Magnetic resonance imaging measurement of blood volume flow in peripheral arteries in healthy subjects

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Objective: **Peripheral arterial disease results in insufficient blood supply to the leg. Assessment of blood flow may provide information about severity of the disease. Magnetic resonance imaging (MRI) has potential use for simple, fast quantitative blood flow measurement. We investigated normal blood flow values for age and sex in the common femoral artery and popliteal artery in 50 healthy volunteers. In addition, we examined reproducibility and determinants of blood flow.**

Methods: **We performed cardiac-triggered phase-contrast quantitative flow measurements in the common femoral artery and popliteal artery, and MRI of the calves in 50 healthy volunteers (age, 26-80 years). Ten persons underwent MRI three times, to analyze reproducibility.**

Results: **All measurements were technically successful. Mean blood flow was 353 mL/min in the femoral artery and 61.9 mL/min in the popliteal artery. Coefficient of variation of femoral measurements was 16%, and of popliteal measurements was 19%. Femoral blood flow was significantly related to age and sex. Popliteal blood flow was significantly related to calf muscle volume, adjusted for age and sex.**

Conclusion: **Normal values for blood flow to the legs are presented. The measurements have reasonable reproducibility. Blood flow to the legs depends on age, sex, and calf muscle volume. (J Vasc Surg 2003;38:1060-6.)**

In peripheral arterial disease (PAD), blood volume flow to the legs is decreased, either after exercise in patients with intermittent claudication or at rest in patients with rest pain or tissue necrosis. Thus far it has not been possible to reliably diagnose decreased blood flow and to measure the effects of treatment in terms of blood volume. Current noninvasive methods for diagnosis and follow-up of PAD, such as segmental pressure measurement, ankle-brachial index, pulse volume recording, Doppler scan waveform analysis, pulsatility index, duplex ultrasound scanning, and color flow Doppler mapping, do not enable measurement of blood flow, and only indirectly provide information about volume of blood to the leg. Plethysmographic methods, such as segmental pressure and pulse volume recordings, can be used to measure changes in extremity volume, and because the only tissue in the extremities that changes volume rapidly is blood, plethysmography essentially measures changes in extremity blood volume. Segmental pressure measurements provide information about decrease in blood pressure along the leg, but not at a specific location. Pulse volume recording enables analysis of the waveform of the blood flow caused by cardiac contractions. Ultrasound offers the possibility of volume flow measurement, but with substantial observer variability (16%-40%[1]), and has therefore not become a clinically useful tool.

With phase-contrast imaging, blood flow can be quantified in a simple and noninvasive manner. This magnetic resonance imaging (MRI) technique is based on the principle that magnetic field gradients introduce a phase shift in the MRI signal arising from the flowing spins that is proportional to blood flow velocity. This enables construction of velocity maps from which the volume of flow can be calculated by simply integrating the velocity measurements over the vessel surface. Recent technologic improvements in electrocardiographic triggering during MRI have considerably enhanced the possibility of reliably measuring pulsatile triphasic volume flow to the legs.

We measured normal blood flow at rest in the common femoral artery and popliteal artery, and investigated its dependence on age, sex, and calf muscle volume. Furthermore, we investigated the reproducibility of these measurements.

METHODS

Institutional review board approval was obtained for the study, and all subjects gave written informed consent.

Study population. Fifty subjects (hospital co-workers and partners in an ongoing vascular study) were examined. We aimed for equal distribution of sex per decade from 30 to 80 years (five men and five women per decade). At clinical examination, study subjects had no evidence of cardiovascular disease (stroke, myocardial infarction, angina pectoris, intermittent claudication, renal artery disease, aortic aneurysm) and were not receiving treatment for a vascular risk factor (hypertension, hyperglycemia, hyper-

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Competition of interest: none.

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0741-5214/2003/$30.00 + 0
doi:10.1016/S0741-5214(03)00706-7

lipidemia, hyperhomocysteinemia). They did not use any medication. Further, they had no contraindications to MRI, such as a pacemaker or severe claustrophobia.

Procedure. Subjects were seated for 10 minutes before imaging, to correct for the influence of walking on blood flow and to accommodate them to the room temperature. In 10 subjects the measurements were repeated three times, on different days (mean interval, 15 days).

All studies were performed with a clinical 1.5T MRI scanner (Gyroscan NT; Philips Medical Systems, Best, The Netherlands) equipped with standard hardware and software. Patients were placed feet-first in the MRI scanner. Quantitative flow measurements of the common femoral and popliteal arteries were performed with an 11 cm diameter circular surface receive coil. For the popliteal artery the coil was placed under the knee; for the femoral artery the coil was placed on the groin. A transverse inflow image of the common femoral arteries was obtained, and quantitative flow measurement was planned on the sagittal and coronal maximum intensity projections, perpendicular to the common femoral artery at the level of the femoral head. For the popliteal artery, transverse scan imaging was planned at the level of the knee joint. If the imaged section turned out to be at the level of or below the femoral bifurcation or the popliteal trifurcation, the imaging plane was placed a little more proximal. Imaging parameters for quantitative flow were as follows: repetition time, 15.0 ms; echo time, 6.0 ms; flip angle, 20 degrees; field of view, 115 mm; section thickness, 6.00 mm; acquisition matrix, 64 × 64; reconstruction matrix, 128 × 128; and 20 heart phases and 2 signals averaged. A 50 mm parallel saturation slab was placed distally for suppression of venous signal and maximum water fat shift. The velocity encoding parameter was set to 90 cm/s popliteal and 120 cm/s femoral.[2] The scanner was equipped with a vector ECG system for cardiac synchronization. With a cardiac frequency of 80 bpm, the scan duration was 115 s. From the 20 velocity images reconstructed from the phase-contrast flow volume images, the volume of flow (in milliliters per minute) was calculated for each time frame by integrating the velocity data over a region of interest exactly containing the entire vessel lumen. This took about 1 minute for each vessel.

To measure calf muscle volume, high-resolution T1-weighted coronal images of the lower legs were acquired in all 50 subjects (repetition time, 7.2 ms; echo time, 4.3 ms; flip angle, 25 degrees; field of view, 398 × 530 mm^2; acquisition matrix, 287 × 382; reconstruction matrix, 512 × 512; 75 coronal sections, 2 mm each). On a graphic workstation (EasyVision; Philips Medical Systems), muscle tissue located between the knee joint and the ankle joint was segmented from the data by performing a simple upper and lower threshold segmentation to exclude high-intensity fat and bone marrow and low-intensity bone tissue. After segmentation the resulting total calf muscle volume in the left and right leg was calculated with the workstation. Measuring calf muscle volume took about 5 minutes per subject.

The total imaging session took about 30 minutes. Volume flow and muscle volume measurements took about 15 minutes.

Statistical analysis. Univariate and multivariate linear regression analysis was used to assess the effects of age, sex, and calf muscle volume on femoral and popliteal blood flow volume. The regression coefficient beta is interpreted as follows: with an increase of the determinant with one unit, the outcome variable blood volume flow increases with beta. The *r* value indicates how much of the outcome blood flow volume is declared by the model.

Mean intrasubject coefficient of variation was calculated for blood flow volume in the 10 subjects who were imaged three times, as described by Armitage et al.[3] In addition, intraobserver and interobserver coefficient of variation for measuring blood flow volume and calf muscle volume in 10 subjects was calculated with the method described by Bland and Altman.[4] The coefficient of variation is a measure of variability, calculated by dividing the sample standard deviation by the sample mean. It expresses mean difference between measurements. We multiplied it by 100 to give percentage.

RESULTS

Fifty healthy subjects (25 men, 25 women; mean age, 55.4 years [range, 26-80 years]) were studied. All images were technically successful, even in 2 persons with a femoral head prosthesis. All flow patterns were triphasic, as expected (Fig 1). All volume flow measurements were successful, as were all calf muscle volume measurements. We excluded one leg (1%) that had been severely affected by tuberculosis and was not representative of a normal healthy leg. One calf volume image was unintentionally not stored, and one calf volume was wrongly planned on the scout image and therefore was excluded.

Mean (± SD) blood flow volume in the common femoral artery was 353 ± 120 mL/min (range, 136-653 mL/min) for all subjects: 411 ± 117 mL/min for men and 297 ± 92 mL/min for women. In the popliteal artery, mean blood volume flow was 61.9 ± 30.2 mL/min (range, 17.1-168 mL/min): 76.8 ± 33.6 mL/min for men and 47.2 ± 16.5 mL/min for women. In the popliteal artery volume flow was about 17% of that in the femoral artery. Left and right blood flow volume were not statistically different in women (femoral, $P = .8$; popliteal, $P = .2$). In men, left and right femoral flow showed no difference ($P = .7$), but popliteal flow was significantly higher in the right leg (82.5 mL/min) compared with the left leg (69.9 mL/min; $P = .05$).

Blood flow volume declined with age (Table I; Fig 2). For total femoral flow (left and right legs), beta was −5.5, *P* .02, and *r* 0.34. For total popliteal flow, beta was −0.88, *P* .12, and *r* 0.23.

We calculated a mean calf muscle volume (per leg) of 2429 ± 529 mL (range, 1456-3811 mL) for all subjects: 2756 ± 384 mL for men and 2082 ± mL for women. Left and right calf muscle volume was not statistically different in men ($P = .8$) and women ($P = .7$).

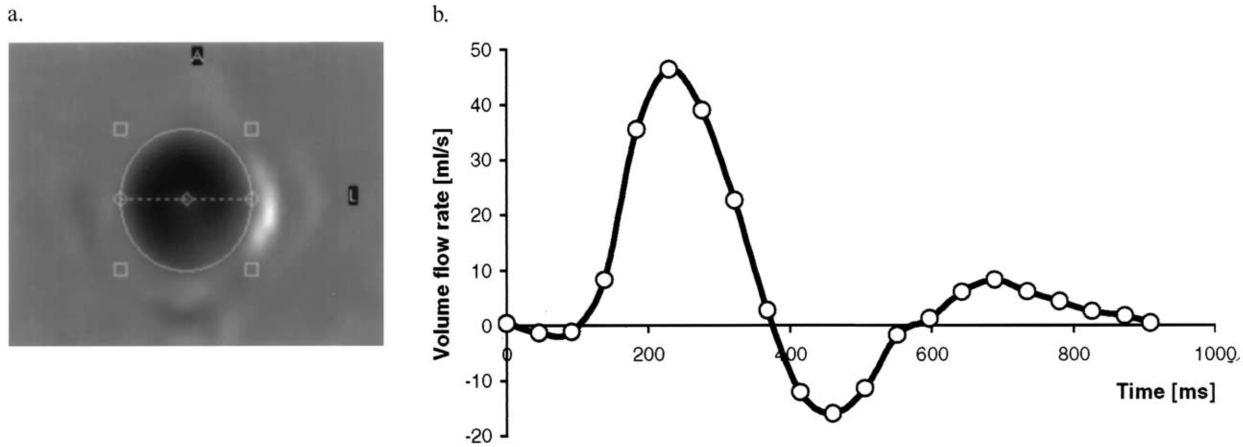

Fig 1. A, Placement of region of interest in the femoral artery. **B,** Triphasic flow in the femoral artery in a healthy subject.

Table I. Mean flow in common femoral artery and popliteal artery according to age and sex

	Common femoral artery				*Popliteal artery*			
	353 (120)				*61.9 (30.2)*			
Mean flow (SD) (mL/min)	*Left (n = 49)*		*Right (n = 50)*		*Left (n = 49)*		*Right (n = 50)*	
Mean flow (mL/min)	*352 (127)*		*355 (113)*		*58.0 (29.4)*		*65.7 (30.7)*	
Age (y) M/F	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*
<40 3/2	463	327	491	303	71.5	54.5	77.6	47.2
40-50 6/7	433	332	405	326	72.3	50.0	84.8	57.0
50-60 7/5	442	324	425	296	90.1	52.6	96.3	53.7
60-70 4/7	453	239	476	284	59.5	36.3	89.5	39.6
>70 5/4	283	278	305	275	48.3	41.1	58.0	45.3

Both femoral and popliteal blood flow volume increased with calf muscle volume (Fig 3). For femoral blood flow volume, beta was 0.099, P .001, and r 0.45. For popliteal flow, beta was 0.034, P .000, and r 0.65.

Univariate linear regression analysis showed that sex, age, and calf muscle volume were significantly correlated with blood flow volume in the common femoral artery (respectively, $P = .000$, $P = .02$, and $P = .001$). In the popliteal artery, correlation with sex and calf muscle volume was also significant; however, correlation with age was not significant (respectively, $P = .000$, $P = .000$, and $P = .12$).

When sex, age, and calf muscle volume were entered in one multivariate linear regression model, it appeared that femoral blood flow volume was significantly correlated with age and sex, and popliteal blood flow volume was significantly correlated with calf muscle volume (Table II).

The coefficient of variation was 16% for the femoral artery and 19% for the popliteal artery. When we included two measurements that were performed in subjects without the required 10 minutes of rest before the imaging session, the coefficient of variation for the popliteal artery (imaged first) was 26%, and for the femoral artery (imaged about 20 minutes later) was unchanged.

Intraobserver and interobserver coefficient of variation for measuring flow volume, that is, placing of the region of interest, was 1.2% and 1.3% for the femoral artery and 6.0% and 5.9% for the popliteal artery. Intraobserver and interobserver coefficient of variation for measuring calf muscle volume was 9.9% and 7.7%, respectively.

DISCUSSION

In 50 healthy subjects, flow to the entire leg depended on age and sex, whereas flow in the lower leg was related to calf muscle volume.

A plausible explanation for this difference is that the popliteal artery supplies only the lower leg, of which the measured calf muscle volume forms a great part. The femoral artery supplies blood to the entire leg, of which the lower leg musculature is only a small part. Indeed, we found that popliteal flow is about 17% of femoral flow. Femoral flow is related more to sex and age than to lower leg muscle volume. We did not measure thigh or entire leg muscle volume. Probably the femoral flow would have demon-

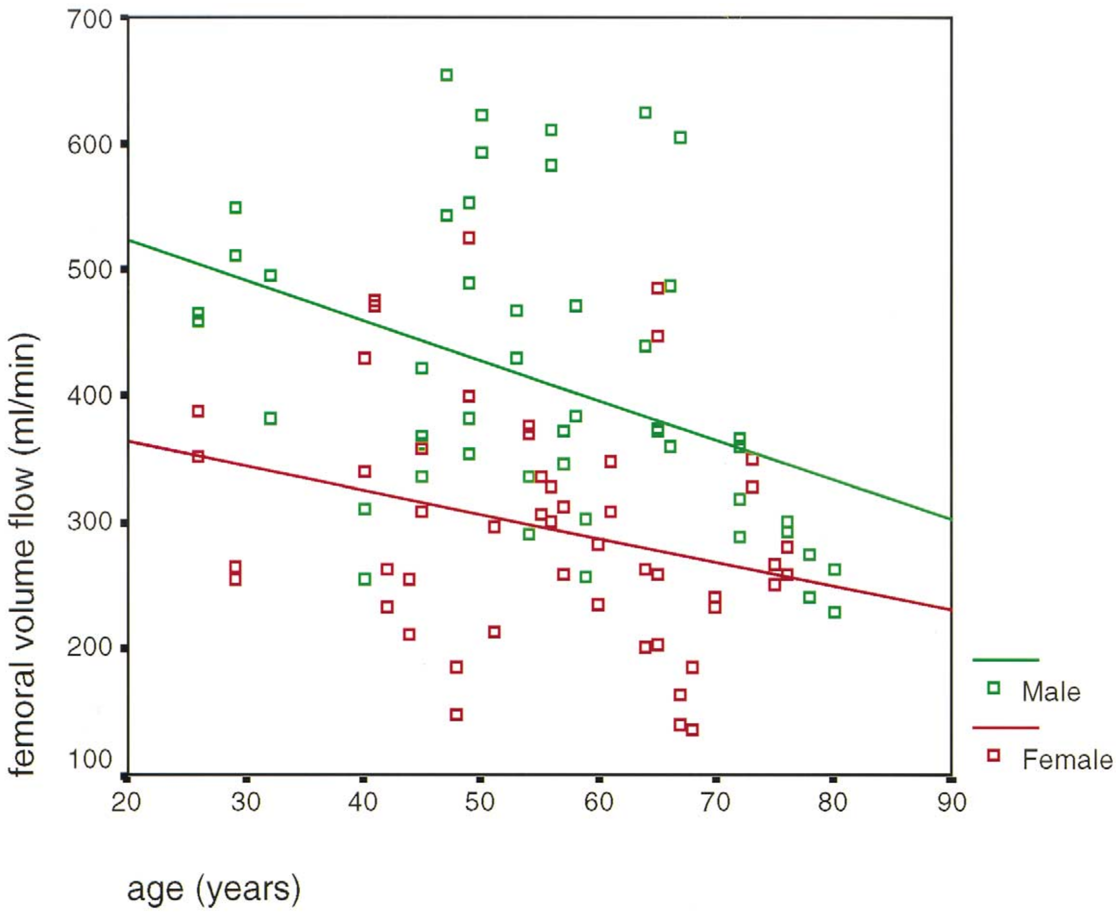

Fig 2. Femoral blood volume flow versus age.

strated significant correlation with those measurements, even when adjusted for age and sex. When interpreting blood flow volume measurements, one must take into account the subject's sex, age, and muscle volume.

Results of this study are similar to those of previous studies[1,5-9] (Table III). Several studies used duplex ultrasound scanning to investigate blood flow volume. In these studies, values for blood flow volume in the common femoral artery and the popliteal artery are consistent with our results. However, in none of these studies was flow volume dependent on age and sex. Holland et al[8] could not find a correlation with calf and thigh circumference as a measure of muscle mass. It may be that the circumference is too imprecise a measure for tissue volume demanding blood supply. In one MRI study[9] with flow volume measurements of the popliteal artery only, eight young healthy subjects were examined. To our knowledge, our study is the first to report blood flow volume measurements in the legs using MRI in a large group of healthy subjects without peripheral artery disease.

We included persons free of vascular disease and vascular risk factors at interrogation. We did not perform any (noninvasive) test to confirm this. Therefore it may be that some subjects were included who were not completely free of vascular disease, and this may have been true especially among the older study subjects.

Reproducibility of blood flow volume in the femoral artery was reasonable: the intrasubject coefficient of variation was 16%. Intrasubject coefficient of variation for the popliteal artery was high, 26%. However, when leaving out the two measurements that were performed without the required 10 minutes of rest before imaging, the coefficient of variation for popliteal flow decreased to 19%, which is reasonable. Intraobserver and interobserver coefficients of variation for flow volume (ie, placing the region of interest) were low, suggesting that most variation in blood flow volume per subject is caused by physiologic changes (assuming that MRI measuring errors are constant and low, 3%[10]). This was also suggested in other studies.[5,8,11]

Symptoms of PAD occur when blood flow to the limb is insufficient. Blood flow volume measurement may provide important information in evaluation of PAD. Current noninvasive methods of measuring blood flow are mainly qualitative and only indirectly provide information about

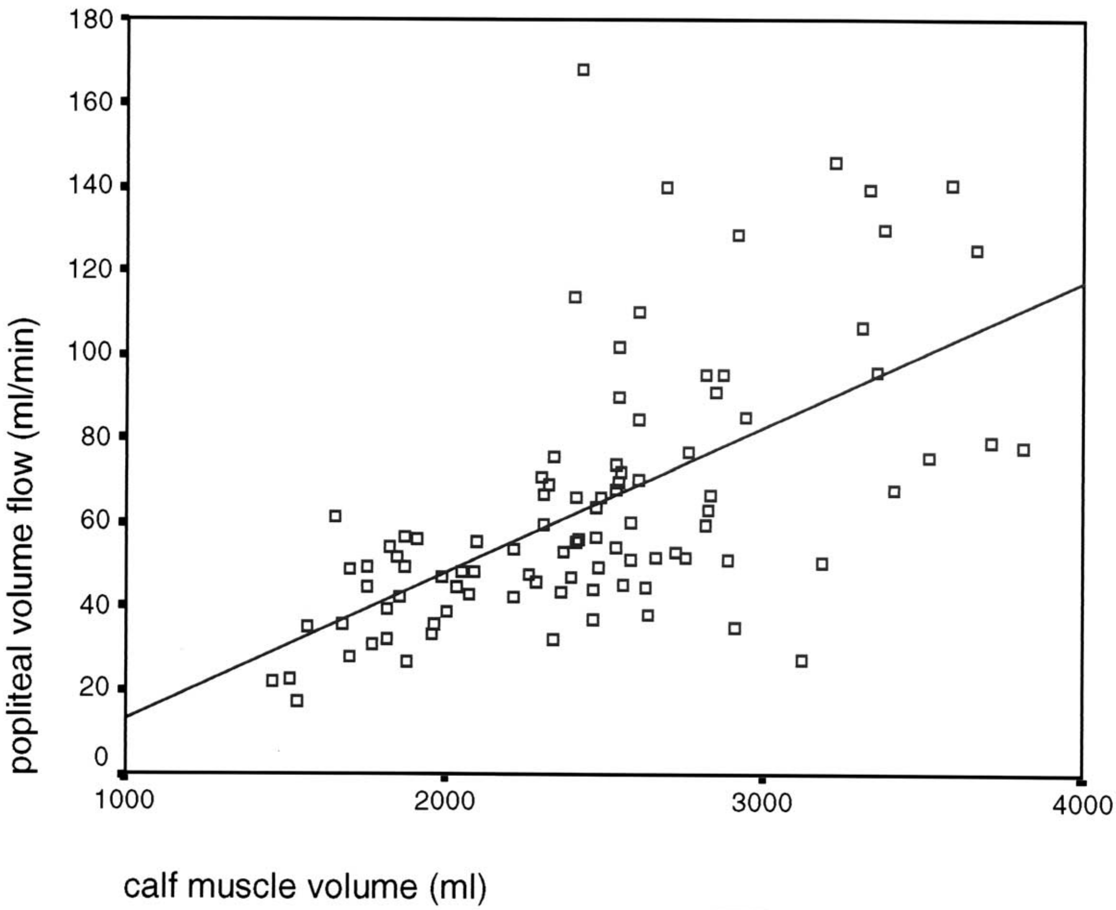

Fig 3. Popliteal blood volume flow versus calf muscle volume.

the quantity of blood flowing. Plethysmography includes a group of techniques used to measure changes in extremity (blood) volume. Plethysmography measures these changes in a limb segment and not at a specific site in one artery. Doppler ultrasound scans can provide both qualitative and quantitative information about blood flow. Flow volume can be calculated with the formula $Q = \pi \times v \times D^2/4$, where V is time-averaged mean velocity across the vessel cross-section, and D is vessel diameter. This is a subjective measurement of the quantity of blood flow and therefore is seldom used in clinical practice. Variability in blood flow volume measured with duplex ultrasound scanning is high,[5,8] because of errors in estimating cross-sectional area and in measuring time-averaged mean velocity, although a great part of variability may also be caused by physiologic changes in subjects.[5] Further, deep-lying arteries, calcified arteries, fat, bowel gas, and low-velocity blood flow will generate suboptimal duplex scans, because of inadequate returning signal strength.

Table II. Determinants of flow: multivariate regression analysis

Volume flow (mL/min)	β	P	*r*
Left femoral artery			
Left calf muscle volume (mL)	0.0378	.4	0.57
Male sex	−89.9	.04*	
Age (y)	−0.270	.03*	
Right femoral artery			
Right calf muscle volume (mL)	0.0257	.5	0.58
Male sex	−98.6	.01*	
Age (y)	−1.98	.06	
Left popliteal artery			
Left calf muscle volume (mL)	0.0227	.02*	0.56
Male sex	−9.39	.3	
Age (y)	−0.287	.3	
Right popliteal artery			
Right calf muscle volume (mL)	0.0308	.001*	0.69
Male sex	−12.1	.2	
Age (y)	−0.103	.7	

*Significant at $P < .05$.

Table III. Normal blood volume flow in legs reported in literature

Author	*Year*	*Method*	*Subjects*	*Mean age (y)*	*Volume blood flow (mL/min) (mean ± SD)*		*Correlation with flow*
					Common femoral artery	*Popliteal artery*	
Lewis et al[5]	1986	Duplex US scanning	51 with no clinical evidence of PAD	44	350 ± 141	NR	NR
Field et al[6]	1989	Duplex US scanning	24 nondiabetic, nonsmoking subjects, without history of cardiac disease or PAD	29	371 ± 27 (SEM)	140 ± 11 (SEM)	Correlation with sex (eliminated when adjusted for body surface area)
Lewis et al[7]	1990	Duplex US scanning	80 without clinical evidence of atherosclerosis	40	344 ± 135	NR	*No* correlation with age or sex
Hussain et al[1]	1996	Duplex US scanning	20 healthy subjects	28	359 ± 114	NR	NR
Holland et al[8]	1998	Duplex US scanning	40 nonhypertensive nonsmokers with ABI >1, no history of cardiovascular disease	39.7	284 ± 119	72 ± 34	*No* correlation with age, sex, weight, height, thigh or calf circumference
Meyer et al[9]	1993	MRI	8	29	NR	55 ± 8.5 (SE)	NR
Current study	2003	MRI	50 without clinical evidence of cardiovascular disease and without medication	55.4	354 ± 120	61.9 ± 30.2	Correlation with age, sex, calf muscle volume

PAD, Peripheral arterial disease; *ABI,* ankle-brachial index; *US,* ultrasound; *MRI,* magnetic resonance imaging; *NR,* not reported.

Two-dimensional phase-contrast flow volume is a reliable technique for measuring flow in the blood vessels. Phantom studies showed that highly pulsatile flow, as in the limbs, needs triggering for flow measurement.[10-12] This increases scanning duration. Our MRI session took 30 minutes. Tissue penetration problems, as seen with ultrasound, are not an issue with MRI. In addition, with MRI it is possibile to examine blood flow volume in several vessels in the same plane at once, because of the large field of view.

MRI was well tolerated by all 50 subjects. None experienced claustrophobia during imaging. This may be because the head remained out of the bore of the imager. Also, with MR angiography for detection of PAD, patients lie feet-first in the imager, and seldom experience claustrophobia.

This preliminary study can serve as a basis for future studies. In a further study we will investigate blood flow volume in patients with PAD and its relation to signs and symptoms of PAD. Applications of MRI blood flow volume measurements have the potential to be used both in diagnosis and in follow-up of patients who underwent an intervention to treat PAD. Probably the images need to be further adapted for the population investigated, as for resolution and velocity encoding. Patients with intermittent claudication probably have normal flow at rest, and a stress test may be necessary. For patients with limb- threatening ischemia, it may be interesting to measure flow volume in the tibial and pedal arteries.

Inasmuch as contrast-enhanced MR angiography has proven to be accurate in showing the anatomy of arteries of the lower extremities.[13-15] Therefore, one scanning session with both MR angiography and flow measurements, for morphologic and hemodynamic information, may be performed in the future.

In conclusion, two-dimensional phase-contrast quantitative flow measurement can be used as an easy, noninvasive method for determining blood flow volume in the arteries of the legs. Age, sex, and leg muscle volume must be taken into account when interpreting flow volume.

We thank I. van der Tweel for assistance with statistical analysis.

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Submitted Jan 8, 2003; accepted Mar 10, 2003.