The prognostic value of the WIFI classification system (wound, ischemia, and foot infection) to predict limb salvage in patients with chronic limb-threatening ischemia

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Background
Chronic limb-threatening ischemia (CLTI) represents the most severe form of peripheral arterial disease and is strongly associated with reduced survival and limb salvage rates. Classification systems are essential for clinical decision making as well as setting meaningful goals and expectations for patients and their families. The Society for Vascular Surgery has proposed the wound, ischemia, and foot infection (WIFI) classification system as a prognostic tool for amputation risk in patients with CLTI.
Aim
To assess the applicability of the WIFI classification in prediction of limb salvage in patients with CLTI (rest pain, ulcers, or gangrene).
Patients and methods
This is a prospective observational cohort study. A total of 40 patients who presented with critical limb ischemia between January 2020 and December 2021 to Ain Shams University hospitals were treated by infra-inguinal peripheral angioplasty. The study assessed the applicability of the WIFI classification in prediction of limb salvage.
Results
The study was done on 40 patients who had critical limb ischemia. There were nine (22.5%) females and 31 (77.5%) males. Their age ranged between 45 and 73 years, with a mean±SD age of 61.75±7.32 years. A total of 11 (27.5%) patients required major amputation; 31 (72.5%) had limb salvage. Amputation rates were 0% for WIFI stage 1, 9.1% for WIFI stage 2, 9.1% for WIFI stage 3, and 81.8% for WIFI stage 4. The amputation group had a significantly higher prevalence of stage 4 patients (P<0.001), whereas the limb salvage group presented predominantly as stages 1–3.
Conclusion
The WIFI classification could be useful to predict possibility of amputation in patients presented with CLTI.

Keywords:
chronic limb-threatening ischemia, ischemia, foot infection classification, limb salvage, wound

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Introduction

Chronic limb-threatening ischemia (CLTI) is a manifestation of peripheral arterial disease (PAD) that is characterized by ischemic pain in the foot while a person is at rest with pain lasting 2 or more weeks, nonhealing wounds, or gangrene [1]. CLTI represents the most severe form of PAD and is strongly associated with reduced survival and limb salvage rates [2]. The prevalence of PAD is ~3–10% in the population as a whole, with this increasing to between 15 and 20% when focusing on older patients (>70 years of age) [3].

Diabetes mellitus is a risk factor of PAD. Up to 85% of amputations done in the people with diabetes are owing to foot ulcer. There is a 50% risk of developing a serious lesion in the second limb in those people with diabetes who had a previous lower limb amputation within 2 years [4].

Diabetic foot ulcers may be broadly categorized into three groups: purely neuropathic, purely ischemic, and neuroischemic (mixed). Based on recent studies, the prevalence of neuroischemic ulcers has steadily risen from ~20–25% in the 1990s to more than 50% of patients currently [5].

Classification systems are powerful tools for providers to use when managing patients with threatened limbs. The ability to define and delineate a heterogeneous group into fine-grained cohorts aids communication between providers and allows for a more accurate analysis of outcomes across treatment strategies. Thus, classification systems are essential for clinical decision making as well as setting meaningful goals and expectations with patients and their families [6].

The Society for Vascular Surgery has proposed the wound, ischemia, and foot infection (WIFI) classification system as a prognostic tool for the 1-year amputation risk and the added value of revascularization in patients with CLTI [7].

The WIFI classification system is provided to be applied to patients with a broad spectrum of lower extremity atherosclerotic occlusive disease of varying severity and distribution. It includes patients with ischemic rest pain in addition to tissue loss with coexisting chronic PAD [3].

Aim

This study aims to assess the applicability of the WIFI classification in prediction of limb salvage in patients with CLTI (rest pain, ulcers, or gangrene).

Patients and methods

This is a prospective observational single-arm cohort study. The study included 40 patients who presented with critical limb ischemia between January 2020 and December 2021 in Ain Shams University hospitals and were treated by infra-inguinal peripheral angioplasty with 6 months of follow-up. It assesses the applicability of the WIFI classification to predict limb salvage and wound healing.

Inclusion criteria

The study included diabetic foot ulcer with ankle-brachial index less than or equal to 0.7, nonhealing foot ulcer and foot/lower extremity gangrene, or ischemic rest pain.

Exclusion criteria

The study excluded critically ill patients, patients with acute ischemia, nonatherosclerotic diseases such as vasospastic disorders, and patients with pure venous ulcers.

All patients who met the aforementioned criteria and accepted to sign a consent form for this study were included and underwent the following measures:

Full detailed clinical history was taken from all patients, including the following:

Personal history included habits of medical importance (smoking, alcohol drinking, and intravenous drug addiction). Family clinical history (previous history in the family of vascular disease) included aortic aneurysm, cerebrovascular disease, or PADs. Clinical history included the evaluation of cardiovascular risk factors and comorbidities, as well as review of the symptoms related to different vascular territories (chest pain or dyspnea and orthopnea). Lifestyle habits, dietary patterns, walking performances, and physical activity were systematically assessed, according to the guidelines. Vascular symptoms of lower limbs such as claudication pain or rest pain were assessed. Different comorbidities were noted such as diabetes, hypertension, hyperlipidemia, and renal impairment. Detailed drug history included all daily medications in details. Surgical history included all previous surgeries, especially previous vascular surgeries. Foot wound assessment included its anatomical site, approximate size, shape, edge, and floor; when exactly the patient noticed the ulcer; is it acute or chronic; is it due to trauma or infection; is it progressive in course or stationary; is it tender or not; and presence of discharge and its type and odor. Peripheral neuropathy included signs and symptoms of peripheral neuropathy, like tingling, numbness, or loss of foot sensation.

Clinical examination was performed for all patients, including the following:

General examination included patients' decubitus, chest condition, presence of any disability or lost or amputated limb, and presence of pallor or tachycardia. Vascular examination for the lower limb arterial tree was done bilaterally including femoral pulses, popliteal pulses, and pedal pulses.

Full preoperative laboratory investigations were ordered for all patients, including the following:

Kidney function tests, as we were going to give the patients contrast during the procedure; full blood count to assess total leukocytic count and degree of sepsis; bleeding time and international normalized ratio to avoid incidence postprocedural hematoma or bleeding from puncture site; liver function tests; glycated hemoglobin for assessment of glycemic control; and serum albumin, as it is important for improvement of wound healing.

Preoperative general investigation was ordered for all patients, including the following:

ECG and ECHO for cardiac patients to assess the cardiac condition, carotid duplex, pulmonary function test for patients with COPD with limited decubitus, thyroid profile for hypo/hyperthyroid patients, and nerve conduction velocity in case of peripheral neuritis.

Preoperative diagnostic methods for PADs were done for all patients, as follows:

We started by ankle-brachial index, which was done for all patients preoperatively, to assess the severity of the disease, which was followed either by arterial duplex in some patients, recording the degree and percent of stenosis, site and type of the lesion, presence of distal run off, and shape of plaque. For patients with borderline kidney function (1.2 or 1.3), we wanted to minimize the amount of contrast given to them by doing intraoperative angiogram. Computed tomography angiogram (CTA) with delayed films showing status of tibial vessels and foot arches was done for those patients who can afford doing CTA and with good kidney function (0.9 or 1), or due to lack of senior staff for doing expert arterial duplex in some areas. The choice between the arterial duplex and CTA was done according to the quality of the arterial duplex (as it is an operator-dependant investigation). We accepted detailed arterial duplex done by senior staff, commenting on PSV and flow rate in tibial vessels. Moreover, to minimize the amount of contrast given to the patients and also for those patients with well-felt popliteal pulse and good signals distally, we decided to compensate it by full intraoperative angiogram. However, in some patients, we needed preoperative CTA, to see the collateral status and identify the run in and run off before the procedure and identify the patency of the foot arch through doing delayed films.

Investigation of foot wounds

Foot radiograph anteroposterior and lateral view was done for all patients to exclude the presence of osteomyelitis or any joint dislocation. Culture and sensitivity swab was taken from all wounds.

Wound care

All patients with infected foot wounds were kept on broad-spectrum antibiotics in the form of third-generation cephalosporins (ceftriaxone adult dose 1–2 g q 12–24 h) till swab results were revealed. All patients' foot ulcers were dressed daily under complete aseptic condition by betadine to avoid flaring of infection. All patients were given medication to improve the circulation like vasoactive drugs (naftidrofuryl 200 mg tab, three times per day), antiplatelets (aspirin 75 mg tab, two tabs once per day after lunch), and lipid-lowering drugs (statins 20 mg tabs once per day at night). Patients' wounds were assessed.

Risk factor control

All patients were instructed while doing the preoperative investigation to follow-up with internal medicine doctors to control their risk factors through the following: stop smoking, control their blood pressure, and glycemic control. All the patients included in the study agreed to go through the procedure and to be included in this study. They signed an informed consent form about the procedure steps and all its possible complications and risks.

Results

This study was conducted at Ain Shams University Hospitals. The study plan was accepted by the Ethical Committee of the Department of Surgery at Ain Shams University. The study was conducted on 40 patients, comprising nine (22.5%) females and 31 (77.5%) males. Their age mean±SD ranged between 45 and 73 years, with a mean age of 61.75 ± 7.32 years. Demographic data are shown in Table 1.

The clinical pictures of CLTI among the studied cases were gangrene in 20 (50%) patients, nonhealing ulcer in 21 (52.5%) patients, and rest pain in 17 (42.5%) patients (Table 2).

There was no statistically significant correlation between age, sex, and comorbidities and limb salvage, whereas a relation was found with smoking, with

Table 1 Description of demographic and comorbidities of the studied patients

	N=40 [*n* (%)]
Age	
Mean±SD	61.75 ± 7.32
Range	45–73
Sex	
Female	9 (22.5)
Male	31 (77.5)
Smoking	
No	16 (40.0)
Yes	24 (60.0)
DM	
No	3 (7.5)
Yes	37 (92.5)
HTN	
No	6 (15.0)
Yes	34 (85.0)
IHD	
No	20 (50.0)
Yes	20 (50.0)
Renal insufficiency	
No	33 (82.5)
Yes	7 (17.5)

DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease.

P value of 0.014. A relatively small sample size may be related to this result (Table 3).

Complete cell count, including total leukocytic count, platelet count, and hemoglobin level, had a statistically significant effect on wound healing and the risk of amputation, but there was no effect of creatinine level or international normalized ratio level (Table 4).

The study showed that the amputation rates were 0% for WIFI stage 1, 9.1% for WIFI stage 2, 9.1% for WIFI stage 3, and 81.8% for WIFI stage 4. Of 40 patients, 11 had major amputation and limb loss according to significance of grades of WIFI classification (Table 5).

Table 2 Description of clinical data of the studied patients

Clinical data	*N*=40 [*n* (%)]
Rest pain	
No	23 (57.5)
Yes	17 (42.5)
Nonhealing ulcer	
No	19 (47.5)
Yes	21 (52.5)
Gangrene	
No	20 (50.0)
Yes	20 (50.0)

Discussion

Our study showed that the WIFI classification was predictive of limb amputation and wound nonhealing and correlated significantly with outcomes predicted by the Society of Vascular Surgery (SVS) consensus panel.

The study showed that amputation rates were 0% for stage 1, 9.1% for stage 2, 9.1% for stage 3, and 81.8% for stage 4.

It also showed that among the 40 patients studied, 11 patients had undergone amputations, which shows the correlation between the risk of amputation and stage in WIFI classification.

The present results are consistent with many other studies following the same concept of our study.

Cull *et al.* [8] examined and graded 139 patients with foot wounds undergoing any lower extremity revascularization and concluded that increases in the WIFI clinical stages correlate with poorer wound healing and lower rates of 1-year limb salvage.

Another study done by Mills *et al.* [5] showed three single-center studies validating the underlying premises

Table 3 Relation of limb salvage with demographic data and comorbidities of the studied patients

	Limb salvage [*n* (%)]		Test value	*P* value	Significance
	Yes	No			
	N=29	*N*=11			
Age					
Mean±SD	60.66±6.83	64.64±8.12	−1.564•	0.126	NS
Range	49–73	45–73			
Sex					
Female	8 (27.6)	1 (9.1)	1.564*	0.211	NS
Male	21 (72.4)	10 (90.9)			
Smoking					
No	15 (51.7)	1 (9.1)	6.040*	0.014	S
Yes	14 (48.3)	10 (90.9)			
DM					
No	2 (6.9)	1 (9.1)	0.055*	0.814	NS
Yes	27 (93.1)	10 (90.9)			
HTN					
No	3 (10.3)	3 (27.3)	1.792*	0.181	NS
Yes	26 (89.7)	8 (72.7)			
IHD					
No	16 (55.2)	4 (36.4)	1.129*	0.288	NS
Yes	13 (44.8)	7 (63.6)			
Renal insufficiency					
No	25 (86.2)	8 (72.7)	1.004*	0.316	NS
Yes	4 (13.8)	3 (27.3)			

DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease.
P value more than 0.05: nonsignificant; *P* value more than 0.05: significant; *P* value less than 0.01: highly significant.
*χ^2 test.
•Independent *t* test.

Table 4 Relation of limb salvage with clinical laboratory findings

Investigations	Limb salvage		Test value	*P* value	Significance
	Yes	No			
	N=29	*N*=11			
TLC					
Mean±SD	12.54 ± 3.91	16.68 ± 6.39	–2.491	0.017	S
Range	6.1–20	6–30			
PLT					
Mean±SD	318.52 ± 104.42	393.73 ± 44.97	–2.295•	0.027	S
Range	190–515	345–458			
HB					
Mean±SD	10.98 ± 1.70	9.77 ± 1.26	2.134•	0.039	S
Range	8.4–15.3	8.2–12.8			
Creatinine					
Mean±SD	1.14 ± 0.36	1.27 ± 0.70	–0.785•	0.438	NS
Range	0.6–1.9	0.5–2.5			
INR					
Mean±SD	1.03 ± 0.08	1.06 ± 0.17	–0.813•	0.421	NS
Range	0.9–1.2	0.9–1.5			

HB, hemoglobin; INR, international normalized ratio; PLT, platelet; TLC, total leukocyte count.
P value more than 0.05: nonsignificant; *P* value less than 0.05: significant; *P* value less than 0.01: highly significant.
•Independent *t* test.

Table 5 Relation between limb salvage and wound, ischemia, and foot infection classification

WIFI classification	Limb salvage [*n* (%)]		Test value	*P* value	Significance
	Yes	No			
	N=29	*N*=11			
Wound grade					
Grade 0	7 (24.1)	1 (9.1)			
Grade 1	18 (62.1)	1 (9.1)			
Grade 2	4 (13.8)	5 (45.5)	19.714	0.000	HS
Grade 3	0	4 (36.4)			
Ischemia grade					
Grade 1	14 (48.3)	1 (9.1)			
Grade 2	13 (44.8)	7 (63.6)	6.479	0.039	S
Grade 3	2 (6.9)	3 (27.3)			
Foot infection grade					
Grade 0	4 (13.8)	1 (9.1)			
Grade 1	12 (41.4)	1 (9.1)			
Grade 2	11 (37.9)	1 (9.1)	18.735	0.000	HS
Grade 3	2 (6.9)	8 (72.7)			
WIFI stage					
Stage 1	4 (13.8)	0			
Stage 2	5 (17.2)	1 (9.1)			
Stage 3	12 (41.4)	1 (9.1)	9.948	0.019	S
Stage 4	8 (27.6)	9 (81.8)			

WIFI, wound, ischemia, and foot infection.
P value more than 0.05: nonsignificant; *P* value less than 0.05: significant; *P* value less than 0.01: highly significant.

and basic concept of the SVS WIFI Threatened Limb Classification System.

The Greenville group recently reported the results of 158 revascularization procedures performed in 139 patients during a 3-year period and classified patients after revascularization based on the SVS WIFI classification. The WIFI clinical stage was predictive of major limb amputation and wound nonhealing and correlated significantly with outcomes predicted by the SVS consensus panel. The reported major amputation rates were 3, 10, 23, and 40% for clinical stages 1, 2, 3, and 4, respectively. The corresponding wound nonhealing rates were 8, 19, 30, and 63% as one progressed from clinical stage up to clinical stage 4.

The University of Arizona group prospectively applied SVS WIFI classification to a group of 201 consecutive patients presenting with threatened limbs during a 2-year period. All patients had wounds at presentation, and 93% of the total cohort had diabetes mellitus. WIFI classifications were calculated at baseline, before initiation of any treatment, and included patients with a broad spectrum of wounds and ischemia and a significant number with infection. No patients in clinical stages 1 and 2 required amputation, 10% of the amputations were in clinical stage 3 patients, and 90% were in clinical stage 4. One-year amputation-free survival (AFS) rates were 100% for clinical stages l and 2, 93% for clinical stage 3, and decreased to 63% for clinical stage 4.

The University of California (San Francisco) group prospectively applied SVS WIFI classification to 63 threatened limbs in 50 patients, and 70% were diabetic. No limbs in stage l or two patients required amputation, but both minor and major amputation rates increased in stage 3 (19 and 6%, respectively) and stage 4 patients (59 and 24%, respectively) (P=14.01).

Those three studies supported furthermore the predictive ability of the WIFI classification in determining 1-year amputation rates. Moreover, they showed that WIFI correlated with nonhealing wound and how revascularization decreased risk of amputation and time of wound healing.

Zhan *et al.* [9] analyzed 201 consecutive patients with threatened limbs treated from 2010 to 2011 in an academic medical center. These patients were stratified into clinical stages 1–4 on the basis of the SVS WIFI classification. The SVS objective performance goals of major amputation, 1-year AFS rate, and wound healing time (WHT) according to WIFI clinical stages were compared. The mean age was 58 years (79% male and 93% with diabetes). A total of 42 (21%) patients required major amputation; 159 (78%) had limb salvage. The amputation group had a significantly higher prevalence of advanced stage 4 patients (P<0.001), whereas the limb salvage group presented predominantly as stages 1–3. Patients in clinical stages 3 and 4 had a significantly higher incidence of amputation (P<0.001), decreased AFS (P<0.001), and delayed WHT (P<0.002) compared with those in stages 1 and 2. Among patients presenting with stage 3, primarily as a result of wound and ischemia grades, revascularization resulted in accelerated WHT (P=0.008).

Beropoulis *et al.* [2] further validated the WIFI classification system in a prospective study of 302 patients with CLTI undergoing endovascular treatment. They found statistical differences in 1-year amputation and survival between clinical stages 1 and 4 but no differences between clinical stages 1–3. Another study by Mathioudakis *et al.* [10] showed that major amputations continued to plague the most severe stage 4 WIFI patients. The 1-year amputation rates were 20–64% among patients with diabetic foot ulcers treated in a multidisciplinary setting. In this study, there were 217 diabetic foot ulcers patients with 439 wounds (mean age of 58.3–60.8 years; 58% male, 63% black), including 28% stage 1, 11% stage 2, 33% stage 3, and 28% stage 4. Major amputation at 1 year was 63.2% in stage 4.

This supports that the WIFI classification system correlated with the risk of major amputation.

Conclusion

The WIFI classification has high accuracy in stratification and assessing the risk of amputations in patients. WIFI classification can be used during assessment of patients with foot ulcers to help in deciding the management and plan of treatment.

This conclusion should be confirmed by a larger sample size study and pooling data from multicenter studies, taking in account the general condition of the patient and whether the patient is bed ridden or active; has other comorbidities; change in staging of foot ulcer during treatment, for example, after revascularization or debridement, as a result the WIFI changes; and the number of cigarettes smoked per day as risk factors for amputation.

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Conflicts of interest

No conflict of interest.

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