Pulsatile blood flow asymmetry in paired human legs

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Summary. Average leg blood flow has been extensively measured using non-invasive methods, but knowledge concerning pulsatile flow at specific leg cross-sections in normal or vascuarily impaired limbs is quite limited. The present study used nuclear magnetic resonance flowmetry to address two fundamental questions; (1) to what extent are pulsatile flow differences present between paired-legs? and (2) is paired-leg flow symmetry affected by the presence of lower extremity arterial disease (LEAD)? Comparisons of left-right leg pulsatile blood flow (ml/min), perfusion (ml/min/100cc), and arterial status index at multiple leg sites showed highly significant correlations between legs ($P<0.001$) in 57 normal and 37 patients with LEAD. To evaluate symmetry, the ratio of lower to higher paired-leg flow parameter values at five below-knee sites were averaged. Results showed all ratios significantly greater in normal subjects ($P<0.001$). These findings establish the distribution and range of leg flow symmetry in vascuarily normal individuals and show significant symmetry reductions accompanying bilateral LEAD. Although the cause of the asymmetry is presently unknown, non-uniform disease progression between paired legs may be involved. These initial findings provide a basis for subsequent research regarding the possible use of bilateral flow asymmetry assessment to further clarify the pathophysiological progression process and the possibility of using symmetry-based parameters to develop early markers of sub-clinical peripheral arterial disease progression.

Key words: flow symmetry, leg blood flow, magnetic resonance, peripheral arterial disease, pulsatile blood flow, vascular disease.

Introduction

Methods for the measurement of average blood flow in human legs for physiological and clinical purposes has long been available using minimally invasive (Lassen, 1964) and non-invasive methods (Sumner & Strandness, 1969; Sumner 1993). As clinical tools, such measurements have been used to study resting and hyperemic flow features of limbs that

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mellitus was present in 41 subjects with a mean duration of 16.8 years (5.43 years, sd=10.8 years).

LEG BLOOD FLOW MEASUREMENT

On a follow-up visit (within one week of screening) eligible participants returned to the laboratory whereupon pulsatile blood flow was evaluated in each leg under resting, supine conditions using the method of nuclear magnetic resonance flowmetry (NMRF). With this method the participant is placed on a moveable table which is advanced by an operator so as to position a specific leg site within the center of a tubular measurement section of the NMRF system (Metriflow AFM100, Milwaukee). Within the measurement section a fixed magnet (0.1 Tesla) causes the hydrogen nuclei of the fluids within the leg to precess at a very precise frequency, and an NMR sensor detects the amount of precession. The main NMR signal detected and processed is due to precession of hydrogen nuclei associated with intravascular water. As the precession frequency is very specific, it is possible to finely tune the detection processor to optimally detect the amount of hydrogen precession within the vascular compartment of the leg which is exposed to the magnetic field. The magnitude of the detected signal is proportional to the number of precessing hydrogen nuclei and is, thus, proportional to the amount of vascular water flowing into and out of the measurement section. Non-pulsatile flow (e.g. tissue water, venous flow) produces small contributions which, in any case, are filtered out by the system. Calibration to obtain absolute blood flow is accomplished using a pulsatile flow pump which drives water, doped with a paramagnetic solute to simulate the NMR characteristics of blood, through a phantom limb composed of simulated vessels which is positioned within the NMRF measurement region. The pump pulsatile flow is registered using an electromagnetic sensor and a range of calibration flows are used (0-120 ml/min) to obtain a calibration curve. The calibration is done each day prior to patient use and a calibration factor relating actual pulsatile flow to NMR magnitude is automatically determined by the system software. Further technical details and theoretical aspects regarding the NMRF may be found in the literature (Battocletti, 1986; Kerr et al., 1991; Kofler et al., 1991; Rice, 1994; Salles-Cunha & Beebe, 1994).

PROTOCOL AND BLOOD FLOW PARAMETERS

For the present study, the measurement protocol started with a 15 min supine acclimation interval after which pulsatile leg blood flow (Q, ml/min; see Fig. 1 for example) was measured bilaterally at five below-knee sites. This measurement includes the sum of all pulsatile arterial flow passing peripherally through the leg cross-section within an axial segment five cm in length. The flow measuring sites were standardized for all participants by first measuring the length (L) between the medial malleolus and the tibial tubercle at the knee. Five leg sites located at 10, 25, 50, 75 and 90% of L as measured from the malleolus were then marked. Leg circumference measurements at each site were used...
Fig. 2. Blood flow relations between paired legs at different anatomical sites. Panels show left-right pulsatile flows (circles) at the 10%, 25%, 50% and 75% leg sites for 91 subjects. The 10% site is closest to the ankle. Solid lines are linear regression lines for data with equations and parameters as shown in each individual panel. All regressions are highly significant ($P<0.001$). A slight increase in the correlation value ($r$) is noted from ankle toward knee.

overall leg comparisons between groups were made on a site-by-site basis and overall leg values were tested using the non-parametric Mann-Whitney U-test.

Results

OVERALL PAIRED LEG RELATIONSHIPS

Figure 2 illustrates the relationship of left to right leg blood flow at four of the measured sites. Significant correlations ($P<0.001$) are present at all sites, but a trend for a decrease in the correlation ($r$-value) from knee toward ankle may be noted. Figure 3 shows the relationship between paired values for leg averaged parameters. Highly significant direct correlations for each are demonstrated with associated regression equations as shown in the figure. For all legs evaluated ($n=182$) flow, perfusion and ASI were found to correlate with ABI in a nonlinear fashion and best fitted in each case with exponential regressions as shown in Fig. 4.

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Fig. 4. Relationship of blood flow parameters to Ankle-Brachial Index. The perfusion and ASI are below-knee averages and flow is that measured at L.=50%. All flow parameters are significantly ($P<0.001$) but nonlinearly related to ABI with regression equations and parameters as shown in the figure. The strongest correlation is noted between ASI and ABI.

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the physiological flow distribution. However, at each site the flow of the LEAD subjects is significantly less than at corresponding sites in the NORM subjects. Separate analyses show that the nonlinear change in site mean flow is well expressed by quadratic regressions as shown in the table legend.

Discussion

Nuclear magnetic resonance flowmetry is a relatively new technology which has been used for the assessment of various aspects of lower extremity arterial pulsatile blood flow. Kerr and co-workers (Kerr et al., 1991) were among the first to report on the potential, as well as the shortcomings, of the first generation commercially available system used in the present study. Sumner (1991), commenting on the usefulness of this method in a clinical setting, pointed out that, even though the method reliably measures pulsatile flow, its clinical usefulness as compared with other, less expensive and already available non-invasive methods was questionable for a variety of well argued reasons. Contrasting, several workers have suggested unique applications of NMRF. Salles-Cunha and co-workers (Salles-Cunha et al., 1989) reported that the beneficial effects of percutaneous transluminal angioplasty in patients with ABI>0.8 are best demonstrated by comparing pre- and post-angioplasty NMR flows. Serial measurements following femoropopliteal angioplasty may also provide early warning of impending graft failure or developing restenosis (Bendick et al., 1992), although an adequate patient base is not yet available to substantiate this concept. However, when considering the role of NMRF in the diagnostic laboratory, the question of cost benefit is prominent. The system cost is greater but in the neighborhood of that required for an advanced color flow duplex ultrasound system, with some additional costs associated with installation. This initial capitalization would need to be reflected against certain operational benefits. In our hands, a complete bilateral leg assessment can be done in about 15 min, thus, freeing significant amounts of technician time. The flow data obtained is objective, reliable, independent of operator subjectivity, and is not subject to artifacts associated with segmental pressure measurements in calcified vessels as may be present in patients with diabetes, end-stage renal disease and other conditions. The fact that the flow measurement is non-contact also allows for assessment of flow in patients with leg bandages in place and at sites of open wounds and burns on the lower extremities. These features have been of particular utility in the authors’ laboratory. However, the main use of the NMRF technique, in our hands, has been as a clinical/physiological research tool (Mayrovitz & Larsen, 1994; 1996) and the present study is similarly targeted.

The main objective of the present study was to determine the physiological symmetry in pulsatile leg blood flow between paired legs, and secondarily to investigate the effect that lower extremity arterial disease presence might have on that symmetry. The pulsatile component of blood flow perfusing the lower extremities is dependent on multiple factors, but the flow symmetry between paired legs is primarily related to the vascular and haemodynamic differences between legs. Differences in flow to paired organs, even
In summary, the present findings establish the range and distribution of leg pulsatile blood flow symmetry in vascularity normal individuals and indicate significant reductions in symmetry accompanying bilateral LEAD. These initial findings provide a basis for subsequent research regarding the possible use of bilateral flow asymmetry assessment to further clarify the pathophysiological progression process and the possible use of symmetry-based parameters in the development of early markers of sub-clinical peripheral arterial disease progression.

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