Vascular Surgery

VOLUME 30 JULY/AUGUST 1996 NUMBER 4

Pulsatile Blood Flow Indices in Lower Extremity Arterial Disease: Leg Only Compared with Leg and Cardiac Parameters

Harvey N. Mayrovitz, Ph.D.
and Parry B. Larsen, M.D.

MIAMI BEACH, FLORIDA

ABSTRACT

The relative diagnostic value of pulsatile leg blood flow and indices with and without normalization to cardiac stroke volume was determined in 100 subjects (200 legs) with and without lower extremity arterial disease (LEAD) who were stratified on the basis of ankle-brachial pressure index (ABI). Leg blood flow parameters (magnetic resonance flowmetry) included absolute pulsatile flow (Q, mL/min), leg flow per stroke (LSV, mL), and an arterial status index (ASI, mL/min/100 cc). Cardiac stroke volume (CSV) was determined by transthoracic bioimpedance cardiography and was used to obtain the normalized leg/cardiac parameter LSV/CSV. Results show that all tested parameters provide significant statistical separation between LEAD and normal limbs ($P < 0.001$) but that normalization by CSV was least good and offers no benefit as compared with the leg parameters. Further, based on analysis of receiver operator curves, the ASI parameter, which is derived from leg blood perfusion data, provides the best sensitivity (93.7%–98.1%) and specificity (81.8%–77.7%) of all parameters tested.

From the Department of Vascular Research, Vascular Laboratory and Wound Healing Center, Miami Heart Research Institute, Miami Beach, Florida.

Research supported by a grant-in-aid, American Heart Association, Florida Affiliate.

Introduction

It is a well-recognized and long-standing principle that the mean level of resting calf blood flow is generally not a useful diagnostic indicator for lower extremity arterial disease (LEAD).[1] However, a number of investigators have attempted to use measurements of leg pulsatile flow and derived indices for diagnostic purposes employing magnetic resonance and bioimpedance techniques.[2-5] Okuda and co-workers[5] used impedance cardiography to estimate cardiac stroke volume (CSV) and impedance plethysmography to estimate leg blood flow stroke volume (LSV) and reported that the ratio LSV/CSV was a reliable diagnostic indicator of arterial disease. Others have used leg flow pulsatile indices directly without normalizing for cardiac stroke volume and have reported favorable results.[2,4] There is a logic to using the ratio of leg to cardiac stroke volumes if the pulsatile component of leg flow is correlated with the magnitude of cardiac stroke volume. Patients with similar levels of LEAD but differing in cardiac stroke volume might present with pulsatile leg flow differences only partially related to the leg pathology, thereby causing larger variances in the data. Similarly, pulsatile leg flow in subjects free of arterial disease may be influenced by cardiac stroke volume if a significant correlation between leg and cardiac stroke volumes exists. The purpose of the present study was to determine whether such a correlation could be detected in subjects with and without LEAD and to determine whether discrimination between these groups is improved by the use of leg/cardiac ratios as compared with leg flow indices alone.

Methods

Cardiovascular Parameters

A total of 100 subjects were evaluated after signing an Institutional Review Board (IRB)-approved informed consent. Before leg blood flow was measured and immediately after, cardiac stroke volume (CSV) assessments were done using the method of transthoracic bioimpedance cardiography[6] with band electrodes in the tetrapolar configuration[7] with the subject supine;[8] the averages of the values obtained before and after leg flow measurements were used (Minnesota Impedance Cardiograph, model 304). Mean blood pressure (MBP) was obtained with an oscillographic automated system (DYNAMAP). CSV multiplied by measured heart rate (HR) yielded cardiac output (CO), and CSV and CO were also expressed as the body surface indices CSVI and CI by dividing by body surface area. Total systemic vascular resistance (TSR) was approximated as the ratio of MBP to CO. The length parameter used in the stroke volume calculation was the mean of the anterior and posterior distance between sensing band electrodes.[7] An extensive literature shows the correlation of bioimpedance values with a variety of other methods for cardiac output monitoring.[9]

Leg Blood Flow Measurement

Following a fifteen-minute supine acclimation interval, pulsatile leg blood flow, (Q, mL/minute) was measured bilaterally at five below-knee sites by the method of magnetic resonance flowmetry (Metriflow AFM100, Milwaukee). Principles of operation, validation studies, and applications of this method have been reported.[2,10] The flow-measuring sites were standardized for all subjects by first measuring the distance between the lateral malleolus and the tibial tubercle. Five leg sites between the malleolus and knee were marked at locations equal to 10%, 25%, 50%, 75%, and 90% malleolus-tubercle distance with the zero reference point at the malleolus. Thus flow measured at the 90% site (referred to as Q90) represents the approximate pulsatile flow perfusing the lower limb. Leg circumference measurements at each site were used together with an algorithim incorporated in the AFM100 system to calculate blood perfusion (Q′) expressed as mL/minute/100 cc of distal tissue volume. For each site, a derived quantity known as arterial status index (ASI) was calculated as the ratio of the perfusion pulse 50% amplitude divided by the corresponding pulse width normalized to the cardiac period. Since the ASI value is sensitive to both the amplitude and relative width of the flow pulse, it has been reported to better discriminate between patients with and without LEAD than perfusion values alone.[3,4] The leg average of all measured sites was used to characterize the ASI of each leg. Brachial and ankle systolic blood pressures were measured at the end of the leg blood flow determinations by Doppler ultrasound, and the ankle/brachial index (ABI) was calculated.

Subject Groupings

For statistical comparisons, subjects were stratified into one of two groupings based on the ABI value; if ABI was <=0.85 in either leg, the subject was assigned to the LEAD subgroup; otherwise the subject was assigned to the normal leg subgroup (Norm).

Results

Overall Relationships

Overall relationships between leg stroke volume (LSV) and cardiac stroke volume (CSV) were tested by separate correlation analysis by use of the LSV of the leg with the lower ABI and the leg with the higher ABI value as the paired variable. In each case LSV was calculated as the pulsatile flow measured at the 90% site (Q90) divided by HR. Similar tests were done using the leg stroke volume index (LSVI, mL/100 cc) calculated as the leg average Q′ divided by HR and correlated with cardiac stroke volume index (CSVI).

For all subjects (n=100) both CSV and CSVI were inversely correlated with subject age (r= 0.373 and 0.389 respectively, $P < 0.001$); neither LSV nor LSVI was age related ($P > 0.50$). For legs with the lower ABI, statistically significant correlations between LSV and CSV (r=0.341, $P < 0.001$) and between LSVI and CSVI (r=0.336, $P < 0.001$) were detected by using partial correlation and controlling for age. Corresponding correlations for the legs with the higher ABI were similar but slightly less; between LSV and CSV r=0.328, $P < 0.001$, and between LSVI and CSVI, r=0.304, $P < 0.002$.

Comparisons Between Subgroups

Table I summarizes and compares the systemic cardiovascular parameters between LEAD and Norm subjects by use of independent t tests. No parameter was significantly different between groups with the exception that LEAD subjects were significantly older. Table II compares the leg parameters (paired leg with the lower value of ABI) between the two groups. All tested parame-

Table I

Systemic Cardiovascular Parameters

	Subject Grouping		
Parameters	LEAD	Norm	P Value
N	31	69	
CSV (mL)	79.6 (5.7)	89.9 (3.8)	0.108
CSVI (mL/m^2)	42.1 (2.9)	47.8 (2.0)	0.120
CO (L/min)	5.2 (0.3)	5.9 (0.2)	0.057
CI (L/min/m^2)	2.7 (0.1)	3.1 (0.1)	0.058
HR (min^{-1})	67.7 (2.2)	67.5 (1.5)	0.840
MBP (mmHg)	104.3 (2.9)	98.3 (1.9)	0.129
Age (yr)	70.7 (1.6)	56.5 (1.9)	0.001

Values are mean and (SEM). CSV and CSVI are cardiac stroke volume and index, CO and CI are cardiac output and index, HR is heart rate, MBP is mean blood pressure. N=number of subjects.

Table II

Parameters for Legs with the Lower ABI

Parameters	Subject Grouping: LEAD	Subject Grouping: Norm	t Value
N	31	69	
LSVI/CSVI (%)	0.04 (0.01)	0.07 (0.01)	4.34
LSV/CSV (%)	0.79 (0.10)	1.24 (0.10)	4.60
Q'_{90} (mL/min/100 cc)	1.12 (0.08)	1.92 (0.08)	4.71
LSV (mL)	0.59 (0.05)	1.02 (0.06)	5.79
LSVI (mL/100 cc)	0.017 (0.001)	0.030 (0.002)	6.35
Q_{90} (mL/min)	38.3 (3.0)	65.8 (3.0)	6.38
Q_{50} (mL/min)	20.8 (1.9)	39.0 (1.6)	6.61
ASI (mL/min/100 cc)	2.69 (0.25)	7.50 (0.31)	12.0
ABI	0.59 (0.03)	1.07 (0.01)	12.4

Values are mean and (SEM). Parameters are listed in ascending order of t value. All LEAD values are significantly less than corresponding Norm values ($P < 0.001$). All leg data are from the limb with the lower ABI value. Subscripts 50 and 90 correspond to the 50% and 90% leg measurement sites. LSV and LSVI are the leg stroke volume and index, ASI is the leg average arterial status index.

ters were significantly less in the LEAD group ($P < 0.001$). Similar comparisons made using only subjects with age greater than sixty years showed similar results (data not shown). It is clear from these data that statistical separation of groups using LSV/CSV does not improve on the separation with LSV alone and that separation is maximum with the ASI parameter. Similar results are obtained when leg flow parameters for all 200 legs evaluated are compared as shown in Table III. All parameters were less in LEAD subjects ($P < 0.001$), but the parameters normalized to cardiac stroke volume and index provided the least statistical separation, whereas the ASI value was the greatest when the associated t values were used as a basis for comparison. These differences arise as a consequence of different relationships of the two parameters to leg ABI values. This is illustrated in the scatter plots of Figure 1, which show that both LSV/CSV and ASI increase with ABI, but a much tighter relationship exists for the ASI parameter as confirmed by the regression values in the figure.

The diagnostic value of ASI was accessed by constructing receiver operator curves[11] with ASI threshold values between 4.0 and 6.5 in 0.5 increments by use of three different threshold levels of ABI (0.85, 0.88, and 0.91) to define disease presence. These curves, shown in the top part of Figure 2, reveal an optimal ASI value of 5.5 yielding sensitivities for ABI thresholds of 0.85, 0.88, and 0.91 of 98.1%, 96.6%, and 93.7% respectively. Corresponding specificities are 77.7%, 80.9%, and 81.8% respectively. A comparison of receiver operator curves using ASI and LSV/CSV criteria for an ABI threshold of 0.85 is shown in the bottom part of the figure.

Discussion

The present results reveal the presence of a statistically significant correlation between LSV and

Table III

Parameters for All Evaluated Legs

Parameters	Subject Grouping		t Value
	LEAD	Norm	
N	53	147	
LSVI/CSVI (%)	0.041 (0.003)	0.067 (0.003)	6.68
LSV/CSV (%)	0.81 (0.05)	1.24 (0.05)	5.89
LSV (mL)	0.60 (0.04)	1.00 (0.04)	7.75
LSVI (mL/100 cc)	0.016 (0.001)	0.029 (0.001)	10.5
Q_{90} (mL/min)	39.2 (2.2)	65.0 (2.0)	8.7
Q'_{90} (mL/min/100 cc)	1.04 (0.06)	1.88 (0.05)	11.6
ASI (mL/min/100 cc)	2.64 (0.17)	7.35 (0.21)	17.4
ABI	0.61 (0.02)	1.08 (0.01)	17.4

Values are mean and (SEM) for all 200 legs evaluated. Parameters are listed in ascending order of t value. All LEAD values are significantly less than corresponding Norm values ($P < 0.001$).

CSV. In spite of this, however, the use of the LSV/CSV ratio did not improve on the statistical separation between LEAD and Norm subjects as compared with use of the LSV alone. The decline in CSV that was detected with increasing age for the studied population does not explain the absence of improvement since similar results were obtained with a subgroup of age-matched LEAD and Norm subjects. The magnitude of the LSV/CSV ratio herein obtained differs considerably from that found by Okuda and co-workers.[5] In normal subjects they reported a ratio of 11.2% (present study 1.05%) and in patients with LEAD a value of 3.1% (present study 0.59%). Since similar methods for the determination of CSV were used in both studies, the major discrepancy in the ratios is likely related to the LSV determination. In the present study LSV was calculated as the pulsatile flow just below the knee divided by the subject's heart rate. This value approximates the flow per stroke perfusing the lower limb. The values of flow herein obtained agree closely with those reported by others.[2,3] In theory, the bioimpedance method used by others[5] for leg flow measurement should have yielded similar results, but neither the actual leg flow nor the stroke volume value obtained was reported. We can only speculate that either the LSV was significantly overestimated or the CSV was underestimated resulting in the overinflated and nonphysiologic estimates reported.

Among the presently evaluated leg blood flow parameters the best statistical separation between LEAD and Norm was achieved with the leg average ASI value. As previously noted this parameter is the ratio of the leg flow pulse (Q′) half amplitude divided by the corresponding relative pulse width. This parameter was further evaluated in regard to its sensitivity and specificity for LEAD detection by use of receiver operator curves with three different ABI threshold levels defining LEAD presence. Results of that analysis reveal good di-

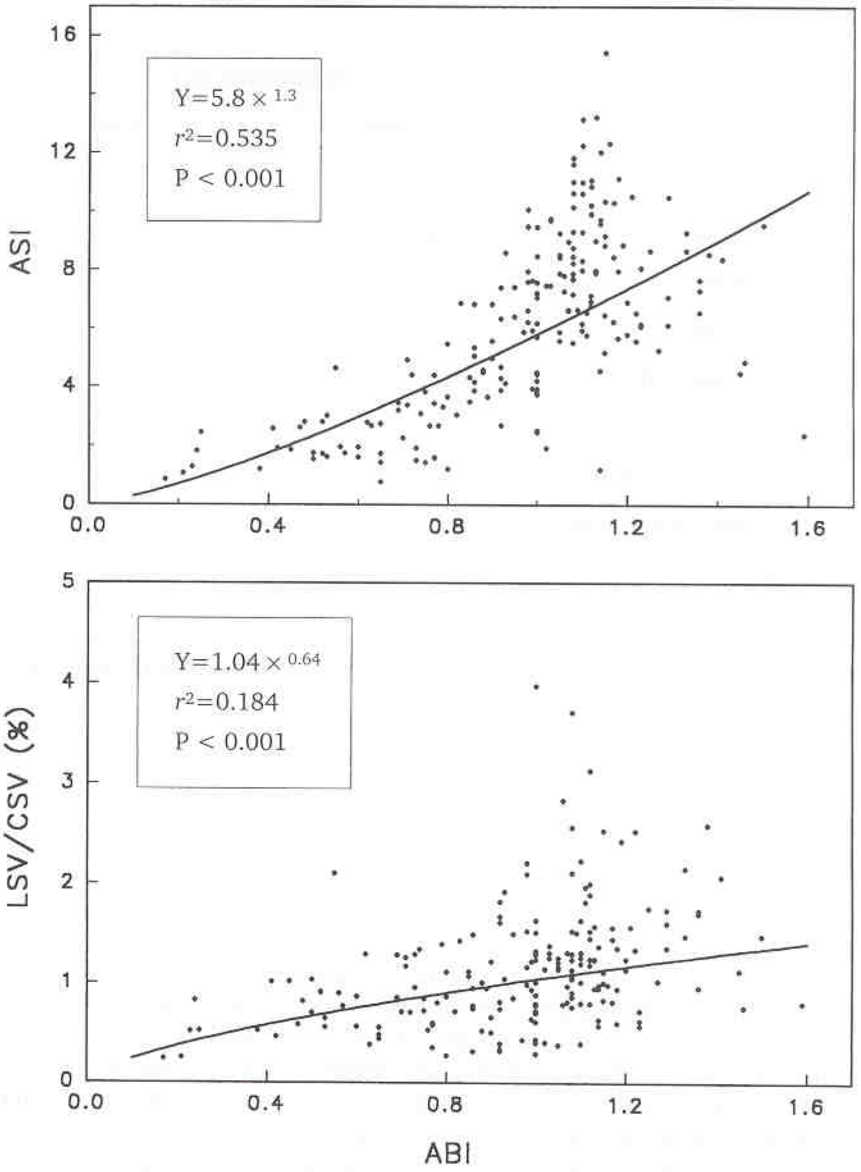

Figure 1. Differences in relationship between ABI and leg arterial status index (ASI, top) and the leg/cardiac parameter LSV/CSV (bottom). Data set includes 200 legs. Solid lines are best fit regression defined by equations and parameters shown in the inset.

agnostic sensitivities (93.7%–98.1%) and specificities (81.8%–77.7%), which were significantly better than those with use of the LSV/CSV parameter but less than the 100% sensitivity and 97.5% specificity reported with use of this same ratio although with different methodology.[5] In view of the fact that in the present study ASI yields the best discrimination, it is unclear how to reconcile these findings with the values otherwise reported based on the LSV/CSV ratio.

Conclusions

The present results do not support the view that the use of leg flow stroke volume normalized to cardiac stroke volume improves the diagnostic value over leg flow itself. The data further indicate that among the leg flow parameters evaluated, the arterial status index provides the best discrimination of LEAD vs Norm. Note, however, that the use of magnetic resonance flowmetry in

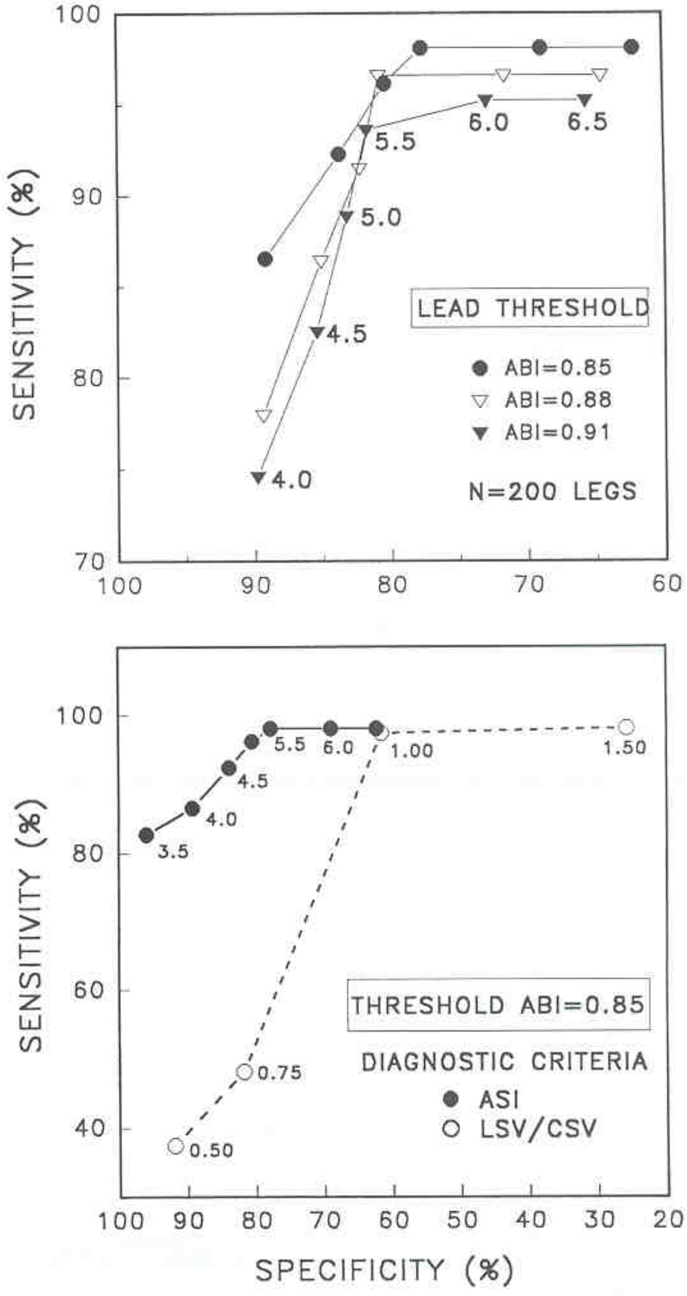

Figure 2. Receiver operator curves. Top: sensitivity vs specificity for three levels of ABI threshold parametrically determined as a function of ASI value from 4.0 to 6.5. Bottom: comparison between ASI and LSV/CSV parameters for a fixed ABI threshold of 0.85.

the present study was targeted to specific research questions in which pulsatile flow quantification was an important element. In most clinical situations, the widely available diagnostic techniques such as ABI, plethysmography, or duplex scanning are generally the more cost-effective alternatives and are adequate and appropriate to define the presence of peripheral arterial disease.

Harvey N. Mayrovitz, Ph.D.
Miami Heart Research Institute
Department of Vascular Research
Vascular Laboratory and Wound
Healing Center
4701 N. Meridian Ave.
Miami Beach, FL 33140

References

1. Sumner DS, Strandness DE: The relationship between calf blood flow and ankle blood pressure in patients with intermittent claudication. Surgery 65:763-771, 1969.
2. Kerr TM, Cranley JJ, Johnson JR, et al: Measurement of blood flow rates in the lower extremities using a nuclear magnetic resonance based instrument. J Vasc Surg 14:649-657, 1991.
3. Bendick PJ, Price JL, Glover JL: An objective measure of hemodynamic improvement after angioplasty. Arch Surg 127:806-811, 1992.
4. Rice KI, Money SR, Pendelton DW, et al: Resting arterial status index predicts exertional arterial compromise. J Vasc Tech 1994 (in press).
5. Okuda N, Masami Y, Feng S, et al: Diagnosis of arteriosclerosis obliterans by impedance technique with special reference to relative blood flow of the lower extremity. Angiology 40:808-813, 1989.
6. Kubicek WG, Karnegis JN, Patterson RP, et al: Development and evaluation of an impedance cardiac output system. Aerospace Med 37:1208-1212, 1966.
7. Kubicek WG, Kottke FJ, Ramos MU, et al: The Minnesota impedance cardiograph—theory and applications. Biomed Eng 9:247-260, 1974.
8. Patterson RP, Raza SB: Impedance cardiography using band and regional electrodes in supine, sitting and during exercise. IEEE Trans Biomed Eng 38:393-400, 1991.
9. Fuller HD: The validity of cardiac output measurement by thoracic impedance: A meta-analysis. Clin Invest Med 2:103-112, 1992.
10. Battocletti JH: Blood flow measurement by NMR. CRC Crit Rev Biomed Engr 13:311-367, 1986.
11. Sumner DS: Evaluation of noninvasive testing procedures: Data analysis and interpretation. In: Vascular Diagnosis, ed. 4, ed. by Bernstein EF. Baltimore: Mosby, 1993, pp 39-63.

DISCUSSION

David S. Sumner, M.D.
Springfield, Illinois

This carefully performed and well-analyzed study demonstrates that an ASI (arterial status index) of 5.5 measured by magnetic resonance flowmetry is highly sensitive (98%) for identifying limbs with ankle-brachial indices (ABIs) less than or equal to 0.85. The specificity was, however, less satisfactory (78%), indicating that a high sensitivity could be achieved only at the expense of an appreciable number of false-positive studies. Further work is required to determine how well other ASI thresholds predict lower ABI levels. In other words, can ASI discriminate among moderate, severe, and limb-threatening arterial obstruction? Figure 1 suggests that this may not be possible.

Magnetic resonance flowmeters are expensive instruments with a limited range of applications. They provide little information that cannot be more readily obtained by other, less complicated methods. As the authors wisely conclude, ABI, plethysmography, and duplex scanning are more widely available and more cost-effective. Although magnetic resonance flowmetry might be useful when ABIs are rendered unreliable by calcification of the ankle arteries, plethysmography and toe pressure measurement are equally diagnostic. Despite its having been introduced almost a decade ago, the role of magnetic resonance flowmetry has yet to be established.