Diagnosis of Arterial Disease of the Lower Extremities With Duplex Scanning: A Validation Study

Rosella S. Arellano, MD; Ma. Teresa B. Abola, MD.

Background --- While standard x-ray arteriography remains the traditional gold standard for peripheral arterial imaging, it has obvious limitations and is associated with significant local and systemic complications. Technological advances in duplex ultrasonography have allowed lower-extremity arterial mapping, primarily of the femoropopliteal segment, based on morphological and hemodynamic parameters. However, inadequate sonographic visualization of the infrapopliteal arteries is seen as a major limiting factor for the liberal use of duplex ultrasonography as a sole preoperative imaging modality. Others have documented the feasibility and reliability of infrapopliteal duplex ultrasound arterial mapping. These divergent results may be partially explained by the operator-dependent nature of this exam and different types of scanners utilized by various investigators. To date, there has been no validation study done in the Philippine Heart Center on the duplex sonographic evaluation of the peripheral arteries in patients suspected of having peripheral arterial occlusive disease. This study was conducted to determine the diagnostic accuracy of duplex scanning in patients suspected of having peripheral arterial disease.

Methods --- This was a cross-sectional validation study involving duplex ultrasonography studies of femoral arterial segments of patients suspected of peripheral arterial disease. The results of these were compared to the results obtained using subtraction angiography. Each segment was graded as normal, <50% stenosis, > 50% stenosis, near total-occlusion , and total occlusion. The duplex scan results were evaluated independently by two vascular specialists while the arteriogram result was evaluated by an experienced interventional cardiologist. The Kappa statistic was used to examine the level of agreement between angiography and ultrasound.

Results --- The Kappa level (95% confidence interval) of agreement between ultrasound and angiographic assessments for distinguishing hemodynamically significant (>50%) stenosis was 0.55. Poorest agreement was observed from ultrasound assessments of the popliteal artery as compared to the other arterial segments studied.

Conclusion --- It has been demonstrated that Duplex ultrasonography produces satisfactory agreement with arteriography for the diagnosis of peripheral arterial occlusive disease, and this technique can even limit the need for arteriography in assessing this subset of patients. *Phil Heart Center J 2007; 13(2):96-100.*

Key Words: Peripheral arterial disease ■ duplex ultrasonography, digital subtraction angiography ■ validation study

Peripheral arterial disease is part of a more generalized involvement of the arteries by atherosclerosis. Risk factors for peripheral arterial disease are the same as those for coronary and carotid artery disease, namely, smoking, hypercholesterolemia, hypertension and diabetes. Its prevalence is difficult to establish because majority of patients are asymptomatic.[1] While standard x-ray arteriography remains the traditional gold standard for peripheral arterial imaging, it has obvious limitations and is associated with significant local and systemic complications. For these reasons, the interest in less invasive arterial imaging techniques has grown recently. Technological advances in duplex ultrasonography have allowed lower-extremity arterial mapping, primarily of the femoropopliteal segment, based on morphological and hemodynamic parameters. In fact, several investigators reported an acceptable correlation between duplex ultrasonography and catheter arteriography. The sensitivity and specificity of duplex ultrasonography for the detection and grading of peripheral arterial disease involving the aorta-iliac and femoropopliteal segments are generally moderate to high, ranging from 70-92%.[2,3,4,5] However, inadequate sonographic visualization of the infrapopliteal arteries, as reported in some series, is a major limiting factor for the liberal use of duplex ultrasonography as a sole preoperative imaging modality.[6] Others have documented the feasibility and reliability of infrapopliteal duplex ultrasound arterial mapping.[7,8] These divergent results may be partially explained by the operator-dependent nature of this exam and different types of scanners utilized by various investigators. To date, there has been no validation study done in the Philippine Heart Center on the duplex sonographic evaluation of the peripheral arteries in patients suspected of having peripheral arterial occlusive disease. This study was therefore conducted to determine the diagnostic.

Correspondence to Rosella S. Arellano, M.D. Division of Adult Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

accuracy of duplex ultrasonography in patients suspected of having peripheral arterial disease. Specifically, the study was aimed to determine the concordance between the duplex ultrasonography and arteriography in patients with peripheral arterial occlusive disease, as well as to compare the accuracy of our local duplex ultrasonography with international validity studies in the detection of peripheral arterial occlusive disease.

Methods

This was a cross-sectional validation study involving patients who underwent catheter arteriography of the lower extremities at the Philippine Heart Center from January1, 2005 to December 31, 2006. The roster of subjects was identified from the Department of Radiology database. The identified names were checked against the Vascular Section database to see if they also had undergone arterial duplex ultrasound. Patients with both duplex ultrasound and catheter arteriography were included in the study, provided that the latter was done within two months after the duplex ultrasound was performed. Catheter arteriography was used as the reference standard.

Duplex Scanning

All the peripheral arterial duplex procedures were done by expert vascular technologists who have had more than 5 years experience in performing the procedure. The color duplex equipment used was Logic 700 Pro-series, General Electric (Japan). Patients were placed supine on the examination table. The bilateral lower extremity arterial segments were insonated at an angle of less than 60 degrees, starting at the level of the distal external iliac artery down to the dorsalis pedis artery using a 5-7 MHz linear transducer. For the purpose of this study, only the data from the distal external iliac artery and femoropopliteal segments were obtained for analysis. In arteries with different categories of lesions, the most severe lesion was taken for comparison with arteriography.

In every arterial segment that was accessible and could be evaluated, gray-scale B-mode imaging, color-flow imaging and pulsed-Doppler spectral waveform analysis were done to get information regarding presence or absence of obstruction, type of obstruction and evaluation of blood flow velocity. Peak systolic velocity (PSV) was measured. The total examination time would take 30-45 minutes.

Catheter Arteriography

Catheter arteriography was performed by experienced interventional radiologists who may or may not be aware of the duplex scan findings. The procedure was performed using 5-F universal flush catheters placed in the infrarenal abdominal aorta at the level of the third lumber vertebra. Non-ionic dye (Ultravist), 370mg iodine/ml, was injected via a power injector at 5 ml/second. After the film was reviewed, a second injection was done in the common femoral artery and a third injection may be done in the mid-distal superficial femoral artery to clearly visualize the distal arterial segments. Each of the lower extremity was assessed. Digital subtraction arteriography (DSA) was employed usually at the popliteal artery level but may be employed in the upper segments if there is technical difficulty in visualizing the upper arterial segments. Approximately, 100 cc of contrast agent was used per procedure.

Image Evaluation

The arterial duplex scan results were analyzed and interpreted independently by two experienced vascular specialists. The B-mode and color flow images as well as the spectral Doppler velocities and waveform patterns in a particular arterial segment were analyzed independently by the two readers. The severity of stenosis was determined by the PSV ratio at the site of the stenosis and the normal adjacent artery and was translated to percent diameter reduction. Stenosis category scale9 used were as follows: 0% diameter reduction (normal), if PSV was within normal limits without presence of plaque/obstruction, and with triphasic waveform pattern (Table 1); 1-19% (mild) if PSV was within normal limits but with presence of plaque/obstruction, with triphasic waveform pattern; 20-49% (moderate) if PSV was increased by 30-99% from the normal adjacent segment and with signs of obstruction, with triphasic waveform pattern; 50-99% (hemodynamically significant) if PSV was increased by >100% from the adjacent normal segment or with biphasic waveform pattern; >75% stenosis was reported if the PSV was >400cm/sec; near-total occlusion if with monophasic or thump waveform pattern and very low PSV; and lastly, total occlusion if there was no Doppler signal seen. The arteriogram result was interpreted by an experienced interventional radiologist. The severity of stenosis was determined by the luminal diameter ratio at the site of the stenosis and the normal adjacent segment, reported as percent diameter reduction. For research purposes, a particular arterial segment stenosis was graded as follows: 0% diameter reduction (normal); 1-49% diameter reduction (hemodynamically insignificant stenosis); 50-99% diameter reduction (hemodynamically significant stenosis); near-total occlusion if there was a hairline flow of the contrast within the stenosed segment; and, total occlusion if there was no flow of contrast within the segment. Other clinically relevant clinical findings were: diffuse long-segment atherosclerotic plaque, thrombotic occlusion, and ulcerated plaques. Plaques may be described as focal or long, calcified or non-calcified, concentric or eccentric, smooth or ulcerated. Multiple projections may be needed to uncover significant stenosis, but the anteroposterior view was the one was uniformly used.

Table 1. Classification of the spectral waveform pattern[9]

Waveform	Characteristics
Triphasic	three waveform "phases" consisting of a sharp systolic forward up rise and fall, an element of reverse flow during diastole, and an element of forward flow during diastole
Biphasic	two waveform "phases" consisting of a systolic forward up rise and fall with loss of reverse flow during early diastole
Monophasic	one waveform "phase" consisting of slow and blunted systolic rise and fall with loss of diastolic flow
Thump	no waveform is seen on the Doppler spectral display

Results

Twenty one non-consecutive patients were included in the study (Table 2). Their average age was 61 years. The youngest was 32 while the oldest was 86 years old. Eighteen were males. Majority of patients were hypertensives (71%), smokers (67%) and with concomitant coronary artery disease. Less than half of the patients were diabetic (38%). One patient had a previous aortofemoral bypass surgery on the left with concomitant above the knee amputation on the right 8 years ago. Another patient had below the knee amputation more than 50 years ago. Table 3 shows the patients indications for the non-invasive and invasive work-ups for their peripheral arterial occlusive disease.

Table 2. Baseline Characteristics of Included Patients

Characteristic	N	(%)	SD
Age (mean)	61		± 15.45
Sex			
Male	18	(86)	
Female	3	(14)	
Diabetes	8	(38)	
Hypertension	15	(71)	
Smoking	14	(67)	
Coronary artery disease	12	(57)	
Previous lower extremity surgery	2	(10)	
Abdominal aortic aneurysm	1	(5)	

Of the 21 patients, 20 patients had their catheter arteriography done within 20 days after their lower extremity arterial ultrasound was done and one patient had his arteriogram done on the 60th day after his ultrasound.

A total of 278 arterial segments were evaluated both by duplex ultrasound and arteriography. The two-way contingency table for classification of disease by duplex ultrasound and arteriography is given in Table 4. Accuracy, sensitivity, specificity, positive predictive value, negative predictive value and kappa values were calculated. Kappa statistic is a method to relate the found agreement between Duplex ultrasound and arteriography to the proportion of agreement expected by chance. A kappa value of 1.0 means a perfect correlation whereas 0 means a total lack of correlation.

Table 3. Frequency of indications for work-up

Indications	No.
Disabling claudication	2
Rest pain	7
Gangrene	5
Non-healing ulcer	2
Acute limb ischemia	2
Popliteal aneurysm	1
Femoral artery aneurysm	2
Total	21

Table 4. Two-way contingency table for results of duplex ultrasound as compared to arteriography (N= 278 segments)

	Arteriogram Classification (% stenosis)				
	0	<50%	≥ 50%	Near-Total Occlusion	Total Occlusion
Duplex Classification (% stenosis)					
0	70	2	0	0	0
< 50%	8	75	7	0	3
≥50%	0	20	30	5	4
Near-Total Occlusion	1	0	5	5	11
Total Occlusion	0	0	0	0	32

There were a total of 32 segments which were seen to be totally occluded on duplex ultrasound and were all confirmed by arteriography. Of the 32 occluded segments, 7 were thrombotic in nature, 2 of which occurred in femoropopliteal aneurysms and 1 occurred inside a bypass graft. The two aneurysms mentioned were clearly demonstrated in the duplex ultrasound but not in the arteriogram. The rest of the total occlusions were brought about by heavy calcified intraluminal plaques. There were three segments which were interpreted as having insignificant arterial occlusive disease on ultrasound but were interpreted as totally occluding lesions by arteriography. Table 5 lists sensitivities, specificities and kappa values for the various arterial segments.

Table 5. Validity Measures of Duplex scanning as compared to arteriography

Segment		n	Kappa	Accuracy %	Sensitivity %	Specificity %	PPV %	NPV %
DEIA		39	0.92	82	92	89	90	97
CFA		39	NA	94	86	92	84	96
DFA		37	NA	73	85	89	89	92
SFA	proximal	41	0.74	76	72	96	96	90
	Mid	40	0.68	70	78	94	83	90
	Distal	41	0.75	73	81	98	98	98
Popliteal A		41	0.56	68	88	84	87	95

Discussion

Arteriography has long been the definitive test for symptomatic aortoiliac and lower extremity arterial disease. However, this approach provides anatomic rather than functional data and has many limitations. Interpretation is also subject to wide inter-observer variability. Because atherosclerotic lesions are often eccentric, the angiographic appearance may be misleading, especially if only unipolar views are obtained. The best way to determine the hemodynamic significance of arterial lesions is to measure the pressure gradient at angiography, but this is not always practical or anatomically possible. Moreover, the invasive nature and relatively high cost of angiography make it unsuitable for screening purposes or routine follow-up. Although MRA and CTA are increasingly used for non-invasive vascular imaging, DUS has proved to be cost-effective and accurate for the detection of significant vascular stenoses and is therefore often used as the first diagnostic modality.

From a clinical standpoint, duplex scanning can localize and classify peripheral arterial stenoses nearly as well as angiography. A normal duplex study excludes significant occlusive disease. In this study, the negative predictive value is 92% which is in agreement with previous reports, and abnormal studies can direct further examination. However, the sensitivity of duplex scanning for detecting hemodynamically[6] significant stenoses was decreased in low-flow segments distal to total occlusions. Recognition of this difficulty should allow us to improve accuracy.

In the validation study by Jager et al[4] using 338 arterial segments of 30 patients, the kappa value for duplex scanning vs. angiography was 0.69, and that for one radiologist's interpretation of the angiograms vs. the other's was 0.63. Kohler et al[14], in their study on symptomatic aortoiliac and femoropopliteal artery disease, found an overall agreement between duplex scanning and arteriography to be slightly less than that of Jager (kappa value 0.55 vs. 0.69), specificity was comparable (92% vs. 98%) and sensitivity was slightly higher (82% vs. 77%). In another study by Polak et al[11], duplex scan had a sensitivity of 0.88 for detecting significant stenoses or occluded segments. Specificity was 0.95 and accuracy was 0.93.

No occlusions were missed in this study. There was an ultrasound finding of total occlusion in an arterial segment that was seen to be patent or normal in the arteriogram. This false- positive segment was noted to be in the popliteal artery and was distal to a high-grade stenosis. Large collaterals were present and most likely decreased the amount of blood carried by these segments. There also seems to be a tendency for duplex ultrasound to classify angiographically normal arteries as minimally diseased and they were seen in seven arterial segments deemed to be normal by arteriography.

Two femoropopliteal thrombosed aneurysms were not by the duplex ultrasound. Negative arteriographic findings such as these are thought to occur in up to 36% of diagnosed popliteal aneurysms.[11] Exact agreement occurred in 207 arterial segments (74%). The finding of total occlusion in the duplex ultrasound has a 100% sensitivity and specificity. For identifying lesions with >50% diameter reducing lesion has a sensitivity of 83%, a specificity of 92%, a positive predictive value(PPV) of 88% and a negative predictive value(NPV) of 92%. The Kappa is 0.55. For identifying lesions that are <50% diameter reducing, the sensitivity and specificity are 89% and 83% respectively. The PPV and NPV are 89% and 91% respectively. The Kappa is 0.62. Kappa values were relatively high in the distal external iliac artery (DEIA) which means that there is very good agreement between the duplex ultrasound and the arteriogram. This finding can be attributed to the size of the DEIA and ease in insonating this particular arterial segment. On the other hand, Kappa values were relatively low for the popliteal artery because of the fact that most of the popliteal arterial segments studied were diseased or there were presence of more proximal stenoses which rendered duplex ultrasound difficult to interpret. Moreover, the accuracy and sensitivity of duplex ultrasound for detecting hemodynamically significant stenosis was decreased in low-flow segments distal to total occlusions. The over-all statistical findings obtained from this study are equivalent to the rates previously reported in studies abroad. It is the limitation of this study that the infrapopliteal segments were not evaluated. The experience with duplex scanning for diagnosis of infrapopliteal stenoses is limited.[8] In fact, the use of arteriography as the gold standard in the diagnosis of peripheral arterial occlusive disease has certain limitations in its application for infrapopliteal segments. It is difficult to judge the infrapopliteal segments optimally in patients with proximal obstruction, considering the technical aspects of the procedure. Therefore, it can be said that at least partially the lack of accuracy of duplex ultrasound , and specially the low specificity concerning hemodynamically relevant lesions, may be a reflection of the limitations of arteriography as the reference method.

Conclusions

It has been demonstrated that Duplex ultrasound produces satisfactory agreement with angiography for the diagnosis of iliac and femoropopliteal arterial occlusive disease. It has grown from an ancillary diagnostic test to a critical component in the diagnostic work-up and even in monitoring of patients after various interventions with its high level of diagnostic accuracy in the femoral and popliteal arteries. Non-invasive testing with duplex ultrasound allows the clinician to choose intervention more wisely be it a selective diagnostic arteriogram, percutaneous angioplasty or surgery. As duplex scanning becomes more sophisticated, it may eliminate the need for routine preoperative contrast studies in the assessment of patients with lower extremity arterial occlusive disease.

It is the recommendation of this paper that a prospective comparative study be done on the infrapopliteal arterial segments using catheter arteriography, magnetic resonance angiography and duplex ultrasonography.

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