Prevent The 1st Event

Approach for patients with peripheral artery disease (PAD) + T2DM: focus on LDL-C control

PAD is a common manifestation of atherosclerosis and encompasses all vascular sites, including:[1]

- **Lower extremity arteries**
- Carotid artery
- Vertebral artery
- Upper extremity arteries
- Mesenteric artery
- Renal artery
- Aorta

New 2024 ESC guidelines for the management of peripheral arterial and aortic diseases (PAAD) show:[2]

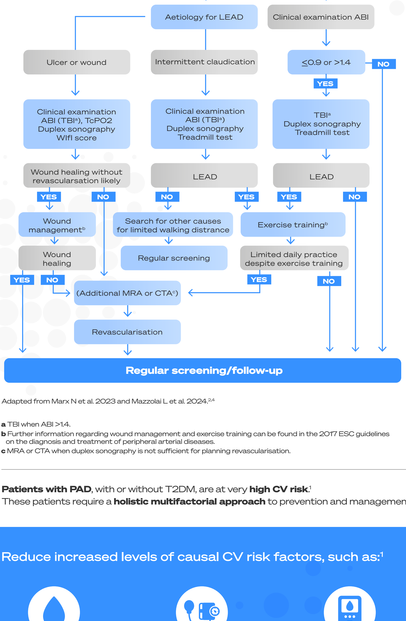
4–5x Increased risk of CV events in patients with PAD compared with those without PAD[2]

Patients with both PAD and T2DM are at a 'very high' risk of cardiovascular events[2]

In a prospective cohort study in Europe, patients with PAD and T2DM had...

~8x Higher risk of CV events* compared to those with neither PAD nor T2DM[3]

Screening for lower-extremity arterial disease (LEAD) is recommended on a regular basis, with clinical assessment and/or ankle-brachial index (ABI) measurement.[2,4]



Adapted from Marx N et al. 2023 and Mazzolai L et al. 2024.[2,4]

a TBI when ABI >1.4.
b Further information regarding wound management and exercise training can be found in the 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases.
c MRA or CTA when duplex sonography is not sufficient for planning revascularisation.

Patients with PAD, with or without T2DM, are at very **high CV risk**.[1]
These patients require a **holistic multifactorial approach** to prevention and management.

Reduce increased levels of causal CV risk factors, such as:[1]

LDL-C
Target: see below

Blood pressure
Target: SBP 120–129 mmHg†

HbA_{1c}
Target is <7.0% (53 mmol/mol)

Reducing LDL-C levels represents the primary target for reducing CV risk[1]
According to the 2019 ESC/EAS dyslipidaemia guidelines, and 2024 ESC chronic coronary syndromes guidelines, all patients with PAD have the following LDL-C goals.[1,2]

An LDL-C reduction of ≥**50% from baseline**‡ and an **LDL-C goal of <55 mg/dL** (<1.4 mmol/L) are recommended

For patients at **very high CV risk** (including those with PAD and T2DM) not achieving their LDL-C goal on a maximum tolerated dose of statin and ezetimibe, combination with **a PCSK9i is recommended.**[1]

Recommendations for pharmacological LDL-C lowering[1]

Step 1 I A
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.

Step 2 I B
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.

Step 3 I A
For secondary prevention, patients at very high risk not achieving their goal on a maximum tolerated dose of a statin and ezetimibe, combination with a PCSK9i is recommended.

Adapted from Mach F et al. 2019 and Mazzolai L et al. 2024.[1,2]

You should aim to assess your patient's response to therapy **6–8 weeks from initiation.**[1]

Prevent The 1st Event for your patients with **PAD + T2DM**¥

*When compared to those with neither PAD nor T2DM, HRs adjusted for age, gender, BMI, smoking, hypertension, LDL-C, and HDL-C were 1.26 (95% CI 0.84, 1.91); P=0.267, HR 4.17 (95% CI 2.97, 5.85); P<0.001, and HR 7.82 (95% CI 5.49, 11.12); P<0.001 for those with T2DM only, for those with PAD only and for those with the combination of PAD plus T2DM, respectively.[3]

†Provided the antihypertensive treatment is well tolerated.

‡The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C-lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.[1]

¥Prevent the first major CV event for your ASCVD patients without prior major CV event.

In a prospective cohort study, cardiovascular events were prospectively recorded over a mean follow-up period of 7.2 ± 2.6 years in 1,049 subjects, encompassing 4 groups: 558 with neither PAD nor diabetes, 153 with T2DM but without PAD, 192 with PAD but without T2DM, and 146 with the combination of PAD and T2DM. 4 PAD patients were defined as those with an ankle brachial index <0.9 or with previous revascularisation of peripheral arteries who underwent routine duplex sonography and in whom PAD was sonographically verified.[3]

ABI = ankle–brachial index; **ASCVD** = atherosclerotic cardiovascular disease; **BMI** = body mass index; **CI** = confidence interval; **CTA** = computed tomography angiography; **CV** = cardiovascular; **EAS** = European Atherosclerosis Society; **ESC** = European Society of Cardiology; **HbA_{1c}** = glycated haemoglobin; **HDL-C** = high-density lipoprotein cholesterol; **HR** = hazard ratio; **LEAD** = lower-extremity artery disease; **LDL-C** = low-density lipoprotein cholesterol; **MRA** = magnetic resonance angiography; **PAAD** = peripheral arterial and aortic disease; **PAD** = peripheral artery disease; **PCSK9i** = proprotein convertase subtilisin/kexin type 9 inhibitor; **SBP** = systolic blood pressure; **TBI** = toe-brachial index; **TcPO2** = transcutaneous oxygen pressure; **T2DM** = type 2 diabetes mellitus; **WIfI** = Wound, Ischaemia, foot Infection.

References:

1. Mach F, Baigent C, Catapano AL, et al. ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111–188.
2. Mazzolai L, Teixido-Tura G, Lanzi S, et al. ESC Scientific Document Group. 2024 ESC Guidelines for the management of peripheral arterial and aortic diseases. Eur Heart J. 2024:ehae179.
3. Saely CH, Schindewolf M, Zanolin D, et al. Single and combined effects of peripheral artery disease and of type 2 diabetes mellitus on the risk of cardiovascular events: A prospective cohort study. Atherosclerosis. 2018;279:32–37.
4. Marx N, Federici M, Schütt K, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC). Eur Heart J 2023;44(39):4043–4140.

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