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Significance of ankle brachial index and collaterals for prediction of critical limb ischemia in infrainguinal peripheral arterial occlusive disease

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ABSTRACT

Purpose: Chronic limb ischemia (CLI) is a clinical diagnosis, but should be approved by technical tests like the ankle-brachial index (ABI). Although the ABI is well established, less is known about the influence of collateralization on clinical stage.
Material/Methods: Magnetic resonance angiographies (MRA) of 129 lower extremities were searched for morphological changes and for the number of collateral vessels according to Sorlie. Ankle pressures were recorded as higher (APmax) and lower (APmin) systolic blood pressures of the two ankle arteries with consecutive calculation of ABImax and ABImin.
Results: In comparisons of ROC curves, APmax (AUC=0.749) did significantly better as a prognostic marker than APmin (AUC=0.642) (p=0.005) and ABImax (AUC=0.744) did significantly better than ABImin (AUC=0.650) (p=0.019). APmax showed a positive likelihood ratio (+LR) of 5.79 and a negative likelihood ratio (-LR) of 0.47 (cutoff ≤55 mmHg). For the number of collateral vessels a +LR 2.27 and a -LR of 0.09 and in patients with an APmax ≤55 mmHg a +LR of 5.50 and a -LR of 0.00 were calculated (cutoff ≤1 collateral vessel).
Conclusion: Whereas APmax is more eligible for verification of CLI, collateral count is better in exclusion of CLI. Both seem to be independent factors for validating the clinical diagnosis of CLI.

Key words: peripheral arterial occlusive disease, critical limb ischemia, ankle-brachial index, collaterals, magnetic resonance angiography

INTRODUCTION

Peripheral arterial occlusive disease of the lower extremity (PAD) affects more than 20% of individuals over 75 years old worldwide [1,2]. Although the majority of these patients are free of symptoms, the prevalence of intermittent claudication (IC) is about 25% to 30% and of critical limb ischemia (CLI) 1% to 3% in the PAD population [3]. Several factors that influence a patient's clinical stage include morphologic, hemodynamic and individual parameters, in which the local perfusion based on macro- and microcirculation may be the most important.

Patients with CLI have chronic ischemic pain or ischemic skin lesions, with either ulcers or gangrene for more than two weeks. Only 1% to 3.3% of IC patients will need a major amputation within a 5-year period whereas 25% of CLI patients will need amputation as primary treatment. Amputations for CLI accounted for almost 60,000 total amputations in Germany in 2008 [3,4]. These patients face a high risk of limb loss and other vascular problems, such as myocardial infarction and stroke because of poor prognosis of CLI. Results indicate a one-year prognosis of 25% mortality, 20% with continuing CLI, 30% amputation and 30% with a resolved CLI [3]. Therefore, it is important to diagnose CLI correctly because alternative diagnoses could be diabetic neuropathy, complex regional pain syndrome or nerve root compression with a better prognosis.

According to the Trans-Atlantic Inter-Society Document on Management of Peripheral Arterial Disease (TASC) II, CLI is a clinical diagnosis but should be verified by objective tests such as ankle pressure (AP), ankle-brachial index (ABI), toe systolic pressure (TSP) or transcutaneous oxygen tension (tcpO2) [3]. Of these, ABI is the easiest to perform in daily clinical routine. It is calculated as the quotient of the highest systolic blood pressure of the two ankle arteries of that limb and the higher of the two brachial systolic blood pressures (BBP) of the upper limbs. However, current publications report about a better sensitivity and overall accuracy to detect PAD by using the lower of the systolic blood pressures of the two ankle arteries to calculate the ABI [5,6].

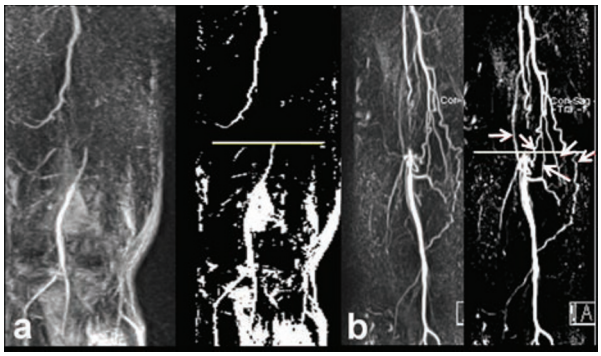
Another important compensatory mechanism in PAD is the degree of collateralization of vascular lesions [7]. Even though the number of collaterals can be determined by angiography, their impact on tissue perfusion is difficult to specify. This may be the reason why collateralization in PAD is rarely published, and guidelines such as TASC II or ACC/AHA guidelines do not consider this point [3, 8]. Whereas ABI and TSP only reflect the impaired macrocirculation in the examined vessel, the degree of collateralization expressed by the number of collaterals may particular influence the extent of microcirculation. Time-consuming technical procedures such as tcPO2 or contrast-enhanced ultrasound (CEUS) can provide information about tissue perfusion and both macro- and microcirculation (including the degree of collateralization) [9,10]. A collateral count in angiograms and an ABI measurement seem easy to perform and are inexpensive methods to obtain similar information.

This study aims to prove the impact and predictive value of ABI and collateralization on diagnosing CLI in arteriosclerotic patients.

PATIENTS AND METHODS

Magnetic resonance angiography (MRA) was performed on seventy-nine patients with PAD at our center for vascular diseases. One hundred and twenty-nine lower extremities of these patients showed an infrainguinal PAD and were included in our study. The medical records and MRA for all included patients were reviewed. From the medical records, sex, age, clinical status (according to Rutherford), and concomitant diseases were extracted retrospectively for each patient. The clinical stage was documented after the exclusion of other differential diagnoses. For ABI and AP measurement, a standard sphygmomanometer and a Doppler ultrasound device with an 8-MHz continuous-wave probe (handydop®, Elcat, Wolfratshausen, Germany) was used. Blood pressure measurement was performed after at least 10 minutes of rest. APs were recorded as APmax and APmin for the higher (APmax) and lower (APmin) of the systolic blood pressures of the two ankle arteries. Subsequently, ABI was calculated as the quotient of the higher (ABImax) and lower (ABI min) of the systolic blood pressures of the two ankle arteries of that limb and the higher of the two brachial systolic blood pressures (ABImax=APmax/BBP; ABImin=APmin/BBP). Patients with suspected mediasclerosis, previous vascular reconstruction, and significant lesions in the aorta, ipsilateral iliac artery, common or deep femoral arterieswere excluded from this study.

Figure 1. **Method described by Sorlie to rate the number of collateral vessels crossing a line at the distal end of the vascular lesion. No collateral vessel (a) and 5 collateral vessels (→) crossing the line (b).**



A 1.5 Tesla Magnetom superconducting magnet (Siemens, Erlangen, Germany), with a moving-table and a whole-body spiral for the lower legs, femoro-popliteal and aorto-iliacal vascular territory, was used to perform all of the MRAs. All MRA source images and MIP reconstructions were independently examined by two observers (A.Z., C.R.) without knowledge of the patient's clinical data. In case of disagreement, a final consensus examination was performed. The quantification of collateral vessels was performed according to Sorlie's method, which counts the collaterals passing the distal ending of the vascular lesion. These collaterals are mainly responsible for compensation of the vascular obstruction *(Fig. 1)* [11].

All statistical analyses were performed using MedCalc® version 9.6.4.0 (MedCalc Software, Mariakerke, Belgium). Normal distribution was excluded using the D'Agostino-Pearson test. The Mann-Whitney-U test for two independent groups and the Kruskal-Wallis test for more than two independent groups were used to compare the level of quantitative data. Spearman's method was used to express the correlation coefficient between clinical stage and number of collaterals. Receiver operating characteristic (ROC) plot analysis was applied to compare the performance of AP, ABI and the number of collaterals in order to discriminate patients with critical and non -critical PAD. Area under the ROC-curve (AUC) was reported to assess overall predictive performance of the different analysis methods. Ninety-five percent confidence intervals were reported for AUCs indicating statistically significant predictive capability if the critical value of 0.5 is not included. The sensitivity and specificity of the ROC curve were used to determine optimal cut-off values for the prognostic markers by using the Youden index (*J*=maximum[