Part IV

Assessment

Noninvasive Assessment of Critical Leg Ischemia

Ali F AbuRahma

Although many physicians still rely entirely upon arteriography as the main tool for evaluation of critical limb ischemia, the role of the vascular laboratory cannot be denied. Various noninvasive vascular diagnostic techniques have been described to assist the clinician in the diagnosis and treatment of vascular patients. Noninvasive vascular tests help the clinician to evaluate the presence or absence of significant arterial occlusive disease, severity and location of disease, and, in the presence of multisegmental disease, which arterial segment is mostly affected. Other challenging questions for physicians dealing with patients with critical limb ischemia include the following: In patients with both arterial occlusive disease and neuropathy, which condition is more likely to be responsible for the pain or ulceration? Will an ulcer or amputation heal at a specific level? Since the traditional diagnostic tools of clinical history and vascular examination are often inadequate in answering some of these questions, and since arteriography is invasive, painful, and provides no physiological information, increasing attention has been focused on the value of the vascular laboratory in these diagnostic challenges.

General indications for obtaining noninvasive assessment of the peripheral arterial system include: absence of normal pulses, suboptimal examiner reliability or experience, a clinical history or examination potentially consistent with peripheral arterial occlusive disease, and a planned vascular procedure, including determining the level of leg amputation and benefit from lumbar sympathectomy (1). Intraoperative measurement of ankle pressures after completion of aortofemoral bypass or aortoiliac endarterectomy can be used to predict the results of the procedure. The determination of segmental pressure measurements in the postoperative period aids in quantitatively assessing the results of aortofemoral bypass.

The most commonly used methods for diagnosis of critical limb ischemia of the lower extremity at present are: segmental Doppler pressures (with or without Doppler wave analysis), pulse volume recording, and color duplex ultrasonography (2).

Segmental Doppler pressures and Doppler waveform analysis

Instrumentation and Physical Principles

A continuous-wave (CW) Doppler velocity detector is used to sense apparent changes in the reflected sound wave frequency produced by the movement of red blood cells relative to an ultrasound probe. An electric oscillator vibrates a piezoelectric crystal (ceramic) at 5 to 10 MHz. This produces an ultrasound wave that is transmitted via an acoustic coupling gel into the body. The ultrasonic beam is reflected back to a receiver in the probe by all the structures in its path, including the moving red blood cells. The movement of the blood cells causes a frequency shift (Doppler shift) in the reflected sound wave. The Doppler shift is proportional to the blood flow velocity. There is a Doppler effect whenever there is relative motion between the source and the receiver of the sound. Blood is the moving target and the transducer is the stationary source. Depending on the direction of the flow relative to the Doppler beam, the reflected frequency is higher or lower than the transmitted frequency (Doppler shift). The signal is electrically mixed with the transmitting frequency and processed to produce a frequency in the audible range. A received ultrasonic beam can be amplified and projected audibly through either a loudspeaker or earphones. A

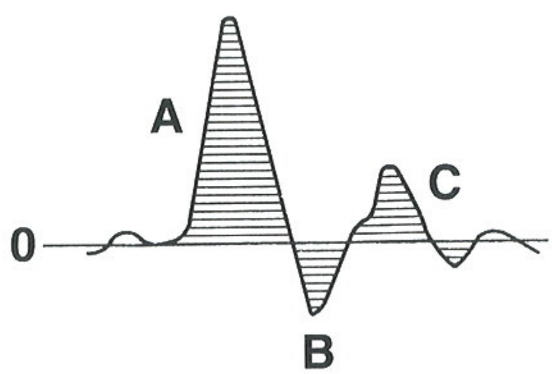


FIGURE 1
Normal arterial velocity tracing (multiphasic). (A = systolic component; B = early diastolic component; C = late diastolic component).

From Critical Lower Limb Ischemia Edited by R Bartolucci, L Battaglia, V D'Andrea, E De Antoni ©2002

second method of displaying the Doppler velocity signal is by converting it to a visible analog waveform. With the analog waveform, the amplified signal is electronically converted and displayed on a channel recorder similar to an ECG (Figure 1).

Therefore, there are several types of Doppler velocimetry:

1. auditory: this processes the Doppler signal as sound. It has the advantage of containing all Doppler frequencies with the exception of those extreme frequencies removed by filtering. A trained technician or physician can easily distinguish normal signals from those received proximal to, within, or distal to a stenosis or occlusion. A higher pitched signal can mean that the probe angle is very acute to the vessel angle or it can indicate a significant arterial occlusion.
2. Analog wave tracing: this method employs a zero crossing frequency meter to display the signals graphically on a strip chart recorder. It has an acceptable overall accuracy, but it is not as sensitive as the spectral analysis and it also has the following drawbacks: noise, and under or overestimation of high and low velocities, respectively.
3. Spectral analysis: this method displays frequency on the vertical axis, time on the horizontal axis, and the amplitude of back-scattered signals at any frequency and time (Figure 2). It has the advantage of displaying the amplitudes at all frequencies, but it is free of many of the disadvantages that were previously described for the analog wave tracing.

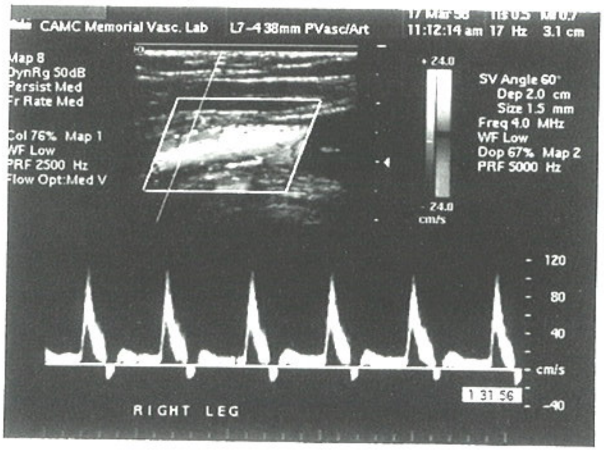


FIGURE 2

A spectral analysis of the right common femoral artery. This method displays frequency on the vertical axis, time on the horizontal axis and the amplitude of backscattered signal at any frequency and time. (This picture was taken by a color duplex ultrasound machine)

Methods

The complete arterial lower extremity Doppler examination consists of three components:

1. analysis of the arterial analog wave tracing,
2. measurement of the segmental systolic limb pressures, and
3. calculation of the ankle/brachial index (ABI).

After the history is taken, the patient is allowed to rest in the supine position on the examining table for ten to 15 minutes to assure the measurement of pressures in the resting state. The patient is placed in the supine position with the extremities at the level of the heart. The head of the bed can be elevated slightly, and the patient's head can rest on a pillow. The patient's hip is generally externally rotated with the knee slightly bent to facilitate the lower extremity evaluation.

The Doppler probe (transducer) must be positioned on the long axis of the vessel. An angle of insonation of approximately 45 to 60 degrees is usually used for this study. The leg pulses (femoral, popliteal, dorsalis pedis, and posterior tibial) are evaluated by palpation and by audible Doppler signals. The Doppler signals are graded as normal (biphasic), abnormal (monophasic), or absent.

Qualitative Doppler Waveform Analysis

For the lower extremities, Doppler velocity waveforms are recorded from the following arteries bilaterally:

1. common femoral artery at the groin level,
2. superficial femoral artery,
3. popliteal artery,
4. posterior tibial artery (at the level of the medial malleolus),
5. dorsalis pedis artery (at the dorsum of the foot),
6. occasionally the peroneal artery (at the level of the lateral malleolus). Auditory signals are obtained. If the examiner is using a headset, the right earphone provides forward (antegrade) flow signals, while the left earphone provides reverse (retrograde) flow signals. The qualities of the auditory signals and the waveforms are observed and analyzed.

The normal arterial velocity signal is multiphasic. That is, it is characterized by one systolic and one or more diastolic components (Figure 1). In the major peripheral arteries, the systolic component is a large positive deflection indicative of a high net forward flow velocity. This is followed by a brief period of net flow reversal. This flow reversal is then followed immediately by another positive deflection, the diastolic forward flow component. The brief period of flow reversal characteristic of the major peripheral arterial velocity signal is a function of the generally high resistance of the extremity vascular bed. Lowering resistance, via vasodilation can eliminate the net flow reversal. The normal arterial velocity signal is also pulsatile, i.e., it cycles with each heartbeat. Thus, the normal nonpulsatile, phasic, low-pitch venous signal is easily differentiated from the pulsatile, multiphasic arterial signal.

Abnormal signals are generally monophasic (Figure 3), non-pulsatile, or absent. Biphasic signals can also be considered abnormal (Figure 3). It is imperative to observe for deterioration of the waveform, e.g. triphasic to biphasic or triphasic to monophasic of the Doppler signal quality from one level to the next level. A monophasic and dampened signal can be obtained proximal to an obstruction as well as distal to it. In the absence of additional obstructions, the distal signal can normalize.

The arterial velocity signal produced just before an occlusion is characteristically of short duration, i.e., a slapping signal of low amplitude. However, the arterial signal produced over a stenotic segment is a high-pitched signal with less prominent diastolic components.

The signal from just beyond the stenotic segment is also characterized by dampened systolic and absent diastolic components, but it is not as high-pitched as the

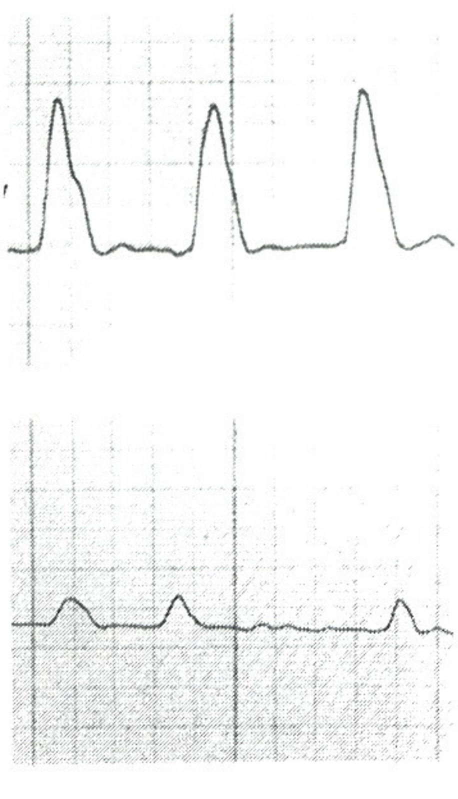


FIGURE 3

This is an abnormal arterial tracing of the lower extremity in a patient with stenosis of the common femoral artery. The upper tracing was recorded from the popliteal artery distal to the obstruction and the lower tracing was taken at the level of the posterior tibial artery. These signals are monophasic.

stenotic signal. The signal beyond an occluded arterial segment is like a poststenotic signal, although the systolic component may be of even lower amplitude. The signal produced by the prominent collateral arterial signal is high-pitched and almost continuous.

As noted in the abnormal wave tracing, a Doppler signal obtained from a common femoral artery which is diseased shows the poor quality of the signal (poor upslope and downslope, with a somewhat rounded peak) (Figure 3).

Quantitative Doppler Waveform Analysis

Pulsatility Index (PI)

This is calculated by dividing the peak-to-peak frequency by the mean (average) frequency (3) as seen in Figure 4. This ratio is independent of the beam-to-vessel Doppler angle when using hand-held Doppler equipment. As seen in Figure 4, the pulsatility index equals P1 to P2 divided by the mean frequency. Normally, the values of the PI increase from the central to peripheral arteries. A PI of >5.5 is normal for the common femoral artery, while a normal PI for the popliteal artery is approximately 8.0. These values decrease in the presence of proximal occlusive disease, e.g. a PI of <5 in the common femoral artery with a patent superficial femoral artery (SFA), indicates proximal aortoiliac occlusive disease. However, the same reduced PI is not diagnostic if the SFA is occluded.

Inverse Damping Factor

This is calculated by dividing the distal PI by the proximal PI of an arterial segment. It indicates the degree to which the wave is dampened as it moves through an

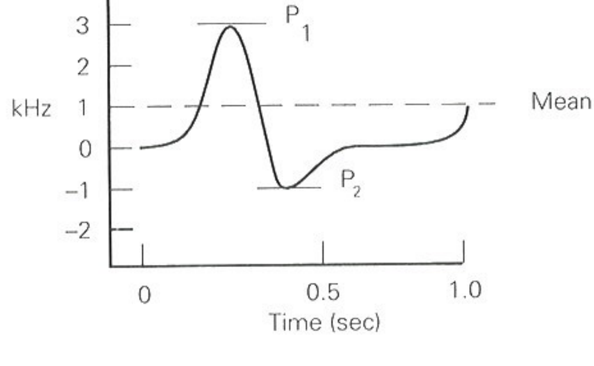


FIGURE 4

This diagram demonstrates the method for calculating the pulsality index.

arterial segment, (3) e.g., severe stenosis or occlusion of the SFA is usually present when the inverse femoral-popliteal dampening factor is less than 0.9 (a normal value = 0.9-1.1).

Acceleration Time or Index

This differentiates inflow from outflow disease. It's based on the principle that arterial obstruction proximal to the site of the Doppler probe prolongs the time between the onset of systolic flow to the point of maximum peak in waveforms at the probe site (Figure 5). Figure 5A shows a normal common femoral artery tracing. There is a quick systolic upslope representing a normal acceleration time, in contrast to Figure 5B which shows a slower upslope from the onset of systole to maximum peak from an abnormal common femoral artery tracing. Acceleration time is not prolonged when there is disease distal to the probe. It is applied to those signals evaluated by spectral analysis because it is necessary to maximize sensitivity and minimize artifacts. Generally, an acceleration time of equal to or less than 133 milliseconds suggests the absence of significant aortoiliac disease. False positive results can occur with technical errors, e.g. a Doppler angle ≥70 degrees, which may dampen the Doppler signal qualities, and in the presence of poor cardiac output since the Doppler flow signal will be attenuated with the waveform detecting slow upstroke, rounded peak, and slow downslope.

Limitations of the Analog Wave Tracing Analysis

The Doppler waveforms may be affected by:

- ambient temperature;
- uncompensated congestive heart failure may result in dampened waveforms following exercise;
- an inability to distinguish stenosis from occlusion;
- an inability to precisely localize the occlusion;
- unable to be applied on patients with casts or extensive bandages that cannot be removed;
- it is technologist-dependent, and the result can vary with the Doppler angle used.

Doppler segmental pressures

Doppler segmental pressures have the same capabilities of analog wave tracing, i.e. to help in identifying the presence and severity of arterial occlusive disease, to provide an objective baseline to follow the progression of peripheral vascular disease of the lower extremity and/or the postoperative course, and to somewhat evaluate the treatment plan. The results of this testing are usually combined with the Doppler velocity waveform analysis. The patient preparation and positioning is similar to that of the Doppler velocity waveform analysis.

Technique of Measuring Doppler Segmental Pressures

The brachial artery Doppler systolic pressures are measured in each arm. Cuffs of appropriate size (bladder dimension 12 x 40 cm) are placed on each arm. The brachial artery is palpated in the antecubital fossa, and a small amount of acoustic gel is applied to the skin over the artery. The arterial signal is found using the Doppler probe, and then the cuff is inflated until the signal disappears (20-30 mmHg beyond last audible Doppler signal). The cuff is slowly deflated until the arterial signal is again audible, at which time the pressure is recorded. Unlike the standard stethoscope, as the cuff is

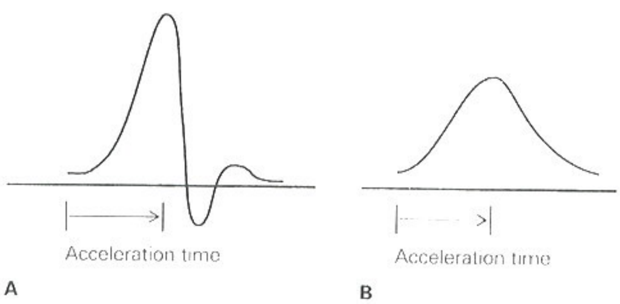


FIGURE 5
This shows a normal common femoral artery tracing with a normal acceleration tima (A), and an abnormal common femoral artery tracing with an abnormal acceleration time (B).

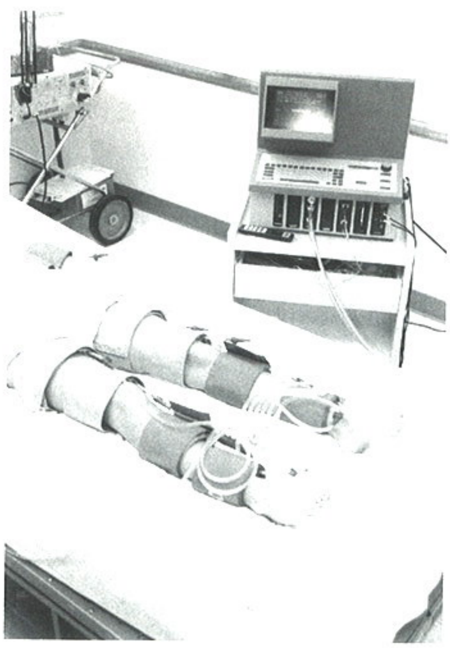


FIGURE 6A
This shows the tecnique for measuring the segmental Doppler pressures using the four cuff method.

further deflated, the velocity signal will not disappear, so the diastolic pressure cannot be determined.

Four 12 x 40 cm pneumatic cuffs are applied at various levels on each leg: as high on the thigh as possible, just above the knee, just below the knee, and above the ankle (Figure 6A). The examiner then listens to the posterior tibial and the dorsalis pedis arterial signals (Figure 6B). Of these vessels the one with the strongest Doppler signal is chosen for the ankle pressure. If none of the vessels can be located with the ultrasound probe, the popliteal artery signal is identified in the popliteal fossa. High-thigh, above-knee, below-knee, and ankle pressure readings are taken. An automatic cuff inflator may be used to save time.

Several important facts concerning cuff characteristics should be noted. It is most important that the pneumatic bladder of the cuff completely encircle the limb. The bladder of the cuff should be placed over the artery. This is especially important when the bladder does not encircle the limb. Just as bladder length affects the pressure determination, bladder width must also be related to the limb diameter. For the most accurate measurement of blood pressure, the width of the pneumatic cuff should be 20% greater than the diameter of the limb. [4]

For all practical purposes, this means that larger arms require wider cuffs. When a cuff is too narrow relative to the limb diameter, an erroneously high pressure (30 to 90 mmHg greater than arm pressure) results.

The four cuffs used in this test to determine the segmental pressures at different levels of the lower limb are all the same width (12 x 40 cm), making the pressures at the widest part of the limb (high thigh) erroneously high. Some laboratories use a large (19 x 40 cm) thigh cuff to satisfy the recommended width/girth relationship and thereby give a more accurate thigh pressure. However, the cuff is so wide that only one can be placed on the thigh. The three-cuff technique utilizes one large cuff placed as high as possible on the thigh. With this technique, a more accurate thigh pressure is obtained (a thigh pressure that is very similar to the higher brachial pressure).

Segmental Doppler pressures of the lower extremity are obtained bilaterally at the following sites and in this order using a hand-held or machine sphegmomanometer with automatic display: ankle pressure (using the posterior tibial artery and dorsalis pedis artery); below-knee pressure (calf pressure), using the best signal of the posterior tibial artery or the dorsalis pedis artery; above-knee pressure (same as below-knee pressure, although the popliteal artery can be used if the ankle Doppler signals are difficult to obtain); and high-thigh pressure (the same as above-knee pressure). If a pressure measurement needs to be repeated, the cuff should be fully deflated for about one minute prior to repeat inflation.

Barnes (5) used a narrower cuff (12 x 40 cm) for measuring the proximal and distal thigh pressures and

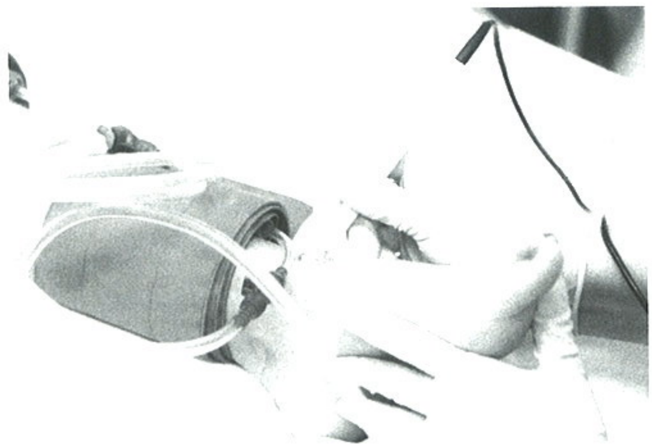


FIGURE 6B
This demonstrates the application of the Doppler probe on the dorsalis pedis artery.

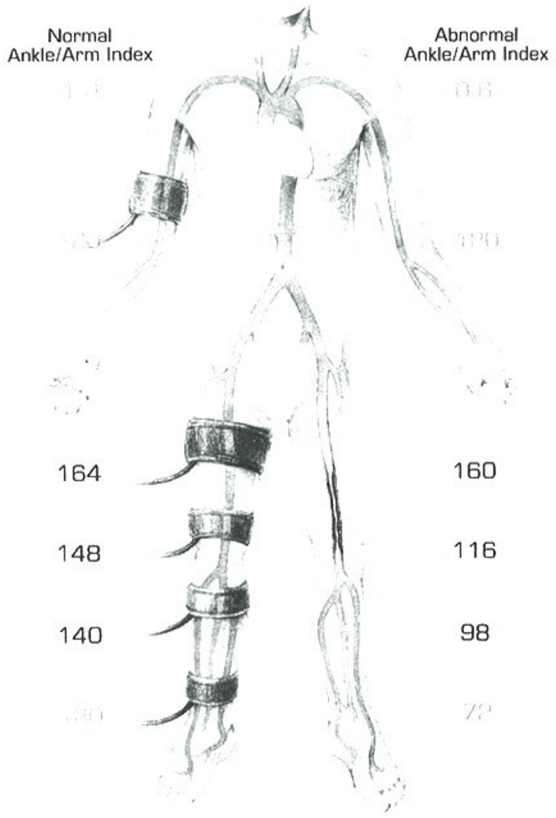


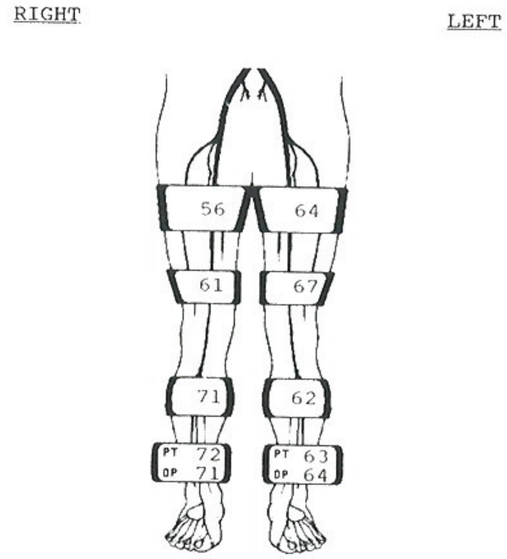
FIGURE 7
Segmental systolic limb pressures of a patient with severe stenosis of the left superficial femoral artery

accepted the artificially high values obtained. This technique allows an approximation of the common femoral (inflow) artery pressure by the proximal cuff and the superficial femoral artery pressure by the above-knee cuff. When only one large cuff is used on the thigh, the single thigh pressure measured does not differentiate aortoiliac from superficial femoral artery occlusive disease. For convenience, the aeroid manometer is used rather than the mercury manometer. The aeroid manometer has the advantage of being portable, inexpensive, easily exchanged from cuff to cuff, and an accurate pressure registering system.

Interpretations

Normally, the proximal thigh pressure should be 20 to 30 mmHg higher than that of the arm, and the pressure gradient between adjacent levels of measurement in the leg should be no greater than 20 to 30 mmHg. A low proximal thigh pressure signifies aortoiliac or common femoral occlusive disease. An abnormal gradient between the proximal thigh and the above-or below-knee cuff is indicative of superficial femoral or popliteal artery occlusive disease. An abnormal gradient between the below-knee and ankle cuffs indicates tibioperoneal disease. Figure 7 shows a patient with occlusion of the left superficial femoral artery as indicated by the pressure differential between the high-thigh and above-knee readings (160 to 116 mmHg respectively).

A horizontal difference of 20 to 30 mmHg or more suggests significant disease at or above the level of the leg with the lower pressure. Figure 8 shows a patient with significant stenosis or occlusion at the aorto-iliac level as indicated by low high thigh pressures bilaterally.



109	BRACHIAL	107
	Indexes	
0.51	U. THIGH	0.59
0.56	L. THIGH	0.61
0.65	CALF	0.57
0.66	ANKLE-PT	0.58
0.65	ANKLE-DP	0.59

(*) Indexes use highest brachial pressure.

FIGURE 8

This represents a patient with significant stenosis or occlusion at the aortoiliac level as indicated by low high-thigh pressures bilaterally.

Thigh Pressure Indexes

Thigh pressure/the higher brachial pressures are normally greater than 1.2, while 0.8-1.2 suggests aorotiliac occlusive disease, and less than 0.8 indicates that proximal occlusion is likely. With the three-cuff technique, the large, single thigh cuff segmental pressure is normally similar to the brachial pressure.

Ankle/Brachial Index (ABI)

From the ankle and brachial systolic pressures, a ratio is obtained which is helpful in determining the presence and magnitude of occlusive disease. Since normal lower limbs have ankle pressures equal to or greater than their ipsilateral arm pressures (recorded in a supine position), a ratio of 1.0 or greater is taken as normal. However, mild to moderate atherosclerotic disease may not affect resting ankle pressures significantly, so all persons having an ABI of 1.0 or greater will probably benefit from stress testing, e.g., treadmill exercise as described in detail later.

It's generally agreed upon that an ABI of 0.9 to 1.0 signifies normalcy or minimal arterial occlusive disease, an ABI of 0.5 to 0.9 signifies a claudication level, less than 0.5 signifies the presence of ischemic rest pain or severe arterial occlusive disease, and less than 0.3 is compatible with trophic changes of the lower extremity. There are those who feel that an absolute ankle pressure of less than 50 mmHg, rather than an ABI of 0.5 is better at predicting symptoms at rest. It has also been suggested that an ABI of equal to or more than 0.5 represents single segment involvement and that lesser values are more indicative of multilevel disease.

Technique for Toe Doppler Systolic Pressure

An appropriately sized cuff, the width of which should be at least 1.2 times that of the toe, is applied to the base of the toe (s). Two 2.5 cm cuffs are usually used for fingers and a 2.5 to 3 cm cuff for the great toe. The digital pulse can be examined using the usual Doppler probe, and a similar technique is applied to measure the Doppler toe pressure.

Normal toe pressures vary from 60% to 80% of the ankle pressures. Values significantly less than this signify digital arterial occlusive disease. The exception to this criteria is when the ankle pressure is artificially high (arterial calcinosis), in which case the toe pressure may be much lower than 80% of the ankle pressure in the absence of digital artery disease. It is generally believed that there is a little difference between the toe pressures in diabetics and non-diabetics, which makes toe pressure determination very helpful in patients with very artificially high segmental Doppler pressures at the ankle level.

Limitations and Sources of Error in Doppler Segmental Pressure Determination

There are a number of limitations and sources of error in Doppler segmental pressure determination:

1. *Hypertension*: when the systemic pressure is elevated, the absolute post-stenotic values are also erroneously high.
2. *Media Sclerosis*: this may cause falsely elevated Doppler pressures in those patients with calcified vessels, e.g. patients with diabetes or end-stage renal disease.
3. *Edema*: in solid edema, especially lipedema, adequate arterial compression may fail, causing erroneously high pressure values.
4. *Congestive Heart Failure*: patients with uncompensated congestive heart failure may show decreased ankle/brachial indexes after exercise.
5. *Measurement of Pressure Post-Exercise*: two examiners should carry out the examination simultaneously after physical exertion to evaluate both extremities, otherwise an adequate rest period between the measurement of the right and a left side is needed. The lower extremity that has the lower resting pressure should be measured first, because the recovery time, post-exercise, is otherwise too long in pathological cases.
6. *Multilevel Occlusive Disease*: patients with multilevel occlusive disease make it difficult to interpret segmental pressures.
7. *Resting Period*: an adequate resting period of 10 to 20 minutes before measurements are taken must be observed. Where there are poorly compensated flow obstructions, the resting period should be longer, in order to avoid measuring erroneously low pressure values.
8. *Deflation Errors*: releasing the cuff pressure too quickly (above 5 mmHg per second) causes erroneously low values. Therefore, a deflation velocity of around 2 mmHg per second should be maintained.
9. *Arm-Leg Measurement Intervals*: the time difference between Doppler pressure measurements should not be too long. Intra-individual systemic blood pressure fluctuations can occur and affect the results.
10. *Subclavian Stenosis or Occlusion*: the systolic blood pressure values measured in this situation are erroneously low; which may give a false impression of normal circulation of the lower extremities.
11. *Flow Velocity in the Arteries Measured*: if the flow velocity in the arteries that are being measured is too low (less than 6 cm/sec), it's not possible to receive a Doppler signal. This phenomena usually occurs at pressures below 30 mmHg.
12. *Effect of the Girth of the Limb*: when the girth of the limb is large in relation to the width of the cuff, the pressure in the cuff may not be transmitted completely to the vessels in the central part of the limb, and the measured pressures may be erroneously exaggerated. Such high false pressures are commonly encountered in the measurement at the level of the thigh.
13. *Effect of Vasomotor Tone Changes*: changes in the vasomotor tone may affect the arterial pressures. When the blood flow is increased during peripheral vasodilatation induced by exercise, heat, or reactive hyperemia, more pressure energy is used in causing flow through stenotic lesions, small distal vessels, and collaterals; therefore distal pressure is reduced. Conversely, when the patient is cool, or when the flow is lower at rest, the pressure tends to be higher. These considerations will explain the normal pressures measured at rest in limbs with mild stenotic lesions and why ankle and digital pressures may be altered significantly by changes in the vasomotor tone. The high tone of the smooth muscle in the wall of the smaller distal vessels of the limbs may result in an artificial reduction of the measured systolic pressure. (6,7)
14. *Stenosis versus Occlusion*: this test cannot distinguish between stenosis and occlusion, and cannot precisely localize the area of occlusion, although it can identify a general location. Similarly, it cannot distinguish between common femoral artery disease and proximal external iliac artery disease.
15. *Stenosis or Occlusion in Parallel Vessels*: when several parallel vessels of comparable size are under the cuff, the measurement will usually reflect the pressure in the artery with the highest pressure and will not detect stenotic or occlusive lesions in the other vessel. Therefore, these measurements will not detect isolated disease in the internal iliac, profunda femoris, tibial, peroneal, ulnar, or individual digital arteries, or interruption of one of the palmer or plantar arches.

Plethysmography

The principle of plethysmography is based on graphic recordings of a change in dimension of a portion of the body in response to each heartbeat or in response to temporary obstruction of the venous system (venous occlusion plethysmography.[8] Most plethysmographs directly or indirectly record the change in column of a digit, limb, or other part of the body. An exception to this is the photoplethysmograph that records the change in reflection of light from the change in number of red blood cells in the cutaneous microcirculation.

Various types of plethysmographs are currently available. Each type employs a different transducer principle for recording the changes in body dimension.

1. The strain-gauge plethysmograph (SPG), originally described by Whitney, (9) uses the principle of the change in the resistance of a column of mercury in an elastic gauge as a sensor of digit or limb volume. This technique is simple and versatile in screening for peripheral arterial and venous disease. Recent modifications of this instrument have permitted electrical calibration of the gauge in situ on the limb [10] and automatic calculation of the limb flow from the excursion of a panel meter needle (11). This technique is less cumbersome than standard volume plethysmography, and has been accepted for measuring limb blood flow (12). It can also be used to obtain pulse volume waveforms, which have been proven to be valuable in the diagnosis of arterial occlusive disease.
2. The photoelectric or photoplethysmograph (PPG), (13) has been used for many years as a pulse sensor. This technique includes an infrared light–emitting diode (14) to transmit light into skin. Light reflected from blood cells is received by either a photocell or a phototransistor, which permits recording of the pulsatile cutaneous microcirculation.
3. Volume or air plethysmography (pulse volume recording) utilizes pneumatic cuffs placed at multiple levels around the extremity. By standardizing the injected volume of air and the pressure within the cuff, momentary volume changes of the limb result in pulsatile pressure changes within the air-filled bladder. These changes can be displayed as segmental pressure pulse contours, which correspond closely to a direct intraarterial recording at that level.

Pulse Volume Recorder

As described in the original pulse volume recorder (PVR) developmental work at Massachusetts Institute of Technology, (15) in order to maintain proper system calibration when a PVR cuff is placed on an extremity, the system and operator must inflate the cuff to a known cuff pressure (i.e. 65 mmHg calf/thigh) and also know the amount of injected atmospheric air necessary to produce the cuff pressure. If the volume of injected air does not meet an established criterion (i.e. 75 ± 10 cm^3, calf; 400 ± 75 cm^3, thigh) the operator must reapply the cuff. Whereas a number of manufacturers market PVR-like devices, some do not include this important calibration. These manufacturers have suggested to operators that after cuff application it is only necessary to inflate the cuff to the recommended pressure. There are manufacturers that provide a good external calibration as described above. These systems provide reproducible PVR data that virtually eliminates operator application and technique errors.

New PVR systems use the popular Windows 95 Operating System with Microsoft Office for word processing, data analysis (electronic spreadsheet), and relational database. The new PVR systems include patient interface ports (i.e. for PVR cuffs and Doppler probes), color monitor, keyboard, and color printer.

The following four parameters, in the limb of interest, must be obtained carefully with a PVR at the correct pneumatic gain settings:

PVR amplitude and contour at the ankle level.
PVR amplitude and contour at the TM level.
PVR amplitude and contour at the 1st digit or most symptomatic digit.
Ankle pressure.

If ankle pressure is <40 mmHg in the non-diabetic patient or <60 mmHg in the diabetic patient resting ischemia may be present. The difference in criteria is based on the fact that diabetics often have medial calcinosis that artificially elevates distal pressures. It should also be stated that in 10-15% of diabetic cases distal pressures cannot be measured at all, due to medial calcinosis; in these cases PVR recordings are the only measurements available.

The diagnosis is secured on the basis of the amplitude of the PVR tracings. If a digit of interest has a flatline PVR amplitude, ischemia is very probable. The probability is further increased if the TM and ankle PVR tracings are also flatline or near flatline. It is not hemodynamically possible to have a flatline tracing proximal to a non-flatline tractíng. If this occurs, the operator should look for a technical error in the testing. In the ischemic setting all tracings should be markedly blunted with no reflected wave present in diastole.

It is possible to have transient borderline ischemia with digital amplitudes as high as 2 mm; however, this is rare.

PVR Reflected Wave

The contour of a PVR tracing is closely associated with the intra-arterial pressure contour. If at rest the reflected wave is absent, this implies the peripheral resistance distal to the point at which the tracing was taken has been reduced. Reduction in peripheral resistance is most often caused by proximal arterial obstruction. Of course, reduced peripheral resistance and loss of PVR reflected wave is expected following exercise (Figure 9).

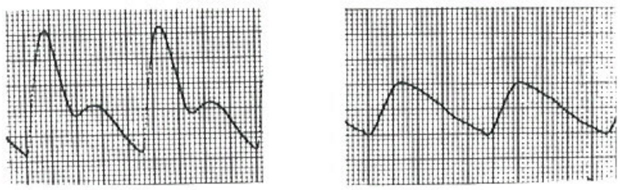


FIGURE 9

Normal (left) and abnormal (right) pulse volume recordings. Ankle level cuff pressure 65 mmHg, cuff volume 75 mL.

PVR Amplitude

The greater the PVR amplitude the greater the local pulsatile component of total flow rate (Qp). Generally, the Qp tracks total flow. Further, PVR amplitude is a function of local pulse pressure and pulse pressure is reduced with arterial occlusion proximal to the point at which the tracing is taken. Therefore, the more reduced the PVR amplitude the greater the proximal obstruction and the poorer the local perfusion.

PVR Amplitude Relationships

When PVR tracings are taken properly calibrated, with an open superficial femoral artery, the PVR calf amplitude is always increased when compared with the thigh and ankle amplitudes. If this is not the case a superficial femoral artery occlusion should be expected. If the PVR tracing at the thigh level is normal with an open aortoiliac system, and the calf PVR tracing amplitude does not augment, an occlusion at the level of Hunter's canal should be suspected.

If the contours of the thigh, calf, and ankle tracings are abnormal (i.e. loss of reflected wave, amplitude reduction) but the calf amplitude is augmented compared with the thigh, this suggests aortoiliac disease with an open superficial femoral/popliteal system.

Whenever there is an abrupt change in PVR amplitude and contour from a proximal measurement to the next segment (i.e. calf to ankle; ankle to TM; TM to digit) occlusion between the two levels should be suspected.

Clinical Applications of Plethysmography

Plethysmographic techniques permit evaluation of peripheral vascular disease by one of the following three techniques: pulse-wave analysis, determination of digit or limb blood pressure, and determination of arterial blood flow. Assessment of digit or limb blood pressure permits semiquantitation of peripheral arterial occlusive disease, and the assessment of limb blood flow permits quantitation of peripheral arterial diseases.

Pulse-Wave Analysis

The contour and amplitude of the plethysmographic pulsation with each heartbeat is a qualitative guide to the presence and degree of peripheral arterial occlusive disease (16). Normally, the pule wave has a steep upslope, a relatively narrow peak, and a dicrotic wave on the downslope which is concave toward the baseline. In the presence of arterial occlusive disease, the pulse-wave contour is damped with a more gradual upslope, a broad rounded peak, and loss of the dicrotic wave on the downslope, which becomes convex away from the baseline. The amplitude or height of the pulse wave diminishes progressively with increasing arterial obstruction (Figure 10). The amplitude of the pulse wave will also decrease in response to sympathetic stimulation, such as that induced by a deep inspiration.

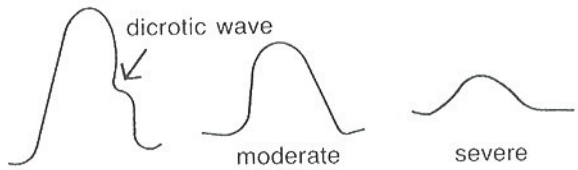


FIGURE 10

Pulse wave tracing. Normal pulse wave has a steep upslope, a relatively narrow peak, and a dicrotic wave on the downslope which is concave toward the baseline. Notice the contour and amplitude in the presence of moderate and severe arterial occlusion.

The digit and segmental limb systolic blood pressures can be determined by plethysmography. However, such determinations are more simply done by Doppler ultrasound. The measurement of high blood pressure usually requires a plethysmography transducer on the distal phalanx (17). Photopulse, strain gauge, or air transducers are suitable for detecting the return of pulsations following deflation of a specially designed blood pressure cuff. Such digit pressure measurements are particularly useful in patients with diabetes mellitus, Raynaud's syndrome, and advanced peripheral arterial occlusive disease.

Determination of digit or limb blood flow by plethysmography provides the most accurate quantitation of peripheral arterial disease. The limb or digit blood flow may be determined by means of venous occlusion plethysmography from the rate of initial increase in limb or digit circumference in response to temporary venous occlusion with a proximal pneumatic cuff (18). The limb blood flow may remain normal in peripheral arterial occlusive disease until the disease becomes far advanced. Thus, it is necessary to measure the abnormal attenuation of increase in limb blood flow during stress, such as that during reactive hyperemia or following limb exercise (19). Normally, arterial blood flow increases by several times the resting level during hyperemia and rapidly returns to normal within a few seconds (reactive hyperemia) or in one or two minutes (postexercise hyperemia). In the presence of arterial occlusive disease, the hyperemia would be attenuated and prolonged in proportion to the degree of the circulatory obstruction.

Color duplex scanning for critical limb ischemia

Duplex ultrasonography provides detailed anatomic and hemodynamic information on the location, extent, morphology, and severity of vascular disease. This information can be used to determine treatment options including medical, surgical bypass/endarterectomy, or endovascular intervention.

The reported diagnostic accuracy of duplex scanning is such that selective use of arteriography is possible in many patients prior to an anticipated intervention (limb revascularization, aneurysms repair) (20-22). Duplex scanning is used to answer specific queries concerning disease morphology (stenosis, occlusion), vessel diameter, extent of atherosclerosis, stenosis severity, or length of vessel occlusion by visualization of exit and re-entry collateral vessels (23).

On the basis of duplex scanning, the majority of patients with limb ischemia manifest by rest pain, tissue loss, or disabling claudication can be classified into an appropriate therapeutic arm, be it PTA or surgical repair/bypass. If endovascular intervention is deemed a treatment option based on finding favorable anatomy, the patient is informed of the risk-benefit ratio for percutaneous balloon dilation or stent placement (PTA) and it is performed at the time of the initial angiographic procedure. PTA may be the sole treatment, or for patients with multilevel disease, involved staged intervention, such as PTA of the aortoiliac segment followed by infrainguinal arterial bypass grafting.

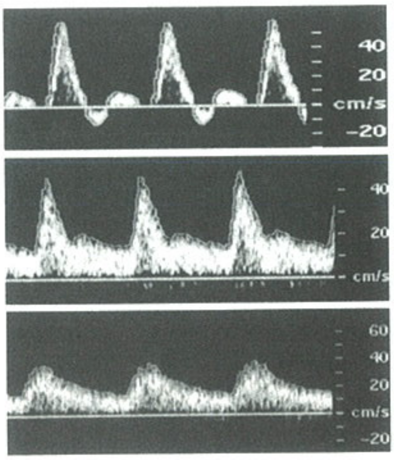
Accepted clinical applications of duplex scanning include:

1. The evaluation of symptomatic patients with abnormal ABIs to guide intervention options (PTA vs. surgery).
2. The reduction of the extent of angiographic imaging (contrast load) in patients with renal insufficiency.
3. The exclusion of occult aortoiliac (inflow) disease in patients with femoral pulses in whom a distal bypass graft is planned.
4. The evaluation of specific diseased arterial segments (stenosis severity, outflow artery atherosclerosis) who hemodynamic significance is not clear following angiographic visualization.
5. The identification of sites of atheroembolism.
6. The surveillance of bypass grafts and PTA sites for stenosis caused by myointimal hyperplasia, fibrosis, or atherosclerosis.

Using color Doppler technology, the arterial tree can be imaged/mapped in a manner analogous to arteriography in body regions accessible to interrogation by ultrasonic energy. The classification of occlusive lesions is based on the same general principles that apply to the duplex evaluation in other arterial circulations. Compared with arteriography, the "gold standard", the diagnostic accuracy of duplex scanning is >80% in the detection of >50% diameter reduction stenosis or occlusion (2,20-25). In the absence of multilevel disease, diagnostic accuracy is higher and exceeds 90% for the detection of high-grade stenosis or occlusion involving the iliac, femoral, or popliteal arteries. When duplex scanning has been used in the evaluation of symptomatic lower limb atherosclerotic disease, approximately 45% of patients have been found to have a lesion suitable for treatment by PTA (26).

Technique

Patients should be scanned in a fasting state to minimize the presence of intestinal gas that obscures imaging of the aortoiliac arterial segment. The patient should be in the supine position with the hip externally rotated and the knee slightly bent. The examination room should be kept warm to avoid vasoconstriction. Scanning begins by imaging the infrarenal aorta at the renal artery origins using a 3-5 MHz phased array transducer to identify occlusive and aneurysmal changes. When clinically indicated, the renal and mesenteric arteries can also be examined. Color Doppler imaging permits rapid location of sites of stenosis by lumen narrowing, color-map aliasing, real-time color flow jet (persistence of high-velocity flow through pulse cycle). Imaging is used for vessel localization, identification of branching and collateral vessels, detection of occlusive or aneurysmal disease, and placement of pulsed Doppler sample volume and Doppler-angle correction. It is important to sample blood flow patterns at closely spaced intervals because the flow disturbances produced by occlusive lesions may only be propagated downstream a short distance. To grade stenosis severity, center stream Doppler angle-corrected (60° or less) pulsed Doppler spectral analysis is carried out proximal to, at the site of maximum flow disturbance, and distal to the stenosis, noting changes in velocity waveform configuration (pulsatility), and measuring peak systolic and end-diastolic blood flow velocities. Duplex interrogation is performed along the aortoiliac and femoropopliteal/tibial arterial segments to classify disease severity in the aorta, common/external iliac arteries, common femoral and proximal deep femoral arteries, superficial femoral/popliteal arteries, and mid-to-distal tibial arteries. Recording the pulsed Doppler velocity spectra from distal tibial or pedal arteries is recommended to correlate waveform pulsatility and peak systolic velocity with measured ABI (Figure 11). This correlation is useful when calcified tibial arteries are imaged, for example in diabetic patients when vessel incompressibility was suspected or documented during measurement of segmental or ankle pressures.



ABI	PSV (cm/s)	PI
1.09	58	8
0.72	45	1.5
0.40	36	1.0

FIGURE 11

Duplex pulsed Doppler velocity spectra recorded from the distal posterior tibial artery at the ankle. Note the changes in velocity waveform configuration (triphasic to monophasic, decrease in pulsatility index (PI) and peak systolic velocity (PSV)) with a progressive decrease in ankle-brachial systolic pressure index (ABI) from normal (ABI > 0.95), tp the level seen in a claudicant (ABI 0.5-0.9), to that typical of severe or critical limb ischemia (ABI < 0.5).

A variety of phased and linear array transducers (5, 7, 10 MHz) can be used to image arteries/bypass grafts distal to the inguinal ligament. Use of multiple scanning windows (aorta: midline, flank; iliac artery: medial to iliac crest; femoral/superficial femoral artery: anterior; popliteal: medial, posterior) may be required for complete insonation/imaging of the peripheral arteries. Imaging limitation include obesity (vessels >15 cm deep), bowel gas, large limbs, edema, surgical incisions/wounds, ulcers, and inability to bend knees, small vessels, and extensive vessel calcification.

TABLE I

Mean arterial diameter and peak systolic flow velocity (PSV) measured by duplex scanning in healthy subjects with normal ABI.

Artery	Diameter ± SD (cm)	Velocity ± SD (cm/s)
External iliac	0.79 ± 0.13	119 ± 22
Common femoral	0.82 ± 0.14	114 ± 25
Superficial femoral (proximal)	0.60 ± 0.12	91 ± 14
Superficial femoral	0.54 ± 0.11	94 ± 14
Popliteal	0.52 ± 0.11	69 ± 14
Tibial		50 – 58 ± 10

ABI, ankle-brachial index; SD, standard deviation.

Duplex Criteria for Grading Stenosis

Although a number of duplex-derived velocity criteria have been validated by comparison with arteriography, the use of maximum peak systolic velocity (PSV), end-diastolic velocity, and velocity ratios (Vr) are recommended to categorize first- and second- order (tandem) stenoses. Standard values for arterial diameter and PSV in the lower extremities have been determined for normal individuals at rest (Table 1) (24). After successful infrainguinal vein bypass grafting, PSV recorded for a normal distal graft segment is in the range of 70cm/s. Prosthetic bypasses and vein grafts to pedal arteries typically have lower PSVs in the 45-70 cm/s range. In investigating patients with lower limb occlusive disease, the finding of a triphasic velocity waveform and normal acceleration time in a proximal arterial segment (i.e. iliac or common femoral artery) is an accurate predictor of no significant inflow (aortoiliac) disease, particularly if the superficial femoral artery is patent. Patients with mild claudication (ABI >0.8) may also have triphasic velocity waveform in the leg arteries at rest (Figure 12); but with exercise ankle pressure decreases and monophasic signal will be recorded distal to the proximal occlusive lesion.

Several classification schemes based on PSV and Vr have been validated with contrast arteriography and are thus useful in grading occlusive lesions from minor to severe stenosis and occlusion (Figure 13, Table 2). (25,27). In general, a significant pressure (>20 mmHg resting systolic pressure gradient) and flow-reducing stenosis is accurately predicted by duplex scanning when there is a (Figure 14):

Loss of triphasic waveform configuration
PSV >250-300 cm/s
EDV >0

TABLE II
Duplex criteria for lower limb arterial occlusive disease.

% stenosis[a]	Duplex-derived velocity spectra: Peak systolic velocity (cm/s)	Velocity ratio[b]	Distal artery waveform
Classification scheme used at University of South Florida[c]			
Normal, 1 – 19%	< 150	< 1.5	Triphasic
20 – 49%	150 – 200	1.5 – 2.0	Triphasic
50 – 75%	200 – 300 EDV > 0	2.0 – 3.9	Post-stenotic turbulence, monophasic distal waveform
> 75%	> 300 EDV > 100	> 4.0	Damped distal waveform with low flow velocity; diastolic velocity in stenosis ≥ pre-stenosis systolic velocity
Occlusion	No flow by color Doppler/pulsed Doppler spectral analysis; length of occlusion estimated from distance between exit and re-entry collateral arteries		
Classification of Cedars-Sinai Medical Center Vascular Laboratory[d,e]			
Normal	< 150	< 1.5	
< 50%	150 – 200	1.5 – 2	
50 – 75%	200 – 400	2 – 4	
> 75%	> 400	> 4	
Occlusion	No flow detected		

[a]EDV, end-diastolic velocity, Diameter reduction.
[b]V_1 is peak systolic velocity at the level of the stenosis, and V_2 is peak systolic velocity of normal caliber artery/graft within 2 diameters length distance from the stenosis.
[c]Adapted from University of Washington criteria.[7,11]
[d]Cossman et al.[3]
[e]*Diagnostic accuracy*: Normal versus abnormal: sensitivity 93%; specificity 83%; > 50% diameter reduction: sensitivity 99%; specificity 87%; artery segment occlusion: sensitivity 99%; specificity 81%.

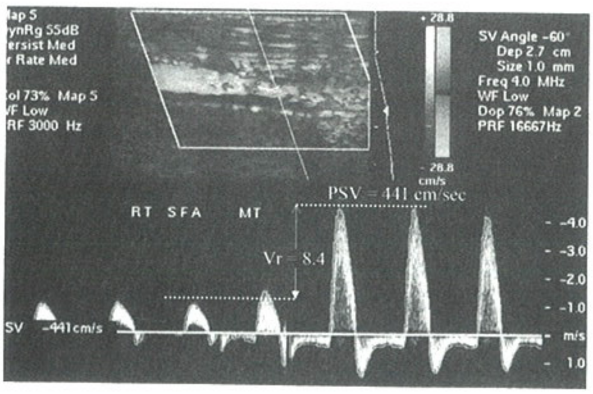


FIGURE 12
Duplex scan of mid-thigh superficial femoral artery stenosis in a patient with calf claudication. At rest, a triphasic waveform was recorded proximal and distal to a focal stenosis with a PSV of 441 cm/s. Treadmill exercise (12% grade at 1.5 mph) resulted in a decrease in ankle pressure from 132 mmHg at rest to 50 mmHg after walking for 2 min. The patient underwent successful balloon dilatation of the lesion with restoration of normal limb hemodynamics.

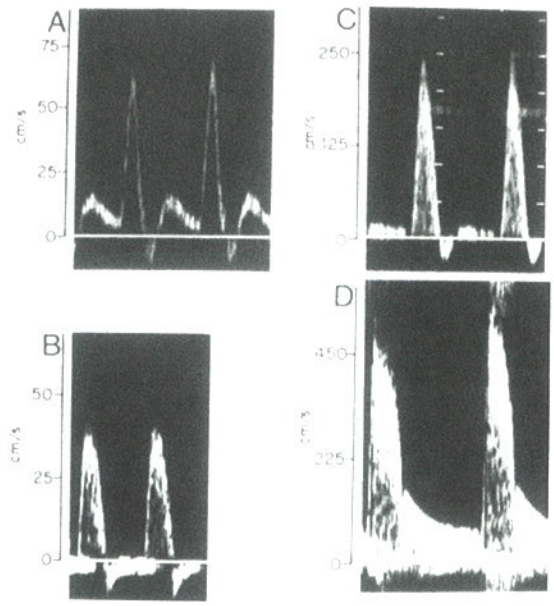


FIGURE 13
Lower extremity spectral waveforms typical of normal (1-19% diameter reduction, DR), 20-49% DR,50-75% DR and > 75% DR stenosis.

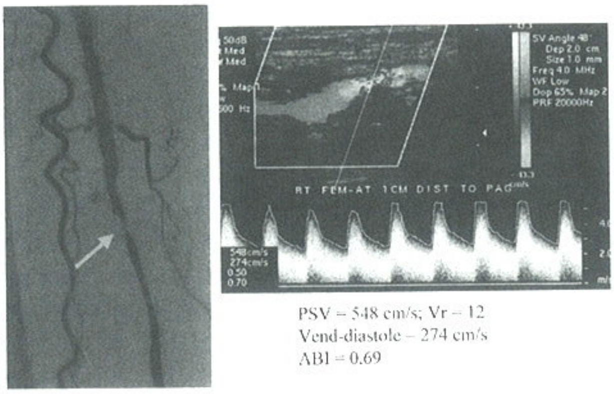


FIGURE 14

Duplex scan of a peripheral artery stenosis (arrow) with features (increased PSV and end-diastolic velocity, turbulent flow, increased Vr) of a pressure-reducing lesion at resting flow rates.

Peak systolic velocity ratio across the stenosis >3

Damping and reduction in pulsatility in the distal artery velocity waveform

Estimation of systolic pressure gradient across stenosis can obtained using maximum PSV at and proximal to the stenosis measured by duplex scanning and a modified Bernoulli equation:

Systolic pressure gradient (mmHg) = $4 \times (PSV_{stenosis} - PSV_{proximal})^2$

Example:

Common iliac stenosis: $PSV_{stenosis} = 3.5$ m/s;

$PSV_{proximal} = 0.5$ m/s

$\Delta P = 4 \times (3.5 - 0.5)^2$

$\Delta P = 36$ mmHg

As stenosis severity increases, the pulsatility and velocity of distal arterial flow decreases, EDV in the stenosis increases, and flows in the inflow vessel decreases and develops a high-resistance flow pattern.

Occlusion of an arterial segment is identified by no color Doppler flow in the lumen, a pre-occlusive thump (staccato waveform), marked damping of distal waveforms, and the presence of exit collaterals. Using real-time Doppler imaging the length of vessel occlusion can be estimated with a precision of ±4 cm based on detection of flow in the lumen and the presence of exit-reentry collaterals (23).

Multilevel disease decreases the diagnostic accuracy of duplex scanning (20). The presence of adjacent stenosis or occlusion reduces diagnostic accuracy of duplex scanning in the aortoiliac segment from >90% to 63% and in the femoropopliteal tract from 93% to 83%. Distal to a severe stenosis or short segment occlusion, the grading of a second-order stenosis relies on both imaging and modified velocity criteria since the inflow Doppler waveform is not triphasic and blood flow velocities are reduced (Table 3). A velocity ratio >2.5 combined with significant lumen narrowing by B-mode imaging indicates a >50% diameter reduction stenosis.(20) The inability of color Doppler mapping accurately to grade stenosis in low-flow conditions when B-mode imaging indicates the presence of atherosclerosis limits its clinical application as the sole diagnostic study prior to tibial bypasses for critical limb ischemia. In these circumstances, angiography prior to or during the procedure is recommended.

Choice of Treatment Based on Duplex Scanning

Based on duplex findings, patients found to have unilateral focal stenosis or short <5 cm occlusions of recent onset (less than 3 months) involving the common iliac or superficial femoral arteries should be considered for PTA (balloon angioplasty/stent with or without catheter-directed thrombolysis). The arterial lesion should be verified by angiography and if a category 1 or 2 lesion based on the Society of Cardiovascular and Interventional Radiology guidelines (28) is confirmed, an endovascular intervention performed. Such treatment results in a high (>95%) technical success and can yield clinical results similar to those following surgical intervention. When duplex scanning indicates features of category 3 or 4 lesions (>4 cm length calcified stenosis, multilevel disease, 5-10 cm length chronic occlusions) use of PTA is possible, but to date endovascular treatment does not yield long-term patency comparable to bypass grafting, especially in treatment of arterial occlusion. PTA of these lesions should only be considered for patients with critical

TABLE III

Duplex criteria for grading first - and second - order peripheral artery stenosis

First-order stenosis ↓	Normal proximal (triphasic) velocity waveform PSV > 150 cm/s Velocity ratio across lesion > 2 Severe spectral broadening and lumen reduction at lesion Loss of triphasic spectral waveform distally
Second-order stenosis ↓	Color duplex lumen reduction with increased velocity Velocity ratio across lesion > 2.5 Decrease in acceleration time and pulsatility of distal velocity waveform
Third-order stenosis	

ischemia who are deemed a surgical risk, or patients with unfavorable anatomy for bypass grafts, or in the absence of a suitable autologous vein for use as a bypass conduit.

Most patients with critical limb ischemia have multilevel occlusive disease and require additional vascular imaging studies (contrast arteriography, magnetic resonance angiography) beyond that afforded by duplex scanning. Duplex scanning can be used to determine whether iliac angioplasty is feasible for patients with combined aortoiliac and infrainguinal disease (29,30). The surgeon can then decide whether to proceed with a staged iliac PTA followed by distal bypass or perform a simultaneous inflow/outflow revascularization. For patients with unilateral or contralateral absence of femoral pulses and long-segment arterial occlusion by duplex imaging, proceeding with aortofemoral, femorofemoral, or axillofemoral bypass grafting without arteriography is appropriate. In treatment of infrainguinal disease, surgical intervention (endarterectomy, bypass grafting) without arteriography is possible in selected patients with single segment occlusive or aneurysmal disease. Femoral endarterectomy with or without profundaplasty, femoropopliteal bypass grafting, and repair of femoral or popliteal aneurysm can be performed based on duplex scan findings. If imaging of the distal vessels is not optimal, intraoperative arteriography can be performed to exclude downstream lesions. Patients with arteriomegaly and diffuse atherosclerosis with multiple tibial artery involvement should undergo preoperative arteriography prior to bypass grafting.

Selective Use of Segmental Doppler Pressures and Color Duplex Imaging in the Localization of Arterial Occlusive Disease of the Lower Extremity

With the recent advances in noninvasive vascular technology, color duplex ultrasound (CDI) has become popular in the diagnosis and localization of aortoiliac and femoropopliteal occlusive disease with a very good correlation to angiography (31-33). However, because of the cost and time involved in performing a CDI of the lower extremity, many vascular laboratories still rely on segmental Doppler pressures to localize arterial occlusive disease, while others still combine both modalities.

In a previously published study, (2) we compared the abilities of segmental Doppler pressures and CDI to accurately categorize the severity of disease. We analyzed 134 patients (268 limbs) who underwent all three tests: segmental Doppler pressures, CDI, and arteriograms. Segmental Doppler pressures and CDI results were examined to determine their accuracy in localizing high-grade (>50%) stenosis at three levels; aortoiliac-common femoral artery (level I), superficial femoral artery (level II), and popliteal artery (level III).

The sensitivity, specificity, positive and negative predictive values, and overall accuracy for segmental Doppler pressures and CDI were: Level I – 63%, 88%, 81%, 75%, and 77%; 93% 99%, 98%, 95% and 96%, respectively ($p<0.01$); Level II – 51%, 99%, 99%, 57%, and 70%; 94%, 98%, 99%, 92%, and 96%, respectively ($p<0.01$); Level III – 55%, 92%, 60%, 90%, and 85%; 78%, 100%, 97%, 95%, and 95%, respectively ($p<0.01$). There was exact agreement between the CDI and arteriogram in regards to the severity of disease in 88% of the limbs (1170 segments). The presence of superficial femoral artery disease in patients with Level I disease or aorto-iliac-common femoral artery disease in patients with Level II disease did not significantly alter the ability of segmental Doppler pressures to localize the disease. The presence of diabetes significantly affected the accuracy of segmental Doppler pressures in localizing superficial femoral and popliteal artery stenosis. An analysis of segmental Doppler pressure's ability to detect any segment as abnormal, as confirmed by arteriogram, revealed a sensitivity of 88%, specificity of 82%, positive predictive value of 96%, negative predictive value of 60%, and overall accuracy of 87%. We concluded that CDI was superior to segmental Doppler pressures in localizing arterial stenosis at all levels. However, since segmental Doppler pressure is cheaper, it can be used initially if no surgical or endovascular intervention is planned.

Transcutaneous PO_2

This technology allows quantitative estimation of cutaneous oxygen delivery that is independent of arterial wall mechanical properties (e.g. medial calcinosis). This monitoring device is a modification of the Clark polarographic oxygen electrode coupled to a servo/controlling heating coil and thermistor. It operates on the principle that vasodilation occurs when the skin heats. At skin temperatures higher than 43 degrees centigrade, the ratio of transcutaneous PO_2 (TCPO2) to arterial PO_2 is constant and approximates 1. Conventional probes are, therefore, set between 43 and 45 degrees centigrade. The relationship is complex and affected by several factors, although the $TCPO_2$ is directly related to skin blood flow. Several attempts have been made to increase the accuracy of predictions based on $TCPO_2$ measurements, e.g. response to maneuvers including oxygen inhalation, post-occlusion reactive hyperemia, exercise, and leg dependency. None of these maneuvers was found to significantly increase the overall accuracy. Other factors that may limit the accuracy and overall usefulness of this methodology include changes in skin temperature, sympathetic tone, age, edema, hyperkerotosis, and cellulitis.

The clinical application of absolute $TCPO_2$ measurement using this technology is limited by the broad overlap of values correlating with the clinical classification of arterial disease. Mild to moderate arterial occlusive disease is generally not detected by reduced $TCPO_2$ levels. The normal range in these patients is around ≥40 mmHg. $TCPO_2$ measurements have maximal sensitivity at critically low levels of tissue perfusion; therefore it is useful in predicting amputation or wound healing in an extremity with severe peripheral vascular occlusive disease. Generally speaking, most wounds or amputations will heal if the $TCPO_2$ is greater than 30 mmHg at that level. For $TCPO_2$ values between and 20 and 30 mmHg, the likelihood of healing is unpredictable. For $TCPO_2$ levels of <20 mmHg, most amputations or wounds will not heal (34).

All the figures in this chapter are reprinted with permission from:
Ali F. AbuRahma and John J. Bergan (Eds) - "Noninvasive Vascular Diagnosis" - Springer 2001

REFERENCES

(1) AbuRahma AF, Robinson PA. *Clinical parameters for predicting response to lumbar sympathectomy with severe lower limb ischemia.* J Cardiovasc Surg 1990;31:101-106.

(2) AbuRahma AF, Khan S, Robinson PA. *Selective use of segmental Doppler pressures and color duplex imaging in the localization of arterial occlusive disease of the lower extremity.* Surgery 1995;118:496-503.

(3) Johnson KW, Maruzzo BC, Kassam M, et al. *Methods for obtaining, processing and quantifying Doppler blood flow velocity waveforms.* In: Yao JST, Nicolaides AN (eds) *Basic investigation in vascular disease.* London, Churchill Livingstone, 1981.

(4) Kirkendall WM, Burton AC, Epstein FJ, et al. *Recommendation for human blood pressure determinations by sphygomanometers: report of sub-committee of the postgraduate education committee, American Heart Association.* Circulation 1967;36:980-988.

(5) Barnes RW. *Noninvasive diagnostic techniques and peripheral vascular disease.* Am Heart J 1979;97:241-258.

(6) Sawka AM, Carter SA. *The effect of temperature on digital systolic pressures in the lower limb in arterial disease.* Circulation 1992;85:1097-1101.

(7) Carter SA, Tate RB. *The effect of body heating and cooling on the ankle and toe systolic pressures in arterial disease.* J Vasc Surg 1992;16:148-153.

(8) Landowne M, Katz LN. *A critique of the plethysmographic method of measuring blood flow in the extremities of man.* Am Heart J 1942;23:644-675.

(9) Whitney RJ. *The measurement of changes in human limb volume by means of mercury-in-rubber strain gauge.* J Physiol (Lond) 1949;109:5P.

(10) Hokanson DE, Sumner DS, Strandness DE Jr. *An electrically calibrated plethysmograph for direct measurement of limb blood flow.* IEEE Trans Biomed Eng 1975;22:25-29.

(11) Barnes RW, Hokanson DE, Wu KK, et al. *Detection of deep vein thrombosis with an automatic electrically-calibrated strain gauge plethysmograph.* Surgery 1977;82:219-223.

(12) Yao JST, Needham TN, Gourmoos C, Irvine WT. *A comparative study of strain-gauge plethysmography and Doppler ultrasound in the assessment of occlusive arterial disease of the lower extremities.* Surgery 1972;71:4-9.

(13) Hertzman AP. *The blood supply of various skin areas as estimated by the photoelectric plethysmograph.* Am J Physiol 1938;124:328-340.

(14) Barnes RW, Clayton JM, Bone GE, et al. *Supraorbital photopulse plethysmography: simple accurate screening from carotid occlusive disease.* J Surg Res 1977;22:319-327.

(15) Raines JK. *Diagnosis and analysis of arteriosclerosis in the lower limbs from the arterial pressure pulse.* PhD thesis, Massachusetts Institute of Technology, Cambridge, 1972.

(16) Strandness DE Jr. *Wave from analysis in the diagnosis of arteriosclerosis obliterans and peripheral arterial disease: a physiologic approach.* Boston, MA: Little, Brown, 1969, pp 92-113.

(17) Gundersen J. *Segmental measurement of systolic blood pressure in the extremities including the thumb and the great toe.* Acta Chir Scand 1972; Suppl 426:1-90.

(18) Brodie PE, Russell AE. *On the determination of the rate of blood flow through an organ.* J Physiol (Lond) 1905;32:47P.

(19) Hillestad LK. *The peripheral blood flow in intermittent claudication. IV. The significance of claudication distance.* Acta Med Scand 1963;173:467-478.

(20) Allard L, Cloutier G, Durant LG, et al. *Limitations of ultrasonic duplex scanning for diagnosing lower limb arterial stenosis in the presence of adjacent segment disease.* J Vasc Surg 1994;19:650-657.

(21) Moneta GL, Yeager RA, Antonovic R, et al. *Accuracy of lower extremity arterial duplex mapping.* J Vasc Surg 1992;15:275-284.

(22) De Smet AA, et al. *Duplex scanning for grading aortoiliac obstructive disease and guiding treatment.* Eur J Vasc Surg 1994;8:711-718.

(23) Cossman DV, Ellison JE, Wagner WH, et al. *Comparison of contrast arteriography to arterial mapping with color-flow duplex imaging in the lower extremities.* J Vasc Surg 1989;10:522-529.

(24) Jager KA, Risketts HJ, Strandness DE Jr. *Duplex scanning for the evaluation of lower limb arterial disease.* In: Bernstein EF (ed) *Noninvasive diagnostic techniques in vascular disease.* St. Louis: CV Mosby, 1985: pp 619-631.

(25) KOHLER TR, NANCE DR, CRAMER MM, ET AL. *Duplex scanning for diagnosis of aortoiliac and femoropopliteal disease: a prospective study.* Circulation 1987;76:1074-1080.

(26) EDWARDS JM, COLDWELL DM, GOLDMAN ML, STRANDNESS DE JR. *The role of duplex scanning in the selection of patients for transluminal angioplasty.* J Vasc Surg 1991;13:69-74.

(27) POLAK JF, ET AL. *Determinant of the extent of lower-extremity peripheral arterial disease with color-assisted duplex sonography: comparison with angiography.* AJR 1990;155:1085-1089.

(28) STANDARDS OF PRACTICE COMMITTEE OF THE SOCIETY OF CARDIOVASCULAR AND INTERVENTIONAL RADIOLOGY. *Guidelines for percutaneous angioplasty.* Radiology 1990;177:619.

(29) VAN DER HEIJDEN FH, ET AL. *Value of duplex scanning in the selection of patients for percutaneous transluminal angioplasty.* Eur J Vasc Surg 1993;7:71-76.

(30) WHELAN JF, ET AL. *Color flow Doppler ultrasound: comparison with peripheral arteriography for the investigation of peripheral arterial disease.* J Clin Ultrasound 1992;20:369-374.

(31) HATSUKAMI TS, PRIMOZICH JF, ZIERLER RE. *Color Doppler imaging of infrainguinal arterial occlusive disease.* J Vasc Surg 1992;16:527-533.

(32) MONETA GL, YEAGER RA, LEE RW. *Noninvasive localization of arterial occlusive disease: a comparison of segmental Doppler pressures and arterial duplex mapping.* J Vasc Surg 1993;17:578-582.

(33) COLLIER P, WILCOX G, BROOKS D. *Improved patient selection for angioplasty utilizing color Doppler imaging.* Am J Surg 1990;160:171-173.

(34) KRAM HB, APPEL PL, SHOEMAKER WC. *Multisensor transcutaneous oximetric mapping to predict below-knee amputation wound healing: use of a critical PO2.* J Vasc Surg 1989;9:796-800.

Peripheral Blood Flow Rates and Microvascular Responses to Orthostatic Pressure Changes Before and After Revascularization

William P Paaske

Methods for exact measurement of blood flow rates in peripheral tissues

Exact determination of the perfusion coefficients in peripheral tissues such as human skin, subcutaneous adipose tissue, and skeletal muscle can be made with the local ^{133}Xenon washout method.

Blood flow in cutaneous tissue can be assessed after atraumatic labelling of the skin with ^{133}Xenon in pure gas form (1-3): The gas is introduced into a small, gas tight, diffusion chamber positioned on the skin, and the gas is allowed to diffuse into the skin for a period of some three min. The diffusion chamber is then removed, surplus gas is blown away, and the activity located in the skin can be detected by a NaI (Tl) crystal (scintillation detector) connected to a ratemeter and a computer. ^{133}Xenon emits gamma radiation with a peak of 81 keV, and the local irradiation of the skin is very low which makes it ideally suited for investigations on human subjects. In addition, there is practically no recirculation since ^{133}Xenon removed from the field by the blood stream will pass from the blood to the alveolar air in the lungs and be exhaled at the first lung transit. A few hundred µm of the skin surface, the upper dry half of the epidermal membrane, is an almost gas tight biological membrane (4), so all gas that has penetrated this biological membrane during the labelling procedure will be removed from the labelled area by convection of the blood in proportion to the blood flow rate. One of the few places in the body where only skin, and no subcutaneous adipose tissue, is present, is the skin fold between the first and second fingers. By collimating the detector to record activity from this area, exclusively, it is possible to get the exact skin blood flow rate by plotting the recorded activity (for example in counts per second) as a function of time in a semilogarithmic diagram and calculate the fractional washout rate constant, k_{skin}, expressed in min^{-1} ($k = \text{lognat } 2 / t_{1/2}$ where $t_{1/2}$ is the half time in minutes, the time for halving of the activity). The curve can be described as $A(t) = a \cdot \exp(-k \cdot t)$ where A(t) is the recorded activity as a function of time, a is the interception of the monoexponential slope, k, with the ordinate, and this time). Using the Kety principle (5), the blood flow rate in the skin can be found as $f_{skin} = k_{skin} \cdot \lambda_{skin} \cdot 100$ (ml blood $\cdot$ (100 g tissue)$^{-1} \cdot min^{-1}$), where λskin is the skin to blood partition coefficient for ^{133}Xenon (a table value, 0.7 ml $\cdot$ g^{-1}).

If a skin area with underlying subcutaneous adipose tissue is atraumatically labelled with the gas, the ^{133}Xenon will be removed from the skin as described above, but it will also be convected as well as diffusing down into the subcutaneous layer from which it will be removed by convection by the blood in proportion to the perfusion coefficient. Experiments have shown that the recorded activity versus time curve will conform to a simple biexponential function and that it is possible to separate this biexponential function into its two monoexponential constituents, one for each tissue. Since the tissue to blood partition coefficient for skin is 0.7 ml $\cdot$ g^{-1} and for subcutaneous adipose tissue 10 ml $\cdot$ g^{-1}, there will be a 14 - 15 times difference in the rate constants for washout at the same blood flow rate in the two tissues which makes it easy to separate the two components by conventional curve resolution, so in this case: $A(t) = a_{skin} \cdot \exp(-k_{skin} \cdot t) + a_{sc} \cdot \exp(-k_{sc} \cdot t)$ where subscript sc denotes the subcutaneous adipose tissue. As above, $f_{skin} = k_{skin} \cdot \lambda_{skin} \cdot 100$ ml blood $\cdot$ (100 g skin tissue)$^{-1} \cdot min^{-1}$ and, further, $f_{sc} = k_{sc} \cdot \lambda_{sc} \cdot 100$ ml blood $\cdot$ (100 g subcutaneous adipose tissue)$^{-1} \cdot min^{-1}$.

The undisturbed blood flow rate in the skin cannot be determined after intracutaneous injection of ^{133}Xenon dissolved in isotonic saline or sterile water (typical concentrations around 555 MBq $\cdot$ ml^{-1}), since the injection itself induces a trauma that elicits a hyperaemic response that lasts as long (20 - 30 min) as detectable ^{133}Xenon is present in that segment (skin). However, the (undisturbed) subcutaneous adipose tissue perfusion rate can be determined by this technique, provided that around 90 min elapses after the intracutaneous injection so that the ^{133}Xenon has disappeared from the skin. All radioactivity will be present in the subcutaneous adipose tissue since the convective and diffusive processes are operative as described above, and the trauma phase in skin has come to an end.

Finally, the gas dissolved in water can be injected directly into the subcutaneous tissue, and after 20 - 30 min the trauma phase will have come to an end, and an undisturbed (monoexponential) washout can be recorded and used for determination of the perfusion coefficient (6).

In skeletal muscle, the countercurrent nature of the

From Critical Lower Limb Ischemia Edited by R Bartolucci, L Battaglia, V D'Andrea, E De Antoni ©2002

microcirculation with shunting by diffusion (7) makes it necessary to take special precautions to ensure correct blood flow determinations (8,9) (proximal lead shield collimation), and the physiological fat inherent to certain muscular regions invalidates determination of true muscle blood flow, if the depot is placed close to an area with fat (10).

Recently, the local heat washout method was introduced for measurement of perfusion rates using heat as the indicator (tracer) for blood flow (11,12). In essence, it is not important whether one uses gas or heat, the principles for kinetic black box analysis and blood flow determinations are identical, and the Kety principle (5) is likewise applied. A Clark type electrode E 5250 (Radiometer a/s, Denmark) is used in this technique. The electrode is constructed with a thermostatically controlled cap to ensure heat delivery in one direction, only (to the skin). Contact fluid is positioned between skin and probe. The electrode is fixed on the skin by a double adhesive, ring shaped membrane and silk tape, and a baseline temperature is recorded. Next, the probe is heated (usually for about five minutes) until the underlying skin reaches a steady state temperature of 41°C as evidenced by constant heat dissipation from the probe. The heat is turned off, and the skin temperature, T, is recorded every 10 seconds until a stable base line temperature, T_b, is obtained after 6 - 10 minutes. $\Delta T = T - T_b$ for each recorded temperature difference measured every 10 seconds is plotted against time in a semilogarithmic diagram. The fractional rate constant, k_{heat}, of ΔT versus time is used to calculate blood flow rate, fheat, from: $f_{heat} = k_{heat} \cdot \lambda_{heat} \cdot 100$ (ml blood $\cdot$ (100 g skin)$^{-1}$ $\cdot$ min^{-1}) where λ_{heat} is the cutaneous tissue to blood partition coefficient for heat. A λ_{heat}-value of 1.0 (ml $\cdot$ g^{-1}) can be used for simplicity (exact value 0.954) (13).

Whereas the ^{133}Xenon local washout method determines the blood flow rate through the nutritive capillaries, the heat washout method determines the blood flow rate in nutritive capillaries plus the blood flow rate in arteriovenous anastomoses (the shunt vessels that have a diameter of 20-70 μm, average 35 μm) when the probe is positioned on the skin in areas with underlying networks of these conduits due to the very high diffusion coefficient of heat (12), as it is about 100 times faster for heat as compared to gases.

The blood flow rates in peripheral tissues of legs

In adults at rest, the normal blood flow rate through nutritive capillaries in skin, subcutaneous adipose tissue, and skeletal muscle is rather low, around 2 - 6 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1}. This value is under normal circumstances subject to modulations induced by sympathetic tone induced by blood pressure and thermoregulation, &c. The blood flow rate in toe pulp skin of normal subjects is around 50 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1} at rest and during thermic equilibrium (14). About 10 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1} pass through the capillaries, and 40 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1} go through the arteriovenous anastomoses. The blood flow rates are also subjected to circadian rhythms; this was most evidently shown in a group of patients with arterial insufficiency who had markedly reduced blood flow rate during sleep (15). Blood flow rates in the pulp of toes and fingers (mainly though arteriovenous anastomoses) decrease with increasing age as the metabolism decreases, and it is around 120 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1} in child toe pulp (14).

When the methods for measurement of blood flow rates in peripheral tissues were introduced, it was hoped that knowledge of the exact perfusion coefficients could be used for differentiation between the three major groups of interest to vascular surgeons, i.e., normal subjects, patients with intermittent claudication, and patients with critical ischemia. Large studies showed, however, that the blood flow rates at rest vary considerably, and overlapping between the three groups was pronounced, so it is not possible from measurements of blood flow rate during rest to classify an individual into either of these groups. Diabetics, too, have normal blood flow rates during rest (16). Wide variations exist, but blood flow rate in ischaemic areas is very low (17), probably below some 0.3 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1}. A special phenomenon is operative in skeletal muscle where arterial and venous vessels are running concomitantly: During muscular exercise, capillaries are "recruited", and during exercise blood flow rate will increase in response to the increased metabolic demands. An exercise blood flow rate of around 100 ml blood $\cdot$ (100 g tissue)$^{-1}$ $\cdot$ min^{-1} is consistent with a capillary recruitment (17) of factor 3.5-4. At rest, the number of perfused capillaries per g tissue is about $1.2 \cdot 10^5$ in skeletal muscle, and the area available for transcapillary exchange is 25 cm^2 $\cdot$ g^{-1}; under heavy exercise (17) the number is $4 \cdot 10^5$, and the area is 100 cm^2 $\cdot$ g^{-1}.

The orthostatic experiment

The orthostatic experiment was devised in order to study the influence of passively induced blood pressure changes within the physiological limits on the peripheral perfusion coefficients.

The subject under study is placed sitting on a chair in a room with comfortable temperature to ensure thermal balance. The study area of the arm, hand, or finger is positioned at a level with the right atrium of the heart (in practice: 5 cm below the jugular notch) on a special lever allowing passive displacements of the arm up and down in relation to the heart. First, a reference blood flow value is measured at heart level, f_{ref1}, the arm is then positioned at an optional level above or below the heart, and the blood flow value is determined in that position, f_{test}; finally, the arm is returned to heart level and a new reference value is measured, f_{ref2}. The results can either be expressed in absolute values or be given as $f_{test}/(0.5 \cdot (f_{ref1} + f_{ref2}))$, *i. e.*, the fractional value at the test level; in the latter way λ cancels out. By the duplicate measurements of the blood flow value at the reference level, it is ensured that reasonably steady state is present with respect to basic blood flow rate during the experiment and that the value obtained at the test level is a true value under this condition. The blood pressures on the arterial and venous sides can be measured simultaneously to allow calculation of the peripheral resistance, R, at the various levels.

If the experiment is being done on the foot or leg, the procedure is the same except for the fact that the subject is lying in supine position on a couch with the leg and foot in the apparatus for lowering or elevating the area under study.

The arterial blood pressure in the distal parts of the extremities is a linear function of the position of the area of interest in relation to the reference level, the right atrium. The hydrostatic pressure, P, is $P = r \cdot g \cdot h$, where r is the density of the whole blood ($1.056\ g \cdot cm^{-3}$), g is the acceleration due to gravitation ($980\ cm \cdot s^{-2}$), and h is distance (cm) above or below the reference level. Since 1 mm Hg is equal to $1330\ dyn \cdot cm^{-2}$, the hydrostatic pressure in a foot vessel 130 cm below the reference level will increase by $(1.056 \cdot 980 \cdot 130)/1330 = 101$ mm Hg, so if the mean arterial pressure is 100 mm Hg at heart level in a supine subject, the arterial mean pressure will be 100 + 101 mm Hg = 201 mm Hg in the foot when it is lowered to 130 cm below heart level. The systemic venous mean pressure is constant and close to zero above heart level, but below a level of about 5 cm below the jugular notch the vein blood pressure increases in parallel to the arterial blood pressure. This implies that the driving pressure (the blood pressure gradient from the arterial side to the venous side) is constant below heart level, and it decreases linearly with the decrease in hydrostatic and arterial blood pressure when the extremity is elevated above heart level.

Local regulation of the blood flow rates in normal subjects

In a series of measurements on cutaneous and subcutaneous adipose tissue of the distal arm it was shown, that the blood flow rate was constant when the area was placed from around 25 cm above to around 25 cm below the reference level (heart). Two different blood pressure conditions are operative within this range: from 5 cm below the jugular notch and upwards, the venous pressure is constant and 0 mm Hg whereas the arterial blood pressure decreases in proportion to the reduction in hydrostatic pressure: This means that the driving pressure is decreased in proportion the reduction in arterial pressure. From 5 cm below the jugular notch and downwards, arterial and venous blood pressures increases in proportion to the increase in hydrostatic pressure: The consequence is that the driving pressure is constant from 5 cm below the jugular notch and downwards ($P_a - P_v$ = constant).

Autoregulation of blood flow is defined as maintenance of constant blood flow rate in spite of changes in arterial pressure when venous pressure is constant. Based on the experimental findings it can be concluded that autoregulation of blood flow, according to the classical definition, is present in normal subjects from about 25 cm above the heart to 5 cm below the jugular notch in cutaneous (18) as well as subcutaneous adipose tissue (19).

The blood flow rate is constant, too, when the extremity is lowered from 5 cm below the jugular notch and downwards to about 25 cm below the reference level, but according to the classical definition, autoregulation in the proper sense is not present in this interval, since venous pressure increases in parallel with the arterial pressure and the hydrostatic pressure.

When the extremity is lowered further down below 25 cm under the reference level, a peculiar finding is observed in both subcutaneous adipose tissue (19) and skin (18): Blood flow rate decreases suddenly to around 60% of that at heart level, and it remains at that value as an on/off mechanism even when the arm or leg is lowered further down below the 25 cm under heart level (which corresponds to a 67% increase in vascular resistance). In a series of experiments on humans, the mechanism behind this reduction in blood flow rate was found to be due to a local, sympathetic venoarteriolar axon reflex: When the veins and venules are dilated over a certain point, the reflex is triggered, and arteriolar constriction follows which decreases local blood flow rates (20,21). Identical findings were seen in skeletal muscle (22,23).

The effect of the local, sympathetic venoarteriolar axon reflex is more pronounced in the distal leg than in the distal arm. When transmural pressure increased 25 mm Hg or more vascular resistance increases about 67% in the dependent forearm but 150% in the dependent leg. Further, vascular resistance after maximum dilatation achieved after 20, 30, and 35 min of induced ischemia was less in the vessels of the arm than in the vessels of the foot. This means that there is local adaptation in the form of structural changes (more developed smooth muscle cells in the arteriolar media) subjected to increased blood pressure in the leg under normal circumstances (24).

In the areas with numerous arteriovenous anastomoses such as the finger or toe pulps, it was found that there is autoregulation of blood flow but no venoarteriolar reflex (11,25).

In patients with diabetic microangiopathy, autoregulation of blood flow is impaired or reduced (16,26), a fact that must be taken into account when interpreting results from vascular surgical patients.

It should be noted that the transcutaneous oxygen tension is also influenced by the local regulation mechanisms in operation during the orthostatic experiment. At maximum elevation the tension decreases about 35% and at lowering about 40% on the foot (27).

Local regulation of the blood flow rates in vascular patients

Intermittent claudication

In a series of examinations on patients with intermittent claudication (Fontaine group II), it was shown that the arteriolar responses in subcutaneous adipose tissue to passively induced changes during the orthostatic experiment are like those of normal subjects (28). Autoregulation of blood flow as well as the venoarteriolar reflex operate normally. In areas with numerous arteriovenous anastomoses (toe and finger pulp) the local venoarteriolar reflex is absent (25). During muscular exercise, blood flow rate in skeletal muscle cannot rise sufficiently. The volume blood flow rate in the femoral artery is around 400 ml · min^{-1} in normal subjects and in typical claudicants; during reactive hyperaemia peak blood flow rate is around 2 l · min^{-1} in normal subjects but only half of that in claudicants. The pressure drop over a haemodynamically significant stenosis will increase, and the distal mean arterial blood pressure will be reduced. Since the arterioles are not paralysed and react normally with vasodilatation, this leads to an increase of the capillary surface area available for perfusion. In this way the linear velocity of the red blood cells within the microcirculation is reduced. The large capillary surface area and the longer transit time of the red blood cells in the capillaries favour the extraction of oxygen (and exchange of solutes) but when demand exceeds supply, the symptoms of claudication develop in parallel with the exercise induced relative local ischemia within the muscles. It should be noted that rheological disturbances are encountered in claudicants with increased aggregation of red blood cells, increased haematocrit value, and increased plasma viscosity.

After some 90 min of sleep, the perfusion is doubled in normal subjects, but in patients with intermittent claudication there is no specific pattern (29).

In a recent series with the heat washout method applied to the toes it was shown that the blood flow rate at heart level was lower in claudicants before reconstruction as compared to a normal control group, and blood flow rate in this area increased and returned to normal in claudicants after intervention. In this way, the heat washout method presents an opportunity to differentiate between normal subjects and claudicants in contrast to the isotope washout methods. Before surgery, blood flow rate in the pulp of the first toe in claudicants increased in median with a factor of 1.79 during lowering. The conclusion is that the disturbances of the microcirculatory responses to orthostatically induced pressure changes in claudicants revert towards normal after arterial reconstruction (30,31). The reason for these findings is probably that claudicants have reduced arteriolar wall thickness (atrophy) induced by the relatively lower arterial blood pressure that results in increased compliance.

Chronic critical ischemia

In patients with chronic critical ischemia (rest pain, Fontaine III) normal responses were present in proximal areas such as the subcutaneous tissue over the head of the fibula and at the lateral malleolus but at the base of the first toe blood flow rate decreases during elevation and increases during dependency (28). The vessels in ischaemic areas act passively and in non ischaemic areas the reactions are normal. This is to be expected since the passive vascular bed will be distended corresponding to the respective compliances due to the increase in transmural pressure which results in a decrease in vascular resistance. The blood flow rate may rise in the ischaemic because of normal vasoconstrictor response during dependency in proximal non ischaemic areas which gives an increase in the arterial perfusion pressure head of the peripheral ischaemic areas. In this way, a redistribution of the total limb blood flow takes place. In other words: If the ischaemic limb is lowered without simultaneous activation of the vein pump, the arterioles in non ischaemic areas will constrict, so the perfusion in ischaemic areas will increase, since the perfusion pressure in these areas increases, and global flow is constant (32). This is the reason why patients with ischaemic rest pain get relief from their pain by letting the leg hang down from the bed during the night; by a slight activation of the vein pump this will still be the case, and hereby the venous blood pressure will decrease, so the driving pressure will be increased which results in an increased perfusion rate in ischaemic areas.

These findings have consequences for the understanding of the local actions of administered vasodilator drugs. The arterioles in non ischaemic areas will dilate after vasodilators, but the perfusion in ischaemic areas will decrease since relatively more blood is now going through the presently dilated and normally functioning arterioles. This paradoxical redistribution of blood flow is called the inverse steal phenomenon, or the inverse Robin Hood syndrome, and it is the reason why patients with peripheral ischemia should not be given vasodilator drugs. On the contrary, vasoconstrictor drugs should have a beneficial effect on the perfusion in ischaemic areas (Robin Hood syndrome, steal).

Ischaemic paralysis of vascular smooth muscle cells should in theory result in a dilated vascular bed, but intravital microscopy of nail fold capillaries in patients with ischaemic periphery has shown that the number of capillaries per unit area is very low, and the tissues are characterized by oedema, intracapillary stagnation, plugging by red blood cells, and activated leukocytes. The local haematocrit fraction is high (and becomes even higher by standing), and local viscosity is increased. This leads to long diffusion distances for oxygen and solutes, trophic changes occur, and the result is ulceration or gangrene.

Normal production of nitrous oxide, NO, demands a normally functioning endothelium. The formation of this lipophilic, unstable radical is stimulated by pulsatile flow and shear stress. The labile gas NO enters the cellular cytoplasm and activates the second messenger system guanylate cyclase, so formation of cyclic guanylic acid is increased. This induces the sequence of protein phosphorylation that leads to smooth muscle cell relaxation and vessel radius increase. This mechanism is abnormal, defective, or absent in patients with diseased endothelium such as in patients with critical limb ischemia. The result of the dysfunctional endothelium is less pronounced endothelium dependent vasodilatation. Leukocytes and red blood cells are more easily deformed in regions with high shear stress and high blood pressure than in low pressure areas such as those found in ischaemic patients. Local acidosis, hyperosmolarity, calcium accumulation, and increased concentrations of fibrinogen in ischaemic areas all contribute to making the red blood cells less deformable, so intracapillary trapping is facilitated. The result is a decrease of local perfusion due to intracapillary plugging leading to perfusion heterogeneity and the no reflow phenomenon. It is also known that there are severe disruptions of the normal rhythmical vasomotion of capillary perfusion in these patients.

The peculiar phenomenon of vasospasms under ischemia has not been satisfactorily addressed and explained. It seems reasonable to assume that paradoxical, local vasospasms are sometimes elicited during ischemia.

When the leg is lowered from 5 to 25 cm below heart level, the capillary filtration rate increases linearly with the increase of the hydrostatic blood pressure. If the leg is lowered further down than 25 cm below heart level, the increase in filtration rate will be reduced by 33%. The capillary filtration coefficient is 0.0012 ml · min^{-1} · (100 g $tissue)^{-1}$ · mm Hg^{-1} at heart level in normal subjects and is practically constant within the whole range of orthostatic pressure changes in normal subjects, so arteriolar constriction during limb lowering decreases the post- and precapillary resistance ratio and counteracts an increase in capillary hydrostatic pressure (33). In addition, arteriolar constriction tends to reduce the number of perfused capillaries leading to a decrease in capillary filtration rate. In this way the superimposed sympathetic venoarteriolar axon reflex counteracts the transcapillary filtration rate increment reinforcing local myogenic vasoconstrictor mechanisms as an oedema preventing mechanism. In patients with ischemia these actions are not operative due to defects in the reflex and there will be disturbed control mechanisms which is the reason behind the, often pronounced, oedema formation in the feet of patients with rest pain. In chronically sympathectomized subjects, the capillary filtration rate increases linearly with venous pressure elevation (34).

Abdominal aortic aneurysm

Very little is known about the microvascular function in patients with non specific infrarenal aortic aneurysm. It has become clear that severe disturbances of the media elastin contents of the aorta characterize these patients, so it was speculated that there might be a peripheral component with abnormal reactions of the arterioles (which have an abundance of elastin). On the other hand the reactions of the arteriovenous anastomoses should be normal since these conduits do not have elastin. In patients previously operated for ruptured aneurysm, the capillary blood flow rate in the subcutaneous adipose tissue of the distal legs was four times higher at rest than in normal subjects at heart level. The aneurysm patients exhibited normal autoregulation of blood flow as well as normal venoarteriolar sympathetic axon reflex. The blood flow rates in the shunt vessels of the toe pulps were the same in aneurysm patients and in normal subjects, and autoregulation as well as the reflex were absent in both aneurysm patients and normal subjects in the pulp. Therefore it is clear that these patients have a peripheral functional component affecting arterioles but not arteriovenous anastomoses (35).

REFERENCES

(1) SEJRSEN P. *Atraumatic local labeling of skin by inert gas: epicutaneous application of xenon 133.* J Appl Physiol 1968;24:570-572.

(2) SEJRSEN P. *Blood flow in cutaneous tissue in man studied by washout of radioactive xenon.* Circ Res 1969;25:215-229.

(3) SEJRSEN P, TØNNESEN KH. *Experimental evaluation of the theory of the local clearance technique. I. The gas diffusion method for atraumatic local labelling.* Scand J Clin Lab Invest Suppl 1967;100:82.

(4) SEJRSEN P. *Epidermal diffusion barrier to 133Xe in man and studies of clearance of 133Xe by sweat.* J Appl Physiol 1968;24:211-216.

(5) KETY SS. *Measurement of regional circulation by the local clearance of radioactive sodium.* Amer Heart J 1949;38:321-328.

(6) NIELSEN SL, SEJRSEN P. *Reactive hyperemia in subcutaneous adipose tissue in man.* Acta Physiol Scand 1972;85:71-77.

(7) SEJRSEN P, TØNNESEN KH. *Shunting by diffusion of inert gas in skeletal muscle.* Acta Physiol Scand 1972;86:82-91.

(8) TØNNESEN KH, SEJRSEN P. *Inert gas diffusion method for measurement of blood flow. Comparison of bolus injection to directly measured blood flow in the isolated gastrocnemius muscle.* Circ Res 1967;20:552-564.

(9) TØNNESEN KH, SEJRSEN P. *Washout of 133Xenon after intramuscular injection and direct measurement of blood flow in skeletal muscle.* Scand J Clin Lab Invest 1970;25:71-81.

(10) SEJRSEN P, TØNNESEN KH. *Inert gas diffusion method for measurement of blood flow using saturation techniques. Comparison with directly measured blood flow in isolated gastrocnemius muscle of the cat.* Circ Res 1968;22:679-693.

(11) MIDTTUN M, SEJRSEN P. *Blood flow rate in arteriovenous anastomoses and capillaries in thumb, first toe, ear lobe, and nose.* Clin Physiol 1996;16:275-289.

(12) MIDTTUN M, SEJRSEN P, COLDING-JØRGENSEN M. *Heat-washout: a new method for measuring cutaneous blood flow rate in areas with and without arteriovenous anastomoses.* Clin Physiol 1996;16:259-274.

(13) PERL W, CUCINELL SA. *Local blood flow in human leg muscle measured by a transient response thermoelectric method.* Biophys J 1965;5:211-230.

(14) MIDTTUN M. *Blood flow rate in arteriovenous anastomoses: from the cradle to the grave.* Clin Physiol 2000;20:360-365.

(15) JELNES R. *Development of gangrene during sleep.* Scand J Clin Lab Invest 1990;50:351-361.

(16) HENRIKSEN O, KASTRUP J, PARVING HH, LASSEN NA. *Loss of autoregulation of blood flow in subcutaneous tissue in juvenile diabetes.* J Cardiovasc Pharmacol 1984;6 Suppl 4:S666-S670.

(17) PAASKE WP. *Capillary permeability in skeletal muscle.* Acta Physiol Scand 1977;101:1-14.

(18) HENRIKSEN O, NIELSEN SL, PAASKE WP, SEJRSEN P. *Autoregulation of blood flow in human cutaneous tissue.* Acta Physiol Scand 1973;89:538-543.

(19) HENRIKSEN O, NIELSEN SL, PAASKE WP. *Autoregulation of blood flow in human adipose tissue.* Acta Physiol Scand 1973;89:531-537.

(20) HENRIKSEN O. *Local sympathetic reflex mechanism in regulation of blood flow in human subcutaneous adipose tissue.* Acta Physiol Scand Suppl 1977;450:1-48.

(21) HENRIKSEN O. *Sympathetic reflex control of blood flow in human peripheral tissues.* Acta Physiol Scand Suppl 1991;603:33-39.

(22) HENRIKSEN O, SEJRSEN P. *Local reflex in microcirculation in human skeletal muscle.* Acta Physiol Scand 1977;99:19-26.

(23) ANDERSON EB, BOESEN F, HENRIKSEN O. *Local and central sympathetic reflex control of blood flow in skeletal muscle and subcutaneous tissue in normal man.* Clin Physiol 1991;11:451-458.

(24) PAASKE WP, HENRIKSEN O. *Vascular resistance in peripheral blood vessels at normotension and at local orthostatic hypertension in healty humans.* Acta Physiol Scand 1975;95:463-469.

(25) MIDTTUN M, SEJRSEN P, PAASKE WP. *Blood flow rate during orthostatic pressure changes in the pulp skin of the first toe.* Eur J Vasc Endovasc Surg 1997;13:278-284.

(26) FARIS I, VAGN NIELSEN H, HENRIKSEN O, PARVING HH, LASSEN NA. *Impaired autoregulation of blood flow in skeletal muscle and subcutaneous tissue in long-term Type 1 (insulin-dependent) diabetic patients with microangiopathy.* Diabetologia 1983;25:486-488.

(27) AABECH J, JENSEN FB, UTZON NP, EICKHOFF JH, PAASKE WP. *Effect of electrode temperature on orthostatic changes in forefoot transcutaneous oxygen tension (tc-PO2).* Scand J Clin Lab Invest 1988;48:475-480.

(28) HENRIKSEN O. *Orthostatic changes of blood flow in subcutaneous tissue in patients with arterial insufficiency of the legs.* Scand J Clin Lab Invest 1974;34:103-109.

(29) JELNES R, TØNNESEN KH. *Nocturnal foot blood flow in patients with arterial insufficiency.* Clin Sci (Colch) 1984;67:89-95.

(30) MIDTTUN M, SEJRSEN P, PAASKE WP. *Peripheral blood flow rates and microvascular responses to orthostatic pressure changes in claudicants before and after revascularisation.* Eur J Vasc Endovasc Surg 1999;17:225-229.

(31) RØRDAM P, SIMONSEN L, JELNES R, HARTLING OJ, CHRISTOFFERSEN JK. *Microvascular circulatory changes in the lower extremities after reconstructive vascular surgery for intermittent claudication.* Eur J Vasc Surg 1988;2:241-244.

(32) EICKHOFF JH, HENRIKSEN O. *Local regulation of subcutaneous forefoot blood flow during orthostatic changes in normal subjects, in sympathetically denervated patients and in patients with occlusive arterial disease.* Cardiovasc Res 1985;19:219-227.

(33) SEJRSEN P, HENRIKSEN O, PAASKE WP. *Effect of orthostatic blood pressure changes upon capillary filtration- absorption rate in the human calf.* Acta Physiol Scand 1981;111:287-291.

(34) HENRIKSEN O, SEJRSEN P, PAASKE WP, EICKHOFF JH. *Effect of chronic sympathetic denervation upon the transcapillary filtration rate induced by venous stasis.* Acta Physiol Scand 1983;117:171-176.

(35) MIDTTUN M, SEJRSEN P, PAASKE WP. *Is non-specific aneurysmal disease of the infrarenal aorta also a peripheral microvascular disease?* Eur J Vasc Endovasc Surg 2000;19:625-629.

Vascular Imaging of Peripheral Vessel Ischemia in the Year 2002

Plinio Rossi

Conventional angiography with the use of iodinated contrast material has been considered for a long time as the gold standard for the evaluation of the vascular system; cross-sectional imaging modalities, however, such as magnetic resonance (MR-angiography) and computed tomography angiography (CT-angiography), have recently emerged as convincing alternatives. MR- and CT-angio-graphy equipments are presently available in many diagnostic centers and these two imaging techniques are more and more employed as effective screening modalities. Conventional angiography still plays an important role, especially for its interventional possibility, but because of its invasiveness and the high radiation dose delivered to both the patient and the operator it has been replaced by these other two techniques.

In most recent years, MR- and CT-angiography have therefore gained an increasing consensus; they are minimally invasive and are able to produce vascular images whose quality is similar to that of conventional angiography but with important additional features. In particular, with the use of axial slices, they allow an accurate assessment of the vessel caliber (dilations or stenoses) and, at the same time, offer a wider visualization of the vascular tree thanks to 3-D reconstructed images. In addition, 3-D images can be magnified, rotated, and examined by innumerable viewing angles, thus providing an easy vessel evaluation and becoming a tool of vital importance for vascular surgeons.

MR- and CT-angiography have both several advantages and drawbacks: the first one offers the great benefit of no ionizing radiations, whereas CT-angiography provides a higher spatial resolution (only when multislice spiral-CT scanners are used) and the depiction of mural calcifications. In addition, CT-angiography can be performed in those patients with contraindications to MR imaging, such as the presence of pacemakers or defibrillators. It should however be noted that both techniques require state-of-the-art equipments to obtain high-quality images (i.e. high-field strength magnets for MR- and multislice spiral-CT scanners for CT-angiography), as well as powerful workstations and dedicated softwares.

With these premises, it is clear that the role of conventional angiography calls for a reappraisal. This modality is presently used either as a diagnostic tool complementary to MR- or CT-angiography, or as a primary screening technique in those centers where highly-sophisticated equipments are missing. Its major advantage is however represented by the possibility of combining a pre-interventional evaluation (especially at the level of distal lower limbs) with the simultaneous possibility of a therapeutic procedure.

In conclusion, this chapter is intended to provide the reader with a comprehensive and exhaustive overview of these three imaging modalities; it has been divided into three parts so that conventional, MR-, and CT-angiography could all be extensively illustrated and described.

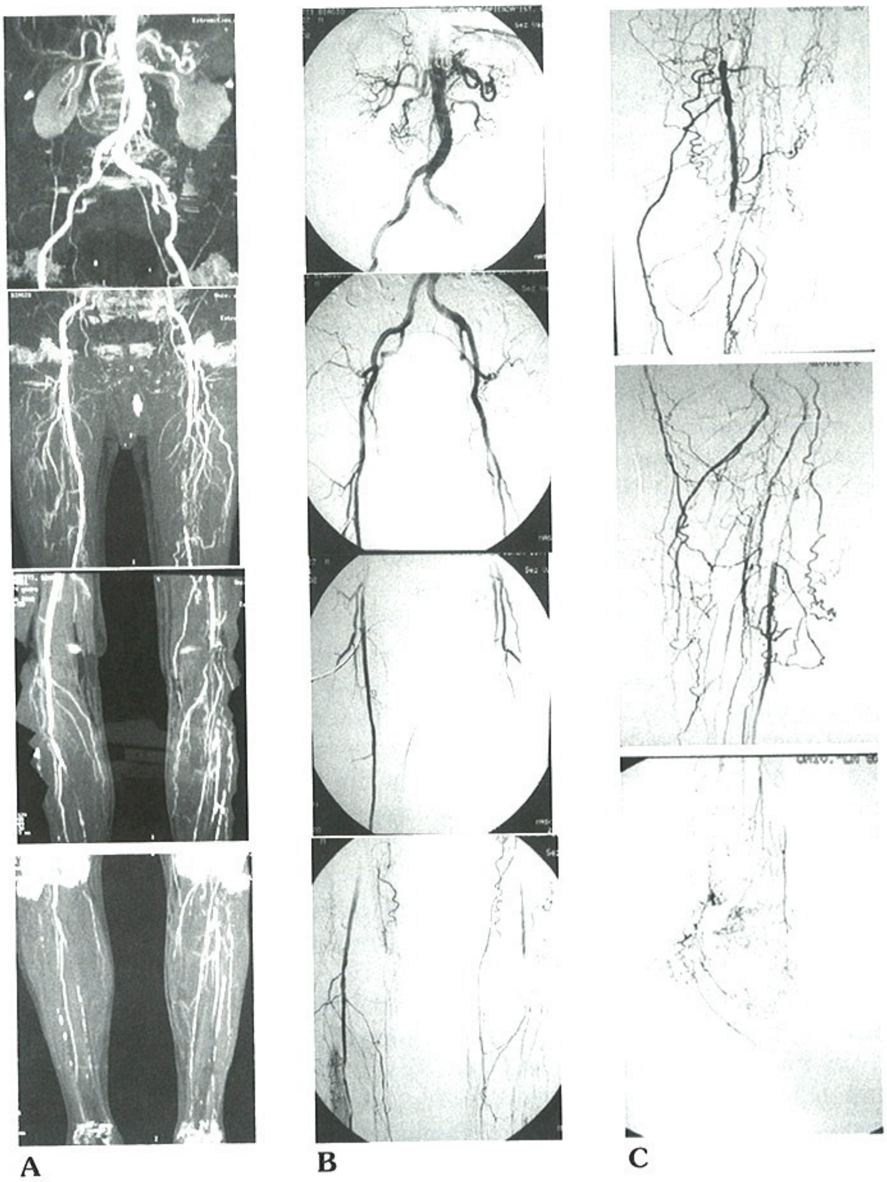
From Critical Lower Limb Ischemia Edited by R Bartolucci, L Battaglia, V D'Andrea, E De Antoni ©2002

Angiographic Imaging and Interventional Procedures in Peripheral Vessels

Fabrizio Fanelli, Filippo M. Salvatori, Simone Vagnarelli, Plinio Rossi

Digital angiography should still be considered the golden standard for peripheral artery visualization only in those institutions where cross sectional MR vascular images, multislice spiral CT-angiography, and USCD are not available. Modern techniques of non-invasive cross sectional imaging, when correctly applied and performed, offer all the information necessary to plan either the surgical or the interventional procedure (Figure 1A-2).

In our Departement, angiography is performed only as the first step of invasive procedures such as recanalizations, or when fine details are important and are not offe-



A B C

FIGURE 1

Comparative study of the same patient with rest pain in the left foot by two imaging modalities: CT-angiography (CTA) and digital subtraction angiography (DSA).
A) CTA: the two stents placed in the left renal and left common iliac arteries are well visualized by CT images although without a clear depiction of the stent lumen. The visualization of the arteries below the inguinal ligament is accurate but it does not permit a true assessment regarding the arteries below the femoral artery obstruction, which could be of valuable importance in the treatment planning.
B) DSA: the depiction of abdominal aorta and peripheral vessels was carried out by multiple injections of contrast medium above the aortic bifurcation and setting of the table at different levels. This technique is able to obtain similar information offered by CTA and with similar limitations regarding the arteries below the obstructed segment. Please, note the excellent visualization of the true arterial lumen at the level of the stents.
C) Selective catheterization of the left iliac artery in the same patient permits a better visualization of the obstructed femoral artery, the popliteal artery and the tibial peroneal trunk. With selective catheterization of the arteries of one lower extremity only, the images can be obtained also in different projections and lateral view. In fact, the angiogram of the foot was obtained in lateral projection demonstrating complete obstruction of the pedidial artery below the ankle and the recanalization of the posterior plantar arch and collateral vessels.

From Critical Lower Limb Ischemia Edited by R Bartolucci, L Battaglia, V D'Andrea, E De Antoni ©2002

red by cross-sectional diagnostic imaging. This technique, therefore, is no longer employed as a diagnostic screening tool.

Technical considerations

DSA does not require any particular preparation, except in case of patients with diabetes mellitus or with renal dysfunction, when the risk/benefit ratio should be taken into careful consideration and the patients must be very well hydrated; also in those patients with cardiovascular insufficiency DSA can be performed, although using a lesser amount of contrast medium (1, 2, 3).

Angiography of the abdominal region is frequently disturbed by superimposing intestinal gases; it is therefore often helpful to immobilize the bowel immediately before the examination by intravenous administration of 20-40 mg of N-butylscopolammonium bromide (e.g., Buscopan, Boehringer).

A retrograde femoral approach is most frequently used to perform angiographic procedures of the lower extremities; the femoral artery is punctured just below the inguinal ligament to maximize the effectiveness of the manual artery compression after catheter removal and to reduce the risk of pelvic and/or retroperitoneal hemorrhage.

The selective catheterization of the arteries of one leg can be performed by different approaches: an ipsilateral antegrade approach with selective catheterization, mostly preferred for infrainguinal vascular interventions, a contralateral retrograde femoral access followed by a cross-over technique, and, more rarely, a trans-brachial approach.

For a complete map of the peripheral vascular system, the visualization of the infrarenal abdominal aorta, the renal arteries, the iliac arteries, and the femoro-popliteal axis should be constantly obtained using a 4-F pig-tail. The catheter is initially positioned 2 cm above the origin of the renal arteries and a non-ionic contrast medium at an intermediate iodine concentration (300 mg/ml) is automatically injected at the flow rate of 20 cc at 20 ml/sec to visualize the renal arteries and the infrarenal abdominal aorta.

The catheter is then pulled back and positioned 1 cm above the aortic bifurcation, where 10 cc of contrast medium are injected at 10 ml/sec to allow an equal opacification of the iliac and the femoral arteries.

In case of aortic mural thrombi or abdominal aortic aneurysms, the contrast medium should be injected at a very low rate (5-6 ml/sec) to avoid the risk of a peripheral embolization due to thrombus dislodgment and subsequent peripheral embolization. Repeated injec-

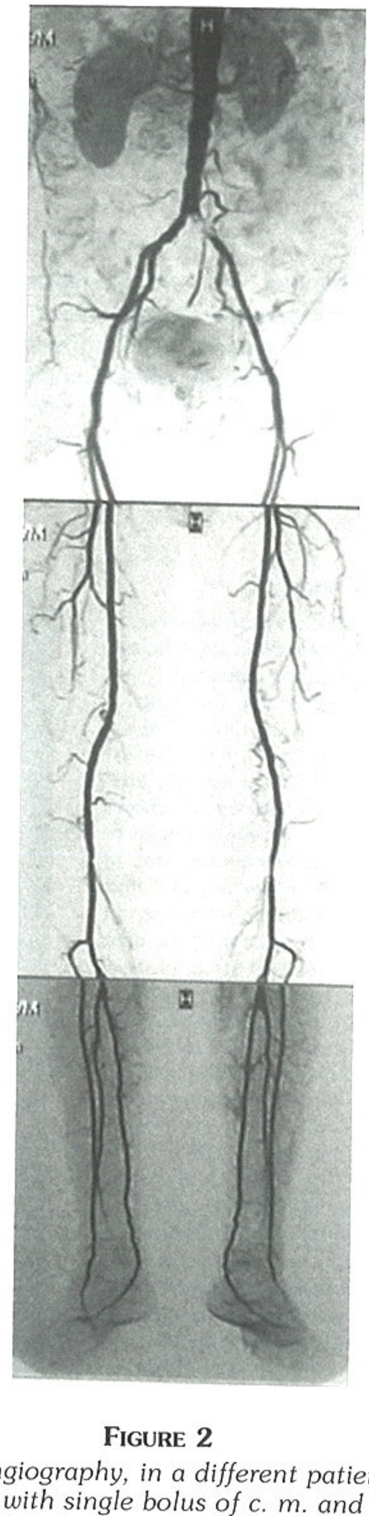


FIGURE 2

MR-angiography, in a different patient, performed with single bolus of c. m. and with a Moby-track technique. At the level of the left common iliac artery, there is a signal loss due to an artifact produced by the presence of a stent. The arterial lumen within the stent is not visualized. Please note the excellent visualization of bilateral femoral, popliteal and tibial arteries to the level of the ankles facilitated by the absence of arterial obstruction.

tions of contrast medium should be done to get the complete visualization of femoral and popliteal arteries, unless the angio-table is programmed to move and follow the passage of contrast medium through the legs. A good opacification of bilateral arteries below the knee requires the injection of a large amount of contrast medium (usually 20-30 cc) at a flow rate of 10 ml/sec (Figure 1).

A better evaluation of the arteries with less contrast medium is however obtained by a selective visualization of the femoro-popliteal axis (Figure 1C). A single leg study is generally performed to improve the definition of vascular structures after a standard run-off procedure or when the interest is focalized on one leg (in case of traumatic injuries, thrombo-embolic occlusions, or as a prelude to interventional procedures) (4-5).

Angiographic procedures in the iliac arteries

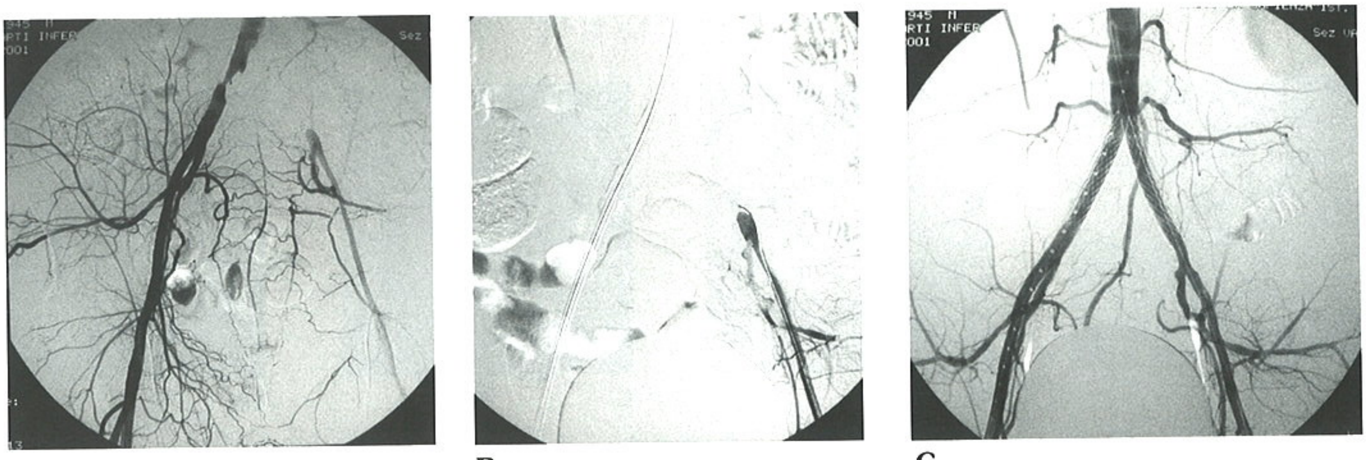
Interventional procedures at level of iliac arteries are generally performed via an ipsilateral femoral access. A 7- or an 8-F introducer sheath (Terumo, Japan), 25 cm in length, is partially introduced. After bypassing the lesion with an angled idrophylic guidewire (Terumo, Japan), a 4-F pig-tail is positioned at the level of the aortic bifurcation to get the visualization of the arterial tree and the severity of the lesion. The introducer is then completely advanced beyond the stenosis, thus favoring a correct stent deployment.

In patients with severe or pre-occlusive stenotic lesions, when the safe passage of a long introducer is not allowed, a predilation should be performed using a low-profile balloon (Wanda, Boston Scientific, USA) placed at the lesion site and slowly inflated with a pressure manometer syringe (Encore, Boston Scientific, USA) for about 20 sec. When the stenosis is correctly dilated, the introducer is then advanced through the lesion to permit an easier release of the selected stent.

In our experience, we prefer the use of primary stenting in case of iliac stenosis or occlusion, according also to the good results reported in the literature. We no longer perform PTA alone to avoid complications due to arterial dilations, such as dissections, intimal flaps, or distal embolizations (6).

Scheinert reported a primary patency rate for iliac stenting of 84% at one year, 81% at two years, 78% at three years, and 76% at four years. Secondary patency rates were 88, 88, 86, and 85%, respectively (7).
In another study reported by Amor using the Palmaz stent, after a six-year follow-up a primary patency rate of 67% was achieved with a secondary patency of 79% (8).

Bare stents are generally used in case of simple stenoses, while covered stents are preferred in more complicated lesions, such as pseudoaneurysms, ulcerated



A B C

FIGURE 3

Recanalization of the obstructed left common iliac artery in a 57-year-old man with a 50-meter claudication.
A) Through a right femoral approach, a selective injection of c.m. at the level of the aortic bifurcation demonstrates an obstruction of the left common iliac artery and a severe stenosis of the right common iliac artery. Both femoral arteries present a normal caliber.
B) Through a retrograde femoral approach, a hydrophylic guidewire was advanced into the abdominal aorta crossing the obstructed segment.
C) Using a "kissing balloon" technique, two e-PTFE covered stent-grafts (Jostent, Jomed, Germany) were simultaneously deployed at the level of the aortic bifurcation with the complete recanalization of both common iliac arteries.
Note that both stents do not extend into the abdominal aorta.

plaques dissections, and in presence of occlusions with fresh thrombi. In case of short lesions and hard calcified plaques, balloon-expandable stents should be selected, since this type of stents has a higher radial force. In case of very tortuous arteries and long stenoses self-expandable stents should be used due to their flexibility.

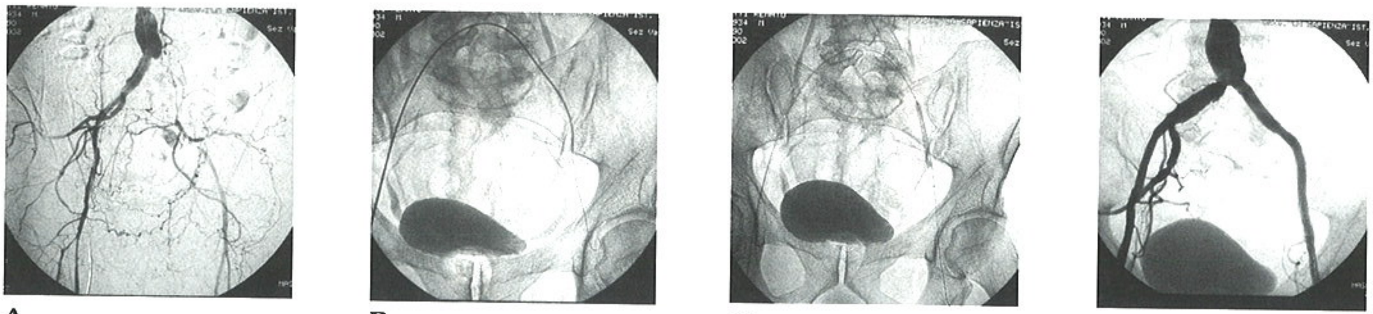
Bilateral disease at the level of common iliac arteries can be treated by a "kissing balloon" technique. From a bilateral femoral access, two low-profile PTA balloons–with or without a pre-mounted stentare advanced up to the aortic bifurcation and simultaneously inflated. Stents should preferably not extend into the abdominal aorta (Figure 3).

To verify hemodynamic results, the intra-arterial pressure should be controlled proximally and distally to the lesion before and after the procedure; if a residual gradient more than 5 mmHg still persists, the procedure cannot be considered correct.

In case of complete occlusion of common or external iliac arteries, if a retrograde passage of the guidewire is impossible, an antegrade approach via a contralateral femoral or brachial access should be attempted (Figure 4).

A percutaneous intentional extraluminal recanalization could be achieved in case of obstruction of the iliac artery when the true lumen is completely obliterated. For the success of this technique, the distal portion of the artery should be reasonably healthy. A 4-F shaped catheter (Multipurpose or Berenstein) is advanced to the occlusion site to easily direct the "Terumo" glidewire into the sub-intimal space. In case of very calcified arteries it would be useful to employ a stiff wire or the back of the wire in order to facilitate the dissection. Once the occlusion is bypassed, the wire is directed back into the true lumen. This represents the most difficult step of the technique, since the dissection often extends proximally or distally to the occluded segment, particularly if the occlusion involves the common iliac artery. Multiple sequential balloon dilations are then performed with a low-profile balloon (Wanda, Boston Scientific, USA) to keep the new sub-intimal channel open. The use of self-expanding stents to fix the subintimal channel is controversial. Murphy (9) recommends their use to keep the sub-intimal channel patent, whereas, according to our experience, we suggest to deploy the stent only at the origin of the dissection to fix the sub-intimal flap. Bolia, however, who is considered the father of the technique, advocates the use of PTA alone without stents (10).

It as been observed that those arteries revascularized by a sub-intimal technique have less propensity to develop a restenosis than those treated using the true lumen. This may be due to the natural migration of smooth muscles from the arteria media into the intima, resulting in fibrotic lesions of intimal hyperplasia after arterial interventions. During a subintimal revascularization, the cleavage plane is similar to that revealed during a surgical endo-arterectomy, but without the stimulation of smooth muscle migration (11).



A **B** **C** **D**

FIGURE 4

Recanalization of the left iliac axis with a "cross-over" technique in a 70-year-old man with a 30-meter claudication on the left side.

(A) The angiogram performed via the right femoral access shows the complete occlusion of the left common iliac artery. A retrograde attempt to recanalize the obstructed iliac artery was not successful; therefore, a cross-over technique was performed.

(B) A Terumo guidewire is advanced from above the obstruction using a Sidewinder 1 catheter (Cordis, Miami, USA) through the thrombus into the external left iliac artery. To avoid perforation of the artery wall, a loop in the guide-wire is formed.

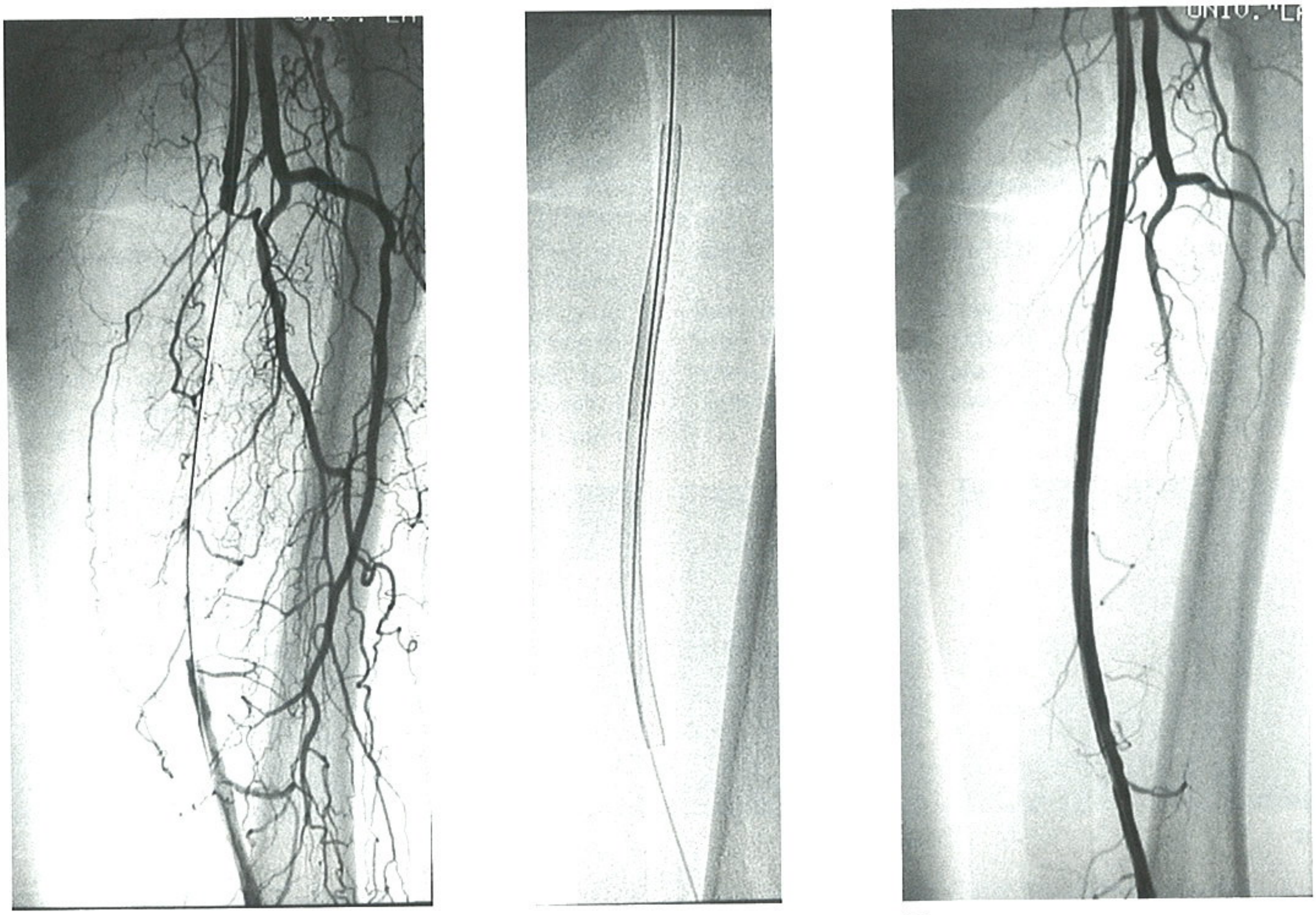
(C) To permit passage of the stent, a pre-dilatation with a 4-mm balloon is performed to enlarge the channel through the thrombus

(D) After deployment of a self-expanding Wallstent (8x50) and balloon-dilation, the final control angiogram shows the complete recanalization of the iliac artery.

In patients with fresh iliac occlusions, an intra-arterial thrombolysis is generally carried out to restore the normal blood flow in the ischemic limb as quickly as possible. From a retrograde ipsilateral or contralateral access and with a cross-over technique, an infusion catheter is coaxially introduced with an hydrophilic guidewire. The thrombus can be easily crossed with a 0.035-inch hydrophilic wire (Terumo, Japan), then the catheter is advanced and positioned with the side holes at the level of the obstruction. A multiple variety of infusion catheters are now available on the market, with different numerous side holes to match the thrombus length. Thrombolysis can be started when there are no contraindications such as: cerebro-vascular events (<2 months), active bleeding diathesis, recent gastrointestinal bleedings (<10 days), neurosurgery, and intracranial traumas within the last three months (12).

Urokinase (UK, Abbott Laboratories) is the most popular lytic agent since it is safe and efficient in peripheral arterial thrombolysis, although it requires many infusion hours. It is a natural protein produced by the kidney obtained from human neonatal kidney cells by tissue culture techniques. Its plasma half-life is 20 minutes (13).

In our experience, after a initial bolus of 200.000/300.000 U.I., a continuous intra-arterial infusion of Urokinase (40.000 to 60.000 UI/hour for 12 hours) should be then injected with a volumetric infusion



A B C

FIGURE 5

Recanalization of the left superficial femoral artery in a 60-year-old woman, heavy smoker, with a 100-meter left leg claudication.

A) A DSA performed through an antegrade femoral access demonstrates a long obstruction (10 cm) of the left superficial femoral artery.

B) After crossing the obstructed segment with a guidewire two Wallstents (10x70 mm and 10x50 mm) are released with a 3-cm overlapping.

C) Final angiogram demonstrating the complete recanalization of the left SFA.

pump with the catheter placed in the proximal portion of the thrombus. We also suggest the association of a continuous systemic infusion of heparin (500-1000 units/hour). When the proximal lysis is obtained, the catheter is advanced into the remaining clot.

A very effective lytic agent of new generation is rt-PA (Activase–Genentech Inc.). It is a recombinantly-derived version of a native protein produced by normal vascular endothelial cells and obtained through cloned mammalian cell cultures. It is a second generation of plasminogen activator with a higher fibrin specificity than UK and a very short plasma half-life (5 minutes). It is generally used at a dose of 0.12 to 2.0 mg/h with a median recommended dose of 0.5-1.0 mg/h (14).

Reteplase (r-PA – Centocore Inc.) is a recombinantly-derived deletion mutation of the native protein alteplase produced from E. coli. It is a third generation plasminogen activator with a higher fibrin specificity than UK and with a plasma half-life of 15 minutes. It is used in a non-weight adjustable dose of 0.25 to 1.0 U/h with or without an initial bolus of 2-5 U (15).

A newest lytic agent is Tenecteplase (TNKase – Genentech Inc.), currently under evaluation for peripheral vascular applications. It was approved in the year 2000 as a single bolus injection for acute myocardial infarctions (16).

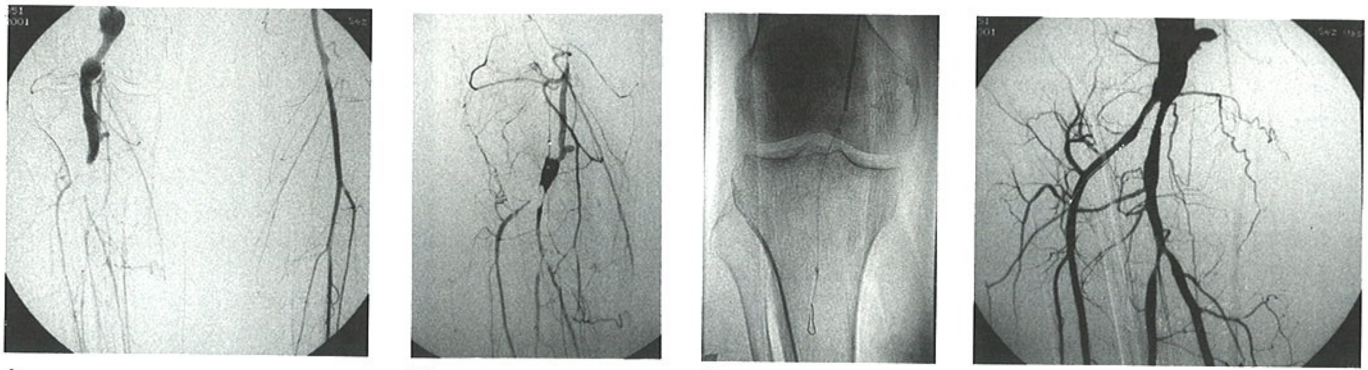
All these lytic agents should however be considered effective in experienced hands only. A review of initial clinical data suggests that there may be some differences between agents with respect to efficacy and complications.

Interventional procedures in the femoro-popliteal arteries

Those stenoses localized in the femoral and popliteal arteries can be crossed as it is done in the iliac arteries. An antegrade approach via an ipsilateral femoral access should be preferred to facilitate wires and catheters manipulation. If the lesion is localized in the proximal portion of the common femoral artery, a retrograde contralateral approach with a cross-over technique could however be used.

Stenoses of the femoral artery can be treated by either PTA alone or with primary stenting. Balloon dilation and stent implantation for claudication and stenosis yield similar long-term patency rates. For more severe femoro-popliteal diseases, the results of stent implantation appear more favorable. Combined three-year patency rates after balloon dilation were: 61% for stenoses and claudication, 48% for occlusions and claudication, 43% for stenoses and critical ischemia, and 30% for occlusions and critical ischemia. Three-year patency rates after stent implantation ranging from 63 to 66% did not correlate with clinical indications and lesion types (17).

Technical success and durability are correlated with several factors: the type of lesion (stenosis or obstruction), its length, the lesion morphology (eccentric or concentric, calcified or not calcified), site of the lesion, and distal run-off. Longer lesions appear to have a lower initial technical success and durability. Jeans found that those stenoses measuring less then 1 cm



A B C D

FIGURE 6

Recanalization of the distal portion of a femoro-popliteal bypass in a 65-year-old man who had undergone a venous femoro-popliteal by-pass of the superficial femoral artery for popliteal entrapment.
A) DSA performed through a contralateral femoral access with direct catheterization of the patent portion of the venous bypass shows a sub-occlusive stenosis at the level of the distal anastomosis and the origin of the antero-tibial and peroneal tibial.
B-C) Balloon dilatation of the distal anastomosis with a 4-mm balloon of the origin of the anterior tibial artery and the tibio-peroneal trunk with a 2.5-mm low-profile balloon.
D) Two bare stents (NIR, Royal, Boston Scientific, 3x18 mm) are deployed at the origin of both the anterior tibial and the tibio-peroneal trunk obtaining an excellent recanalization of the distal arteries.
Note the looped guidewire used to cross the obstruction and the stenosis in a less invasive way.

fared significantly better than longer lesions (>1cm) with a five-year patency rate of 76% and 50%, respectively (18).

Localization of the lesion in the femoral artery is also very important; Amor reported in fact a four-year patency rate of 82% for those lesions localized in the proximal portion of the SFA and 44% for those in the lower portion and the popliteal artery (19). These data are correlated with the anatomical characteristics of the femoral artery. SFA is not uniform and is not subjected to the same extrinsic forces at all levels. Arterial compression and shortening are limited in the proximal part of the femoral artery, whereas at distal ends as well as in the popliteal artery compression, flexion, and shortening are significant.

The durability of femoro-popliteal PTA seems to be also correlated to distal run-off: the three-year patency rate was 78% in presence of a 2/3 vessel run-off, and 25% in case of a poor distal run-off (18).

Because of their flexibility, good adaptation to the arterial morphology, constant force to the arterial wall, and high expansion ratio, self-expanding stents represent the primary choice at the level of the femoral arteries; moreover, they do not collapse in case of external pressure (Figure 5). In the SFA, balloon-expandable stents can also be employed in case of very short lesions.

However, popliteal artery stenting is performed rarely and is not a fully accepted technique. This is due to the anatomical location of the popliteal artery, posteriorly to the knee joint, which requires accommodation during the limb movement and may even cause stent fracture. Strecker reported a two-year primary patency rate of 72%, with a standard error of 10% (20).

Self-expanding stents should be preferred in the popliteal artery also. A study comparing balloon-expandable stents with flexible Nitinol stents, reported a four-year patency rate of 50% for Palmaz stents and 84% for Nitinol stents. These favorable results are explained by the advantageous flexibility and non-compressibility of this type of prostheses (21).

As for the iliac arteries, stent-grafts are preferred only in case of pseudoaneurysms or arterial damages; their long-term validity, in fact, is not proven yet (22).

In case of partial or complete arterial obstructions, recanalization can be achieved by local pharmacological fibrinolysis or sub-intimal recanalization. These two techniques are performed the same way as reported for the iliac arteries.

In presence of very calcified lesions with very tight stenoses, their debulking can be obtained by using mechanical devices or laser.

Rotational atherotomy devices, such as "Rotarex" and "Rotablator," are now available on the market, permitting the creation of a wider lumen through the lesion crossed with a 0.10- or 0.18-inch guidewire; a balloon dilatation should follow. Controversial results are reported in the literature using these devices. Our experience in this field is very limited; we therefore do not express an opinion on this matter (23).

A new percutaneous revascularization technique is represented by the cool laser (24,25). The pulsed excimer laser has been extensively evaluated for its ability to debulk athero-sclerotic material both *in vivo* and *in vitro*, and the photoablative effect of the laser light–capable of recanalizing even long and tight stenoses for very long arterial segments–has been demonstrated. After introducing a 6/8-F sheath, a hydrophilic guidewire is advanced into the origin of the occlusion. Two different techniques can be used to cross the lesion: in one approach, the wire navigates through the lesion, supported by a 4- or 5-F multipurpose guiding catheter. The activated laser catheter is then advanced over the wire (*over-the-wire technique*). Alternatively, to enter the occlusion or to pass a segment resistant to the crossing of the guidewire, an activated laser catheter is advanced in a stepwise fashion for a short distance (<5 mm) without the wire, followed by further crossing with the guidewire (*step-by-step technique*). A fluoroscopic roadmapping is generally used to verify the alignment of wires and catheters to the vessel lumen. Before activating the laser, the contrast medium should be washed out from the vessel by a saline solution. Saline facilitates the trasmission of the laser light to the atherosclerotic tissue while the absorption of the ultraviolet light by the contrast might induce shock waves which can cause dissection of the vessel wall. In most cases, an additional balloon dilation is required to achieve a sufficient lumen. Several randomized trials were performed to compare different laser sources with PTA, but the laser superiority has not been statistically demonstrated. This is probably due to the small diameters of probe commercially available. When a 2-mm probe is used in a 6-mm SFA, little benefit from the laser could be observed. A technical success rate up to 91% was reported with the combined treatment laser + PTA (26-27).

One of the major problems in femoral stenting is the high incidence of restenosis but, although several suggestions have been offered to prevent sub-intimal overgrowth with restenosis, the only tecnique who has given good results is brachytherapy (28).

However, cardiologists have recently experimented drug-eluting stents in the coronary arteries and found that stents covered with Rapamicine are effective in completely eliminating restenosis in six months (29-30).

Interventional procedures of the arteries below the knee

The primary goal of tibial PTA in the limb salvage is not the hemodynamic patency, but to avoid major amputation and to salvage the functioning of the foot. The development of special materials studied for the small vessels is having a big success in interventional procedures performed in the arteries below the knee.

Via an antegrade femoral access, a hydrophilic coated guidewire (Terumo, Japan) can be used in association with a 4-F shaped catheter or a low-profile PTA balloon (Wanda, Boston Scientific, USA) to overpass the lesion. The use of an angled-tip catheter facilitates the correct direction of the guidewire into the artery, especially from the tibioperoneal trunk to the peroneal or the posterior tibial artery.

With the introduction of low-profile, small angioplasty balloons (2-5 mm in diameter) on very small catheter shafts which require a <0.014-inch diameter guidewire, PTA has become the method of choice in case of artery obstruction below the knee. The new generation of PTA balloon catheters presents a stiff, yet flexible, shaft to allow the advancement into long and heavily calcified obstructions, with a high-grade pushability and trackability.

The limb salvage rate obtained with PTA for the management of stenosed or obstructed arteries below the knee is comparable with that obtained by conventional surgery. The higher mortality and morbidity rates of surgery, however, support the use of the endovascular treatment (31).

Solder et al. reported a PTA overall success rate of 84% in case of stenosis and 61% in case of occlusion, higher rates than those obtained by surgical by-passes (32).

Small bare stents can also be implanted at the tibial level, after balloon angioplasty; since controversial results are reported in the literature, it is however generally preferred to treat the lesions below the knee with PTA only (Figure 6) (33).

Subintimal recanalization of the obstructed arteries can also be performed as reported for the iliac arteries.

However, for the success of this technique, the distal portion of the artery should be reasonably healthy. A better quality of the run-off ensures a greater chance of a successful recanalization. Very diseased and poor distal segments beyond an occlusion is a relative contraindication to the sub-intimal recanalization technique.

Moreover, tibial vessels are delicate and the tip of the glidewire may be an easy cause of perforations. To avoid this, it would be preferable to enter the occlusion with the looped glide-wire and not with the tip. During the attempted recanalization, after having dissected the popliteal artery, there is the choice of three vessels at the trifurcation for the glide-wire to follow. All the three vessels may be distally suitable and it would be preferable to recanalize the popliteal artery into all these three vessels to achieve optimal results (10).

Recanalization of very hard lesions can be achieved also using rotational atherotomy devices (Rotablator) and cool laser devices with the same technique previously reported. Laser devices are more efficient in the artery below the knee where a 2-mm probe can achieve the complete ablation of the atherosclerotic lesion (34).

In case of acute arterial occlusions due to fresh thrombotic or embolic diseases, a local intraarterial fibrinolysis can be done using Urokinase or r-tPA with good results.

REFERENCES

(1) Solomon R, Werner C, Mann V, et al. *Effects of saline, mannitol and furosemide to prevent acute disease in renal function induced by radio-contrast agents.* N Engl J Med 1994;331:1416-14.

(2) Spinosa DJ, Angle FJ, Hagspiel KD, et al. *Lower extremity arteriography with use of iodinated contrast material or gadodiamide to supplement CO2 angiography in patients with renal insufficiency.* J Vasc Intervent Radiol 2000;11:35-43.

(3) Eisenberg RL, Bank WO, Hedgock MW. *Renal failure after major angiography can be avoided with hydration.* AJR Am J Roentgenol. 1981 May;136(5):859-61.

(4) Key H, Jackson PC, Thomas EA, et al. *The accuracy of digital subtraction angiography for the quantification of atherosclerosis.* Br J Radiol 1987;60:1083-1088.

(5) Koelemay MJW, Legemate DA, Reekers JA, et al. *Interobserver variation in interpretation of arteriography and management of severe lower leg arterial disease.* Eur J Vasc Endovasc Surg 2001;21:417-422.

(6) Ginsburg R, Thorpe P, Bowles CR, Wright AM, Wexler L. *Pull-through approach to percutaneous angioplasty of totally occluded common iliac arteries.* Radiology. 1989 Jul;172(1):111-3.

(7) Scheinert D., Schroder M., Ludwig J., et al. *Stent-supported recanalization of chronic iliac artery occlusions.* Am J Med 2001; 110: 708-715.

(8) Henry M, Amor M, Ethevenot G, et al. *Palmaz stent placement in iliac and femoropopliteal arteries: primary and secondary patency in 310 patients with 2-4 year follow-up.* Radiology 1995;197:167-174.

(9) MURPHY TP. *Sub-intimal revascularization of chronic iliac artery occlusions.* J Vasc interv Radiol 1996;7:47-51.

(10) BOLIA A. *Percutaneous intentional extraluminal (subintimal) recanalization of crural arteries.* Eur J Rad 1998;28:199-204.

(11) BOLIA A, MILES KA, BRENNAN J, ET AL. *Percutaneous transluminal angioplasty of occlusions of the femoral and popliteal arteies by subintimal dissection.* Cardiovasc Interv Radiol 1990;13:357-363.

(12) SEMBA CP. *Overview of available thrombolytics.* International Symposium on Endovascular Therapy (ISET) 2002.

(13) UROKINASE. *Full prescribing information.* Physicians Desk Reference, Medical Economics CO, Montvale, 1999.

(14) SCVIR ADVISORY PANEL ON CATHETER-DIRECTED THROMBOLYTIC THERAPY. *Alteplase as an alternative to Urokinase.* J Vasc Intervent Radiol 2000;11:279-87.

(15) SCVIR CONSULTANS CONFERENCE. *Thrombolytic and antiplatelet therapy in peripheral vascular disease with use of Reteplase and-or abciximab.* J Vasc intervent Radiol 2001;12:795-805.

(16) RAZAVI MK, WONG H, SZE DY, ET AL. *Initial clinical results of Tenecteplase in catheter directed thrombolytic therapy.* Abstract, SCVIR, April 2002, Baltimore.

(17) MURADIN GS, BOSCH JL, STIJENEN T, HUNINK MG. *Balloon dilatation and stent implantation for treatment of femoropopliteal arterial disease: meta-anlysis.* Radiology 2001 Oct; 221(1): 137-45.

(18) JEANS WD, ARMSTRONG S, COLE SEA, ET AL. *Fate of patients undergoing transluminal angioplasty for lower-limb ischemia.* Radiology 1990;177:559-564.

(19) AMOR M, HENRY M, KLONARIS C. *Role of self-expandable stents in infrainguinal arterial disease.* International Symposium on Endovascular Therapy (ISET) 2002.

(20) STREKER EP, BOOS IB, GOTTMANN D, ET AL. *Popliteal artery stenting using flexible tantalum stents.* Cardiovasc Intervent Radiol 2001;24:168-175).

(21) HENRY M, AMOR M, CHATI Z, ET AL. *Femoropopliteal stenting: results, indications, and choice of stents.* Cardiovasc Intervent Radiol 1999;22,2:S116.

(22) LUNDQUIST PB, KALIN B, OLOFSSON P, ET AL. *Endovascular treatment of atherosclerotic lower limb lesions using a PTFE-collared stent-graft.* J Endovasc Ther 2000;7:221-226.

(23) BRILLU C, PICQUET J, VILLAPADIERNA F, ET AL. *Percutaneous transluminal angioplasty for management of critical ischemia in arteries below the knee.* Ann Vasc Surg 2001;15:175-181.

(24) SCHEINERT D, LAIRD JR, SCHRODER M, ET AL. *Excimer laser assisted recanalization of long chronic superficial femoral artery occlusions.* J Endovasc Ther 2001;8:156-166.

(25) ABELA GS. *Laser arterial Recanalization: a current perspective.* J Am Coll Cardiol 1998;12:103-105.

(26) MILFORD MA, WEAVER FA, LUNDELL CJ, ET AL. *Femoropopliteal percutaneous transluminal angioplasty for limb salvage.* J Vasc Surg 1988;8:292-299.

(27) BAKAL CW, CYNAMON J, SPRAYREGEN S. *Infrapopliteal percutanmeous transluminal angioplasty: what we know.* Radiology 1996;200:36-43.

(28) STUCKLE CA, LAUFER U, KIRCHNER J, ET ALL. *Successful treatment of intimal hyperplasia in renal arteries by endovascular brachytherapy.* Cardiovasc Radiat Med. 2001 Apr-Jun; 2(2): 114-8.

(29) SOUSA JE, COSTA MA, ABIZAID A, ET AL. *Lack of neointimal proliferation after implantation of Sirolimus-coated stents in human coronary arteries.* Circulation 2001; 103: 192-195.

(30) SERRUYS PW, MORICE MC, SOUSA JE, ET AL. *The RAVEL study : a randomized study with the sirolimus coated Bx velocity balloon-expandable stent in the treatment of patients with de novo native coronary artery lesions.* Europ Heart J 2001; 22: 484.

(31) SCHWARZENBACH BP, GROSCURTH P, LANG A, SCHOPKE W, HOFFMANN U, BOLLINGER A. *Significance of arterial anastomoses of the distal calf and proximal foot for compensation of peripheral arterial occlusive disease.* Vasa 1996;25(4):331-6.

(32) SOLDER HK, MANNINEN HI, JAAKKOLA P, ET AL. *Prospective trial of infrapopliteal artery balloon angioplasty for critical limb ischemia: angiographic and clinical results.* J Vasc Interv Radiol 2000;11:1021-1031.

(33) DORROS G, JAFF MR, DORROS AM, ET AL. *Tibioperoneal (outflow lesion) angioplasty can be used as primary treatment in 235 patients with critical limb ischemia. Five-year follow-up.* Circulation 2001;104:2057-2062.

(34) DIETHRICH EB. *Below the knee arterial occlusive disease-the cool laser is in!* International Symposium on Endovascular Therapy (ISET) 2002.

Multidetector-row Spiral CT Peripheral Angiography in Leg Ischemia

Carlo Catalano, Alessandro Napoli, Francesco Fraioli, Piergiorgio Nardis, Simona Fiori, Roberto Passariello

In the past ten years we have assisted to rapid technological developments aimed at achieving non-invasive imaging modalities for the assessment of vascular pathologies.

Among these, spiral CT-angiography has provided excellent results, particularly in the evaluation of thoracic and abdominal aorta with their branches and pulmonary arteries (1,2,3,4). Nevertheless, because of the technical limitations that impaired the acquisition of large volumes at high resolution, spiral CT-angiography could be employed in large districts only when small vessels such as the peripheral vasculature had to be studied.

The recent introduction of multi-slice spiral CT (MSCT), which allows the simultaneous acquisition of four slices per single gantry rotation, has opened new frontiers in the vascular imaging with computed tomography; in addition, further developments are in progress and, soon, more slices per rotation will be possible. The limitation of volume coverage, in fact, has been surpassed, as well as the spatial resolution along the z-axis, thanks to the near-isotropy of the voxels (5,6,7). Presently, therefore, the clinical advantages of transaxial acquisition typical of computed tomography, such as vessel wall imaging, can be applied also to the assessment of the entire aorta and run-off vessels, after one single bolus of contrast agent administration (8). In consideration of the volume length, the amount of data produced after such acquisition is extremely large and should be analyzed on dedicated workstations. The tree-dimensional data set analysis using several types of reconstruction algorithms should be considered part of the MSCT examination (Figure 1).

Scanning protocol

The patient's feet are positioned first, by securing his/her legs in a slight internal rotation, in order to separate the bones from the arteries below the knee; this expedient allows the editing of osseous segments during the post-processing phase.

A large topogram (1024 mm) is obtained from the diaphragm to the feet with the positioning of an acquisition volume, in order to examine the

A B

FIGURE 1

Normal peripheral vascular tree.
Multi slice spiral CT angiography of the entire run off vasculature from the celiac trunk to the calf vessels acquired in a few seconds after a single bolus contrast media administration.
Both MIP (1a) and perspective VR (1b) images show an excellent arterial delineation of the main arteries of the legs as well as smaller vessels.

From Critical Lower Limb Ischemia Edited by R Bartolucci, L Battaglia, V D'Andrea, E De Antoni ©2002

arterial district from the celiac trunk to the pedal circulation.

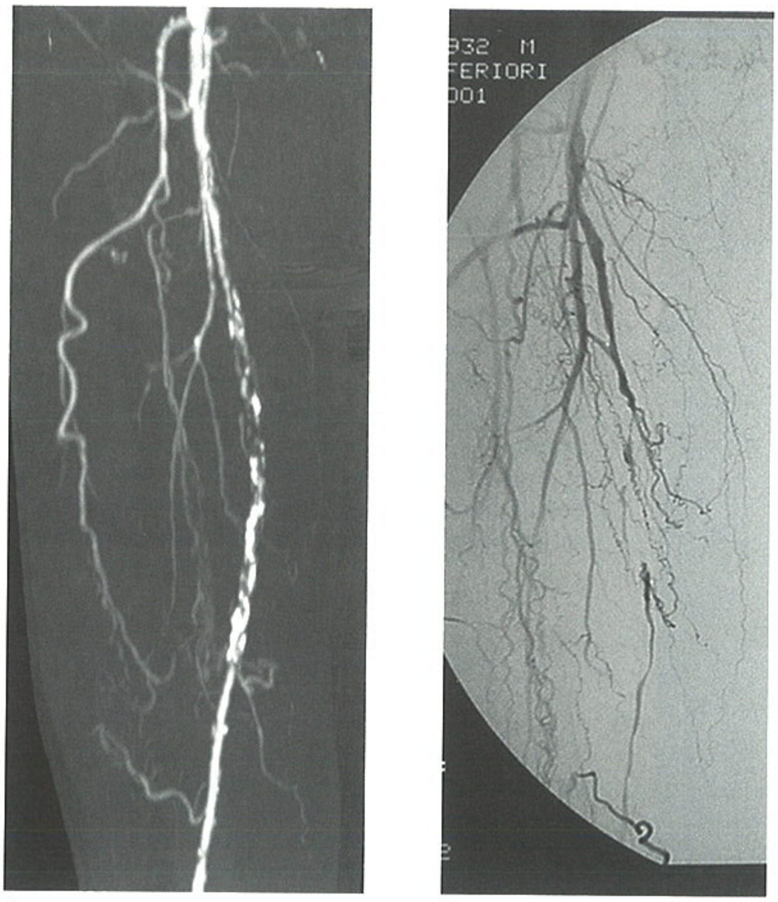
The protocol we usually adopt using a 0.5 sec gantry rotation time multidetector-row spiral CT consists in the following parameters: 4 x 2.5 mm collimation; 3 mm slice thickness; 3 mm reconstruction interval; 15 mm (30 mm/s) feed/rotation. To obtain more details, additional reconstructions at thinner intervals can be performed. This is particularly useful at the level of the renal arteries or the trifurcation vessels, where a better delineation is desirable and images can be reconstructed with 1.5 mm slice intervals (9).

Contrast agent administration

Optimization of contrast media administration is the key factor to achieve a good peripheral MSCT-angiography. Flow rate, iodine concentration, amount of contrast agent, and delay time, all of these factors affect the image quality. Our two-year experience shows that best results are achieved when an 18-G i.v. cannula is utilized, which easily allows a flow rate of 3.5 ml/s and more (4-4.5 ml/s). In the routine practice, we administer 42g/I per patient injected at a flow rate of 4 ml/s. Best results can be obtained with high iodine concentration contrast agents (we routinely use 370-400 mgI/ml contrast agents), which provide a significantly greater arterial enhancement as compared with lower iodine concentration agents (300 mgI/ml). When we first started our experience with MSCT-angiography of the run-off vessels in the mid 1999, no methods for the assessment of the delay time was available on the scanner. After a preliminary evaluation, we therefore decided to routinely use a standard delay time of 28 seconds, which provided good results in more than 200 patients with peripheral arterio-pathy, with technical failures in about 2% of subjects. In case of aneurysmal disease or in patients with a low cardiac output, the delay time may be increased to 30-32 seconds (10). In case of an asymmetric flow, differences in the enhancement of the two extremities may occur, particularly in those patients with unilateral occlusive or dilative disease; in most of the cases, however, the distal enhancement is bilaterally adequate for the diagnosis. As far as image degradation from the veins is concerned, previous studies have shown that venous enhancement occurs after approximately 120 seconds; nevertheless, there might be venous enhancement in those cases of cutaneous trophic lesions or in patients with artero-venous fistulas or varices. In our experience and according to other studies also, in none of the cases the venous enhancement degraded the image quality (11).

3-D image analysis

When performing a MSCT peripheral vascular study, a large amount of data is routinely produced. For an easier management, the volume data set is then transmitted to a dedicated workstation where all CTA studies are analyzed by using a 3-D rendering software (12,13). No pre-defined reconstruc-



A B

FIGURE 2

Obstructed right femoral artery with heavy calcifications

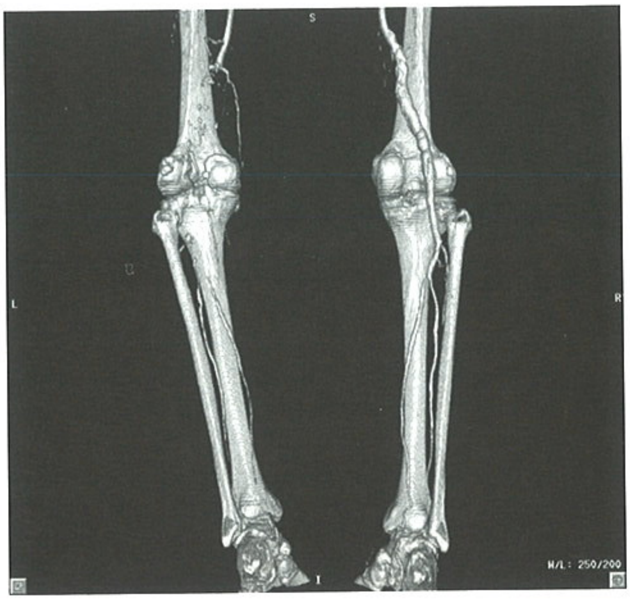
Obstruction of the superficial right femoral artery with collaterals arising from the deep femoral artery on MIP image (2a) after bone segmentation, with excellent correlation with DSA (2b). Presence of calcifications is well demonstrated by CTA and it never is an obstacle to the lumen visualization which patency is always assessed using cross-sectional images.

tions, planes, or projections are obtained by the technicians. The 3-D analysis, which presently requires 15-20 minutes approximately for each case, is performed directly by the readers. Bone segmentation is not considered as being routinely necessary, but performed in a few selected cases only.

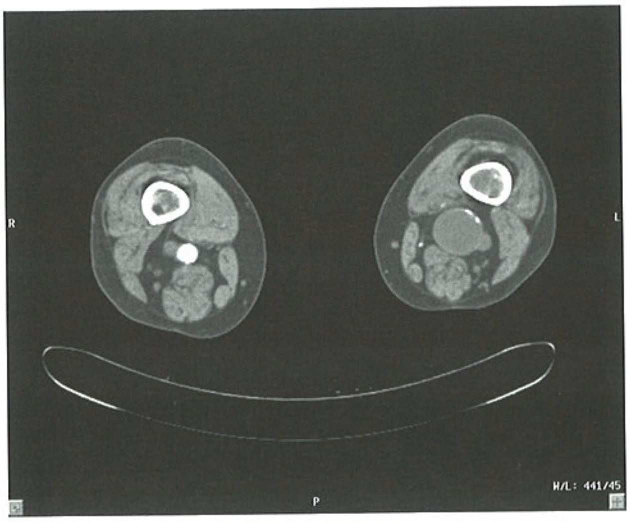
A rapid scrolling of axial images is always carried out as first step of the reviewing process in all MSCT-angiography examinations by the reader; he selects different planes among all the types of reconstruction algorithms provided by the workstation: multiplanar reformatting (MPR), maximum intensity projection (MIP), thin MIP, and volume rendering. By using this approach, the reader can display and select interactively any portion of the scan volume, thus generating any useful plane or perspective. This approach, although time-consuming when performed by non-experienced operators, allows a careful analysis and avoids routine bone segmentation, another time-consuming operation (14). The employment of technicians for the acquisition of 3-D images has shown to be successful in some institutions, but we believe, and so do other authors, that real-time interaction permits an optimal use of the radiologists time. In our experience with MSCT (not only when assessing vascular pathologies), the radiologist is the direct user of real time data and the first interpreter of the images obtained.

Clinical evaluation

In the assessment of peripheral arterial occlusive disease, DSA still remains the gold standard for peripheral



A



B

C

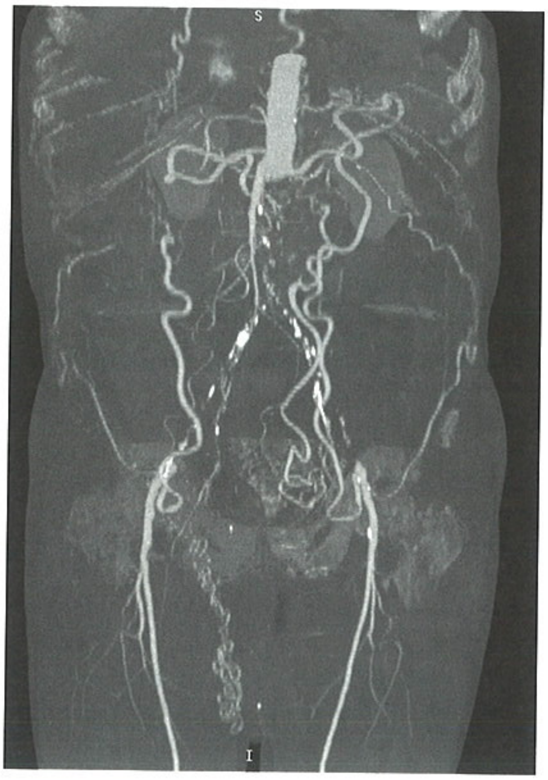
FIGURE 3

Occlusion due to thrombosed popliteal aneurism VR on a posterior view (3a, left leg is on left side of the picture) shows obstruction of the left popliteal artery with good distal run off. Axial (3b) and sagittal (3c) MPRs show the presence of a popliteal artery thrombosed aneurysm.

ischemia. Nevertheless, in consideration of its invasiveness, costs, and a minimal complication rate, a non-invasive technique, able to demonstrate vascular peripheral occlusions or arterial stenoses, is desirable (15,16).

Our results show that, as it has already been demonstrated in other vascular districts with single-slice spiral-CT, computed tomography is very accurate also in the assessment of peripheral vascular disease (Figure 2). As compared with DSA, there is a slight tendency to overestimate degree of stenosis, while a very few cases are underestimated. A comparative evaluation of 50 patients assessed with catheter angiography has shown a statistically significant difference only in the differentiation between normal and mildly diseased arteries; no change in the therapeutic approach is therefore deter-

A



B

C

FIGURE 4

Leriche's syndrome with the recanalization of both common femoral artery

Thick coronal image shows obstruction of the juxta-renal aorta due to a thrombus within the abdominal aorta and iliac arteries below the renal arteries (4a). Multi slice CT MIP angiogram shows recanalization of both distal common femoral artery through several collateral vessels arising from the intercostal, mammary, epigastric, lumbar and mesenteric arteries (4b). Intravenous contrast administration allows an excellent opacification of distal vessels to the obstruction (4c) that could not be obtained with DSA because the injection of contrast media has made above the obstruction and it doesn't allow the opacification of intercostal and mammary arteries that are the major supply in case of obstruction of the abdominal aorta.

mined by erroneous interpretations. Although in our experience there was a tendency of MSCT-angiography to overestimate slight parietal alterations, the visualization of the vessel walls intrinsic to axial acquisitions was a significant advantage of computed tomography, not only as compared with DSA but also with other non-invasive imaging modalities, such as contrast-enhanced MRA. In our study, the analysis of axial slices together with multiplanar reconstructions provided superior information in the visualization of those occlusions secondary to an aneurysmal disease and in the treatment planning, particularly regarding plaque-morphology. Discordances were also seen in differentiating focal from diffuse severe disease, especially in distal vessels.

The main difficulty in the determination of single or multiple stenoses is represented by the presence of circumferential and heavy parietal, diffuse calcifications, which may impair the assessment of the real degree and extent of the stenosis, particularly in small-caliber vessels. In presence of calcified plaques, the real-time interaction approach with the 3-D data set provided better results; our experience suggests that all possible reconstructions should be used, since all of them may offer different information. The use of MIP, thin MIP, and volume-rendering only may impair the quantification of stenoses, particularly if heavy parietal calcifications are present. In this respect, acquisitions along the transverse plane represent an advantage over other non-invasive imaging modalities, such as contrast-enhanced MR-angiography (MRA), acquired along longitudinal planes (17,18). In our experience, in fact, the use of transverse planes provided superior information on the stenoses degree, in depicting associated aneurysms (in some cases thrombosed, especially in the femoro-popliteal district) (19), and in determining the plaque-morphology (Figure 3).

In those patients with an obstructive disease, MSCT reveals another significant advantage: as compared with catheter arteriography, in fact, the venous administration of contrast agent allows the opacification of all collaterals, thus resulting also in the excellent opacification of those vessels distal to the occlusion, hardly enhanced when an intraarterial injection is performed (Figure 4).

In conclusion, although MSCT angiography of the aorta and lower extremity arteries is in its infancy, the technique is very accurate, reproducible and, in most cases, it may replace catheter-based DSA.

REFERENCES

(1) CINAT M, LANE CT, PHAM H, LEE A, WILSON SE, GORDON I. *Helical CT angiography in the preoperative evaluation of carotid artery stenosis.* J Vasc Surg 1998; 28: 290-300.

(2) RUBIN GD. *3D spiral CT angiography of the aorta and its branches.* In: Fishman EK, Jeffrey RB, eds. Spiral CT: *principles, techniques and clinical applications.* Philadelphia, PA: Lippincott-Raven, 1998; 361-403.

(3) VAN HOE L, BAERT AL, GRYSPEERDT S, ET AL. *Supra- and juxtarenal aneurysms of the abdominal aorta: preoperative assessment with thin section spiral CT.* Radiology 1996; 198: 443-448.

(4) KAATEE R, BEEK FJ, DE LANGE EE, ET AL. *Renal artery stenosis: detection and quantification with spiral CT angiography versus optimized digital subtraction angiography.* Radiology 1997; 205: 121-127.

(5) HU H. *Multi-slice helical CT: scan and reconstruction.* Med Phys 1999; 6:5-18.

(6) RUBIN GD, SHIAU MC, SCHMIDT AJ, ET AL. *Computed tomographic angiography: historical perspective and new state-of-the-art using multi detector-row helical computed tomography.* J Comput Assist Tomogr 1999; 23 (suppl 1): s83-s90.

(7) KLINGENBECK-REGN K, SCHALLER S, FLOHR T, OHNESORGE B, KOPP AF, BAUM U. *Subsecond multislice computed tomography: basics and applications.* Eur J Radiol 1999; 31:110-124

(8) RUBIN GD, SHIAU MC, LEUNG AN, KEE ST, LOGAN LJ, SOFILOS MC. *Aorta and iliac arteries: single versus multiple detector-row helical CT angiography.* Radiology 2000; 215: 670-676.

(9) CATALANO C, GROSSI A, NAPOLI A, FRAIOLI F. *Fast high-resolution computed tomography angiography of peripheral vessels. In: Marincek B, Ros PR, Reiser M, Baker ME, eds. Multislice CT: a practical guide.* Berlin Heidelberg New York: Springer-Verlag, 2000; 134-142.

(10) MACARI M, ISRAEL GM, BERMAN P, LISI M, TOLIA AJ, ADELMAN M, MEGIBOW AJ. *Infrarenal abdominal aortic aneurysms at multidetector row CT angiography: intravascular enhancement without a timing acquisition.* Radiology 2001; 220: 519-523.

(11) RUBIN GD, SCHMIDT AJ, LOGAN LJ, SOFILOS MC. *Multi-detector row CT angiography of lower extremity arterial inflow and runoff: initial experience.* Radiology 2001; 221: 146-158.

(12) FISHMAN EK. *Real time visualization of volume data: applications in computed tomography angiography. In: Marincek B, Ros PR, Reiser M, Baker ME, eds. Multislice CT: a practical guide.* Berlin Heidelberg New York: Springer-Verlag, 2000; 125-133.

(13) RUBIN GD, DAKE DS, SEMBA CB. *Current status of three-dimensional spiral CT scanning for imaging the vasculature.* Radiol Clin North Am 1995; 33: 51-70.

(14) KATZ DS, HON M. *CT angiography of the lower extremities and aortoiliac system with a multi-detector row helical CT scanner: promise of new opportunities fulfilled.* Radiology 2001; 221: 7-10.

(15) ABURAHMA AF, ROBINSON PA, BOLAND JP, ET AL. *Complications of arteriography in a recent series of 707 cases: factors affecting outcome.* Ann VascSurg 1993; 7: 122-129.

(16) WAUGH JR, SACHARIAS N. *Arteriographic complications in the DSA era.* Radiology 1992; 182: 243-246.

(17) VISSER K, HUNINK MGM. *Peripheral arterial disease: gadolinium-enhanced MR angiography versus color-guided duplex US - a meta-analysis.* Radiology 2000; 216: 67-77.

(18) ROFSKY NM, ADELMAN MA. *MR angiography in the evaluation of atherosclerotic peripheral vascular disease.* Radiology 2000; 214: 325-9.

(19) BEREGI JP, DJABBARI M, DESMOUCELLE F, WILLOTEAUX S, WATTINNE L, LOUVEGNY S. *Popliteal vascular disease: evaluation with spiral CT angiography.* Radiology 1997; 203: 477-483.

Peripheral Mr Angiography

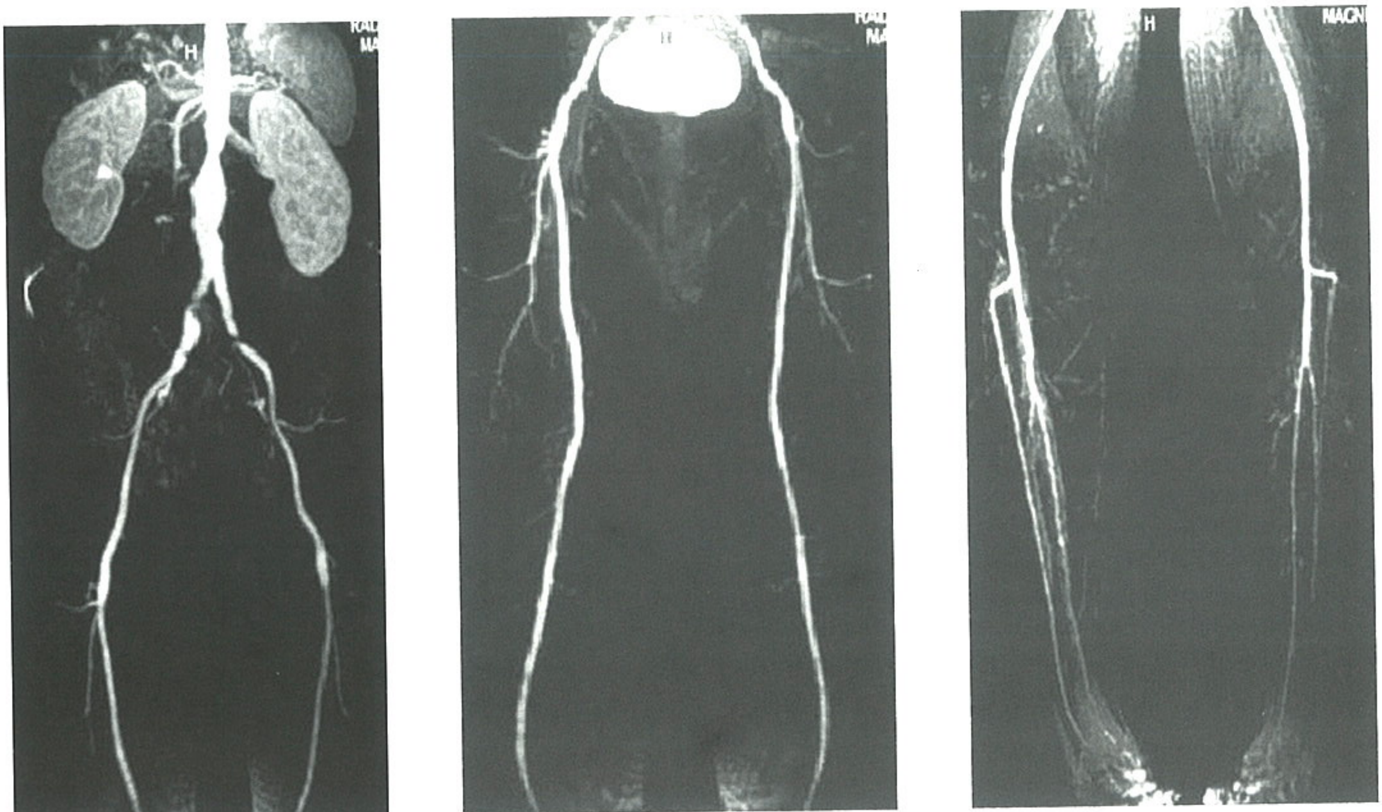
Laura Broglia, Andrea Laghi, Riccardo Iannaccone, Plinio Rossi

In the anatomic assessment of peripheral arteries, digital subtraction angiography (DSA) with iodinated contrast media is considered the standard of reference to search for vascular lesions. Technical improvements in Magnetic Resonance Imaging (MRI) have widened diagnostic horizon in this field and MR Angiography (MRA) is now able to offer all the information required in order to plan a re-vascularization procedure. In fact, the introduction of gadolinium-enhanced 3D gradient echo techniques has definitely overcome most of the limitations that affected the older, non-enhanced, MRA methods, generating MR Angiograms with uniform intravascular signal intensity in less that 30 seconds (1,2).

In this chapter we review the most common study techniques together with clinical indications and results.

Study technique

The wideness of the district to be examined in patients with peripheral vascular disease, requiring an anatomic coverage from the infra-renal portion of the



A B C

FIGURE 1

Multi-step contrast-enhanced MR angiography. Three different stations are subsequently acquired. On the first station (a) aorto-iliac district is completely evaluated from the supra-renal aorta to the common femoral arteries; slight dilatation of the infra-renal abdominal aorta is observed as well as the presence of severe stenoses at the level of the common iliac arteries bilaterally. On the second station (b), complete representation of the common, superficial and deep femoral arteries is obtained. On the third station (c) popliteal arteries, anterior and posterior tibial arteries and interosseus arteries are observed.

abdominal aorta to the foot, makes this examination challenging.

Un-enhanced MRA techniques (i.e., Time of Flight and Phase Contrast) (3,4) have been abandoned in favor of contrast-enhanced 3D MRA, due to limitations related to long acquisition time, signal losses from in-plane saturation, turbulent flow and susceptibility effects in the region of surgical clips and vascular stents; flow-related artifacts were also the cause of diagnostic mistakes such as overestimation of length and severity of a stricture (5,6).

Contrast-enhanced MRA provides rapid, high contrast arterial imaging with results comparable to DSA in the aorto-iliac district. However, in patients with peripheral arterial occlusive disease, imaging of the entire lower extremity from the abdominal aorta to the foot is required in extremely short time, during the arterial pass of contrast agent. The technical demand cannot be satisfied by commercially available MR equipments where anatomic coverage in the cranio-caudal plane never exceeds 50 cm, not enough to image the entire region of interest.

To overcome this limitation different strategies have been developed, mainly represented by: 1) multi-step contrast-enhanced MRA (7,8); 2) moving bed infusion-tracking MRA (Mobitrack; Philips Medical System, Da Best, The Netherlands) (9). The choice among these different techniques is influenced by local availability, MR systems and patient cooperation. However, all the modalities are able to offer a good and reproducible representation of the peripheral vascular tree.

1) Multi-step CE MRA. Contrast enhanced 3D MRA is performed subsequently at three different levels: firstly from the distal aorta to the common femoral artery; secondly from the femoral to the popliteal region and eventually from the distal popliteal artery to the tibial and peroneal arteries. For each region, three consecutive measurements with a T1-weighted 3D Gradient-Echo sequence are obtained with a phased array coil, during the injection of a single dose of gadolinium chelate at a flow rate of 1 ml/sec in order to have a mask, an arterial enhanced phase and a delayed arterial enhanced phase. To increase contrast/noise ratio the mask should be subtracted from the arterial phase. Images are reconstructed with MIP algorithm (10) (Figure1).
2) Moving bed infusion-tracking MRA. In order to reduce the dose of contrast media and examination time, a bolus chase concept has been introduced in contrast-enhanced MRA (11). The aim is to image sequential anatomic districts during a time when concentration of contrast media in the blood is high. This can be obtained by moving the patient during the acquisition of a 3D contrast-enhanced MRA sequence, either by manually moving the table (12) or by using automated table moving (13) (Figure 2).

In the first experience called "moving-bed infusion-tracking MRA" the patient is positioned in a supine feet-first position, with knee and ankles raised at the same level so that all the vessels can be included in a 10 cm coronal imaging volume (9). Now dedicated support are

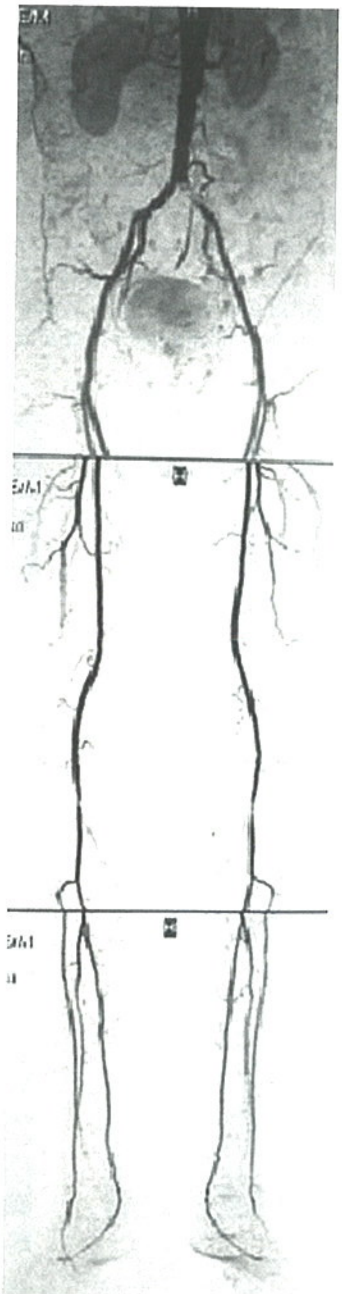


FIGURE 2

Ce-MR angiography obtained with a moving-bed technique. Image shows a tight stricture of the left common iliac artery and normal representation of the other vascular structures from the aorta to the arteries of the legs.

available from companies to immobilize the patient and to avoid motion artifacts during acquisition. A 3D GRE dynamic sequence is implemented to acquire three identical coronal volumes. The alignment of thighs and legs makes possible to image the peripheral arteries by moving the table into or out of the MR equipment. The dynamic study is acquired twice, before and during the injection of about 40 ml of Gd-DTPA at a flow rate of 0.3-0.5ml/sec, followed by 10ml saline flush. Subtraction of un-enhanced from enhanced study is performed for all the anatomical regions.

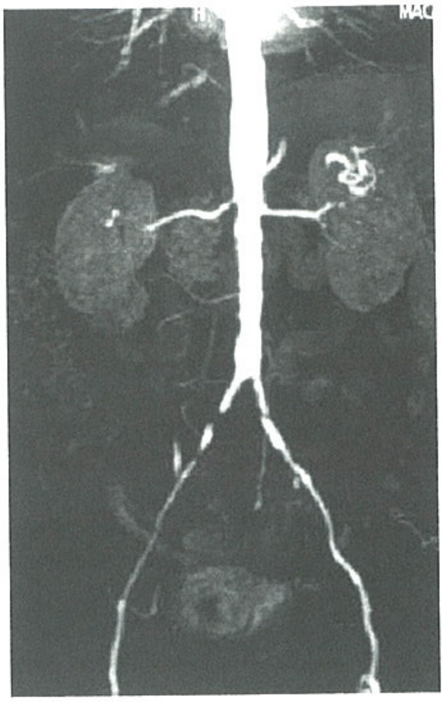
3) New technical perspectives. Technical advances include hardware and software implementations, i.e. new MR scanners and development of faster sequences. In terms of MR scanners, new dedicated "cardio-vascular" systems operating at 1.5T are being developed, with critical features represented by gradient amplitude (up to 50 mT/m) and rise time (less than 100 ms). These highly specialized devices offer excellent results for vascular studies, thanks to faster acquisition times and higher spatial resolution, but at the expenses of higher costs compared with conventional MR scanners, limiting their use to specialized referral centers for vascular diagnosis and intervention. Further improvements are expected by new 3T magnets, whose application in areas other than neuro-imaging are at the moment too preliminary.

Software implementations allow MR Angiography to provide a comprehensive non invasive approach for screening assessment of the arterial vasculature, from supra-aortic arteries to distal runoff vessels (14). "Whole body" MR Angiography consists of the acquisition of five 3D data sets in rapid succession, each with acquisition time of 10-12 seconds and a total scan time of 72 seconds during the single injection of a dose of 0.3mmol/Kg b.w. Patient is positioned on a rolling table platform ("Angio-SURF", System for Unlimited Rolling Field of View) with integrated surface coil, mounted on the top of the original patient table. Image are of good quality and comparable to DSA in the detection of substantial vascular disease (sensitivities: 91% and 94%; specificities:93% and 90% respectively) (14).

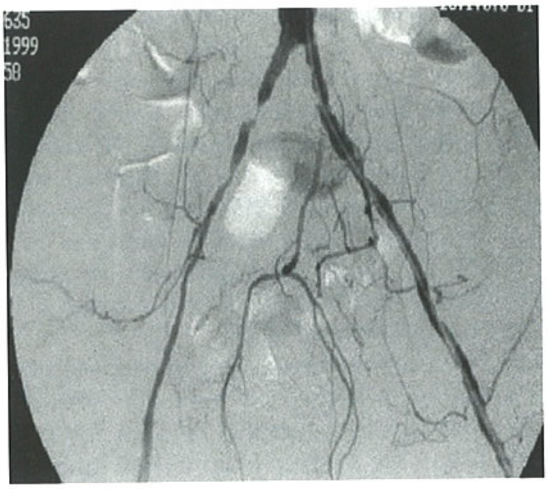
Other advancements include time resolved high spatial resolution images with multi injection acquisition ("TRICKS technique"). This technique uses the combination of an integrated mask, complex subtraction and the detection of the peak arterial frame for selective reconstruction (15,16). The integrated mask removes the contrast present in the vein from the previous injection and image quality is not impaired by venous contamination. The peak arterial frame is automatically detected without significant time delay during image reconstruction.

Clinical indications and results

Clinical indications for MRA of peripheral arteries are represented by 1) morphological evaluation of



A



B

FIGURE 3

Multi-step contrast-enhanced MR angiography (a) versus DSA (b). Note the optimal correlation between the techniques, both showing a pre-occlusive stenotic lesion and more distal severe stenosis of the right common iliac artery and a severe stenosis of the left common iliac artery.

vascular status in peripheral arterial occlusive disease in patients with symptoms represented by claudication, rest pain or tissue loss; 2) monitorization of the response to medical therapy; 3) acquisition of a vascular map prior to endovascular or surgical therapy; 4) follow-up after angioplasty; 5) surveillance of peripheral arterial by-pass grafts.

In peripheral arterial occlusive disease, first experience with contrast-enhanced 3D MRA showed good results in assessing the presence and the degree of stenosis in comparison with un-enhanced studies, especially in tortuous vessels and in post-stenotic tract, where signal voids are generated by turbulent flow (2,17). Contrast-enhanced 3D MRA has a lower in-plane spatial resolution in comparison with DSA, therefore overestimation of stenosis can occur, especially in the lower leg where the caliber of the vessel is smaller. On the other hand, contrast enhanced MRA acquires an entire 3D data set and reconstruction algorithms allow for projectional images from many directions without requiring further acquisition or contrast injection. In this way it is possible to visualize all the structures that can be hidden in the frontal view.

Different experiences are reported in the literature where authors use several technical approaches. Using a multi-step acquisition a sensitivity of 100% and specificity of 96% in detecting hemodinamically significant stenoses and a sensitivity of 100% and a specificity of 93% in detecting vascular occlusion are reported (10). However, slight overestimation of the degree of stenosis may occur and it is more common in the lower leg than in the upper leg or in the pelvic region (18) (Figure 3).

The introduction of a moving bed infusion-tracking MRA technique has revolutionized imaging of the peripheral arteries, offering a non invasive technique to obtain a panoramic and comprehensive view of the vascular tree, from the abdominal-aorta to the ankle, similar to the angiographic study (Figure 4). Sensitivity and specificity for detecting and grading diseased segments are reported between 81-99% and 75-95% and in hemodinamically significant stenosis between 91-95% and 98% (9,13,19). Venous overlap occurs rarely, only if the acquisition time is longer than 2 minutes and this can interfere with image quality.

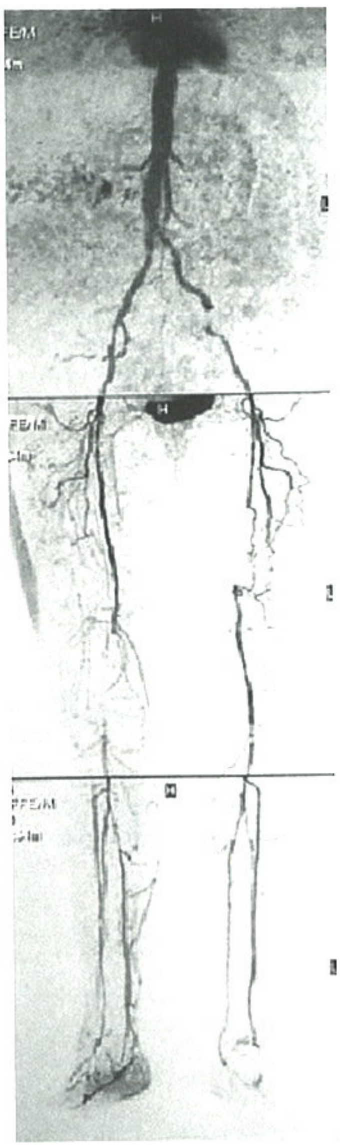
Generation of a vascular map prior to endovascular or surgical therapy is a further indication for MRA. In this case MRA is a valuable adjunct to DSA for pre-interventional diagnostic work-up of aortic and peripheral arterial aneurysms, as it provides exact evaluation of aneurysm dimensions and information about partial thrombosis. In fact, the value of DSA for the measurement of aortic and peripheral arterial aneurysm dimensions is limited by projection effects. In a recent study (20) the authors evaluated if additional contrast-enhanced 3D MRA could compensate for the disadvantages of DSA in a population of patients with aneurysms in the abdominal aorta, iliac and femoro-popliteal vessels. Results showed that diameter and length of aneurysms were underestimated on DSA with deviation ranging from 15% in the aorta to 21% in the iliac vessels. Only with calibrated catheters as reference the distances on DSA correlated well with MRA. Moreover contrast-enhanced 3D MRA detected aneurysmal thrombosis with difference between length of inner lumen dilatation on DSA and whole aneurysm length. Other Authors (21) reported an agreement between MRA and DSA in treatment planning in 71% of the cases. MRA had a sensitivity of 100% and PPV of 92% for identifying lesions resulting in intervention. MR angiography had a treatment specific predictive value of 88% for each lesion identified, and 95% for lesions identified in patients evaluated for claudication. If treatment plans were based on MR angiography only, 46% of patients would have avoided catheter arteriography (21).

Follow-up after angioplasty is another potential indication for MRA. However, it should be reminded that the presence of vascular stent might affect the quality of MRA examination due to metallic-induced susceptibility artifacts.

Surveillance of peripheral arterial by-pass grafts represents a further indication for peripheral MRA. Graft surveillance is of particular importance because flow impairment is the major cause of graft failure and the early detection of graft stenosis is the best way to improve the secondary by-pass patency rate. Contrast-enhanced 3D MRA is well suited for the morphologic assessment of peripheral grafts as well as for the depiction of occlusions, stenoses and ectatic or aneurisymatic changes affecting the graft, as reported by a recent paper (22) where sensitivity and specificity were 100% for 87 evaluable segments with correlation with digital subtraction angiography. As a consequence MR angiography might be considered into a graft assessment strategy as a second step morphologic technique after duplex sonography examination.

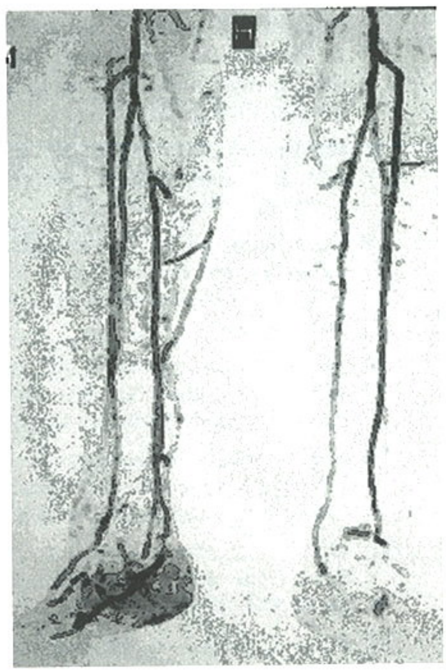
Comparison with CT angiography

First studies on CT angiography of peripheral arteries date back to 1995 (23) where an accuracy of 95% for identification of occluded vessels as well as stenoses of major vessels greater than 50% was reported. However, it is with the advent of multidetector CT angiography that a revolution in CT imaging of peripheral arteries has occurred. In fact, there are no tradeoffs in coverage or z-axis resolution because the entire abdominal aorta through to the feet can be imaged with one contrast material bolus and one acquisition ensuring that inflow aortoiliac disease, including stenoses, occlusions, collateral vessels and aneurysms is identified as is outflow disease in the distal popliteal and calf arteries. Results recently reported by Rubin et al (24) show optimal opacification of arterial vessels with minor venous enhancement in all the 504 segments which were depicted and analyzable in a 34 patient population. Thus, a comparison with MR angiography is not proposable at the moment since both techniques are in continuous evolution and no comparative data are available (25). Major disadvantages of CT angiography are represented by dose exposure and the use of iodinated contrast material. The advantages are in the relatively faster examination time compared with MRA and the higher spatial resolution; in addition, some of the newer MRA protocols still do not permit coverage of most of all of the abdominal aorta as opposite to multislice CT angiography.



A

B



C

FIGURE 4

Ce-MR angiography obtained with a moving-bed technique. A) On the panoramic view multiple vascular atherosclerotic alterations are observed. In the aorto-iliac district severe stenosis of the left common iliac artery is identified. B) The magnified view of the femoral district shows occlusion of the right superficial femoral artery at the middle third with distal rehabitation at the level of the popliteal artery and proximal occlusion of the left superficial femoral artery with multiple collateral vessels rehabitating the vessels 5-cm distally. C) Magnified view of the leg vessels shows good distal run-off bilaterally.

REFERENCES

(1) KOROSEC FR,FRAYNE R, GRIST TM, MISTRETTA CA. *Time resolved contrast-enhanced 3D MR Angiography.* Magn Reson Med 1996;36:345-351.

(2) MAKY JH, PRINCE MR, LONDY FJ, CHENEVERT TL. *The effects of time varying intravascular signal intensity and k-space acquisition order on three-dimensional MR angiography image quality.* J Magn Reson Imaging 1996;6:642-651.

(3) YUCEL EK, KAUFMAN JA, GELLER SC, WALTMAN AC. *Atherosclerotic occlusive disease of the lower extremity: prospective evaluation with two-dimensional time-of-flight MR Angiography.* Radiology 1993;187:181-188.

(4) HO KY, DE HAAN MW, OEI TK, ET AL. *MR angiography of the iliac and upper femoral arteries using four different inflow techniques.* AJR 1997;169:45-53.

(5) KAUFMAN JA, MCCARTER D, GELLER SC, WALTMAN AC. *Two-dimensional time-of-flight MR Angiography of the lower extremities: artifacts and pitfalls.* AJR1998;171:129-135.

(6) MITCHELL DJ, TASCIYAN T, ORTEGA HV, OUTWATER E, *Vinitski S. Pulsation artifact in short TR MR imaging and angiography: exacerbation with signal averaging.* J Magn Reson Imaging 1994;4:709-718.

(7) ROFSKY NM, ADELMAN MA. *MR Angiography in the evaluation of Atherosclerotic peripheral vascular disease.* Radiology 2000;214:325-338.

(8) QUINN SF, SHELEY RC, SEMONSEN KJ, ET AL. *Aortic and Lower estremity arterial disease: evaluation with MR Angiography versus conventional angiography.* Radiology 1998;206;693-701.

(9) HO KY, LEINER T, DE HAAN MW ET AL. *Peripheral vascular tree stenoses: evaluation with Moving-bed Infusion-traking MR Angiography.* Radiology 1998;206:683-692.

(10) HUBER A, HEUCK A, BAUR A, ET AL. *Dynamic contrast enhanced MR Angiography of the distal aorta to the ankle joint with a step-by-step technique.* AJR 2000;175:1291-1298.

(11) WANG Y, LEE HM, AVAKIAN R ET AL. *Timing algorythm for bolus chase MR digital subtraction angiography.* Magn Reson Med 1998;39:691-696.

(12) EARLS JP, DESENA S, BLUEMKE DA. *Gedolinium-enhanced three-dimensional MR Angiography of the entire aorta and iliac arteries with dynamic manual table translation.* Radiology 1998;209:844-849.

(13) MEANEY JF, RIDGWAY JP, CHAKTRAVERTY S, ET AL. *Stepping table gadolinium enhanced Digital subtraction MR Angiography of the Aorta and lower extremities arteries: preliminary esperience.* Radiology 1999;211:59-67.

(14) RUEHM SG, GOYEN M, BARKHAUSEN J, ET AL. *Rapid Magnetic Resonance Angiography for detection of atherosclerosis.* Lancet 2001;7;357.

(15) KOROSEK FR, FRAYNE R, GRIST TM, MISTRETTA CA. *Time resolved contrast enhanced 3D MR Angiography.* Magn Reson Med 1996;36;345-351.

(16) HANY TF, CARROLL TJ, OMARY RA. *Aorta and run-off vessels: single injection MR Angiography with automated table movement compared with multiinjection time-resolved MR Angiography. Inital results.* Radiology 2001;221:266-272.

(17) MCDERMOTT VG, MEAKEM TJ, CARPENTER JP,ET AL. *Magnetic Resonance imaging of the distal lower extremity.* Clin Radiol 1995;50:741-743.

(18) KRUG B, KUGEL H, HARNISCHMACHER U, ET AL. *Diagnostic performance of digital subtraction angiography and magnetic resonance angiography: preliminary results in vascular occlusive disase of the abdominal and lower extremities vessels.* Eur J Radiol 1995;19:77-85.

(19) HANY TF, CARROLL TJ, OMARY RA. *Aorta and run-off vessels: single injection MR Angiography with automated table movement compared with multiinjection time-resolved MR Angiography. Inital results.* Radiology 2001;221:266-272.

(20) BIEDERER J, LINK J, STEFFENS JC, FRONIUS M, HELLER M. *Contrast media-enhanced 3D MR a ngiography before endovascular treatment of aneurysm in the abdominal aorta, iliac artery and peripheral vessels.* Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 2000 Dec;172(12):985-91.

(21) REID SK, PAGAN-MARIN HR, MENZOIAN JO, WOODSON J, YUCEL EK. *Contrast-enhanced Moving-Table MR Angiography: Prospective Comparison to Catheter Arteriography for Treatment Planning in Peripheral Arterial Occlusive Disease.* J Vasc Interv Radiol 2001; 12:45–53.

(22) BERTSCHINGER K, CASSINA PC, DEBATIN JF, RUEHM SG. SURVEILLANCE OF PERIPHERAL ARTERIAL BYPASS GRAFTS WITH THREE-DIMENSIONAL MR ANGIOGRAPHY: COMPARISON WITH DIGITAL SUBTRACTION ANGIOGRAPHY. AJR 2001; 176: 215-220.

(23) LAWRENCE JA, KIM D, KENT KC, STEHLING MK, ROSEN MP, RAPTOPOULOS V. *Lower extremity spiral CT angiography versus catheter angiography.* Radiology 1995; 194: 903-908.

(24) RUBIN GD, SCHMIDT AJ, LOGAN LJ, SOFILOS MC. *Multi-detector row CT angiography of lower extremity arterial inflow and runoff: initial experience.* Radiology 221; 146-158, 2001.

(25) KATZ DS, HON M. *CT angiography of the lower extremities and aortoiliac system with a multi-detector row helical CT scanner: promise of new opportunities fulfilled.* Radiology 221; 7-10, 2001.