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Clinical Research

In Patients with Severe Peripheral Arterial Disease, Revascularization-Induced Improvement in Lower Extremity Ischemia Can Be Detected by Laser Speckle Contrast Imaging of the Fluctuation in Blood Perfusion after Local Heating

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Background: We previously reported the utility of the perfusion value (PV) fluctuation slope for detecting severe ischemia in the lower limb. Our approach was based on a thermal load test mimicking the well-known physiological reaction termed ''cold-induced vasodilation,'' which is known to occur as a 3-phase phenomenon. The slope parameter quantifies the decrease in PVs accompanying the relative cooling (third phase) following the transient increase in blood flow (second phase) induced by the applied thermal load. This phenomenon of ''relative'' cold-induced vasodilation (rCIVD) can be monitored using laser speckle contrast imaging (LSCI) after applying the thermal load (LTL test). Here, we aimed to determine whether the slope parameter obtained via the LTL test also reflects the improvement in hemodynamics after revascularization.

Methods: The study enrolled 16 patients (18 limbs), who underwent revascularization for peripheral arterial disease (PAD). The measurements were performed at 2 sites in each limb (in total, 34 sites; 2 sites in one patient were excluded because of significant movement during the measurement). For each site, we recorded the slope describing the behavior of PVs (decrease or plateau) in the third phase of rCIVD, following the initial, heating-induced increase in perfusion (second phase of rCIVD). The plateau group (group P), which included patients with an abnormal rCIVD, and the decrease group (group D), which included patients with a normal rCIVD, were defined based on perfusion slope values of <0.20 and ≥ 0.20 perfusion units/min, respectively. We also quantified the transient increase in perfusion (from baseline to peak) as a descriptor of perfusion behavior during the second phase of rCIVD.

Results: In group P, the change in median values (25−75%) of the slope, transcutaneous oxygen tension, and ankle-brachial index (ABI) from before to after operation was (−0.02 [−0.04 to 0.02]; 4 [1−11]; and 0.08 [0−0.27]) to (0.39 [0.32−0.59]; 46 [37−54]; and 0.81 [0.72−0.90]). Conversely, in group D, the change in the median values of the slope, transcutaneous oxygen tension, and ABI between before and after operation was (0.38 [0.32−0.49]; 40.5 [35−45];

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and0.58 [0.57−0.65]) to (0.44 [0.30−0.64]; 52 [43−56]; and 0.92 [0.81−0.99]). Sites exhibiting perfusion pattern of group D in the third phase of rCIVD showed no significant change in slope after revascularization ($P = 0.21$), whereas the slope in group P increased significantly after revascularization, becoming similar to the postoperative slopes in group D ($P = 0.81$). The amount of transient increase in perfusion, which quantified the behavior in the second phase of rCIVD, showed a similar behavior. Preoperatively, all patients in group P had rest pain and/or ulcer of the foot, whereas only few patients in group D had such symptoms.

Conclusions: Normal rCIVD response in the LTL test indicates less-than-severe ischemia, while abnormal rCIVD response measured via the LTL test indicates severe ischemic symptoms, such as critical limb ischemia. Notably, patients with an abnormal rCIVD response can develop a normal rCIVD response following revascularization, thereby reflecting an improvement in blood flow. The LTL test assessing rCIVD response can be useful for detecting severe limb ischemia, such as critical limb ischemia (CLI), and determining the departure from severe limb ischemia by revascularization.

INTRODUCTION

According to the Fontaine and Rutherford classifications, critical limb ischemia (CLI) is a symptom of peripheral arterial disease (PAD) involving typical chronic ischemic rest pain or ischemic skin lesions in the form of ulcers or gangrene.[1,2] Although a diagnosis of CLI should be confirmed by objective measurements, such as the ankle-brachial index (ABI) or transcutaneous oxygen tension ($tcPO_2$), it is well known than there is no complete consensus regarding the vascular hemodynamic parameters required to establish the diagnosis of CLI.[1]

To perform a more accurate and physiologically relevant assessment of perfusion, we focused on the physiological reaction, termed ''cold-induced vasodilation'' (CIVD) or the ''hunting reaction.'' CIVD is believed to serve as a protective mechanism to prevent cold weather injury to the extremities and is characterized by a triphasic response to local cooling, which consists of an initial, rapid vasoconstriction as the first phase, followed by transient vasodilation as the second phase, and prolonged vasoconstriction as the third phase.[3−6] In our previous study, we confirmed that the fluctuation in blood flow due to ''relative'' cooling after local heating induced using laser speckle contrast imaging (LSCI) is similar to CIVD, and therefore have termed this behavior, ''relative'' cold-induced vasodilation (rCIVD). We quantified the decrease in blood flow in the third phase of rCIVD induced by such an LSCI thermal load (LTL) test in terms of the corresponding linear regression slope. When stratifying the measurement sites according to the slope parameter (i.e., greater versus smaller slope, representing a sharp decrease versus plateau of perfusion in the third phase of rCIVD), we were able to predict severe limb ischemia with high accuracy (sensitivity, 78.7%; specificity, 96.2%) among patients with a plateau pattern of perfusion and $tcPO_2$ below 30 mm Hg.[7] Thus, we defined group plateau (group P) as those patients with a slope < 0.20 (perfusion unit [PU]/min), which indicated a deficiency in prolonged vasoconstriction during the third phase of rCIVD, which has since been termed ''abnormal rCIVD.'' Conversely, we defined group decrease (group D) as those patients with a slope ≥ 0.20(PU/min), which indicated a typical prolonged vasoconstriction during the third phase of rCIVD, which has since been termed ''normal rCIVD.'' It is unknown how blood flow improvement obtained by revascularization is reflected in the perfusion behavior during the second and third phase of rCIVD. The aim of the present study was to confirm the usefulness of the LTL test as a new evaluation method for detecting severe limb ischemia and complementing the assessment of revascularization outcomes in patients with PAD. For this purpose, we compared the prerevascularization and postrevascularization values of parameters, including the slope obtained in the LTL test, against the values of ABI and $tcPO_2$, which are conventional parameters used for assessing limb ischemia in PAD.

MATERIALS AND METHODS

Patients and Study Protocol

Between January and June 2015, patients who were hospitalized at our vascular surgery unit for more than 6 days after revascularization for PAD were recruited. PAD was diagnosed based on the presence of >50% vessel stenosis due to lesions in the lower limbs, which were assessed on computed tomography (CT) angiography, duplex ultrasound sonography, and/or magnetic resonance (MR) angiography. We excluded patients with acute leg ischemia due to emboli. Furthermore, we excluded patients with an axillary temperature over 37.0°C, inflammatory diseases, such as malignancy, and