Erythrocyte Mean Corpuscular Volume Associated with Severity of Peripheral Arterial Disease: An Angiographic Evaluation

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Elevated erythrocyte mean corpuscular volume (MCV) may be a risk factor for peripheral arterial disease (PAD). The aim of the present study was to evaluate whether MCV was associated with the severity of atherosclerotic findings in the lower limbs of PAD patients, as measured by an angiographic scoring system based on vessel lumen reduction. One hundred male patients with symptomatic PAD were studied. MCV was significantly correlated with the angiographic score ($r_a = 0.247, p = 0.013$). PAD patients with an angiographic score in the lower third were compared to those with values in the upper third using a logistic regression model with age, smoking, hypertension, MCV, homocysteine, and total cholesterol and triglycerides as independent variables. This model revealed significant odds ratios (OR) for MCV (OR = 2.02 for an increment of 5 fl, 95% CI = 1.08-3.8) and for age (OR = 2.41 for an increment of 10 years, 95% CI = 1.21-4.81) and facilitated classification of 71% of all subjects correctly. In conclusion, MCV may be associated with angiographically determined disease severity in patients with PAD. This finding supports the hypothesis that MCV is a risk factor for PAD, although the mechanism by which MCV may contribute to the presence and severity of the disease is not yet determined.

INTRODUCTION

Research has confirmed that increasing age, male gender, cigarette smoking, and diabetes mellitus are particularly important risk factors for peripheral arterial disease (PAD).1,2 Other risk factors for PAD include hypertension,1,2 disturbances in lipoprotein patterns3-5 and blood coagulation,2,6,7 as well as elevated total serum homocysteine.8-10 Recently, an elevated mean corpuscular volume (MCV) has been suggested to be a risk factor for PAD.11 It was postulated that a deficiency of folate and/or vitamin B12 might be responsible for this observation, as indicated by the reported correlation of MCV with total serum homocysteine. Because of an additional association of MCV with smoking, an unhealthy lifestyle with a low vitamin intake was thought to cause elevated MCV values in patients with PAD.

To test the hypothesis that MCV is a risk factor for PAD, we carried out a study to evaluate whether MCV was associated with the severity of atherosclerotic manifestation in the lower limbs of PAD patients, as measured by an angiographic scoring system based on vessel lumen reduction. The study population included 100 patients with symptomatic PAD confirmed by angiography and has been previously described in detail.11
There are numerous different angiographic scoring systems for PAD patients, but none of them is generally recommended for assessment of disease severity. Each of these systems is based on the number and severity of atherosclerotic lesions as indicated by a code number. The sum of these numbers usually represents the angiographically documented disease severity. Limitations arise, since these systems use different cutoff values for lumen reduction, and some do not include observations of all segments of the lower limbs.

In contrast, there is one scoring system that has been recommended by the SVS/ISCVS, but this score was developed mainly to gauge the outcome of bypass grafting. Its utility is hindered, however, by its great complexity. As a consequence, we decided to use a modified angiographic scoring system to determine disease severity, as recently described. This allowed the analysis of routine angiographic images by taking into consideration all three arterial segments of the lower limbs in a graduated manner.

**PATIENTS AND METHODS**

We studied 100 consecutive nondiabetic male patients admitted with symptoms of PAD (97 with claudication, 2 patients with rest pain, and 1 patient with an ulceration), aged 40 to 80 years (mean age 60.6 years), who had not undergone previous vascular surgery or percutaneous transluminal angioplasty or amputation, had no symptomatic coronary artery disease or cerebrovascular insufficiency, nor any malignant disease, and who were not on any medication known to influence MCV and/or homocysteine values. The characteristics of the study population and the laboratory methods used have been reported elsewhere in detail. In brief, noninvasive laboratory investigations, consisting of Doppler segmental blood pressure of lower limbs (ATL, HDI 5000) as well as resting anklebrachial index (ABI) measurements, were performed in the study participants. All of them had an ABI ≤0.9 and underwent distal aortofemoral angiography for determination of the location and extent of wall changes. Subjects with systolic blood pressure >145 mmHg and/or diastolic >95 mmHg and subjects using antihypertensive medication were classified as hypertensive. Diabetes mellitus was ruled out by fasting blood glucose levels <126 mg/dL or a glycated hemoglobin <7% without use of glucose-lowering medication. Smoking was specified as the current use of any tobacco. Blood was collected by venipuncture after an overnight fast. MCV, glucose, glycated hemoglobin (HbA1c), and total cholesterol and serum triglycerides were determined by established procedures. Total serum homocysteine values were measured by high-pressure liquid chromatography. Informed consent was obtained from all subjects, and the study was approved by the local ethics committee.

All 100 patients with symptomatic PAD underwent distal aortofemoral angiography (i.e. DSA, Siemens Multistar) with the Seldinger technique via a femoral approach. Studies were done in the anterior-posterior plane with the feet in external rotation. As in the report by Faglia and co-workers, our angiographic study took into consideration the iliac trunk and common femoral artery (treated as a single artery), the superficial femoral artery, the profound femoral artery, the popliteal artery, the anterior tibial artery, the posterior tibial artery, and the peroneal artery, from both limbs. Stenoses in these seven arteries were scored on the basis of vessel lumen reduction, according to the system used by Faglia et al. The sum of points assigned to each of these arteries was called the angiographic score, which was used to estimate the severity of atherosclerosis in the lower limbs. In contrast, our study group divided the points assigned from the calves (the anterior tibial artery, the posterior tibial artery, and the peroneal artery) by 3 and then added this value to the sum of points of the other four arteries (the iliac trunk and common femoral artery, the superficial femoral artery, the profound femoral artery, the popliteal artery). This was summed for both limbs, resulting in a total possible range of 0-30 points. This variation on the procedure was used so that the crural segment, would not be overestimated, since some stenoses in one of the three calf arteries are known to result in a minor reduction of the hemodynamic state, resulting in clinical symptoms.

Statistical analysis was performed with the SPSS 10.0 program. Dichotomous variables are given as prevalence in percent, continuous data are expressed as median (25th-75th percentile). Univariate comparisons of risk factors and other dichotomous variables among study groups were