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Characterizing tissue perfusion after lower extremity intervention using two-dimensional color-coded digital subtraction angiography

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ABSTRACT

Objective: Digital subtraction angiography (DSA) of the peripheral arterial vasculature provides lumenographic information but only a qualitative assessment of blood flow. The ability to quantify adequate tissue perfusion of the lower extremities would enable real-time perfusion assessment during DSA of patients with peripheral arterial disease (PAD). In this study, we used a novel real-time imaging software to delineate tissue perfusion parameters in the foot in PAD patients.

Methods: Between March 2015 and June 2016, patients (N = 31) underwent lower extremity angiography using a two-dimensional perfusion (2DP) imaging protocol (Philips Healthcare, Andover, Mass). Of the 31 enrolled patients, 16 patients received preintervention and postintervention DSA images (18 angiograms), while contrast agent injection settings and the position of the foot, catheter, and C-arm were kept constant. The region of interest for perfusion measurements was taken at the level of the medial malleolus. Perfusion parameters included arrival time (AT) of contrast material, wash-in rate (WIR), time to peak (TTP) contrast intensity, and area under the curve (AUC).

Results: Patients (mean age, 67 years; male, 61%) undergoing 2DP had limbs classified as Rutherford class 3 (n = 9 limbs), class 4 (n = 11), and class 5 (n = 14) ischemia with a mean ankle-brachial index of 0.63. For the whole cohort, median (interquartile range) AT measured 5.20 (3.10-7.25) seconds; WIR, 61.95 (43.53-86.43) signal intensity (SI)/s; TTP, 3.80 (2.88-4.50) seconds; peak intensity, 725.00 (613.75-1138.00) SI; and AUC, 12,084.00 (6742.80-17,059.70) SI*s. A subset of patients had 2DP performed before and after intervention (n = 18 cases). A detectable improvement in SI and two-dimensional flow parameters was seen after intervention. Average AT of contrast material to the region of interest shortened after intervention with percentage decrease of 30.1% ± 49.1%, corresponding decrease in TTP of 17.6% ± 24.7%, increase in WIR of 68.8% ± 94.2% and in AUC of 10.5% ± 37.6%, decrease in mean transit time of 18.7% ± 28.1%, and increase in peak of 34.4% ± 42.2%.

Conclusions: The 2DP imaging allows measurement of blood flow in real time as an adjunct to DSA. The AT may be the most sensitive marker of perfusion change in the lower extremity. Quantitative thresholds based on 2DP hold promise for immediate treatment effectiveness assessment in patients with PAD. (J Vasc Surg 2017;■:1-9.)

Evaluation for peripheral arterial disease (PAD) can be accomplished through several noninvasive measures. The ankle-brachial index (ABI) has been validated against contrast angiography to yield sensitivity of 79% to 95% and specificity of 96% to 100% in predicting a 50% stenosis.[1-3] Although it is a useful screening tool, it cannot be used during angiography to provide real-time objective feedback to the operator about treatment efficacy. In addition, ABIs are not accurate in patients with noncompressible vessels, such as those often seen in diabetics, and it cannot localize diseased vasculature in the foot.

Whereas noninvasive testing provides objective data with prognostic value, contrast angiography is the "gold standard" for evaluating vascular anatomy. Angiography in conjunction with digital subtraction permits a subjective visual assessment of intraluminal vessel diameter and flow down the limb while allowing concurrent endovascular interventions.[4] However, visualization with this approach is limited in small vessels distal to the knee and in settings of poor inflow.[5] Furthermore, visual assessment of flow is dependent on the operator's judgment and thus may be inconsistent across operators.

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Two-dimensional perfusion (2DP) imaging is one tool that may address this deficit. It is a postprocessing software that color codes the flow of contrast material using digital subtraction angiography (DSA) images. As contrast material flows through a specified region of interest (ROI), the 2DP software detects an increased pixel density, or signal intensity (SI), and extrapolates quantitative information by generating SI curves within the ROI. This allows the operator to make rapid assessment of perfusion during angiography without the need for additional DSA runs. The 2DP tool allows measurements of six different parameters, some of which include arrival time (AT), time to peak signal density (TTP), the rate of contrast material wash-in (WIR), and overall signal density in the area (Table I). In addition to intraoperative analysis, a second look can also be conducted at a workstation after the procedure. It has been previously used in analysis of cerebral flow after an intervention[6-9] and in the peripheral vasculature.[10-14] Here in a prospective study, we sought to determine the feasibility of using the 2DP (Philips Healthcare, Andover, Mass) color-coded angiography to measure hemodynamic changes in the lower extremities after an endovascular intervention in patients with known PAD. We hypothesize that because contrast material would move more slowly down an extremity with severe PAD, two-dimensional (2D) parameters that reflect transit time, such as AT, transit time down the leg, and TTP, would increase, whereas parameters reflecting volume or velocity, such as SI, area under the curve (AUC), and WIR, would decrease.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective single-center cohort study
- **Take Home Message:** This study evaluated a novel real-time imaging software tool (two-dimensional perfusion) in 31 patients with peripheral arterial disease to quantify tissue perfusion, from which 18 angiographies included a pre- and postintervention perfusion imaging, and found that arrival time of contrast material may be the most sensitive marker of perfusion change.
- **Recommendation:** The study suggests that two-dimensional perfusion imaging may be a useful software tool to assess effectiveness immediately after intervention for peripheral arterial disease.

METHODS

Patient enrollment. Enrollment occurred from March 2015 to June 2016. After Institutional Review Board approval, patients undergoing lower extremity angiography for PAD as demonstrated on a noninvasive vascular laboratory study or for symptoms of claudication, rest pain, or minor tissue loss were approached for this study and enrolled after written consent. Exclusion criteria included presence of renal dysfunction (creatinine concentration >2.5 mg/dL) that did not require dialysis and history of previous foot amputations. After the patient was enrolled, an ABI of the affected limb was performed before the procedure. This ABI was either obtained at an accredited vascular laboratory or performed manually by the study team at the time of encounter. After intervention, another ABI was obtained immediately postoperatively. Preintervention demographic and clinical characteristics data were captured and are outlined in Table II, *A* and *B*, for the entire cohort and the preintervention vs postintervention cohort, respectively. Our power calculation demonstrated 0.8 power with an effect size of 0.5 and a significance level of .05, requiring 31 patients for enrollment.

Table I. Perfusion parameter descriptions

Parameter	Description
AT, seconds	Time interval from the start of DSA imaging to contrast material entry into the ROI; estimation of blood velocity
LTT, seconds	Time interval for contrast material to travel from injection site to the ROI; AT + DSA delay time; estimation of blood velocity
TTP, seconds	Time to peak SI within an ROI; estimation of blood flow rate within an ROI
Width, seconds	Duration of elevated SI within an ROI as measured by the midpoints of the upstroke and downstroke of the SI curve; reflective of wash-in and wash-out rate
MTT, seconds	Duration of elevated SI within an ROI as measured by arrival of contrast material to an ROI to the center of gravity of the SI curve; estimation of blood volume and reflective of wash-in and wash-out rate
WIR, SI/s	Change in the SI over time; estimation of blood volume and blood flow rate
AUC, SI*s	AUC as measured from the contrast material AT to contrast material exit from the ROI; estimation of blood volume
Peak intensity, SI	A measurement of the highest contrast material concentration within an ROI; indirect estimation of volume

AT, Arrival time; *AUC,* area under the curve; *DSA,* digital subtraction angiography; *LTT,* leg transit time; *MTT,* mean transit time; *ROI,* region of interest; *SI,* signal intensity; *TTP,* time to peak; *WIR,* wash-in rate.

2DP protocol. The 2DP software provides measurements of six different parameters, characterizing the change in contrast SI over time within an ROI. AT is the time between the start of DSA and the detection of contrast material within the ROI. TTP is the time between the first detection of contrast material and the peak SI, and WIR is the slope of the SI curve. These three parameters help elucidate the briskness of blood flow down the lower extremity. The total volume of blood reaching