collateral formation
Faster progress with higher risk of amputation

ADA Guidelines for PAD Care in Diabetes

Facts and Figures:

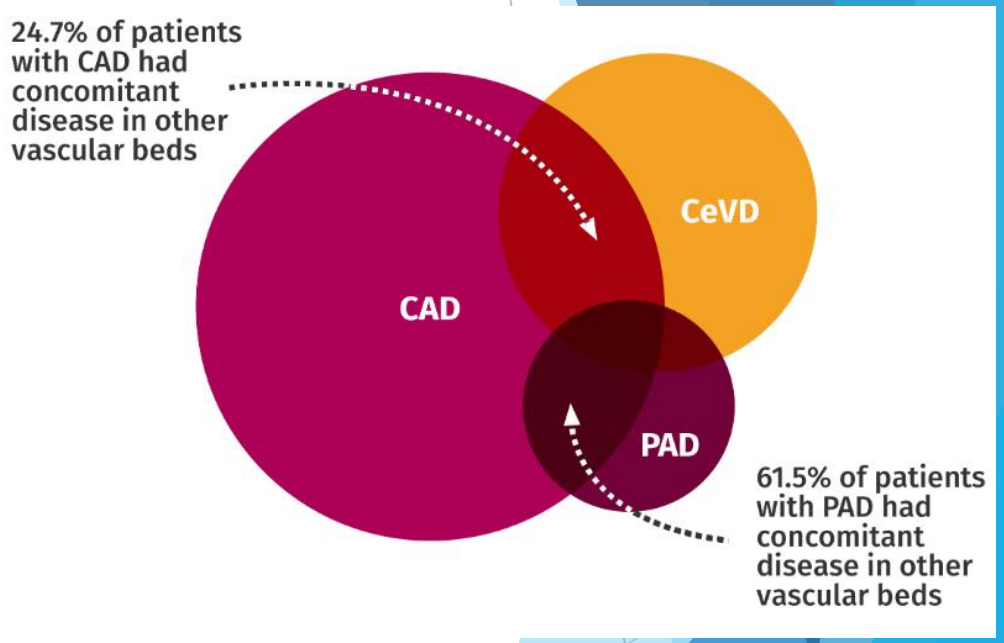
- 29% Prevalence of PAD in diabetics over age of 50 years
- Failing to detect PAD made lead to
  - lower limb amputations
  - Increased five-year risk of MI or stroke with mortality rate of about 33%

Peripheral Arterial Disease in People With Diabetes, Diabetes Care 2003 Dec; 26(12): 3333-3341.

- It is estimated that in middle and high income countries **up to 50%** of patients with **diabetes and foot ulceration** have underlying peripheral artery disease (PAD)

PAD is a polyvascular disease

In the multinational Reduction of Atherothrombosis for Continued Health **(REACH)** registry (N=67,888), 61.5% of patients with PAD had concomitant vascular disease in other vascular bed.



EM, et al. JAMA 2006; 295: 180-9 **Impact of Diabetes on Hospitalization for Heart Failure, Cardiovascular Events, and Death: Outcomes at 4 Years from the REACH Registry**

PAD Underdiagnose in Diabetics

Facts and Figures:

- Of all patients with PAD, **half are asymptomatic**
  - Peripheral Neuropathy in diabetics make the condition asymptomatic

- **One third have claudication**

- Remaining patient have sever disease

Screening and Diagnosis (ADA)

- The **foot examination** should include **neuropathy** and **vascular assessment** including **pulses in the legs and feet**. B
- Patients with **symptoms of claudication** or **decreased or absent of pedal pulses** should be referred for **ankle-brachial index** and further vascular assessment. C

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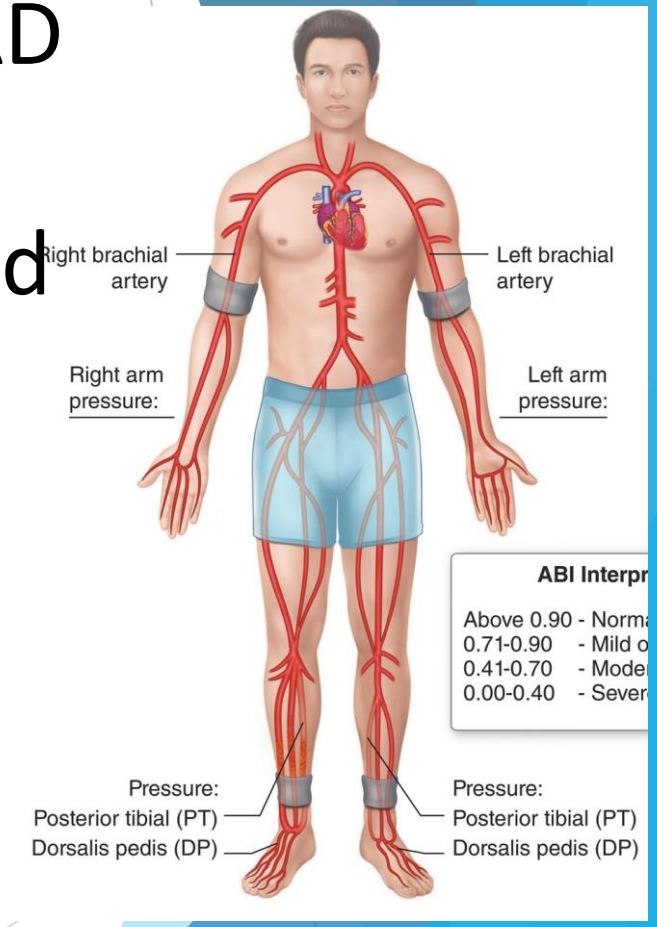
Screening and Diagnosis

- The major cardiovascular societies advise measuring an ABI in every diabetic over 50.
- And in those **younger than 50** years in coexisting hypertension, smoking, hypercholesterolemia, or duration of diabetes more than 10 years.
- If normal, ABI should repeated every 5 years.

Ankle-Brachial Index (ABI)

- ABI is a quick, noninvasive way to check for PAD
- ABI is the systolic pressure at the ankle, divided by the systolic pressure at the arm
- ABI is 95% sensitive and almost 100 specific compared with angiography



Xu Det al.Can J Cardiol. 2013;29(4):492-8.

Table 3.2. ABI categories to estimate degrees of PAD severity in the absence of mediasclerosis.

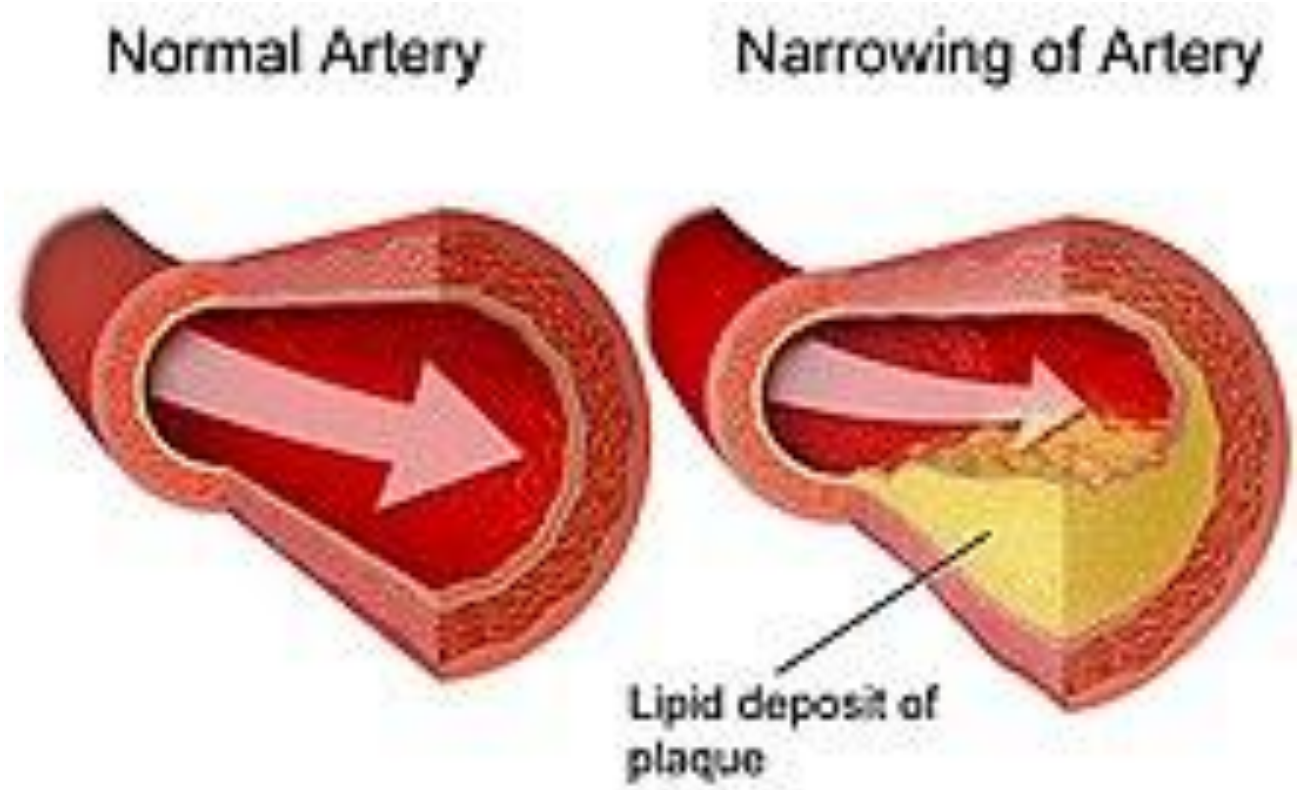
ABI value	Degree of PAD severity
> 1.3	Falsely high value (suspected medial calcific sclerosis)
≥ 0.9	Normal finding
0.75–0.9	Mild PAD
0.5–0.75	Moderate PAD
< 0.5	Severe PAD

Comment: This classification is only valid in the absence of mediasclerosis: If mediasclerosis is suspected, we strongly recommend toe pressure measurement.

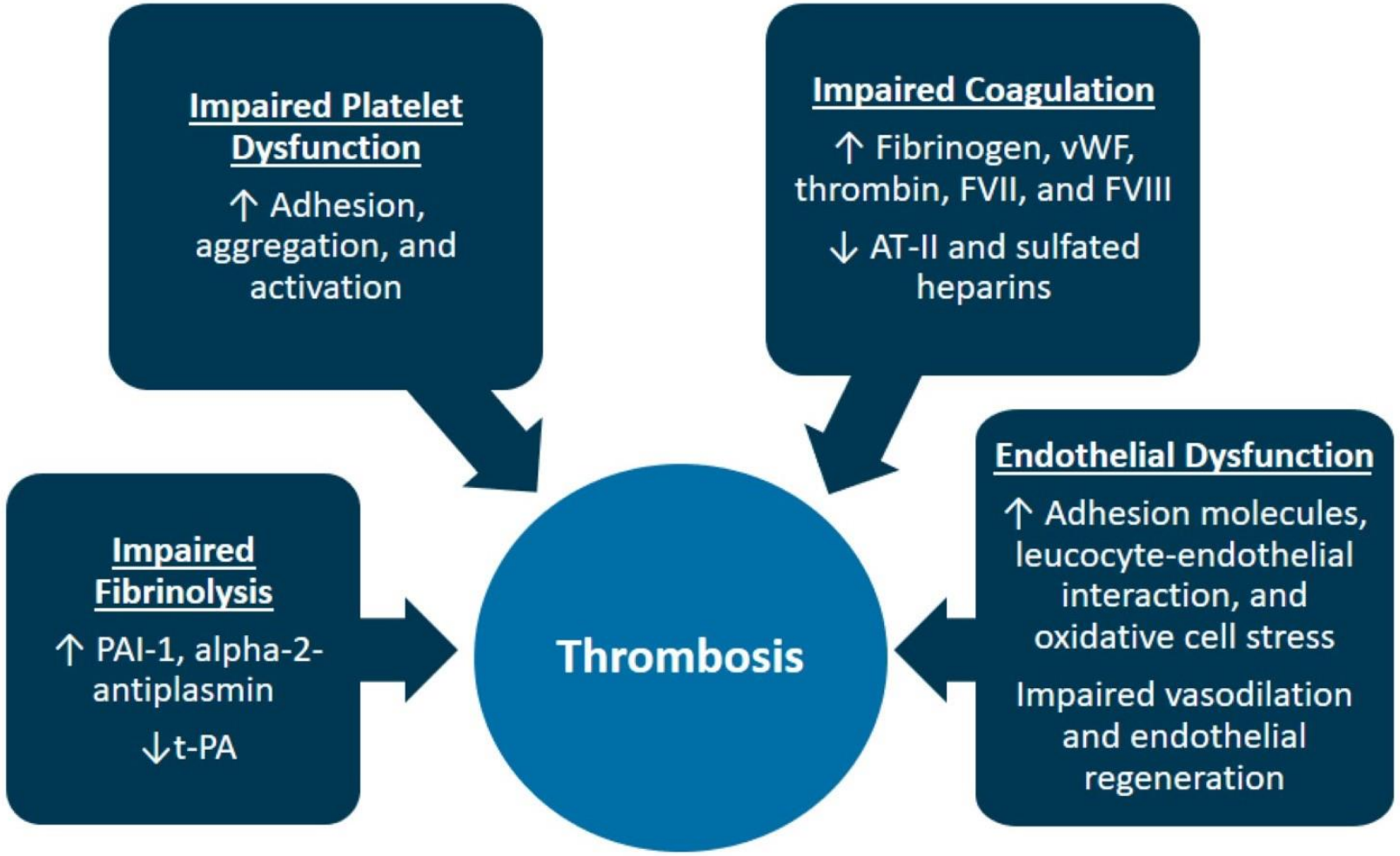
The prognosis of a patient with diabetes

- PAD and foot ulceration requiring amputation is worse than many common cancers – **up to 50% of patients will not survive 5 years**

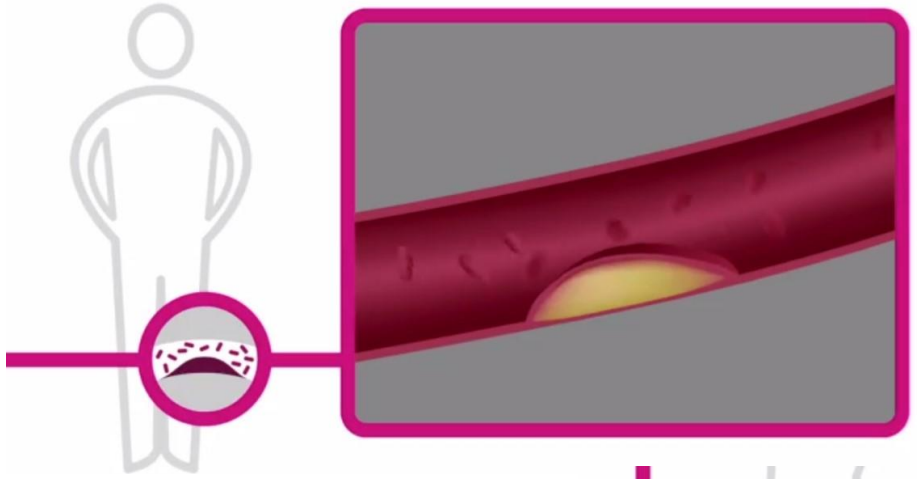
Stenosis or Thrombosis?

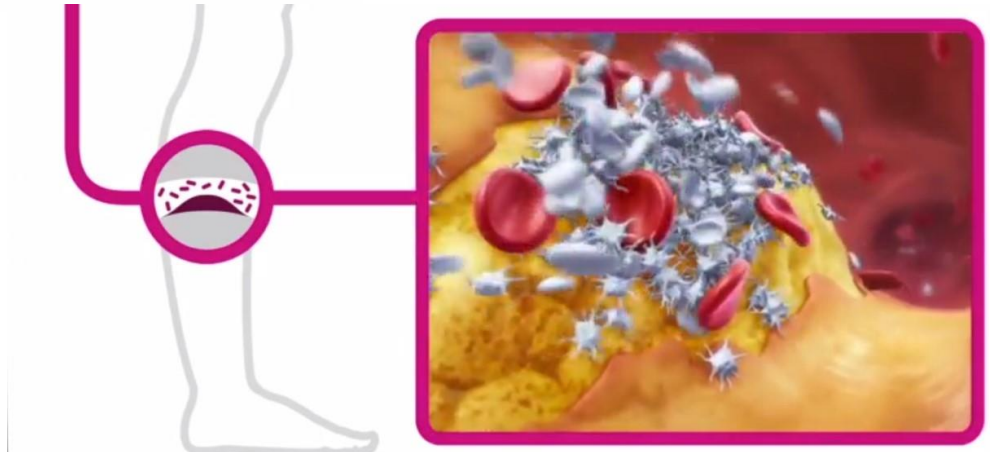


Diabetes as a Prothrombotic State



Angiollilo DJ. *Curr Opin Endocrinol Diabetes Obes*. 2007;14:124-131.





2019 ESC Guidelines
How to Prevent CV Disease in Patients With DM

Lipid control

- Statins remain standard lipid-lowering treatment
- Ezetimibe or PCSK9 inhibitor alone or with a statin can improve CV outcomes and reduce CV mortality

Glucose control

- Glucose control to target a near-normal HbA1c (< 7.0% or < 53 mmol/mol) will decrease microvascular complication
- Tighter glucose control initiated early in younger patients leads to reduced CV outcomes over 20 years

Thrombosis control

- No evidence to support different antiplatelet strategies in patients with ACS or CCS with/without DM
- Those at moderate CV risk: aspirin for primary prevention is not recommended
- Those at high/very high CV risk: aspirin may be considered in primary prevention

Consentino F, et al. *Eur Heart J*. 2019. [Epub ahead of print]

Need for Chronic Antithrombotic Treatment

- Diabetes incrementally increases CV events, such as CV death, MI, and stroke
- High residual risk over time in patients with DM and CVD despite GBMT
- GBMT includes single antithrombotic (primarily aspirin) for secondary prevention (Class I)
  - 2019 ESC Guidelines include dual antiplatelet or dual pathway inhibition in high-risk patients (Class Ia)

Cosentino F, et al. *Eur Heart J*. 2020;41:255-323.

GBMT: guideline based medical treatment

Recommendation	Class of recommendation	Level of evidence
Based on the results of the COMPASS trial, the combined therapy of ASA 100 mg/d and rivaroxaban 2 × 2.5 mg/d should be considered in PAD patients without a high risk of bleeding, or other contraindications.	IIa	B

Vasa (2019), *48* (Supplement 102)

ADA 2021

Combination therapy with aspirin plus low-dose rivaroxaban should be considered for patients with stable coronary and/or peripheral artery disease and low bleeding risk to prevent major adverse limb and cardiovascular events. **A**

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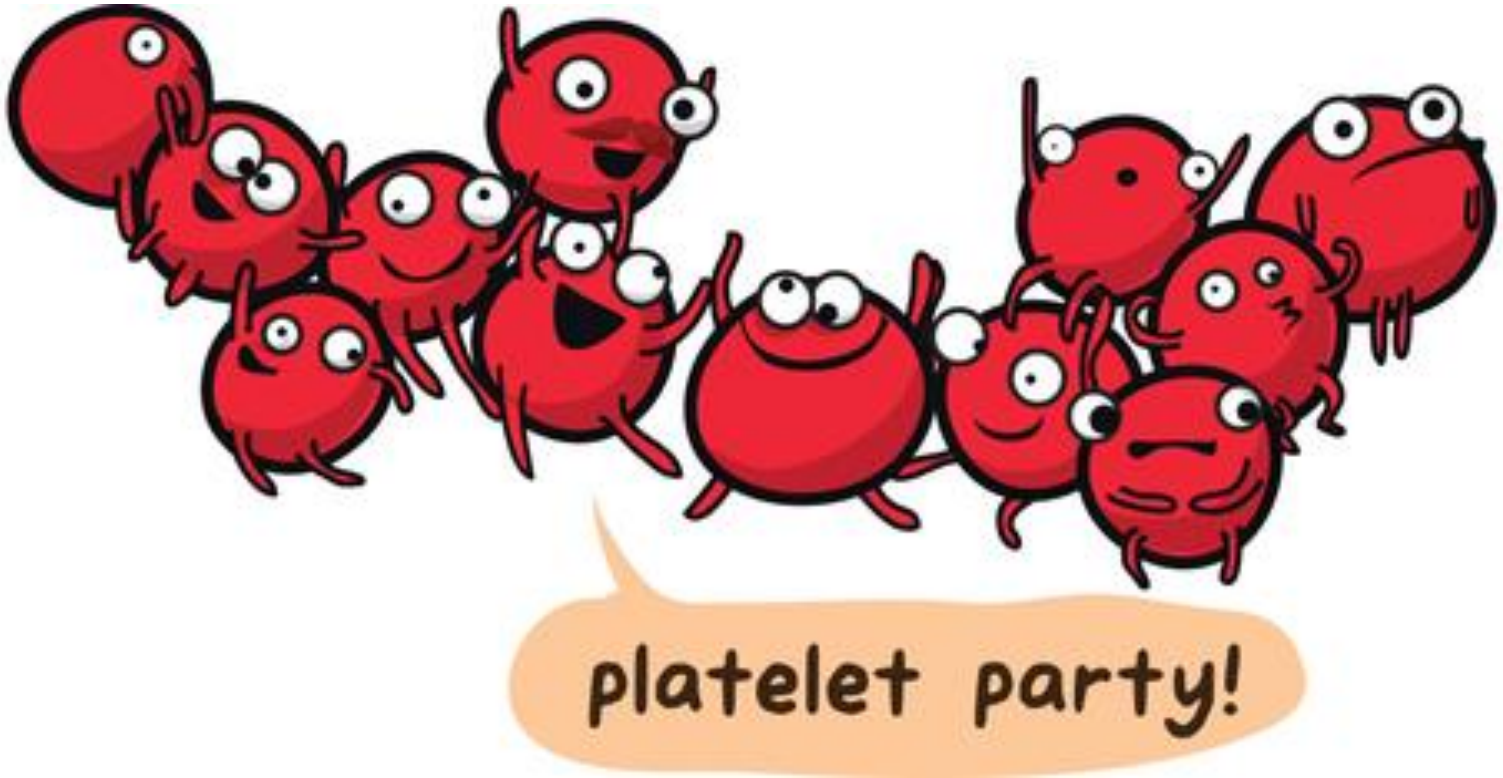
platelet party!