ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 27(1): 16-21, 2022
DOI: 10.5505/ejm.2022.91328

Superficial Femoral Artery Mirror Lesions; Risk Factors, Diagnosis, and Clinical Presentation

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ABSTRACT

Two-sided atherosclerotic involvement of peripheral arteries is common in clinical practice; however, the data about it in the literature is limited. This study aimed to investigate the frequency, clinical characteristics, and predictors of bilateral symmetric total superficial femoral artery (SFA) occlusions (mirror lesions).

Between January 2015 and April 2020, 167 patients with symptomatic total SFA occlusions were retrospectively analyzed. Unilateral and bilateral SFA occlusions were determined, and the risk factors and clinical presentation were investigated between the two groups.

Among 167 patients, 95 (57%) had bilateral SFA lesions, and 30 (18%) presented with critical limb ischemia (CLI). In the bilateral SFA occlusion group, male sex was dominant (p=0.002), and peripheral artery disease (PAD) history was higher (p=0.030). Additional iliac lesions (p = 0.003) and below-knee lesions (p <0.001) were more common in the bilateral SFA occlusion group. The sensitivity of Doppler ultrasonography in detecting SFA occlusions was 83.9%. In multivariate logistic regression analysis, younger age (OR; 0.95 CI; 0.91-0.99 p = 0.030) and history of PAD (OR; 2.08 CI; 1.02- 4, 24 p = 0.040) were identified as independent markers for predicting mirror SFA occlusions

Our study demonstrates that the mirror lesion pattern is common in patients with symptomatic SFA total occlusion. Thus, the non-index leg evaluation should be recommended. The younger the age, and PAD history were the predictors of mirror total SFA occlusions.

Keywords: Superficial femoral artery, peripheral artery disease, duplex Doppler ultrasonography

Introduction

Complex, long-segment atherosclerosis of the superficial femoral artery (SFA) is a challenging clinical predicament (1). The risk factors for SFA lesions are; age, smoking, hypertension (HT), diabetes mellitus (DM) and hypercholesterolemia (1,2). SFA atherosclerosis is a common disease characterized by the presence of moderate to severe calcification (3). Previous studies have shown that symptoms like claudication, cramps, or numbness contribute to a substantial loss in the quality of life and are among the factors determining the treatment strategy in SFA lesions (4,5). These signs are commonly defined as critical signs and show the disease progression; however, the absence of these symptoms does not exclude the presence of occult atherosclerotic disease (6).

Two-sided atherosclerotic involvement of peripheral arteries is common in clinical practice; however, the data about it in the literature is limited. A recent study examined the clinical importance of mirror pattern in peripheral arterial disease (PAD) found a high rate of bilateral stenosis in patients with PAD history (7). Similarly, autopsy studies have demonstrated a bilateral correlation between mean plaque size, remodeling, and lipid-rich plaque formation in the SFA lesions (8).

This study aimed to examine the co-existence of the same-level (mirror lesions) total occlusions in both SFAs and their frequency, clinical characteristics,

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Received: 29.09.2021, **Accepted:** 08.11.2021

predictors, and relationship with other lower extremity lesions. In addition, we investigated the predictive value of Doppler ultrasonography (DUS) in detecting bilateral lesions, which is the standard screening tool for the diagnosis of PAD.

Material and Methods

This single-center retrospective study included patients who underwent peripheral angiography with critical limb ischemia (CLI) or claudication symptoms and had total SFA lesions between January 2015 and April 2020. After exclusion criteria (history of vasculitis, previous lower extremity artery revascularization), a total of 167 patients were included in the study. Patients were divided into two groups as unilateral total SFA occlusions (72 patients) and bilateral total SFA occlusions (95 patients) groups.

Clinical and demographic characteristics of the patients like DM, HT, dyslipidemia, smoking, presence of arterial disease (coronary, carotid, peripheric) were recorded.

Symptoms were defined according to the Rutherford classification as claudication (Rutherford classification II-III) and CLI (Rutherford classification IV-V) (9).

Blood specimens were collected from the antecubital vein immediately upon admission to the hospital before any heparin therapy or reperfusion procedure. Full blood count for hemoglobin was measured. In addition, plasma levels of fasting total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, creatinine, albumin, and C-reactive protein (CRP) were measured. Peripheral angiograms (Infinitt Healthcare Co, Phillips-burg, NJ, United States), which were digitized for quantitative analysis, were analyzed by two expert interventional cardiologists retrospectively. Beginning from the common iliac artery until dorsalis pedis artery, all lower extremity arteries were respectively evaluated.

Furthermore, bilateral DUS was conducted in all subjects. Before angiography, all subjects underwent bilateral lower extremity ultrasonography to examine the lesions' location, extension, and severity. Significant stenosis was determined as follows: an at least doubling peak systolic velocity and the lack of a reverse flow pattern (10). In addition, all lower-extremity arteries were routinely assessed. The institutional ethics committee approved the study and the study protocol conformed to the Declaration of Helsinki.

Statistical Analysis: Statistical analysis was conducted using R software v. 4.0 (R Corporation, Vienna, Austria) using "rms" and "hmisc" packages. Statistical tests were 2-sided and P-value <0.5 was considered statistically significant. Continuous variables were represented as median (interquartile range, 25–75). Categorical variables were expressed as the number and percentage of patients. Medians for continuous variables were compared by applying the Mann-Whitney U test. Categorical variables were compared by applying Chi-square tests or Fischer's exact test. Correlation analysis was assessed utilizing the Pearson correlation coefficient. Finally, multivariate logistic regression analysis was applied to predict the mirror pattern. The probability of the age variable in the regression model for predicting the mirror pattern was shown with the partial effect plot.

Results

Among 167 patients included in the study, the median age was 67 (62-73), 147 (88%) were male, 95 (56.9%) had bilateral SFA occlusions and 30 (18%) presented with CLI. In the bilateral SFA occlusion group male sex was dominant (p=0.002) and the PAD history was higher (p=0.030). The pre-procedural hyperlipidemia treatment was lower in patients with mirror lesions than patients without (p=0.004). Regarding laboratory findings, only CRP levels were higher in the bilateral SFA occlusion groups (p=<0.001). Table 1 shows patients' demographics, clinical and laboratory findings according to 2 groups.

Of the patients included in the study, 95 (56.9%) had a clinical "mirror pattern" of SFA occlusions (Figure 1). Additional iliac lesions (p=0.003) and below-knee lesions (p<0.001) were more common in the bilateral SFA occlusion group. There was no difference between the two groups in terms of CLI (p=0.160).

DUS was applied to all patients before angiography and showed significant stenosis in 140 (83.9%) of the 167 patients (Table 2). Among 95 cases with bilateral SFA occlusion, the Doppler results were positive in both extremities in 62 cases (65.3%), unilateral positive in 25 cases (26.3%), and bilateral false negative in 8 cases (4%). In unilaterally occluded limbs, Doppler detected 53(73.7%) of the 72 cases.

In multivariate logistic regression analysis, the younger age (OR; 0.95 CI; 0.91-0.99 p = 0.030, Figure 2) and history of PAD (OR; 2.08 CI; 1.02- 4, 24 p=0.040) were detected as independent markers for predicting mirror SFA occlusions (Table 3).

Discussion

The results of this study, which aimed to examine the frequency, clinical features, and predictors of mirror

Table 1. Clinical Characteristics of the Patients

	All patients n=167	Bilateral Occlusions n=95	Unilateral Occlusions n=72	p value
Demographics and clinical characteristics				
Median age (years)	67 (62-73,5)	67 (61-72)	67 (63-75)	0.160
Male, n (%)	147 (88)	90 (94,7)	57 (79,2)	0.002
Hypertension, n (%)	113 (67,7)	67 (70,5)	46 (63,9)	0.450
Hyperlipidemia treatment, n (%)	120 /71,9)	60 (63,2)	60 (83,3)	0.004
Diabetes Mellitus, n (%)	95 (56,9)	53 (55,8)	42 (58,3)	0.480
Chronic obstructive pulmonary disease, n (%)	24 (14,4)	14 (14,7)	10 (13,9)	0.870
Chronic kidney failure, n (%)	35 (21)	17 (17,9)	18 (25)	0.260
Previous stroke, n (%)	11 (6,6)	5 (5,3)	6 (8,3)	0.630
Previous peripheral artery disease, n (%)	64 (38,3)	43 (45,3)	21 (29,2)	0.030
Previous coronary artery disease, n (%)	105 (62,9)	58 (61,1)	47 (65,3)	0.570
Previous PCI/CABG, n (%)	96 (57,5)	53 (55,8)	43 (59,7)	0.610
Claudication, n (%)	137 (82)	74 (77,9)	63 (87,5)	0.110
Critical limb ischemia, n (%)	30 (18)	21 (22,1)	9 (12,5)	0.160
Biochemistry				
Albumin (g/dl)	3,8 (3,2-4,0)	3,88 (3,20-4,7)	3,72 (3,18-4,0)	0.250
Hemoglobin (g/dl)	13,2 (12,0-14,4)	13,4 (11,9-14,7)	13,1(12,1-14,9	0.200
C-reactive protein (mg/dl)	3,5 (1,6-9,0)	7,76 (3,26-9,0)	2,0 (1-3,85)	0.001
Creatinine (mg/dl)	0,93 (0,76-1,1)	0,88 (0,76-1,08)	0,98 (0,77-1,15)	0.160
Total cholesterol (mg/dl)	194 (158-220)	197 (156-222)	191 (157-219)	0.430
Lesion characteristics				
Additional critical iliac disease, n (%)	20 (12)	18 (18,9)	2 (2,8)	0.003
Additional infrapopliteal disease, n (%)				0.001
None	17 (10,2)	9 (9,5)	8 (11,1)	
Single-vessel	91 (54,5)	42 (44,2)	49 (68,1)	
2 vessels	57 (34,1)	44 (46,3)	13 (18,1)	
3 vessels	2 (1,2)	0	2 (2,8)	

Continuous variables were represented as median (interquartile range, 25–75). Categorical variables were expressed as the number and percentage (n (%)) of patients. Medians for continuous variables were compared by applying the Mann-Whitney U test. Categorical variables were compared by applying Chi-square tests or Fischer's exact test.
Table footnote: PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft

Table 2. Doppler Ultrasonography Results

Angiographic findings	Doppler findings	n (%)
Bilateral total occlusions, (n=95)	Stenosis detected- both limbs	62 (65,3)
	Stenosis detected- one limb	25 (26,3)
	Stenosis undetected	8 (8,4)
Unilateral total occlusions, (n=72)	Stenosis detected	53 (73,7)
	Stenosis undetected	19 (26,3)

Categorical variables were expressed as the number and percentage (n (%) of patients

Table 3. Parameters Predicting Mirror Lesions, Multivariable Logistic Regression Analysis

	Odds ratio	Confidence interval	p value
Mean age	0,95	0,91-0,99	0.030
Female	3,29	0,99-10,99	0.063
Hypertension	0,64	0,28-1,44	0.280
Diabetes Mellitus	0,61	0,29-1,27	0.180
Hyperlipidemia treatment	0,48	0,17-1,33	0.231
Creatinine	0,95	0,66-1,37	0.764
C-reactive protein	1,02	0,99-1,05	0.110
Previous peripheral artery disease	2,08	1,02-4,24	0.040
Previous coronary artery disease	0,95	0,46-1,94	0.891

The parameters predicting mirror lesions were assessed with multivariable logistic regression analysis

SFA lesions, revealed that bilateral lesions were not rare in patients with SFA occlusion, and younger age and PAD history were independent predictors of mirror lesions. As a widely available and inexpensive imaging tool, DUS can be used to diagnose these patients with high sensitivity.

The phenomenon of the mirror lesion pattern, two-sided atherosclerotic involvement of similar arteries, seems to be linked to systemic factors (8,11). Moreover, the wall shear stress (WSS), which is known to have an essential role in atherosclerotic disease pathophysiology, may partly explicate the mirror lesions pathogenesis (12). Such particular factors like vessel diameter, presence of bifurcation, bifurcation angle may increase WSS and hence raise the risk of atherosclerotic plaque progression and arterial remodeling. Caplan et al. demonstrated that atherosclerotic lesion locations were changed depending on the variables such as gender and race; and affected by genetic factors (13). Moreover, smoking and hyperlipemia promote plaque formation, especially in certain locations (14). However, unilateral involvement appears to be primarily affected by local parameters like focal inflammation (11).

Current guidelines recommend ultrasonography as one of the first imaging modalities in examining patients with non-diagnostic ankle-brachial index (15). In our study, the sensitivity of Doppler was 84%, and this is consistent with the previous reports in the literature (16). The sensitivity of DUS in SFA mirror occlusions was 91.6%, confirming its efficacy. Hence, it is important always to perform a bilateral arterial DUS and the DUS study should not be limited to the symptomatic limb.

There is a lack of data about SFA mirror lesions in the literature. A recent study revealed a mirror lesion pattern in a quarter of included cases with lower extremity atherosclerosis (7) however mirror SFA pattern was higher in our study and found in 57% of the cases. In parallel to the progression of atherosclerotic disease, the mirror pattern became more prominent, and the incidence of the mirror pattern enhanced as the number of atherosclerotic arteries/segments raised. In our study, patients with critical lesions were equally prone to atherosclerosis in

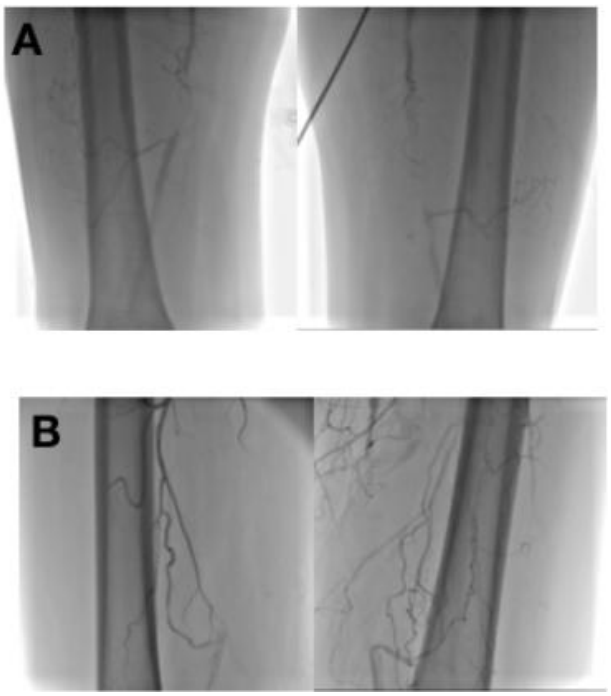

Fig. 1. The mirror image of lower extremity arterial disease, bilateral superficial femoral artery (SFA) total occlusions: A; bilateral SFA lesions with short total occlusions. B; bilateral SFA lesions with long total occlusions

the contralateral limb. The younger the age (%5 increase) and history of PAD (2.1 fold increase) were also found to be predictors of SFA mirror occlusions. Consistent with our finding, younger age was directly related to the severity of PAD in another study (17). Furthermore, younger patients who require an aortoiliac intervention are becoming symptomatic at an earlier age and more prone to atherosclerotic disease after therapy and following patency loss, and are likely to display a more aggressive form of the disease (18,19).

Lower extremity peripheral arterial disease is a systemic disease that seriously affects the quality of life and is mostly present in patients with an increased atherosclerotic disease burden. In patients undergoing DUS for symptomatic PAD, the non-index limb should also be scanned even if it is asymptomatic. Evaluation of the non-index leg with DUS, a low-cost, easily approachable, and highly sensitive imaging modality, may reveal the presence of mirror lesions and play a vital role in preventing future undesirable events. On the other hand, the treatment of asymptomatic disease is yet to be in the contemporary standard of care. Although limb salvage is highly recommended in CLI, current PAD guidelines remain unclear for non-index extremity treatment (20). The 2016 AHA/ACC guidelines do not recommend "preventive interventions" in patients with claudication and indicate that only 10% of these

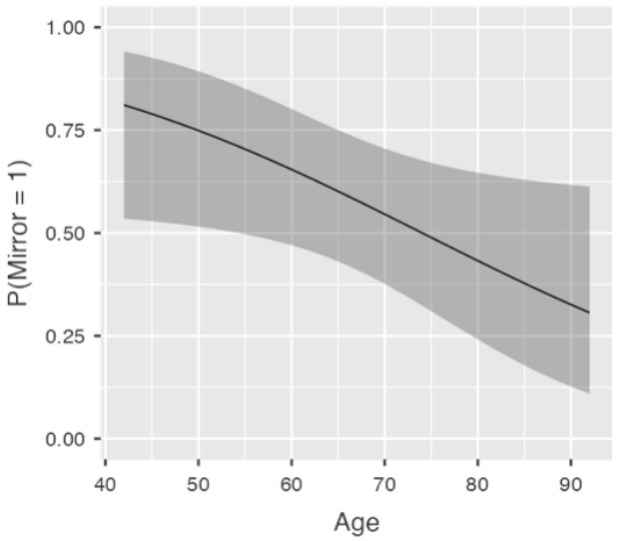

Fig. 2. Predicted probability of restenosis according to patient's age. The probability of restenosis is decreasing by the increasing age

patients will progress to CLI (15). In our study, in terms of CLI, no differences were observed between the two groups. The boundary of symptoms that makes the treatment of non-index limb requisite in CLI patients requires further research.

Limitations: Our study has some limitations. First, it was a retrospective single-center analysis with a small sample size. Prospective large-scale multicenter studies with large numbers of cases are likely to provide better results with clinically useful odds ratios. Secondly, PAD risk factors were reported based on the hospital archive, which can affect the accuracy of the data.

Conclusions: In patients with symptomatic SFA total occlusion, the mirror lesion pattern is common; hence the non-index leg evaluation should be recommended. The younger the age and PAD history were observed as predictors of mirror SFA lesions; therefore, bilateral lower extremity artery examination may be more beneficial in these groups.

Declaration of Conflicting Interests: The authors declared no conflicts of interest concerning the authorship and publication of this article.

Funding: The authors received no financial support for the research and authorship of this article.

Acknowledgment: None

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