

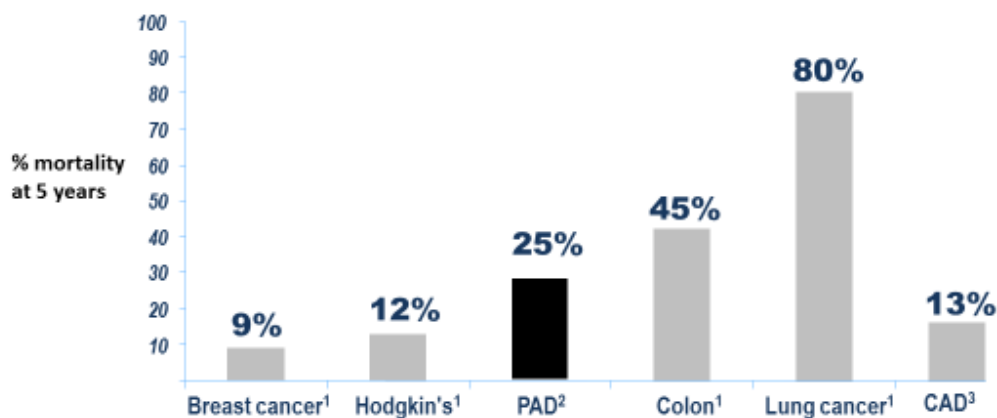
Peripheral Arterial Disease and the need for a SIGN Guideline

Scope of the problem: PAD is underdiagnosed and undertreated

Atherosclerotic disease affecting the arteries of the legs represent a large and growing health burden throughout Europe. It is estimated that peripheral arterial disease (PAD) may affect more than 20% of elderly people worldwide^{1,2}. The burden of aging multimorbid PAD patients with several significant vascular problems is rising² and their outcome is very poor.

Secondary care data on PAD patients shows that the prognosis of many PAD patients is as bad as that of patients with Duke's stage 2b colon cancer³. In 1985 Michael Criqui published the San Diego study⁴ showing a 25% mortality rate at 5 years in intermittent claudication (IC) and 50% from critical limb ischemia (CLI). Worryingly these figures are as true today as in 1985⁵ ie 34 years ago (Fig 1). Whilst morbidity and mortality from coronary disease continues to fall⁶, with mortality at 13% at 6 years, cardiovascular events in PAD have remained the same with the mortality rate persisting at 25%^{7,8} at 5yrs. This dichotomy reflects, in part, an inappropriate divergence from best clinical practice for patients with PAD compared to those with coronary artery disease.

Relative 5-year PAD mortality rates versus common Cancers



¹American Cancer Society. Cancer Facts and Figures – <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf>

² Bartley et al. Eur J Vasc Endovasc Surg. 2018 Apr;55(4):529-536. doi: 10.1016/j.ejvs.2018.01.019

³ Dros-Perroteau C. Six-year survival study after myocardial infarction: The EDLE prospective cohort study. Long-term survival after MI. <https://doi.org/10.1016/j.therap.2019.02.001>

Underdiagnosed.

There are a number of reasons why PAD is underdiagnosed⁹ with about 1/2 of patients having atypical pain¹⁰. Further this is an elderly population who themselves put 'pain in the leg's down to arthritis or 'back troubles'. GPs can do the same, and understandably are reluctant to palpate peripheral pulses within a 10 min appointment slot, with the knowledge that 1/3rd of palpations are wrong in inexperienced hands. So, PAD is an under-diagnosed disease, and the consequence of missing it is a missed opportunity to prevent future cardiovascular (CV) events.

Under-treated

Further, once diagnosed, PAD is grossly under-treated in terms of cardiovascular risk^{REF11, REF12}. The REACH Registry¹³ and other recent papers¹⁴ clearly link CV endpoints in PAD to poor risk management of these patients, and show improved outcome with positive management. Even within this past 12 months publications show disproportionate levels of fatal and non-fatal CV events¹⁵. Again, there are a number of reasons for this, including in the UK the failure of the Quality Outcomes Framework (QoF) to include PAD in its outcome measures (only stroke and Cardiac disease recorded), and this neglect down-prioritised PAD diagnosis and treatment with, I believe, a hangover effect felt today.

Further secondary care for patients with PAD is delivered by Vascular Surgeons whose training is predominantly surgical, and it is only very recently that statin therapy and antiplatelet agents were introduced by Vascular Surgeons, and few surgeons treat to target (ie 40% decrease in non HDL as recommended by SIGN 149¹⁶). Whilst some surgeons are excellent at managing risk, this is certainly not across the board and not to the same competency as in cardiology or via vascular physicians in mainland Europe where Angiology/Vascular Medicine is a sub-speciality of Internal Medicine in 16 EU Countries. Understandably a surgical training does not lend itself to vascular risk management with medical treatments. In summary compared to coronary disease, the sub-optimal management of vascular risk in these patients is well documented, resulting in an unacceptably high incidence of myocardial infarction, stroke, and cardiovascular (CV) death¹⁷.

Proper diagnostics, medical, and interventional treatments as well as follow up, are a priority. Only a multidisciplinary approach with a strong SIGN Guideline targeted to those who actually manage these patients (Primary Care, Vascular Surgeons, and other Vascular clinicians) can address the problem.

The Problem is now compounded by recent trials of medical treatments to decrease amputation

Whilst one might assume that CV risk factor management could be managed with reference to SIGN Guideline 149¹⁶ I wonder how many Vascular Surgeons have read it? This could be an interesting study, but as not specifically targeted to them I doubt it will be many. However recent studies regarding the limb need to be brought to their attention as both the surgeon, and the patient, very much have the limb as a priority, for obvious reasons. Such evidence will, I believe significantly change surgical behaviour and enhance patient compliance when it can be shown that medical treatments benefit the limb.

So for example the 4S study¹⁸ showed that patients on a statin had less likelihood of developing IC, a few small but interesting studies, requiring critical evaluation, show increased walking distance with statins^{19,20}, better endovascular outcomes^{21,22}, again the studies requiring critical evaluation, and importantly fewer amputations in a number of large population based studies of intensive statin therapy²³ (Fig 2)

Statins Have a Dose-dependent Effect on Amputation Risk and Survival in PAD

Association of statin intensity dose with PAD outcomes: amputation risk and mortality at 1, 3 and 5 years

Statin intensity dose	Amputation risk (%)			Mortality (%)		
	1-year	3-year	5-year	1-year	3-year	5-year
No	4.97	7.03	8.33	8.92	22.83	33.85
Low-moderate	4.06	5.84	6.93	5.91	18.13	29.02
High	4.41	5.82	6.43	5.58	14.51	20.20
<i>P-value (chi square)</i>	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

208,275 patients with PAD [Males: 98.1%; Mean age: 67.4 yrs (SD 9.9)], 17,643 amputations and 99,951 deaths occurred in a median follow up of 5.2 years.

Arya S et al. Arterioscler Thromb Vasc Biol 2016;36:A109

PAD, peripheral arterial disease

Such a beneficial effect on the limb if emphasised in Guidelines (or not as per evidence) would greatly enhance surgical uptake and patient compliance.

Further other recent studies have shown medical treatment to not only decrease CV Events but also amputation. This includes the Fourier study²⁴ with a PCSK9 inhibitor, and COMPASS²⁵ with a vascular dose of rivaroxaban and aspirin.

PAD Specific Treatment is neglected

One of the most effective treatments for IC is structured exercise training. Do you know how many units offer this service? Very, very few, and yet the evidence is convincing²⁶, and it appears in all Guidelines²⁷. At best patients are offered cardiac rehab, for which there is no evidence, and at worst told to 'go and exercise' which has been shown to be ineffective. The need for careful podiatry and other management skills is recognised but not practised, again we are failing these patients.

Summary: Why we need a specific PAD SIGN Guideline

- PAD is underdiagnosed, if CV risk management is started before other organ damage ie heart attack and stroke, then outcome is much better.
- PAD is undertreated. This reflects the pathway of care management and a Guideline targeted to the clinicians who look after these patients is crucial
- This undertreatments leads to Cardiac and stroke events but also amputation. Newer treatments decrease limb events as well as CV events elsewhere
- Management of other aspects of PAD is sub-optimal eg structured exercise classes
- I am asking SIGN to redress this inequality of care

JJFB Sept 2019

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