



Acute limb ischemia: Role of preoperative and postoperative duplex in differentiating acute embolic from thrombotic ischemia[☆]

Ahmed Talaat El-Gengehe^{*}, Waleed Abdelsalam Ammar, Essam Baligh Ewiss, Soliman Ghareeb Mahdy, Dina Osama

Department of Cardiovascular Medicine, Cairo Hospital, 41 Manial Street, Cairo 11451, Egypt

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ABSTRACT

Background: Acute limb ischemia (ALI) represents an emergency in which delayed intervention results in significant morbidity, and potentially, death.

Purpose: To assess the role of duplex in differentiating embolic from thrombotic ALI.

Methods and Materials: We prospectively recruited 57 patients; with 62 non-traumatic ALI. We measured the diameter at the occluded site (d_o) and the corresponding contralateral healthy side (d_c). The absolute (Δ) and percent change ($\Delta\%$) between the two diameters were calculated as: $(d_o - d_c)$ and $[(\Delta/d_c) \times 100]$ respectively. According to the reference standard (contrast angiography or surgery), limbs were classified into embolic (E-group:37 limbs) and thrombotic (T-group:25 limbs) groups. Postoperative duplex was done in 34 patients after embolectomy and the absolute (Δ_p) and percent change ($\Delta_p\%$) between the postoperative (d_p) and preoperative (d_o) diameters at the occlusion were calculated as: $(d_p - d_o)$ and $[(\Delta_p/d_o) \times 100]$ respectively.

Results: The baseline clinical characteristics were similar between both groups. However, in the E-group, ($\Delta\%$) was $21.96 \pm 17.53\%$ vs. $-11.03 \pm 16.16\%$ in the T-group, ($p < 0.001$). A cutoff value of $>1.41\%$ for ($\Delta\%$) had 100% sensitivity and 76% specificity for the diagnosis of embolic vs. thrombotic occlusion with AUC 0.95 (95% CI: 0.901–0.999, $p < 0.001$). Postoperatively ($\Delta_p\%$) was $-11.8 \pm 8.2\%$ with a significant negative correlation found between (Δ) and (Δ_p); Spearman's coefficient (ρ) = -0.912 , $P < 0.001$.

Conclusions: A cut off value of 1.41% as percent dilatation or diminution in the diameter of occluded artery is the most important duplex sign for predicting embolic or thrombotic ALI respectively. Postoperative reduction in the diameter of occluded artery after embolectomy confirms this sign.

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1. Introduction

According to the 2007 Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II), acute limb ischemia is defined as: a sudden decrease in limb perfusion that causes a potential threat to limb viability (manifested by ischemic rest pain, ischemic ulcers, and/or gangrene) in patients who present within two weeks of the acute event [1].

There are diverse etiologies for ALI, with the two most common etiologies being embolus and thrombosis in situ secondary to underlying disease such as atherosclerosis. Differentiation between the two can sometimes be difficult; the latter is far more common in occluded bypass grafts [2].

The appropriate and early clinical evaluation of acute limb ischemia is crucial to identify the etiology (embolic or thrombotic) of the ischemic limb. Early intervention can lead to limb salvage, whereas

delayed recognition can place the patient at high risk of significant morbidity, including limb loss and, potentially, mortality [3].

Patients in whom urgent or semi-urgent surgical or endovascular revascularization is indicated may undergo catheter angiography unless there is a contraindication, such as profound critical limb ischemia, renal dysfunction, or contrast allergy. Alternative imaging modalities include ultrasound, contrast-enhanced computed tomographic angiography, and magnetic resonance angiography [4].

Many previous studies proposed that duplex scanning can replace effectively preoperative contrast angiography and to be the sole preoperative imaging in the setting of chronic limb ischemia [5–8]; however it has not been properly evaluated in the setting of acute limb ischemia [9].

2. Material and methods

2.1. Patient selection

Fifty-seven consecutive patients with sixty-two cases of ALI admitted to the vascular surgery emergency room and cardiovascular department of Cairo University were studied prospectively.

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^{*} Corresponding author. 97 Emtedad El Amal Bldgs., Floor 11, Flat 113, Maadi, Cairo 11731, Egypt. Tel.: +20 2 27007211, +20 2 01065979896.

E-mail address: drgeengehe@gmail.com (A.T. El-Gengehe).

Exclusion criteria were patients with past history of peripheral arterial graft or arteriovenous fistula, patients with traumatic limb ischemia and patients with non-atherosclerotic peripheral arterial disease (e.g. arteritis and dissection).

2.2. Study design

Eligible patients were subjected to physical examination, electrocardiogram, echocardiography (\pm transesophageal echocardiography), and duplex scanning. ALI was classified according to the functional classification of the Society of Vascular Surgery/International Society of Cardiovascular Surgery (SVS/ISCVS). Based on the duration of presentation of ischemia, patients were classified into hyperacute (24 h), acute A (1–7 days) and acute B (8–14 days) [10].

2.2.1. Duplex ultrasound scanning (DUS)

All examinations were performed by two operators, who are experienced DUS operators and who were blinded to the clinical data of the patients. All limbs were scanned from the aorta to the pedal arteries in the lower limb and from the subclavian to the distal ulnar and radial arteries in the upper limb to detect the occluded segment using Advanced Technology Laboratories HDI (high-definition imaging) 5000, Siemens Elegra, and HP Sonos 2000 systems. All had a high-resolution broadband-width linear array transducer (L7 MHz).

The aorta, iliac, femoral and anterior tibial arteries were examined with the patient in the supine position, whereas the popliteal, the peroneal and the posterior tibial arteries were examined with the patient in lateral decubitus position. Arterial segments were identified upon detection of a color signal or, if the artery was occluded, by the identification of a vessel wall accompanied by a vein or two veins in the calf. The following features were used to diagnose occlusion: segmental loss of signal in the insonated vessel, dampened distal signal compared with the proximal signal and proximal exit collaterals as well as distal re-entry collaterals.

Duplex scan was used to assess the state of the arterial wall whether healthy or atherosclerotic. Atherosclerosis was defined by the presence of plaques or intima-media thickness of ≥ 1 mm. The presence of calcification or collaterals was reported. The arterial diameters at the site of occlusion (d_o) and at the corresponding

contralateral healthy side (d_c) were measured. The absolute change (Δ) and percent change ($\Delta\%$) between the two diameters were calculated as: ($d_o - d_c$) and $(\Delta/d_c) \times 100$, respectively.

According to surgical findings and contrast angiography, limbs were classified into embolic (E group = 38 limbs) and thrombotic (T group = 25limbs) groups.

Postoperative duplex study was done in 34 patients after embolectomy and the absolute change (Δ_p) and percent change ($\Delta_p\%$) between the postoperative (d_p) and preoperative (d_o) diameters at the site of occlusion were calculated as: ($d_p - d_o$) and $(\Delta P/d_o) \times 100$, respectively.

In order to assess the interobserver reliability of duplex ultrasound in measuring the dimensions of different peripheral arterial segments (which is a cornerstone in our study), a subset of 20 healthy volunteers with no reported history of peripheral arterial diseases was recruited. Measurements were taken consecutively with only two observers (AMT, DO) for the SFA diameter (just after the CFA bifurcation) and both observers were blinded to the results of each other. Data were given as the average determined from three optimized measurements. Comparison between measurements of the superficial femoral arteries by both operators was done.

Also a subset of 30 healthy volunteers with no reported history of peripheral arterial diseases was recruited to assess the degree of homogeneity between the diameters of the different peripheral arterial segments measured at the same level bilaterally to validate using the segment contralateral to the occlusion and at the same level as a reference segment. The diameter of the superficial femoral artery just after its origin and the popliteal artery at the popliteal crease were measured in both limbs by a single operator (AMT) and then comparison was done between both sides.

2.3. Statistical analysis

The categorical variables were expressed as numbers and percentages, and continuous variables as the mean \pm SD. Differences between the 2 groups (embolic and thrombotic occlusion) were calculated using chi-square test for categorical variables and independent sample t-test for continuous parameters. Pearson correlation coefficient (r) and its significance (p) were calculated between (Δ), ($\Delta\%$) and the diameter of the contralateral healthy side (d_c). Statistical significance was accepted for all p values ≤ 0.05 . In parallel, non-parametric tests were also performed because of wide

Table 1
Baseline clinical characteristics of E and T groups.

Variables	E-Group 37 (59.7%)	T-Group 25 (40.3%)	p value
Age (mean \pm SD)	50.9 \pm 15.6	57.5 \pm 15.6	NS
Male gender	16 (43.2%)	13 (52%)	NS
Diabetes	8 (21.6%)	8 (32%)	NS
Hypertension	15 (40.5%)	8 (32%)	NS
Smoking	10 (27.0%)	9 (36%)	NS
Ischemic heart disease	8 (21.6%)	6 (24%)	NS
Heart failure	6 (16.2%)	4 (16%)	NS
Atrial fibrillation	11 (29.7%)	5 (20%)	NS
Cerebrovascular diseases	4 (10.8%)	4 (16%)	NS
Time of presentation			
Hyperacute	9 (24.3%)	3 (12%)	NS
Acute A	16 (43.2%)	12 (48%)	NS
Acute B	12 (32.4%)	10 (40%)	NS
Mode of presentation			
Pain	37 (100%)	25 (100%)	NS
Paresthesia	20 (54.1%)	10 (40%)	NS
Paralysis	4 (10.8%)	4 (16%)	NS
Coldness	26 (70.3%)	19 (76%)	NS
Color changes	21 (56.8%)	16 (64%)	NS
SVS/ISCVS Classification			
Class I	11 (29.7%)	5 (20%)	NS
Class IIa	16 (43.2%)	11(44%)	NS
Class IIb	9 (24.3%)	6 (24%)	NS
Class III	1 (2.7%)	3 (12%)	NS

Data are expressed as mean \pm SD or no. (%) of patients.

Table 2
Duplex data of E and T groups.

Variables	E Group 37 (59.7%)	T Group 25 (40.3%)	p value
Site of occlusion			
Common iliac artery	10 (27.0%)	2 (8%)	NS
External iliac artery	-	1 (4%)	NS
Common femoral artery	4 (10.8%)	-	NS
Profunda femoral artery	-	2 (8%)	NS
Superficial femoral artery	2 (5.4%)	12 (48%)	<0.001
Popliteal artery	19 (51.4%)	4 (16%)	0.004
Infrapopliteal artery	1 (2.7%)	3 (12%)	NS
Subclavian artery	-	1 (4%)	NS
Brachial artery	1 (2.7%)	-	NS
State of arterial wall at site of occlusion			
Healthy	27 (73.0%)	13 (52%)	NS
Atherosclerotic	10 (27.0%)	12 (48%)	NS
Calcification	7 (18.9%)	7 (28%)	NS
Distal runoff	20 (54.1%)	9 (36%)	NS
Collateral	5 (13.5%)	3 (12%)	NS
(Δ) (mm)	1.21 \pm 1.22	-0.68 \pm 1.02	<0.001
($\Delta\%$)	21.96 \pm 17.53	-11.03 \pm 16.16	<0.001

Data are expressed as mean \pm SD or No. (%) of patients.

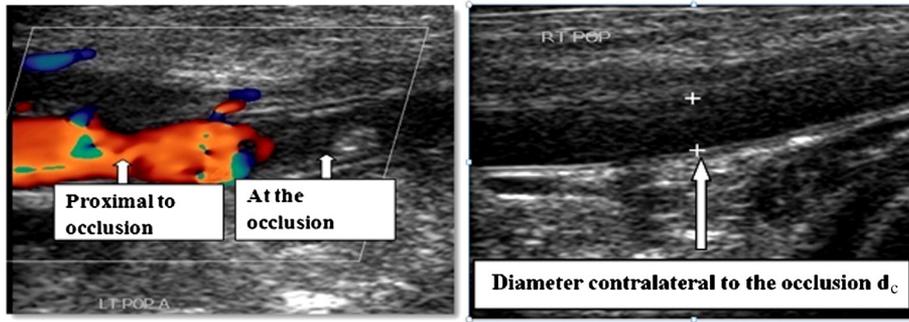


Fig. 1. Embolic occlusion of the popliteal artery with the diameter at site of occlusion = 4.11 mm (left). Diameter of the corresponding contralateral segment = 3.64 mm (right) with (Δ) and $(\Delta\%)$ calculated as 0.47 mm and 12.91%, respectively.

dispersion of some of the data (Mann–Whitney, Spearman correlation, each when appropriate).

Receiver operating characteristic curve (ROC) analysis was used to determine the optimal cutoff of different duplex measurements for differentiating acute embolic from thrombotic limb occlusion with best sensitivity and specificity.

Multiple stepwise logistic regression was done for detection of the most important independent variables that can detect embolic and thrombotic occlusion.

Interobserver reliability was expressed as intraclass correlation coefficients (ICCs). An ICC <0.20 is considered as poor agreement, 0.21–0.40 as fair agreement, 0.41–0.60 as moderate agreement, 0.61–0.80 as good agreement and 0.81–1.00 as very good agreement.

3. Results

3.1. Patient characteristics

This study recruited 57 consecutive patients with 62 occlusions (5 patients had two occlusions at two different sites). Mean age was 53.6 ± 15.8 years with age range between 20 and 85 years, 53.2% occlusions were detected in females while 46.8% occlusions were detected in males. The baseline clinical characteristics of the patients with embolic or thrombotic ALI are shown in (Table 1) with no significant difference was noted between embolic or thrombotic occlusion.

3.2. Preoperative duplex ultrasound scanning

The preoperative duplex data of the patients with embolic or thrombotic ALI are shown in (Table 2) with no significant difference was noted between embolic or thrombotic occlusion except at the site of occlusion (popliteal artery and superficial femoral artery), (Δ) and $(\Delta\%)$ as shown in (Figs. 1 and 2).

The optimal cutoff point of (Δ) and $(\Delta\%)$ for differentiation between embolic and thrombotic occlusion determined by ROC curve analysis was 0.4 mm and 1.41% respectively. Applying this value resulted in a sensitivity of 81.1% and specificity of 100% when using (Δ) and a sensitivity of 100% and specificity of 76% when using $(\Delta\%)$. The area under the receiver operating characteristic curve when using (Δ) for the differentiation between embolic and thrombotic ALI was 0.965 (95% CI: 0.930 to 1.0, $p < 0.001$) and 0.95(95% CI: 0.901–0.999, $p < 0.001$) when using $(\Delta\%)$ as shown in (Figs. 3 and 4).

Multiple stepwise logistic regression analysis was performed using multiple clinical, electrocardiographic, echocardiographic and duplex data; the percent change $(\Delta\%)$ between the diameter at occlusion (d_o) and the corresponding contralateral side (d_c) was the most important independent predictor of embolic versus thrombotic occlusion [OR (95% CI): 1.32 (1.07–1.61), $p < 0.001$].

In order to determine the effect of the initial size of the artery on the magnitude of change of the diameter of the occluded segment in acute embolic or thrombotic occlusion, correlation was done between (Δ) and (d_c) with a significant positive correlation found in embolic occlusion ($r = 0.41$, $p = 0.01$) and a statistically significant negative correlation in thrombotic occlusion ($r = -0.52$, $p = 0.007$), whereas there was no significant correlation between $(\Delta\%)$ and (d_c) in acute embolic or thrombotic occlusion.

3.3. Postoperative duplex ultrasound scanning

From the 37 cases with acute embolic limb occlusion, 34 cases underwent embolectomy. Comparison was done between the preoperative and postoperative diameter at the site of occlusion with a statistically significant difference was found between the preoperative and postoperative diameters (postoperative diameter is smaller than the preoperative diameter) as shown in (Table 3, Fig. 5).

Postoperatively (Δ_p) and $(\Delta_p\%)$ was -0.82 ± 0.77 mm and $-11.8\% \pm 8.2\%$ respectively with a statistically significant negative

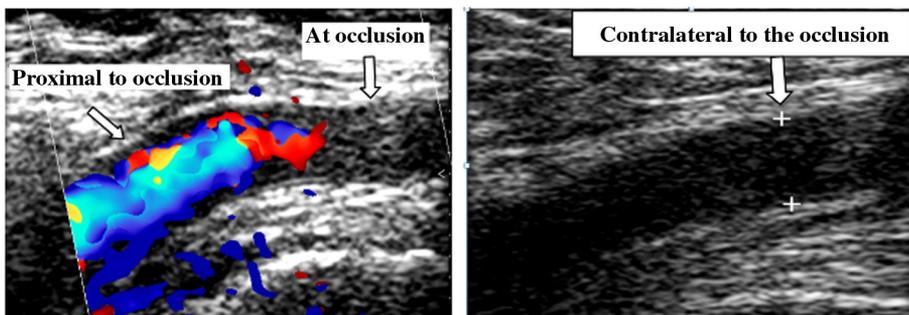


Fig. 2. Thrombotic occlusion of the external iliac artery with the diameter at site of occlusion = 4.14 mm (left). Diameter of the corresponding contralateral segment = 5.39 mm (right) with (Δ) and $(\Delta\%)$ calculated as -1.25 mm and -23.2% , respectively.

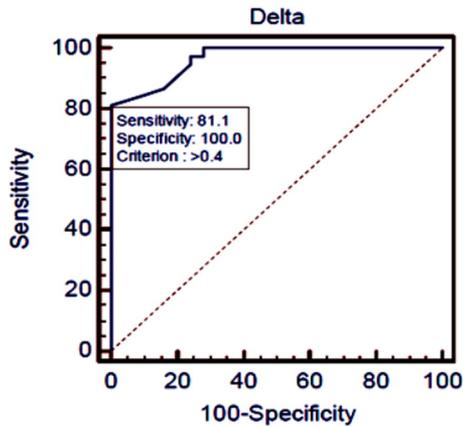


Fig. 3. ROC curve for (Δ).

correlation was found between (Δ) and (ΔP), Spearman's coefficient (ρ) = 0.912, $P < 0.001$.

3.4. Reliability

Interobserver agreement was expressed as intraclass correlation coefficients (ICCs). ICC values of the interobserver agreement for the determination of diameter of the different arterial segments on B-mode images are listed in the (Table 4) which shows very good agreement.

Comparison between measurements of the diameter of the right and left superficial femoral and popliteal arteries in 30 healthy volunteers revealed no statistically significant difference found between both sides as listed in the table (Table 5) and this validates using the segment contralateral to the occlusion and at the same level as a reference segment.

4. Discussion

Duplex scan has changed the diagnostic approach in vascular surgery in the last two decades. However its application in patients with acute limb ischemia has been scarce. The aim of this study was to assess the reliability of duplex scanning in differentiating embolic from thrombotic acute arterial limb occlusion. In our experience, patients with acute embolic or thrombotic limb ischemia can be accurately operated upon with the only preoperative aid of duplex scan.

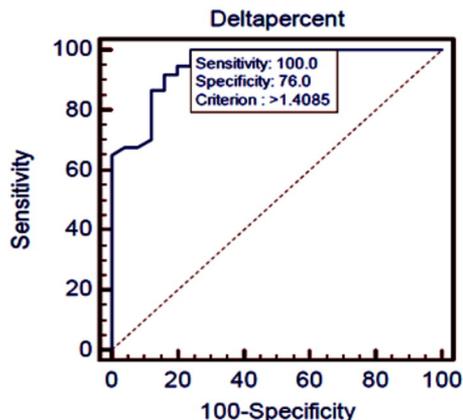


Fig. 4. ROC curve for ($\Delta\%$).

Table 3
Comparison of the diameter at site of occlusion preoperatively and postoperatively.

Variables	Preoperatively 34	Postoperatively 34	p value
Diameter at site of occlusion (mm)	7 ± 2.7	6.1 ± 2.4	$p < 0.001$

Although contrast angiography is still considered the gold standard for preoperative testing because of its known reliability, contrast angiography also has a known complication rate of 2%, is time-consuming, and is costly [11]. These disadvantages have created increasing interest in alternative preoperative imaging studies [5–8,12–16].

This study provides several important clinical implications. First, the arterial segment at the site of acute embolic occlusion is dilated relatively to the arterial segment at the site of thrombotic occlusion with a cutoff value of >0.4 mm for absolute dilatation of the artery having a sensitivity of 81.1% and specificity of 100% with $AUC = 0.965$ (95% CI: 0.930–1.0, $p < 0.001$) for diagnosis of acute embolic vs. thrombotic occlusion and a cutoff value of $>1.41\%$ for the percent dilatation of the artery having a sensitivity of 100% and specificity of 76% with $AUC = 0.95$ (95% CI: 0.901–0.999, $p < 0.001$) for diagnosis of acute embolic vs. thrombotic occlusion and this was in agreement with a recent study [17].

There is a potential explanation for this phenomenon: the kinetic energy caused by the inertia of the moving embolus in the blood stream is transformed to a mechanical energy during impaction of the embolus at the site of occlusion causing dilatation of the artery at the site of occlusion in embolic ALI, however thrombotic occlusion is in situ process which may cause diminution of the size of the occluded segment due to the effect of clot retraction. Further studies will be necessary to elucidate the exact mechanism for this phenomenon and if there is any potential role of the interpersonal and intrapersonal hemodynamic status on the magnitude of this phenomenon by influencing the kinetics of the moving embolus.

Second, the baseline clinical characteristics were similar between the embolic and thrombotic group and only the preoperative duplex data (Δ), ($\Delta\%$) and the site of occlusion (popliteal or superficial femoral artery) showed a statistically significant difference between embolic and thrombotic occlusion.

Third, interestingly, the present study and in comparison to the previous study [17] uses the percent change and not only the absolute change of the diameter of the occluded artery in relation to the reference artery (i.e. ($\Delta\%$) instead of (Δ)) for the following reasons: 1) Abolishing any possible effect of the initial size of the artery on the magnitude of change of the diameter of the occluded segment in acute embolic or thrombotic occlusion and this by being measuring the percent of change of the diameter of the occluded artery in relation to the reference artery (for example the absolute morphological changes in the big arteries e.g. the iliac arteries is more in magnitude than the small arteries e.g. infrapopliteal arteries) and thus allows for more accurate, precise and unified measurements for the comparison between arterial segments of different diameters. 2) It is not ideal to put a cutoff point measured in mm (i.e. Δ) for differentiation between acute embolic and thrombotic ischemia in arteries with big differences in size. (For example, in our thesis the diameter of the artery at the site of occlusion ranges from 1.6 to 14.5 mm with up to 9 folds difference in diameter.)

However, an argument can be made that the reference artery diameter (d_c) may influence the percent change of the diameter of the occluded artery ($\Delta\%$) in relation to the reference artery if we assume that for any given absolute change in the diameter of the artery after occlusion (Δ), a larger baseline diameter (d_c) yields a smaller measure of the percent change of diameter of the artery after occlusion ($\Delta\%$). But this is not applicable here because of the difference in the absolute change in the diameter of the artery after

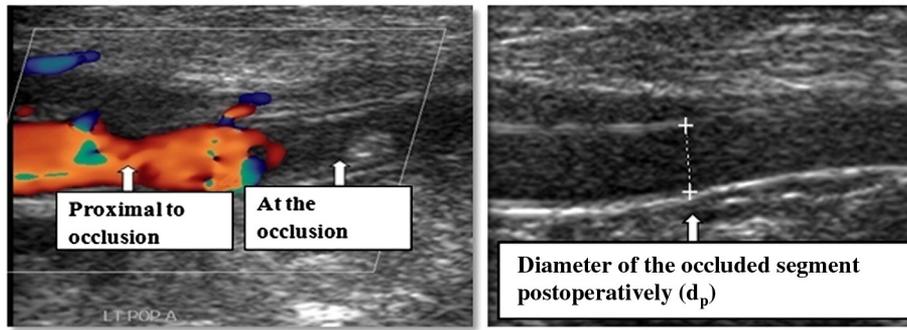


Fig. 5. Embolic occlusion of the popliteal artery with the diameter at site of occlusion = 4.11 mm (left). Diameter of the previously occluded segment after embolectomy = 3.78 mm (right). (Δ_p) and ($\Delta_p\%$) calculated as -0.33 mm and -8.03% , respectively.

Table 4
Comparison between the measurements performed by two different operators for the superficial femoral artery diameter.

Variables	1st operator 20	2nd operator 20	ICC	95% CI
Superficial femoral artery (mm)	5.76 ± 1.35	5.82 ± 1.44	0.990	0.977–0.996

occlusion (Δ) between arterial segments with different diameters; were the absolute change in the diameter appears to be relatively bigger in large arteries than in smaller ones. This is probably because of the bigger size of the embolus and hence the bigger inertia of the embolus needed to occlude the bigger artery in embolic ALI and also because of the longer distance of the smaller embolus it will travels before it is impacted in the smaller distal arteries with the more obstacles it will meet at the kinks and the branching points causing decrease of its velocity before impaction. Also, in thrombotic ALI this may be because of the bigger thrombus burden with the bigger absolute clot retraction effect. So it seems better to use ($\Delta\%$) instead of (Δ) because it abolish any possible effect of the initial size of the artery on the magnitude of the absolute change of the diameter of the occluded segment in acute embolic or thrombotic occlusion. However, the best policy may be to measure and report the reference artery diameter, the absolute change and percent change in diameter.

Fourth, postoperative duplex done for patients with embolic ALI revealed an evidence of reversal of the absolute (Δ) and percent ($\Delta\%$) diameter changes associated with acute embolic occlusion after embolectomy and this evidence confirms the specificity of these changes to acute embolic occlusion. Postoperative duplex was not done for patients with acute embolic occlusion, with the sites of the occluded segment are the same sites of arteriotomy done for embolectomy and patients with thrombotic occlusion. Assessment was not done postoperatively in these two groups because of the interference to the morphology of the previously occluded segment postoperatively by the arteriotomy incision, it's suturing and healing in case of embolic occlusion or by the endarterectomy (with or without patch angioplasty) procedure in case of thrombotic occlusion.

Fifth, there is a statistically significant degree of homogeneity between the diameters of different arterial segments measured at the

Table 5
Comparison of diameter of superficial femoral artery and popliteal artery between both sides.

Variables	Right side 30	Left side 30	p value
Superficial femoral artery (mm)	6.07 ± 0.91	6.07 ± 0.90	NS
Popliteal artery (mm)	5.24 ± 0.75	5.26 ± 0.74	NS

same level bilaterally and thus the segment contralateral to the occlusion and at the same level can be taken as a reference segment for the occluded segment.

Sixth, in line with previous studies [18–20] diameter measurements on B-mode images are largely observer independent with very good interobserver agreement.

5. Conclusion

A cut off value of 1.41% as a percent dilatation or diminution in the diameter of occluded artery is a useful tool for predicting embolic or thrombotic occlusion respectively. Postoperative reduction in the diameter of occluded artery after embolectomy confirms this sign. Diameter measurements on B-mode images are largely observer independent with a very good interobserver agreement.

The present study has some limitation. First, the relative small number of patients with upper limb and infrapopliteal ALI enrolled in this study, so a larger number of patients are needed to confirm the results obtained. Second, limited usage of pharmacological thrombolysis in the management of ALI limits our ability to follow up the morphological changes of the thrombotic occlusion after successful thrombolysis so conducting studies using pharmacological thrombolysis in the management of ALI will help to follow up the morphological changes of the thrombotic occlusion after successful thrombolysis. Finally, interobserver reliability was not assessed in the infrapopliteal arteries.

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