Original Article

Evaluation of global vascular guidelines strategy in infra-inguinal occlusive disease: Revisited using global limb anatomic staging system

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ABSTRACT

Introduction: Evaluate the global limb anatomic staging system (GLASS) with clinical outcomes in patients with extensive forms of atherosclerosis submitted to infra-inguinal lesions revisited and how it affects the decision-making and clinical outcome of the patients.

Patients and Methods: This is a prospective randomized study conducted between February 2018 and February 2022 in a single tertiary referral center.

Results: A total of 100 patients studied 120 limbs. Their ages ranged from 45 to 77 mean of 62.2±7.44, there was male predominance: 81 (81%) males and 19 (19%) females. According to the limb anatomic staging system, 90 (75%) of the limbs were considered as GLASS stage III and 12 (13.3%) of these patients had femoral-popliteal GLASS stage IV with infra-popliteal GLASS stage IV; limb-based patency (LBP) was lost in 52 (48.1%) limbs, with 20/42 (47.6%) after surgical bypass and 32/66 (48.5%) after endovascular interventions. Most major limb amputations occurred after the loss of LBP, 17/52 (32.69%). Three patients lost their limbs with a patent reconstruction and subsequently presented with advanced infection. All were poorly controlled diabetes who underwent revascularization for wound, ischemia, and foot infection (WIFI) wound scores of all or higher, patients who lost LBP after either endovascular versus open revascularization were equally likely to undergo major amputation (*P=0.695*). Limbs initially presenting with WIFI stage IV represent 20/29 limbs in which major limb amputations were performed in this cohort. Among these WIFI stage IV cases, 48 (55.17%) limbs maintained LBP, and 39 (44.8%) limbs lost LBP during follow-up. WIFI stage IV limbs that lost LBP were more likely to have undergone a major amputation at the time of data closure (*P<0.001*).

Conclusion: It was apparent clearly that the GLASS staging system adequately stratified the patients to be revascularized through either endovascular intervention or bypass surgery, similar to what was published in different studies and systematic review analyses.

Key Words: Global limb anatomic staging system, infra-inguinal occlusive disease, wound, ischemia, and foot infection.

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INTRODUCTION

Peripheral artery disease is the second and most severe advanced symptom of the atherothrombotic event worldwide[1,2].

Chronic limb-threatening ischemia (CLTI) develops in 11% of patients with peripheral artery disease, threatening both the life and limb with estimated 1-year mortality and major amputation 20%[3] and 5-year mortality up to 50%[4] and 45% mortality rate after major amputation[5].

The choice of revascularization technique is not standardized and usually depends on lesion-based strategy; the TASC anatomic classification system considers the location of lesions either aortoiliac, femoral-popliteal, or infra-popliteal regions as a separate entity.

This classification correlates poorly, or it did not correlate at all to the clinical outcome of limb revascularization and limb amputation-free survival.

Global vascular guidelines is a patient-central approach that depends on patient risk, limb status [wound, ischemia, and foot infection (WIFI)], and a new anatomic classification system; the global limb anatomic staging system (GLASS) which correlates to functional limb outcome.

It is assumed that GLASS poses an important improvement over the TASC lesion classification system. GLASS fundamentals include restoration of in-line flow to the ankle as the anatomic goal of revascularization in CLTI[6]. This based on the new concept of target artery revascularization pathway (TAP) which is defined as the primary in-line blood flow to the ankle based on target

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infra-popliteal (IP) vessel to the ankle for achieving effective revascularization and limb based patency (LBP) at 1 year which is defined as continued patency of the entire length of the TAP from the groin to the ankle[1-7].

Aim

The aim of this study was to evaluate the GLASS staging system with clinical outcomes in patients with extensive forms of atherosclerosis submitted to infra-inguinal lesions revisited and how it affects decision-making and clinical outcomes of the patients.

PATIENTS AND METHODS:

This is a prospective randomized study conducted between February 2018 and February 2022 in a single tertiary referral center.

The patients signed an institutional approved informed consent. Kasr Al Ainy, Cairo University institutional review board approved the present study.

Patient selection

The subsequent patients experienced a 30-day failure rate following peripheral angioplasty for femoral-popliteal lesions.WIFI grades III and IV significant foot lesions were found in all individuals. The current study did not include any patients whose limbs had imaging results indicating GLASS stage 0 illness. For the study cohort, baseline demographics, comorbidities, functional status, and prior procedure information were documented.

Procedure and postprocedure care

All patients underwent a computed tomography angiography after a clinical assessment of their condition and the tissue loss in their foot (WIFI), with the exception of those in whom the procedure was clinically contraindicated (such as patients whose estimated glomerular filtration rate was <30 ml/min/1.73 m^2); in these cases, a duplex study was performed by a skilled operator to evaluate the anatomic pattern of each limb using the distal waveform analysis that was obtained.

In order to find the best low resistance outflow, the diameter of the artery, the presence of substantial calcification, the integrity of the pedal arch, and the number of collaterals were used to establish the best target runoff vessel. All limbs were prospectively classified using the limb GLASS system. An extrapreliminary analysis was conducted on the pedal GLASS modifier, which is not yet included in the GLASS.

An examination of the operation report revealed the TAP for every treated limb. The revascularization plan is determined by the treating surgeon. Preoperative planning sessions on a frequent basis help to facilitate the decisions. Presenting the alternatives and available evidence to the patients encourages shared decision-making. When measuring vein diameters when the patient was in an orthostatic position, our first preference was the great saphenous vein.

The decisions ranged from redo angioplasty, open surgical bypass, primary amputation, or combined treatment.

These decisions depend on patient risk, limb risk (WIFI grade of the foot), GLASS stage (cause of failure of previous angioplasty intervention), and presence of TAP.

The procedures performed in the angio-suite or hybrid operating room. Inverted great saphenous vein was the preferred conduit when the decision was surgical bypass complemented by angiography or intraoperative duplex study. In endovascular procedures; the approach to the femoral-popliteal and tibial vessels considered via the ante-grade contralateral or ipsilateral common femoral artery. Concomitant aortoiliac lesions were treated before endovascular intervention.

The anterior tibial, peroneal, and posterior tibial arteries were considered treated if the revascularization was successful in establishing an inline flow to inframalleolar vessels; the dorsalis pedis, distal peroneal artery, and distal posterior tibial artery, respectively.

Standard percutaneous balloon angioplasty was used for entire vessels.

Severe residual stenosis, calcification, and flow-limiting dissection were the reasons for stent placement in the superficial femoral artery or popliteal artery. Bare metal stents or drug-eluting stents were used. If popliteal artery stenting was indicated, a Supera stent was chosen.

No stents were used in the tibial vessels.

Primary LBP was defined as the absence of hemodynamic compromise (~50% stenosis in the TAP or a decrease in the ABI of 0.15 or the toe–brachial index of 0.10) with recurrent or unresolved clinical symptoms of CLTI, as well as the absence of occlusion or critical stenosis (>30%) within the TAP or reintervention affecting any portion of the TAP.

Postprocedural care

Medication for lipid-lowering, antithrombotic, and antiplatelet purposes is part of the postoperative medical treatment. The anticoagulant of choice was either direct antifactor X or warfarin. Patients were receiving wound care, and until full healing occurred, they would attend the outpatient clinic once a week. If 4–6 weeks following revascularization, clinical status does not improve or if clinical deterioration occurs, WIFI staging will be carried out again.

Clinical evaluation of wound healing, ischemia indicators, the existence of a foot infection, and physiologic tests (ankle pressures or ankle wave forms analysis) were all included in the surveillance. Usually, surveillance was carried out once, 3, and 6 months, and then again every 6 months following that. Recurring CLTI signs and symptoms, wound regression, or failure to heal will be taken into consideration for follow-up care.

Statistical analysis

Statistical Package for the Social Science IBM SPSS (IBM corp., Armonk, N.Y., USA), version 25.0 was used for data management and analysis. Mean, SD, median, range, numbers, and percentages described quantities data. Independent t test was used to compare means of more than 2 independent groups when numerical variables were displaying normal distribution. Cox regression analysis provides a risk ratio of clinically relevant factors for ulcer healing. The *P value* was two-tailed and considered significant at 0.05 level.

RESULTS:

A total of 100 patients studied 120 limbs. Their ages ranged from 45 to 77, with a mean of 62.2±7.44, there was male predominance: 81 (81%) males and 19 (19%) females. Diabetes and hypertension were the most common risk factors. (Figure 1) illustrates the distribution of the study population risk factors.

Most intervention was performed due to tissue loss (92.5%). (Figure 2) illustrates the distribution of patients according to their clinical presentation, and most of the patients had advanced wound grade according to WIFI classification: 87 (72.5%) was WIFI grade IV, and 33 (27.5%) was WIFI grade III. (Figure 3) illustrated the distribution of foot lesions according to WIFI.

According to the limb anatomic staging system, 90 (75%) of the limbs were considered as GLASS stage III, and 12 (13.3%)of these patients had femoral-popliteal GLASS stage IV with infra-popliteal GLASS stage IV. (Figure 4) illustrates the distribution of GLASS scores.

Revascularization using the open bypass in 42 (35%) limbs (Table 1) and endovascular revascularization in 66 (55%) limbs (Table 2).

In six (5%) limbs, hybrid techniques were performed, either inflow AI lesion stenting or inflow CFA endarterectomy. According to global vascular guidelines, 12 (10%) limbs primary major amputation was the decision after the original procedure (Fig. 5).

Tables 1 and 2 detailed the management options for this population study.

Overall limb-specific outcome

Ninety percent of the treated limbs remained intact after an average follow-up of 12 months (Fig. 6). At 12 months, 56 (51.85%) limbs were evaluated to be free from LBP loss. There was no correlation between the revascularization approach and the presence of LBP (*P=0.861*). Fifty-two (48.1%) limbs lost LBP; following surgical bypass, 20/42 (47.6%) and following endovascular intervention, 32/66 (48.5%) limbs lost LBP. The majority of significant limb amputations – 17/52 (32.69%) – occurred following the loss of LBP. Three patients who underwent amputation had a patent repair but later showed signs of advanced infection. None of the patients received dialysis; all had poorly managed diabetes and underwent revascularization for wounds with a score of III or higher. Major amputation was equally likely to occur in patients who lost LBP following endovascular or open revascularization (*P=0.695*).

Twenty limbs saw the effective reestablishment of secondary LBP following reinterventions in 23 limbs. Three of the limbs that had a reintervention, underwent major amputations. Twenty (86.96%) limbs out of the limbs that had lost LBP but were eventually saved were successfully recovered to function as secondary LBP with reintervention.

About half (15/29) of the 29 limbs that lost LBP and did not receive a reintervention did not exhibit active CLTI symptoms at the time of patency loss, and all of these patients were still in possession of their limbs at the study’s conclusion. These were some of the other reasons for not reintervening included that the limbs were deemed unsalvageable by the multidisciplinary team on 14/29; all underwent major amputation; there was no technical option for revascularization on 9/14 with major amputation; and the patient was medically unfit or refused major amputation on 5/14.

Outcomes in wound, ischemia, and foot infection stage IV based on limb-based patency status

The 20/29 limbs in this group that underwent major limb amputations are represented by the limbs that initially presented with WIFI stage IV. Forty-eight (55.17%) limbs of these WIFI stage IV patients kept their LBP throughout follow-up, whereas 39 (44.8%) limbs lost it. A major amputation was more likely to have occurred at the time of data closure for WIFI stage IV limbs that lost LBP (P<0.001). Thirteen (76.47%) of the 17 of the 39 WIFI stage IV limbs that lost LBP responded favorably to reintervention.

Two (50%) out of four patients where reinterventions failed to recover LBP completely, resulted in major limb amputation. The lack of active CLTI at the time of LBP loss (10/22; no major amputations), extensive tissue loss without limb salvage potential (6/22; six major amputations), lack of remaining technical option for revascularization (3/22; two major amputations), and medically unfit or patient refusal for amputation (3/22; one major amputation) were the reasons for not performing reintervention in 22 limbs. Predictors of LBP: GLASS stage III, race, and smoking status were significant univariate predictors of LBP following intra-inguinal revascularization.

Neither the use of a prosthetic conduit (*P=0.320*) nor a single-segment greater saphenous vein graft (*P=0.517*) was shown to be significantly linked with lower LBP in these subgroups. Within these tiny subsets. 43/90 (47.7%) limbs of limbs with GLASS stage III anatomy and 9/30 (30%) limbs of limbs with GLASS stage II anatomy had lost lower LBP. Eighty-six percent of LBP occurrences happened in the context of GLASS stage III anatomy. A history of smoking was positively correlated with a decrease in LBP following endovascular intervention (*P=0.033*). The decrease of LBP during open bypass was significantly predicted by advanced age (*P=0.014*).

Major limb amputation was not significantly correlated with the revascularization technique (open vs. endovascular; *P=0.695*).

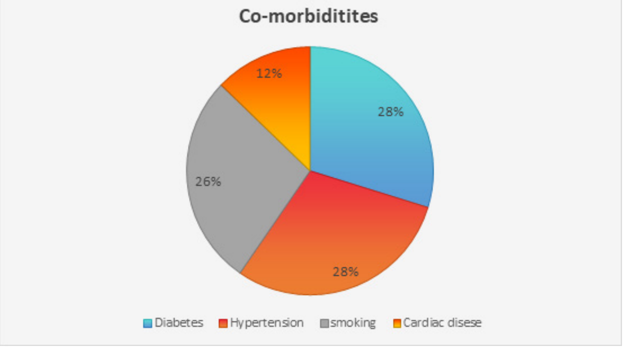

Fig. 1: Comorbidities.

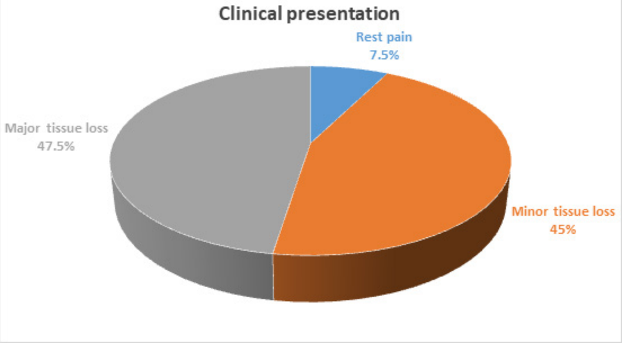

Fig. 2: Clinical presentation.

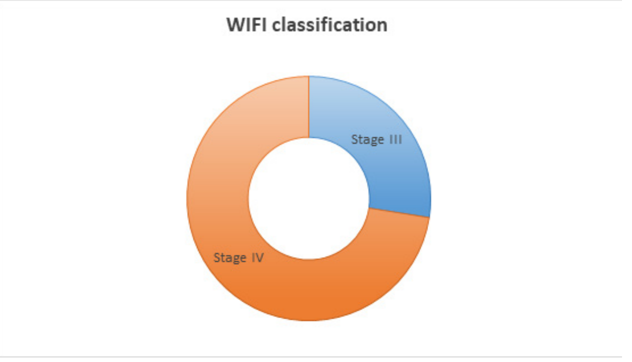

Fig. 3: WIFI classification. WIFI, wound, ischemia, and foot infection.

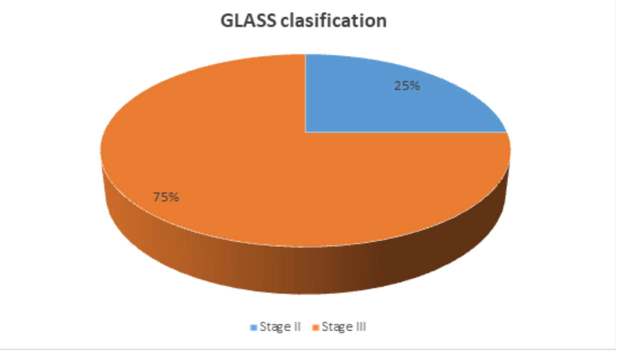

Fig. 4: GLASS classification. GLASS, global limb anatomic staging system.

Table 1: The management options for this population study

	Total (*N*=42)
Procedure	
Bypass	30
Endarterectomy and bypass	12
Bypass	
Fem pop	36
Fem distal	6
Conduit	
GSV	33
Synthetic graft	9
Distal run-off	
ATA	3
PTA	9
Peroneal	9
Multiple	7
Inflow revascularization	
AI	3
CFA	6
PFA	3

Table 2 Management options for this population study

	Total (N=66)
Intervention	
Stenting	60
Balloon angioplasty	6
Access site	
Ipsilateral	18
Contralateral	30
Combined	18
Wire passage	
Intraluminal	12
Subintimal	54
Balloon type	
Plain balloon	60
Drug-coated balloon	6
Stent type	
Bare metal stent	54
Covered stent	6
Supera stent	6
Distal run off	
ATA	9
PTA	6
Peroneal	48
Multiple	3
Inflow revascularization	
AI stenting	3
CFA and PFA	3
Inframalleolar revascularization	
DPA	3
Distal PTA	9

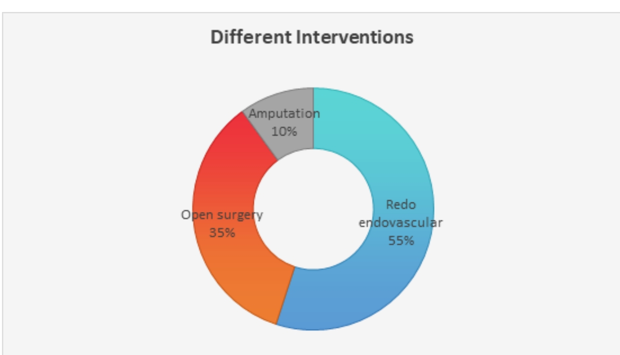

Fig. 5: Different intervention modalities.

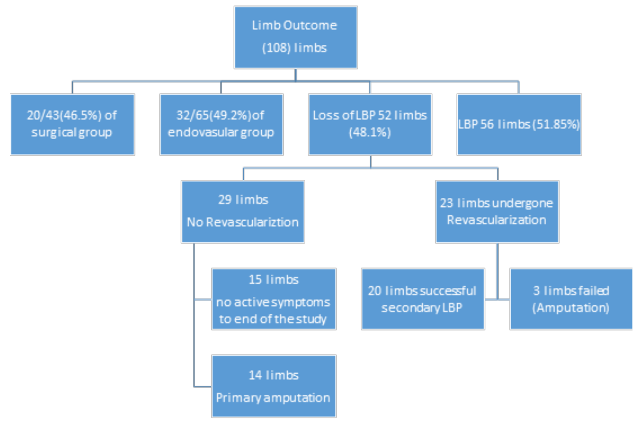

Fig. 6: Limb outcome.

DISCUSSION

Most of the patients presented to the vascular clinic have CLTI with advanced infected wounds. Management of such complex multilevel atherosclerotic lesions with advanced high-grade infected wounds increases the economic burden on the health care system and families.

The concept of lesion based patency rate or the concept of anatomic durability of the reconstruction does not take into the consideration the proximal and distal atherosclerotic disease progression. This was overestimate the patency rate in relation to the new concept of limb based patency which dependent on target artery pathway (TAP) that ensure continuous inline blood flow to the foot. This take in consideration the relation between lesion patency and whole hemodynamic improvement of the whole limb in what is known limb based revascularization (LBP)[8].

LBP concept along with the WIFI classification system; foot severity score, GLASS, and patient risk calculation that tailor a certain revascularization strategy to each patient and different revascularization strategies compared to each other[1].

This cohort study is complex than published cohort in literatures, these patients were redo cases from the start with 90 (75%) patients had high anatomic grading score; GLASS III and 87 (72.5%) patients had high limb severity scoring system WIFI stage IV; 10% of cases underwent primary amputation from the start, 17 limbs (14.16 %) at mean follow up of a year had major amputation, most of these cases presented with unsalvageable limb with high WIFI grade which was proven as an important predictor factor for major amputation[9], high GLASS stage; loss the window of revascularization.

Loss of LBP is strongly associated with major amputation irrespective to the method of revascularization either open, endovascular or hybrid technique.

The importance of LBP has implications for optimal selection of the revascularization strategy, the potential impact of technologies to improve patency, post-procedural medical therapy, re-interventions, and surveillance in CLTI patients. Endovascular first approach under complex circumstances,advanced GLASS and advanced WIFI stages, may result in an increased re-intervention or major amputation risk with subsequent secondary re-vascularization associated with worse outcomes[10–12].

There was no significant difference in LBP between patients managed in the open surgical group 35% versus managed in endovascular group 55%. These results were coincide to which published by El Khoury *et al* and Hicks *et al*, but it was different to Utsunomiya *et al*.[13].

CONCLUSION

It was apparent clearly that the GLASS staging system adequately stratified the patients to be revascularized either through endovascular intervention or bypass surgery, similar to what was published in different studies and systematic review analyses.

Study limitations

There are several important limitations to consider in the present study. First, this was a single-center study; second and most importantly, the number of limbs was too small to investigate and evaluate the possible correlations of the GLASS stage with clinical outcomes. Third, devices, including atherectomy devices, and drug-coated balloon and drug eluted stents were not freely available in all cases (limited resources).

CONFLICT OF INTEREST

There are no conflicts of interest.

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