

Characterisation of Patients with Peripheral Artery Disease at Increased Risk for Cardiovascular Events and Mortality

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Background: Peripheral artery disease (PAD) is characterised by atherosclerotic narrowing of peripheral arteries. Despite current medical treatment strategies, the incidence of cardiovascular events and mortality remains high in PAD populations.

Aims: To characterise PAD patients at increased risk for cardiovascular events and mortality.

Methods: Between 2018 and 2020, 250 PAD outpatients (17 newly diagnosed, 233 with known PAD) were enrolled in this observational cohort study. The study was approved by the ethical review board of MUMC+ and all participants gave written informed consent. Patient data and blood samples were collected upon inclusion and the composite endpoint (myocardial infarction, elective coronary revascularisation, stroke, acute limb ischemia, mortality) was evaluated after one year. Platelet reactivity was assessed using citrated platelet-poor plasma in the VerifyNow assay and medication adherence was assessed by the licensed Morisky Medication Adherence Scale-8 (MMAS-8) developed by Morisky et al, categorised as high (8 points), medium (6-7) and low (<6).

Results: The cohort comprised 211 claudicants and 39 chronic limb ischemia patients. Twenty-six patients reached the composite endpoint (*Table 1*). Prior myocardial infarction (OR 3.2 (1.4-7.3)), stroke (OR 4.4 (1.8-10.6)), aortic plaque formation (OR 3.2 (1-10.8)) and higher creatinine (OR 5.1 (2.1-12.1)), but lower high-density lipoprotein (OR 4.1 (1.5-11.4)) and haemoglobin levels (OR 3 (1.3-6.8)) were associated with events. Overall medication adherence was sufficient (75.6% highly adherent), although high adherence was associated with events (OR 4.3 (1-18.7)) due to increased awareness. Patients with events had more high on-treatment platelet reactivity (HTPR) on aspirin (OR 6.1 (1-3-28.3)) and clopidogrel (OR 4.5 (1-20.7)) (*Figure 1*).

	Whole cohort Mean±SD / n (%)	Event group Mean±SD / n (%)	No event group Mean±SD / n (%)	P-value
Age	68.7±9.1	71.5±7.9	68.3±9.2	0.094
Male gender	144 (57.6)	17 (65.4)	127 (56.7)	0.396
Current smoking	95 (38)	11 (42.3)	84 (37.5)	0.633
Body Mass Index	26.5±4.4	27.4±5.9	26.4±4.2	0.403
Diabetes Mellitus II	69 (27.6)	10 (38.5)	59 (26.3)	0.191
Lipid-lowering agents	225 (90)	23 (88.5)	202 (90.2)	0.388
Antihypertensive agents	183 (73.2)	19 (73.1)	164 (73.2)	0.832

Antiplatelet agents	250 (100)	26 (100)	224 (100)	1.000
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Baseline characteristics for the whole cohort and distribution between patients with and without cardiovascular events and mortality during follow-up.

Platelet reactivity measured by the use of the VerifyNow assay in Aspirin Reactions Units (ARU) for aspirin users and P2Y12 Reaction Units (PRU) for clopidogrel users. Dotted lines represent HTPR which is an ARU > 550 for aspirin and a PRU > 208 for clopidogrel.

Conclusions: PAD patients at increased risk for events had more often a prior myocardial infarction or stroke, extensive atherosclerosis with aortic plaque formation and renal insufficiency. Moreover, cardiovascular medication appeared insufficiently protective as lower levels of high-density lipoprotein and more HTPR were observed in patients with events despite adequate medication adherence.

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