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The extent of atherosclerotic lesions in crural arteries predicts survival of patients with lower limb peripheral artery disease: A new classification of crural atherosclerosis

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ABSTRACT

Background and aims: Several studies report correlation of ankle brachial index (ABI) values and mortality. However, no studies exist on the predictive value of anatomical distribution of atherosclerotic lesions and the extent of atherosclerosis at defined arterial segments on life expectancy. The aim of the present study was to evaluate the significance of both extent and localisation of atherosclerotic lesions to mid-term patient survival.

Methods: Digital subtraction angiography (DSA) images of 887 consecutive patients admitted to the Department of Vascular Surgery at Turku University Hospital (Turku, Finland) were retrospectively analysed. Each angiography was classified according to the TASC II classification for aorto-iliac and femoro-popliteal segments, and a similar four-grade index was created for crural arteries. Patients were followed until 36-months post DSA.

Results: During 36-month follow-up 295 (33%) deaths occurred. Death during follow-up was strongly associated with extensive crural disease, but not with extensive proximal disease (Crural Index III-IV, $p = 0.044$ and < 0.001, respectively). In a Cox regression analysis incorporating baseline variables, Crural Index IV and most severe atherosclerosis on crural vessels were the strongest predictors of poor prognosis (HR 2.20 95% CI 1.3−3.7, $p = 0.003$ and HR 2.45 95% CI 1.5−4.0, $p < 0.001$ respectively).

Conclusions: The extent of crural atherosclerosis is independently associated with poor mid term life expectancy. Therefore, a classification of the extent of crural atherosclerosis could serve as an indicator of mortality among PAD patients and aid in clinical decision making.

1. Introduction

Peripheral artery disease (PAD) is an important cause of morbidity and mortality in western countries. PAD-associated disability and death has increased in all age groups during the past 20 years [1]. The life expectancy of patients with diagnosed large vessel PAD has been shown to be shorter than that of patients without diagnosed PAD [2,3]. Furthermore, widespread atherosclerosis of lower extremity arteries is associated with high mortality compared to that of atherosclerosis localised to other vascular beds [4]. Most of these studies are reporting the predictive value of ankle-brachial index (ABI) on mortality. However, the risk of death and its relation to the extent of atherosclerosis in different vascular segments of the lower limb has not been investigated and there are very few clinical scores assessing mortality risk in PAD [5].

No current classification utilises the extent and distribution of lower limb PAD for risk-analysis of PAD patient outcome. The best current descriptive classifications for characterising lesion extent and severity in lower extremity arteries are aimed at invasive treatment of limb ischaemia in the TASC [6] and TASC II [7,8]

List of abbreviations: ABI, Ankle brachial index; AFS, Amputation free survival; CAD, Coronary arterial disease; COPD, Chronic obstructive pulmonary disease; CI, Confidence interval; CVD, Cerebrovascular disease; DSA, Digital subtraction angiography; ERDS, End-stage renal disease; MACCE, Major adverse cardiovascular and cerebrovascular events; PAD, Peripheral arterial disease; SE, Standard error; SD, Standard deviation; TASC, *Trans*-Atlantic Inter-Society Consensus; WIfI, Wound, Ischemia, and foot Infection.

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recommendations. Additional classifications of severity and distribution of occlusive arterial lesions in the lower extremity have been characterised [9,10], but none of these have been shown to have predictive value regarding patient outcome. Recently, the runoff score of lower limb arteries has been shown to associate with patient outcome and cardiovascular events [11].

The need for new methods for risk assessment of PAD patients has been emphasised [12]. Earlier observations have strongly suggested that atherosclerosis detected with digital subtraction angiography (DSA) could be a useful marker for patient outcome [13,14]. The aim of the present study was to analyse whether the extent of atherosclerotic lesions in the lower limb arteries has predictive value on the outcome of PAD patients.

2. Materials and methods

2.1. Patient cohort

The present study is a retrospective study of all 887 consecutive Caucasian patients admitted to the Department of Vascular Surgery at the Turku University Hospital (Turku, Finland) either for diagnostic DSA or for endovascular treatment of PAD from January 1st, 2009 to July 30th, 2011. All patients were included regardless of earlier PAD history. DSA was the gold standard imaging modality to visualize atherosclerotic changes in lower limb arteries at our department during the study period. The DSA from the clinically more severely affected lower limb was analysed. When both limbs met the criteria for critical limb ischaemia, the limb with the lowest toe pressures was considered worse and entered into the study. If a patient had repeated DSAs during the study period, only data from the first period of hospitalisation was analysed. The study cohort consists of both elective and urgent patients. The local Ethical Committee of the Hospital District of South-Western Finland approved this study.

Patient baseline characteristics were retrospectively collected from our electronic hospital database. Only ICD-10 coded diagnoses were registered. The following risk factors were collected for analysis; coronary artery disease (CAD), carotid artery disease, hypertension, active smoking, diabetes, sleep apnoea, chronic obstructive pulmonary disease (COPD), end-stage renal disease (ESRD), dyslipidaemia, ABI, toe pressures, revascularisation modality and medical treatment (anticoagulant, antithrombotic and statin). The Rutherford classification [15] was retrospectively determined from patient files to assess the clinical severity of ischemia. All patient files were followed up to 38 months to determine all-cause mortality and amputation free survival (AFS) as the hospital registry has a delay of up to 2 weeks in updating mortality data. Furthermore, the date and cause of death was provided by the Cause of death registry of Statistics Finland. Deaths within the patient cohort were registered for the first 36 months, which was the cut-off point for follow-up.

2.2. DSA analysis and description of the crural index

All DSA images were analysed by the corresponding author. The index classification was as described in TASC II for aorto-iliac and femoro-popliteal segments. Aorto-iliac and femoro-popliteal segments (TASC II classification A-D) were modified as follows; no disease was coded as 0, TASC II A was coded as 1, TASC II B was coded as 2, TASC II C was coded as 3 and TASC II D was coded as 4 for the statistical analyses.

For the crural region, all three vessels were first analysed separately. Each crural vessel was coded as follows: No detectable occlusive disease, or minor stenosis 0; Total occlusion less than 5 cm: 1; Total occlusion less than 10 cm: 2; Total occlusion less than 15 cm: 3; Total occlusion more than 15 cm: 4. Only total occlusions were measured, other atherosclerotic lesions were not taken into account. The Crural Index was created by a sum of the three values obtained from each individual crural vessel. If the sum was 0 the Index was 0, if the sum was between 1 and 3 the Index was I, if the sum was 4–6 the Index was II, if the sum was 7–9 the Index was III, and if the sum was 10–12 the Index was IV.

To assess different vascular segments against each other, each patient was assigned into a specific group of disease localisation: 1) aorto-iliac, 2) femoro-popliteal or 3) crural, based on which 0 – IV rating gave the highest number. For example, according to the TASC II classification, a patient had proximal lesions of grade 0 – II, but a Crural Index of III, the patient was assigned to the crural group. However, if the highest grade was equal in two or even three localisations the patient was assigned to the group of the more proximal lesion. For example, a patient with grade IV lesions in all localisations (aorto-iliac, femoro-popliteal, crural) would have been assigned to the aorto-iliac group.

2.3. Statistical analyses

All statistical analyses were performed using the IBM SPSS version 22 statistics program. Categorical variables were expressed as frequency and percentage. For continuous variables, patient characteristics were expressed as mean ± either standard deviation (SD) or standard error (SE). Normal distribution was assessed with Shapiro-Wilk tests. Survival analyses were assessed by Kaplan-Meier curves and Log-rank statistics. Survival and death between groups were compared with ANOVA. A Cox regression analysis was performed to assess the final predictive value of factors affecting survival. Factors with $p < 0.2$ in univariate analysis were selected as independent variables to the Cox proportional hazard model.

3. Results

3.1. Patient characteristics

The male-to-female ratio in the study cohort is 57% and 43%, respectively. During the follow-up time 295 (33%) deaths were registered. Mean age of the patient cohort was 72.4 years ranging from 40 to 98 years. Baseline characteristics are summarized in Table 1. Crural Index grades 0-IV were compared based on patient characteristics and Rutherford class in Table 2. Patient characteristics by most severely diseased arterial segment are shown in Table 3. ABI measurements were available for 792 patients and toe pressures for 791 patients. Measurements were lacking due to either painful crural wounds, absent toes, gangrene, emergent

Table 1
Baseline characteristics (number of patients) of study cohort. Number of patients is 887 in each group except for medication (anticoagulants, antithrombotic and statins) (n = 825).

Cohort demographics	Prevalence
CAD (385)	43.4%
CVD (147)	16.6%
Hypertension (618)	69.7%
Diabetes (379)	42.7%
Sleep apnoea (51)	5.7%
ESRD (92)	10.4%
Dyslipidaemia (310)	34.9%
Smoking history (237)	26.7%
COPD (108)	12.2%
Antithrombotic (599)	73%
Anticoagulants (198)	24%
Statins (473)	57%

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