Abstract: **P1540**

**Major adverse limb events (MALE) and the relation with classical risk factors in patients with symptomatic cardiovascular disease**

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**On behalf:** UCC-SMART

**Topic(s):**
Risk Factors and Prevention – Epidemiology

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Background: Patients with symptomatic cardiovascular disease are at high risk for recurrent major adverse cardiovascular events (MACE). Major adverse limb events (MALE) are only rarely reported as a (primary) outcome in trials and cohorts although MALE often lead to significant morbidity and disability.

Purpose: The aim of this study was to determine the incidence of MALE in patients with coronary artery disease (CAD), cerebrovascular disease (CVD), peripheral arterial disease (PAD) or abdominal aortic aneurysm (AAA) and to assess to what extent the classical modifiable risk factors systolic blood pressure (SBP), smoking and non-high density lipoprotein cholesterol (non-HDL-c) affect the risk of MALE.

Methods: Patients with symptomatic vascular disease were included from the ongoing UCC-SMART cohort (1996 – 2017, n=8139). MALE was defined as a major amputation, peripheral revascularization or thrombolysis of the lower limb. A major amputation included all amputations at the level of the forefoot or higher due to a vascular cause. For non-HDL-c, smoking (per category: non-smoking, former smoking and current smoking) and SBP, the risk for MALE was analyzed with Cox proportional hazard models adjusted for potential confounders. All results were stratified for the presence of PAD/AAA or CAD/CVD at baseline. To calculate the population attributable fraction, non-HDL-c was dichotomized at 1.8 mmol/L and SBP at 140 mmHg.

Results: A total of 577 MALE were observed in 65,402 person-years (median follow up 7.6 years, IQR 3.9-11.7 years) (figure 1A), of which 32 major amputations. In PAD/AAA patients 413 MALE were observed (incidence rate 24.9/1000 person-years). In the CAD/CVD patients 164 MALE were observed (incidence rate 3.4/1000 person-years). The MALE risk per 1 mmol/L higher non-HDL-c was not elevated: HR 1.01 (95%CI 0.94-1.09) for patients with PAD/AAA and HR 1.03 (95%CI 0.91-1.18) for patients with CAD/CVD (figure 1B). The MALE risk per 10mmHg higher SBP was HR 1.10 (95%CI 1.05-1.15) for PAD/AAA patients and HR 1.14 (95%CI 1.06-1.22) for CAD/CVD patients. In patients with PAD/AAA the risk for MALE by former smoking was HR 1.34 (95%CI 0.92-1.97) and for current smoking HR 1.66 (95%CI 1.14-2.44). In CAD/CVD patients, this was for former smoking HR 2.98 (95%CI 1.65-5.39) and for current smoking HR 6.81 (95%CI 3.72-12.45). The population attributable fraction was 0.13 (95%CI 0.07-0.32) for non-HDL-c, 0.21 (95%CI 0.13-0.28) for SBP and 0.28 (95%CI 0.22-0.33) for current smoking.

Conclusions: The incidence of MALE is high in patients with PAD/AAA, and much lower in patients with CAD or CVD. Systolic blood pressure and smoking increase the risk of MALE in PAD/AAA and CAD/CVD patients. Non-HDL-c was not related to the risk of MALE. These findings confirm the importance of MALE as an outcome in patients with clinical manifest vascular disease and underline the importance of the management of classical risk factors to prevent these disabling clinical events.
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(A) MALE-free or MACE-free survival

(B) Relation between risk factors and risk of MALE

Patients with PAD/AAA:
Non-HDL-c (per mmol/L)
SBP (per 10 mmHg)
Former smoking
Current smoking

Patients with CVD/CAD:
Non-HDL-c (per mmol/L)
SBP (per 10 mmHg)
Former smoking
Current smoking

Models adjusted for (when applicable): age, sex, smoking status, systolic blood pressure, non-HDL cholesterol, diabetes mellitus, body mass index, CRP, eGFR (CKD-EPI)

Abbr: MALE = major adverse limb events; MACE = major adverse cardiovascular events; PAD = peripheral arterial disease; AAA = abdominal aortic aneurysm; non-HDL-c = non high-density lipoprotein cholesterol; SBP = systolic blood pressure; CVD = cerebrovascular disease; CAD = coronary artery disease.