Clinical Research, Basic Science

Grades of Below-the-Ankle Arterial Occlusive Disease following the Angiosome Perfusion: A New Morphological Assessment and Correlations with the Inframalleolar GVG Stratification in CLTI Patients

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Purpose: To assess a specific classification of the foot atherosclerotic disease concerning the angiosomal source arteries, the connected foot arches and attached collaterals for Rutherford 5, CLTI patients. To compare eventual analogies of this novel grading system with previously reported GLASS/GVG inframalleolar patterns of occlusive disease (P0-P2).
Materials and Methods: A series of 336 ischemic feet (221 diabetics) were selected and retrospectively analyzed. For each angiographic pattern of inframalleolar atherosclerotic disease, 4 severity classes of targeted angiosomal artery path (TAAP), associating 4 other classes concerning linked foot arches (LFA) and collaterals occlusive disease were described. By associating the 4 TAAP with the 4 others parallel LFA and collaterals classes, 4 novel anatomical "Grades" (A-D) of occlusive disease were described. Limb salvage was studied between groups of diabetic and non-diabetic patients.
Results: Using a primary endovascular approach, limb preservation comparison of grade A/B proved without significance for diabetics ($P = 0.032$) and non-diabetics ($P = 0.226$). Comparison in diabetics and/or non-diabetics between A/C ($P = 0.045$ and 0.046), A/D ($P = 0.027$ and 0.030, B/C ($P = 0.009$ and 0.038), and B/D ($P = 0.006$ and $P = 0.042$), as well as C/D groups ($P = 0.048$ and $P = 0.034$) proved ponderous. Parallel analysis of similar grades (A/A, B/B, etc.) with, or without diabetes appeared without significance ($P > 0.05$). Further comparison between grades A+B (assigned as P0/GVG), versus C (P1), and D (P2), proved significant ($P < 0.0001$).
Conclusion: The present grading system proposes a useful correlation between the severity of foot angiosomal arteries, arches, and collaterals disease and limb salvage, confirming the clinical significance of P0-P2 GVG severity score. This analysis also points the limits of EVT to be probably avoided in grade D patients.

The Authors have no conflict of interest to disclose.

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INTRODUCTION

During the last decade, the angiosome model (AM) has generated growing ~~experience~~ application in current vascular practice. There have been an increasing number of encouraging clinical results about its usefulness in chronic limb-threatening ischemia (CLTI) revascularization, ischemic wound healing, and limb salvage.[1-3]

An increasing number of publications have supported this model during the recent years; however, only a few of these studies acknowledge the angiosomal "source arteries" and the "foot collaterals" as determining factors for clinical success in topographic foot reperfusion.[3-7] The new Global Vascular Guidelines (GVG) document on the current CLTI treatment comprises a milestone in the management of this worldwide and growing health care concern,[8] despite lack of concrete validation up to date. Novel diagnostic strategies and definitions such as the Global Limb Anatomic Staging System (GLASS) are sustained by both morphologic and hemodynamic vascular assessments.[8] Improved stratification of femoropopliteal and tibial vessel atherosclerotic disease by specific grades and stages allows for more accurate TAP selection and treatment. Inasmuch TAP and LBP associating or not the AM, allow a more objective differentiation between various CLTI patterns,[8] a complementary evaluation of inframalleolar (IM) foot angiosomal source arteries, related foot arches, and groups of collaterals is still lacking.

The present study proposes a complementary arterial morphological ranking that focuses on below-the-ankle (BTA), Rutherford category 5 [5-8] CLTI presentations. It analyzes specific angiosomal source-arteries (SAs) occlusive disease defined as "target angiosomal artery path" (TAAP), their associated linked foot arches (LFA), and global collateral atherosclerotic disease from a four-grade stratification perspective. This novel grading method applies data previously published by our multidisciplinary group.[7]

METHODS

Patients

The database used in this study primarily associated two institutions 439 initial inferior limb files, from which 369 (84%) were scheduled for primary endovascular treatment (EVT), 35 (8%) others for primary bypass, and 15 (3%) others for primary amputation. The remaining 20 (5%) files were excluded because of incomplete required clinical data. Among the initially EVT selected candidates, in 33 (9%) limbs concomitant tibial reperfusion failed and these patients equally were omitted from further evaluation. The remnant 336 (91%) limbs in 304 CLTI patients received primary IM endovascular approaches having an appropriate upstream inflow and were further analyzed. The mean age of the patients was 71.9 years (45-98 years).

The "first-approach" EVT files were retrospectively studied throughout an eight-year recruitment period (2011-2019) and approved by the institution's ethics committees. The initial 336 limbs group was divided in a total of 221 diabetic and 115 nondiabetic ischemic limbs with various tissue defects (Rutherford grade III, category 5) 8 that were analyzed in this project, issuing from two institutional health registers.[7] This study's diabetic arm also gathered a group of patients enrolled in a previous prospective observational registry published by our research team.[7] Table I shows a comparison of the main demographic and anatomic atherosclerotic features between the two populations (diabetic versus non-diabetic cases). More than two-thirds of the diabetic patients had an initial diagnosis of diabetes for at least ten years, and 20% were insulin-dependent. Different stages of perceivable peripheral neuropathy, graded according to the UK screening test scale,[7] were noted in 91% of the limbs in the diabetic cohort. Concomitant latent or symptomatic coronary disease was observed in 81% and 69% of the diabetic and non-diabetic patients, respectively, while concomitant cerebrovascular disease was observed in 20% and 13% of these multilevel vascular patients, respectively (Table I).

Each foot atherosclerotic pattern for TAAP, LFA, and joined collateral occlusive disease was correlated to the individual wound topography (when achievable) and scheduled for independent radiological and surgical evaluation. All angiographic assessments were performed using similar imaging modalities and devices, owing to reproducible interventional protocols. Parallel Duplex evaluation was performed and included topographic Doppler flow measurements of the foot arteries and arches.[4-9] Adjoined preoperative Angio-CT, and/or Angio-MRI exams were performed, in addition to systematic perioperative angiographic evaluation. With regard to intraoperative digital subtraction arteriography (DSA), distinct contrast injections at the popliteal and ankle levels were completed by specific injections for each SA, LFA, and the dependent groups of collaterals.[7, 10-12]

Table I. Patients characteristics.

Patients with PTA characteristics database (limbs $n = 336$)	Diabeticlimbs $n = 221$	Non-Diabeticlimbs $n = 115$	*P*
Age >70 years	143 (65%)	84 (73%)	0.529
Male gender	156 (71%)	86 (75%)	0.790
Hypertension	181 (82%)	84 (73%)	0.541
Smoking	68 (31%)	46 (40%)	0.258
Coronary disease	179 (81%)	79 (69%)	0.378
Cardiac Insufficiency and LVEF < 30%	64 (29%)	17 (15%)	0.023
Chronic renal insufficiency	60 (27%)	15 (13%)	0.019
Chronic dialysis	20 (9%)	5 (4%)	0.187
Hypercholesterolemia	159 (72%)	78 (68%)	0.787
Cerebrovascular disease	44 (20%)	15 (13%)	0.229
COPD	60 (27%)	38 (33%)	0.403
Concomitant wound sepsis	183 (83%)	83 (72%)	0.607
Previous tissue fibrosis, scars or minor amputations	49 (22%)	17 (15%)	0.199
2, or 3 tibial trunks occluded	210 (95%)	82 (71%)	0.041
Targeted ATA+DP lesions	91 (41%)	43 (37%)	0.745
Targeted PTA+PA lesions	106 (48%)	59 (52%)	0.764
Multiple angiosomal lesions	53 (24%)	21 (18%)	0.413
Associated 2-3 ischemic wounds	29 (13%)	10 (9%)	0.369
Tandem femoropopliteal significant disease	37 (17%)	30 (26%)	0.124
Inflammation and high CRP levels	201 (91%)	91 (79%)	0.443
ASA III-IV class of perioperative risk	199 (90%)	78 (68%)	0.116

Table II. Targeted angiosome artery path (TAAP)* and/or Classes of atherosclerotic disease.

Targeted angiosome artery path (TAAP)* / Classes of atherosclerotic disease	
Class 1	Isolate stenose, or focal occlusion of the TAAP.
Class 2	Short TAAP occlusion ± 1 cm, (or <1/3 vessel).
Class 3	Occlusion of TAAP > 1 cm, (or 1/3 - 2/3 vessel).
Class 4	Extended occlusion of TAAP (or > 2/3 vessel).

TAAP*, Targeted Angiosome Artery Path.

Angiographic assessment

Each individual IM atherosclerotic pattern of arterial disease was weighted and scored on a newly formulated 4-class severity scale. In this article an original four-class IM angiosomal source artery occlusive disease stratification was described matching with the recently proposed GVG document model.[8] These new IM four TAAP disease classes were described and correlated to the previously used TAP designation in the GVG document.[8] These same four TAAP new classes were further assimilated to ~~the~~ other four concomitant classes of foot arches (LFA) and visible (large-to-small) collaterals disease. More ~~precisely~~ explicitly, for each inframalleolar TAP,[8] a correspondent "target angiosomal artery path" (TAAP) was designated upon the angiosome model. This TAAP represents a new entity in endovascular exercise proposed in this study that embodies previous TAP (GVG) characteristics,8 with complementary topographic, or "wound-directed" orientation.[6-10] TAAP atherosclerotic disease was further scored as per four classes presented in Table II and Fig.1. A parallel four-class stratification pertaining to the LFA and to the visible collaterals (a second original angiographic entity used in this study) was added (Fig. 2) and directly linked to each concomitant TAAP pattern of atherosclerotic disease (Table III).

In this study each BTA occlusive disease presentation (four TAAP classes adding four LFA and collaterals classes) was connected to the individual ischemic wound topography in the foot.

By combining the four (1-4) TAAP *classes* (Fig. 1) with the other four parallel LFA and collateral *classes* (Fig. 2), a resulting four-grade (A-D) stratification of the foot's atherosclerotic disease and related interventional challenge were obtained (Fig. 3 and Table IV). This new combined classification (Fig. 1-3) is further detailed in the "results" section.

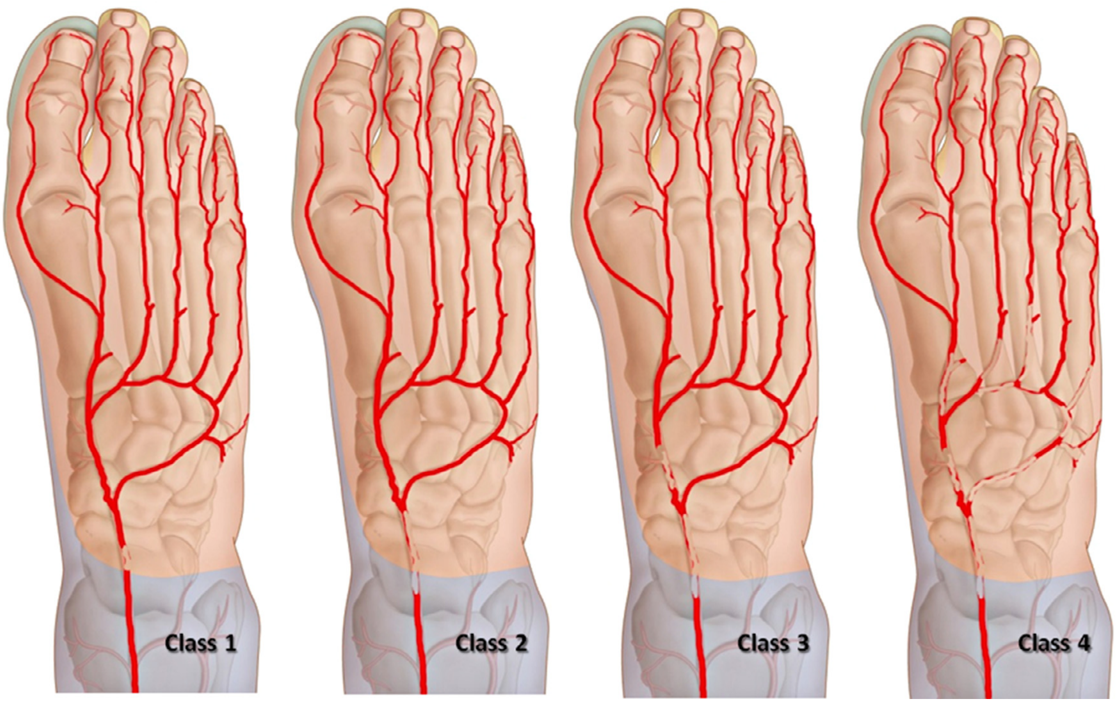

Fig. 1. The TAAP (Target Angiosomal Artery Path) 4 classes for BTA atherosclerotic disease. In this example TAAP is represented by the Dorsalis Pedis artery and its correspondent angiosome. The features of TAAP classes 1-4 are additionally detailed in Table II.

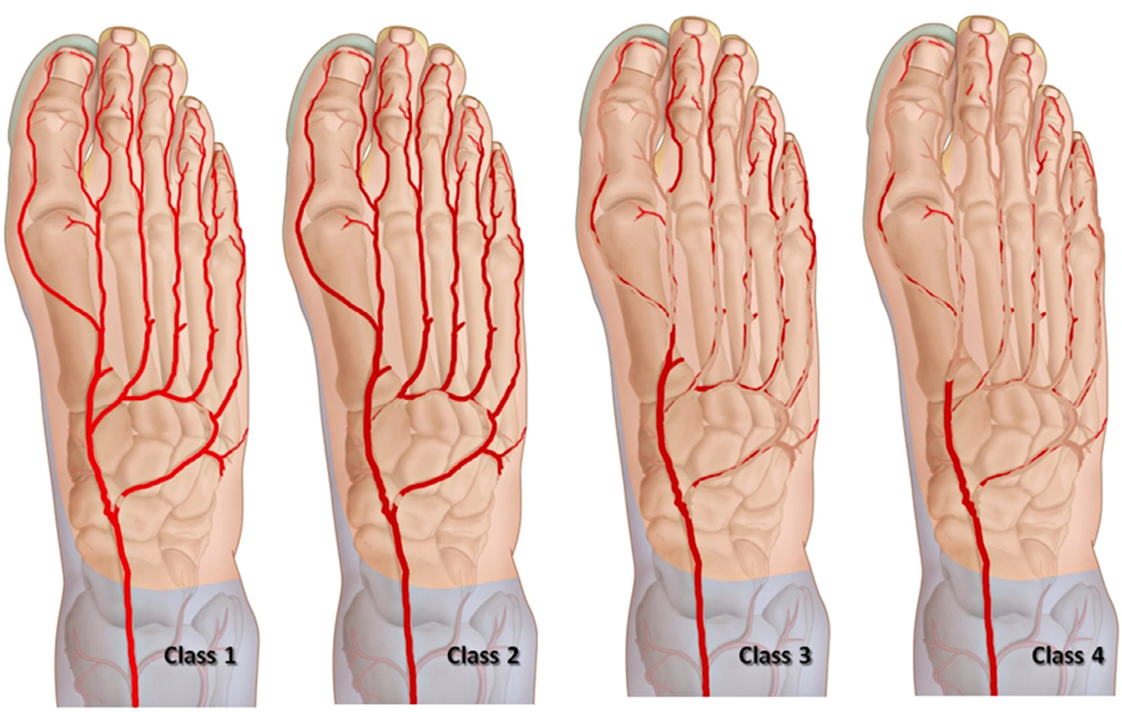

Fig. 2. The parallel LFA (Linked Foot Arches) and visible collaterals 4 classes for BTA atherosclerotic disease. In this example LFA is represented by the dorsal Arcuate Artery (AA) related to the Dorsalis Pedis artery and angiosome (TAAP) and its related collaterals. The characteristics of LFA classes 1-4 are additionally detailed in Table III.

Table III. Linked foot arches (LFA**) and collaterals and/or Classes of atherosclerotic disease.

Linked foot arches (LFA**) and collaterals / Classes of atherosclerotic disease	
Class 1	Focally diseased LFA and visible large (1 mm), and medium-to-small (<1 mm) collaterals.
Class 2	Short LFA occlusion ± 1 cm (or <1/3 vessel) and visible large (1 mm) and medium-to-small (<1 mm) collaterals.
Class 3	Occlusions of LFA > 1 cm (or 1/3 – 2/3 vessel), adding occlusions in the opposite foot arch, and the large collaterals (1 mm); only sparse medium-to-small (<1mm) collaterals are visible.
Class 4	Subtotal or total occlusions of LFA (or > 2/3 vessel), adding occlusion of the opposite foot arch, and all related collaterals.

LFA**, Linked Foot Arches (to the main TAAP).

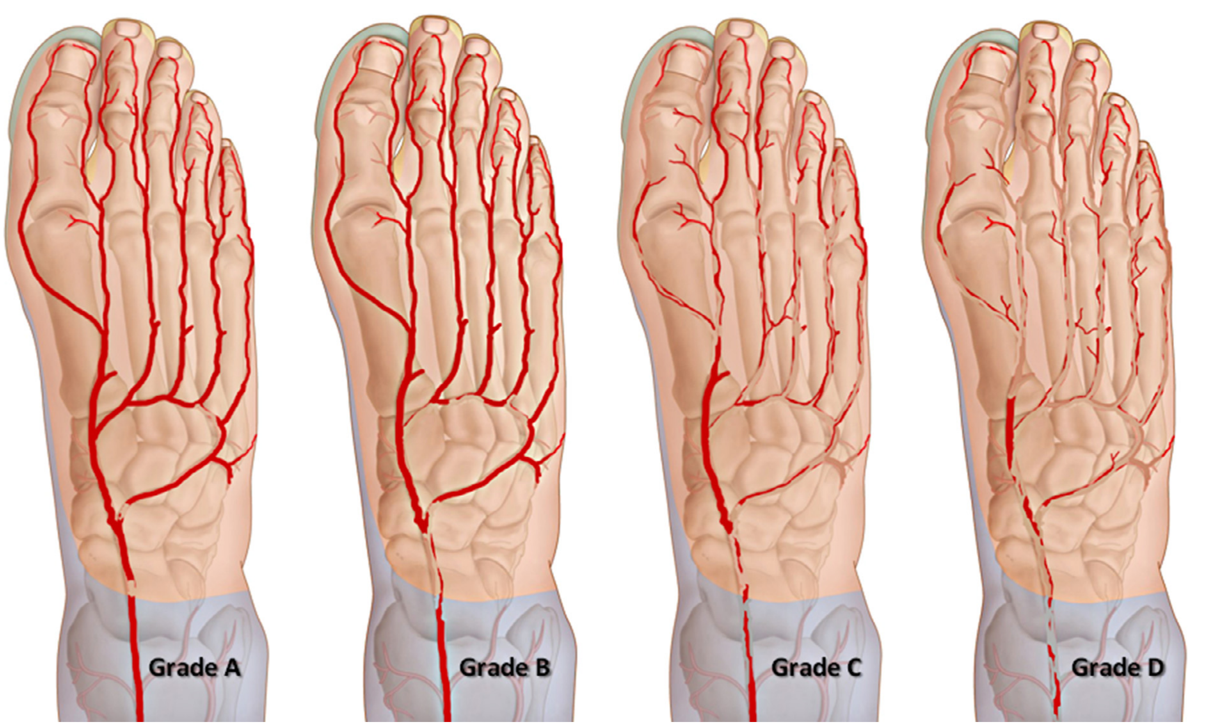

Fig. 3. By adjoining the 4 TAAP classes to the other 4 parallel LFA and collaterals classes, 4 new resulting Grades of inframalleolar arterial occlusive disease are obtained (Table IV). For a better apprehension, these 4 resulting Grades (A-D) are illustrated using the same Dorsalis Pedis example (as for the TAAP & LFA), and are additionally developed in Table VI.

Table IV. Grades of TAAP and LFA and/or collaterals atherosclerotic disease and estimated technical challenge.

Grade A	Grade B	Grade C	Grade D
TAAP Class 1 + LFA Class 1	TAAP Class 1 + LFA Class 4	TAAP Class 2 + LFA Class 4	TAAP Class 3 + LFA Class 4
TAAP Class 1 + LFA Class 2	TAAP Class 2 + LFA Class 2	TAAP Class 3 + LFA Class 2	TAAP Class 4 + LFA Class 2
TAAP Class 1 + LFA Class 3	TAAP Class 2 + LFA Class 3	TAAP Class 3 + LFA Class 3	TAAP Class 4 + LFA Class 3
TAAP Class 2 + LFA Class 1	TAAP Class 3 + LFA Class 1	TAAP Class 4 + LFA Class 1	TAAP Class 4 + LFA Class 4

Standard anteroposterior acquisitions coupled to lateral views were used to more comprehensively explore each topographic collateral pattern. Delayed acquisitions were necessary in specific presentations for demonstrating a collateral "blush" and a late retrograde enhancement of the arches and the connected communicants.

All angiographic data were studied in relation to each foot angiosome, the TAAP, the patency of foot arches, the full-channel arterial-arterial

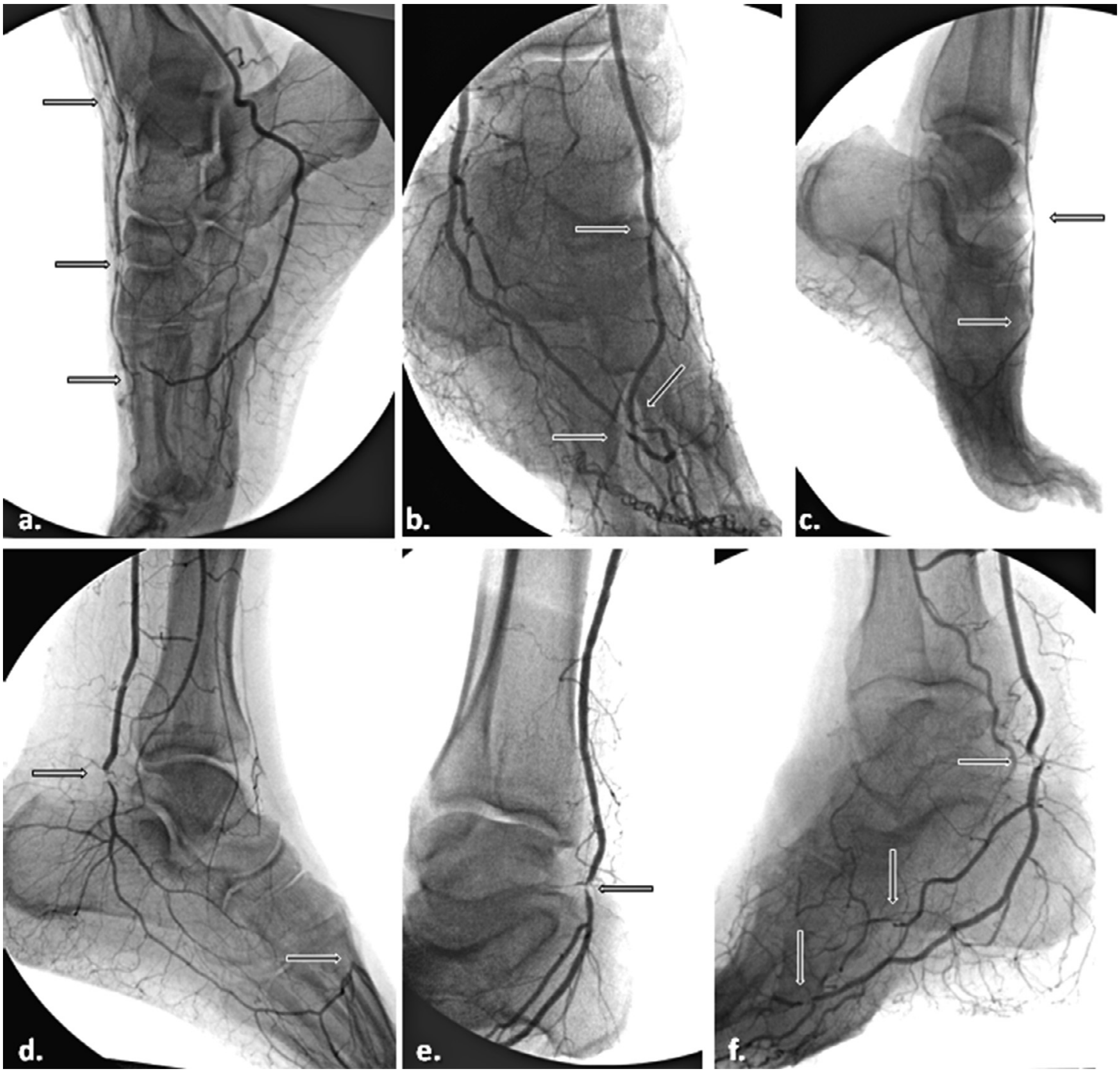

Fig. 4. A few examples of Grade A: TAAP, LFA, and main collaterals angiographic presentations. The A, B, and C images concern the Dorsalis Pedis (DP), while the D, E, and F angiographies refer to the Posterior Tibial (PT) and the Plantar arteries.

(A) A *TAAP class 1+ LFA class 1* presentation. Several short (± 1 cm) TAAP serial occlusions of DP (arrows), associating a brisk LFA occlusion of the dorsal arch are evinced (viewed by popliteal injection). (B) Another *TAAP class 1+ LFA class 1* case. Two short occlusions affecting the forefoot irrigation (via femoral injection): the first is located on the distal DP course, while the second lasts on the inter-arcuate connection via the 1st metatarsal perforator (arrows). (C) A *TAAP class 2+ LFA class 1* presentation. Similar aspects of succeeding short (± 1 cm) occlusions on the DP and dorsal AA (obtained by specific TAAP/AT injection). (D) and (E) Two *TAAP class 1+ LFA class 1* cases. Short or focal occlusions (<1 cm) on the PT artery's distal segment (owing specific PT injections) are present near to the plantar arteries bifurcation (arrows). A lack of connection between the plantar flow and the dorsal arch is also observed on the left image (arrow). (F) A *TAAP class 1+ LFA class 2 pattern.* Associated PT (± 1 cm) and plantar arteries short (<1 cm), serial occlusions (arrows) are obtained in this setting, by selective PT angiography.

communicants, the metatarsal perforators, and the patency of visible large-to-small collaterals (Fig. 4-8). In cases in which two distinct foot angiosomes showed concomitant ischemic involvement, the TAAP was designated in concordance with the dominant wound features, as per a regional microcirculatory assessment.[7, 10] Since two, three, or more foot angiosomes were affected, the two main dorsal and plantar foot arterial axes were systematically targeted as TAAPs for EVT; alternatively, only one arterial axis that was consistently connected to the patent LFA and the

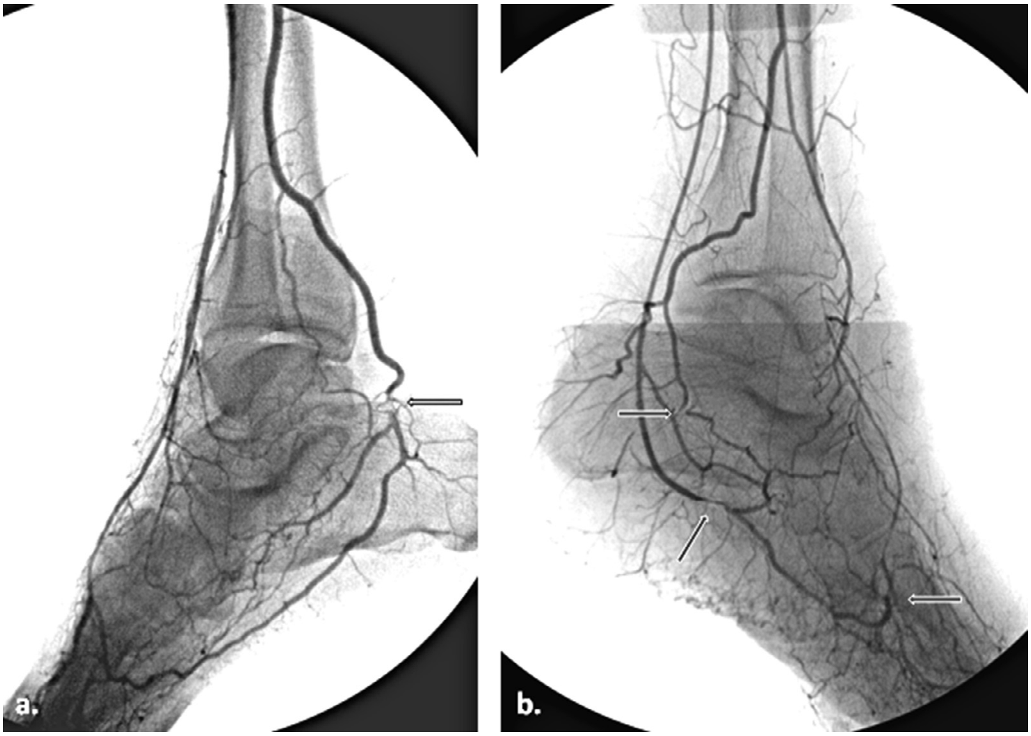

Fig. 5. Two other examples of Grade A, TAAP and LFA occlusive lesions in two relatively rare presentations showing anomalous dominant peroneal arteries perfusion (by popliteal injection):
(A) A *TAAP class 1+ LFA class 2 presentation*. A dominant Peroneal vessel that replaces the PT perfusion (in this case the TAAP) and exhibits a <1 cm length distal and calcified occlusion. (B) A *TAAP class 1+ LFA class 2 case.* A hypertrophic posterior communicant collateral of the Peroneal artery that completes the PT (TAAP) perfusion. Both vessels and appended LFA show brisk occlusions (± 1 cm) evinced by femoral injection (arrows).

appended large functional collaterals was targeted for EVT.

Arterial calcifications were appraised using a semiquantitative evaluation scale as follows: "scarce" or category 1, "moderate" or category 2 (<50% of the lesion's length), and "severe" or category 3 (>50% of vessel's lesion length, included circular and continuous calcifications) [7]. When present, particularly in diabetic and renal patients, category 3 calcification determined an augmentation by one grade in the final morphological grading level of the patient (Table IV).

Endovascular interventions

All patients received aspirin (160 mg/d) or clopidogrel (75 mg/d) premedication for at least 72 hours before the intervention. All interventions were performed in the institutional OR using a mobile C-arm device. Primary inframalleolar angioplasty (usually by intraluminal way) was conducted in each case, with upstream dilations in the tibial, popliteal, and superficial femoral artery as needed. In the majority of cases, the tibial and pedal vessels were catheterized and traversed using the drilling technique with a 0.014-inch hydrophilic guidewire (Terumo, Tokyo, Japan) assisted by a stiff 4- or 5-F support catheter as working platform. Long inflations (2–3 minutes) of various types of conventional low-profile balloons with diameters between 1.5 and 2 mm were applied. In cases in which TAAP reopening was technically unachievable, alternative collateral-sustained foot vessels revascularization utilizing permeable arches, large, and medium-to-small collaterals toward the wound zone was attempted.

The patient selection protocol

Both cohorts in the study had homogeneous patient, wound, and angiographic characteristics, owing to comparable macrovascular and microvascular risk factors (Table I).

Inclusion criteria

Clinical and angiographic analyses were performed for all diabetic and non-diabetic patients with CLTI. The selected cases presented with Rutherford category 5 [8] and corresponding Wagner grade 2-4,[13] or University of Texas (UT) grade 1-3 neuro-ischemic diabetic foot ulcers,14 with or without concomitant skin, deep tissue, or bone infection.

Exclusion criteria

Patients with life-threatening sepsis (systemic manifestations), those with > 3 spreading wounds, > 3 involved angiosomes, with subtotal or total foot necrosis (Rutherford grade III, category 6), or irreversible foot gangrene, (Wagner grade 5,[13] or UT Grade 3, Stage D [14] for diabetic patients), and all those requiring inevitable or urgent major amputation, were excluded from further analysis. Patients with micro-embolic pathologies, infrainguinal aneurysmal disease, thrombophilic conditions, acute ischemia presentations, previous forefoot amputations, stem cell treatment, or cases that underwent iterative IM revascularizations were also not considered for clinical and angiographic staging evaluation.

The anatomic and physiologic angiosome definitions

The six anatomical foot angiosomes and their tissue boundaries were delineated according to previous published descriptions.[4, 9]

A thorough clinical observation was completed by systematic macrovascular and microvascular evaluation [4-7, 10, 16] (before and after tissue debridement).

Functional angiosomes were defined in each presentation following detailed Doppler examination of pedal flow throughout the patent arches and the main “true” large-caliber collaterals.[4-7, 10, 17]

The TAAP for the dorsalis pedis artery (Fig. 4, 6, 7) was defined as the arterial segment contained from the foot extensor's muscles retinaculum, down to the emergence of the 1st dorsal metatarsal artery. For the plantar arteries, the TAAP was represented by the posterior tibial artery course (Fig. 4, 6, 7) below the foot flexor's muscles retinaculum, and along the two plantar arteries and angiosomes (medial and lateral plantar). The same segment of the distal posterior tibial artery containing its calcanean branch (below the flexor's muscles retinaculum), superior to the emergence of the plantar arteries, counted for the medial heel TAAP. The lateral heel and the anterior ankle TAAPs were delineated by the terminal third of the peroneal artery, in addition to its two anterior and posterior communicants and the lateral hindfoot branches.[4-7, 16]

For more clarity, all forefoot wound presentations were merged as ischemic occurrences of at least two neighboring angiosomes.[4-7, 16] In these cases, the local pedal artery (dorsal or plantar) with the highest technical feasibility was considered as the TAAP. LFA were separately assessed for every individualized TAAP (Fig. 4, 6, 7) by distal foot DSA and by conspicuous preoperative Doppler evaluation, coupled to the running physiological (functional) angiosome mapping.[4, 7, 16]

Wounds

All CLTI foot wounds were analyzed by a core-lab multidisciplinary team using the Rutherford scale coupled to the Wagner [(13)] and the University of Texas (UT) 14 tissue evaluation systems for patients with diabetes. A clinical-angiographical correlation between ulcer location and the main TAAP [14, 17, 18] adjoining the foot arches and the regional collateral flow was performed in all eligible patients. This topographic assessment associated the macrocirculatory information (ABI, AP, Doppler, DSA, Angio-CT, and Angio-MRI) with the regular microcirculatory measurements such as the transcutaneous oxygen pressure ($TcPO_2$) (coupled in a majority of cases, with SPECT-Scan scintigraphy). Two-dimensional (2-D) DSA was performed for specific foot run-off analysis (by delayed blush collateral sequences) in all cases. For complementary tibial or pedal vessel anatomical details, multiple angiographic incidences were requested, particularly for cases with extensive calcifications (grade 2-3), dormant collaterals, or blurry distal flow issuing from the collaterals of long tibial CTOs. If two distinct wounds belonged to two separate foot angiosomes, the dominant wound (evaluated by surface, depth, and microvascular assessment) was considered for further TAAP revascularization.

All tissue defects were continuously monitored through a thorough multidisciplinary examination.

Interventions

TAAP was favored as the primary interventional goal in all instances. In cases in which neither TAAP nor specific LFA or large collaterals could be reopened, an indirect EVT following non-angiosomal trunks and branches was attempted. A second-intention distal bypass was performed when the primary EVT failed, and if the following criteria were satisfied: adequate foot run-off collaterals, appropriate superficial veins for bypass, and fit general condition for surgery.[8] Alternative below-the-knee (BTK) deep calf or foot vein arterialization

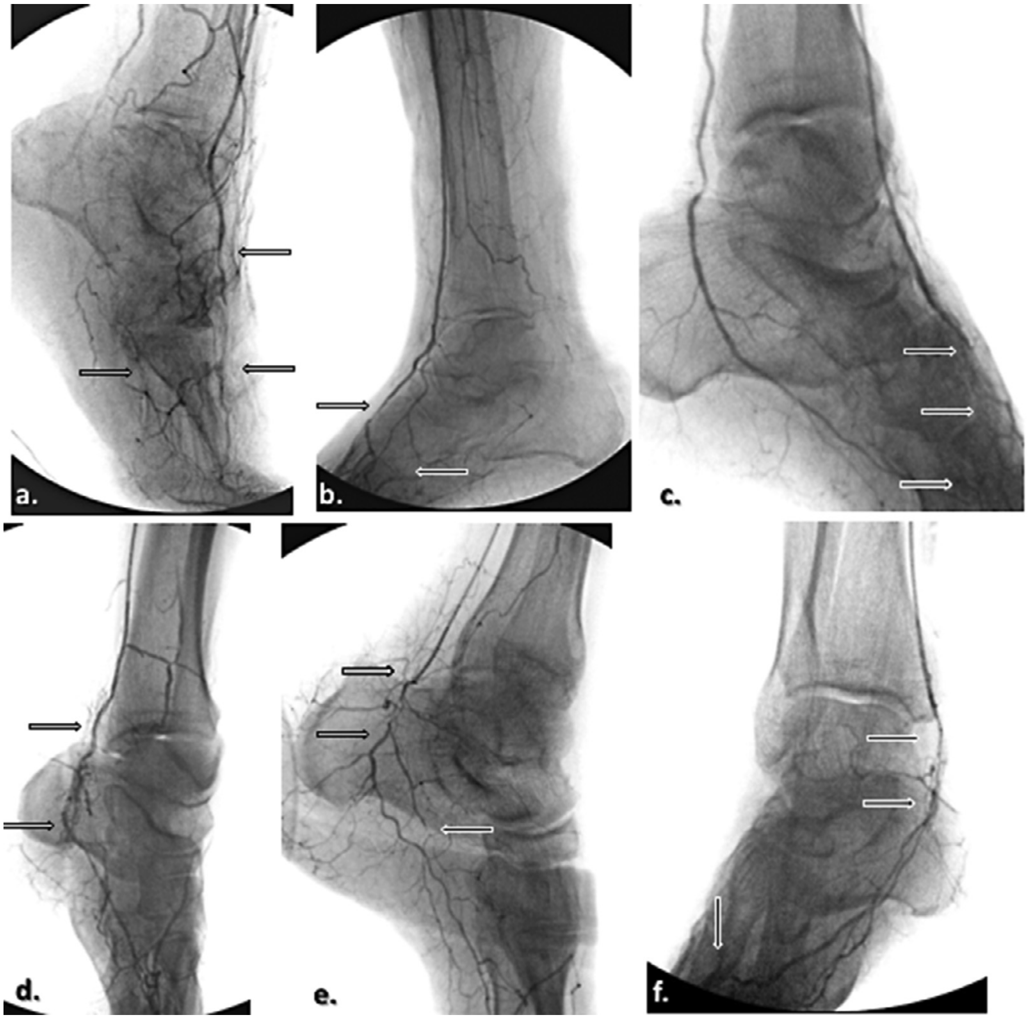

Fig. 6. Several examples of Grade B: TAAP, LFA and appended collaterals foot presentations. The A, B, C, images show several DP aspects, while D, E, F, refer to the PT and Plantar arteries lesions.

(A) A *TAAP class 2+ LFA class 3 case.* Several occlusions (± 2 cm) on DP (the TAAP) pointed by arrows, associate a >2 cm, and >1/3-length LFA occlusion in the dorsal arch (evinced by popliteal injection). (B) A *TAAP class 2+ LFA class 2 pattern.* A ± 1 cm DP occlusion affecting the forefoot irrigation is connected to a 1 cm LFA obstruction (showed via selective AT injection). (C) A *TAAP class 3+ LFA class 1 presentation.* Similar Grade B aspect of a >1 cm distal DP occlusion associated to incomplete (± 1 cm) occlusion of the dorsal LFA, and lack of direct flow to the plantar arteries (viewed by popliteal injection). (D) and (E) Two *TAAP class 2+ LFA class 3 cases.* Grade B specific ± 1 cm TAAP occlusions of the distal PT arteries, that associate ± 1 cm, and >1/3 LFA respectively, discontinuities (arrows) of the plantar arches (obtained by PT injections). (E) Another *TAAP class 3+ LFA class 1 pattern* that associates a PT (TAAP) >1 cm (or 1/3 length) occlusion (arrows), adding another ± 1 cm plantar arteries and LFA occlusion, with lack of communication towards the dorsal foot perfusion (showed by selective PT angiography).

was attempted in specific cases eligible for surgery, if all conventional arterial revascularization methods failed or proved technically impracticable.

Statistical analysis

The Kaplan-Meier life-table method was utilized to determine the risk of major amputation for each grade of atherosclerotic IM and pedal arterial disease. Categorical variables are presented as numbers (percentages) and were compared using the Fisher's exact test. Since no major statistical deviations were observed by this two-fold analysis in the initial patient distribution between groups (Table I), additional analysis using the multivariate Cox regression method was not considered at this stage of the work. A "*P*" value < 0.05 was accepted as statistically significant. The Log-Rank (Mantel-Cox) test was further used to compare limb preservation between different grades (A-D) within

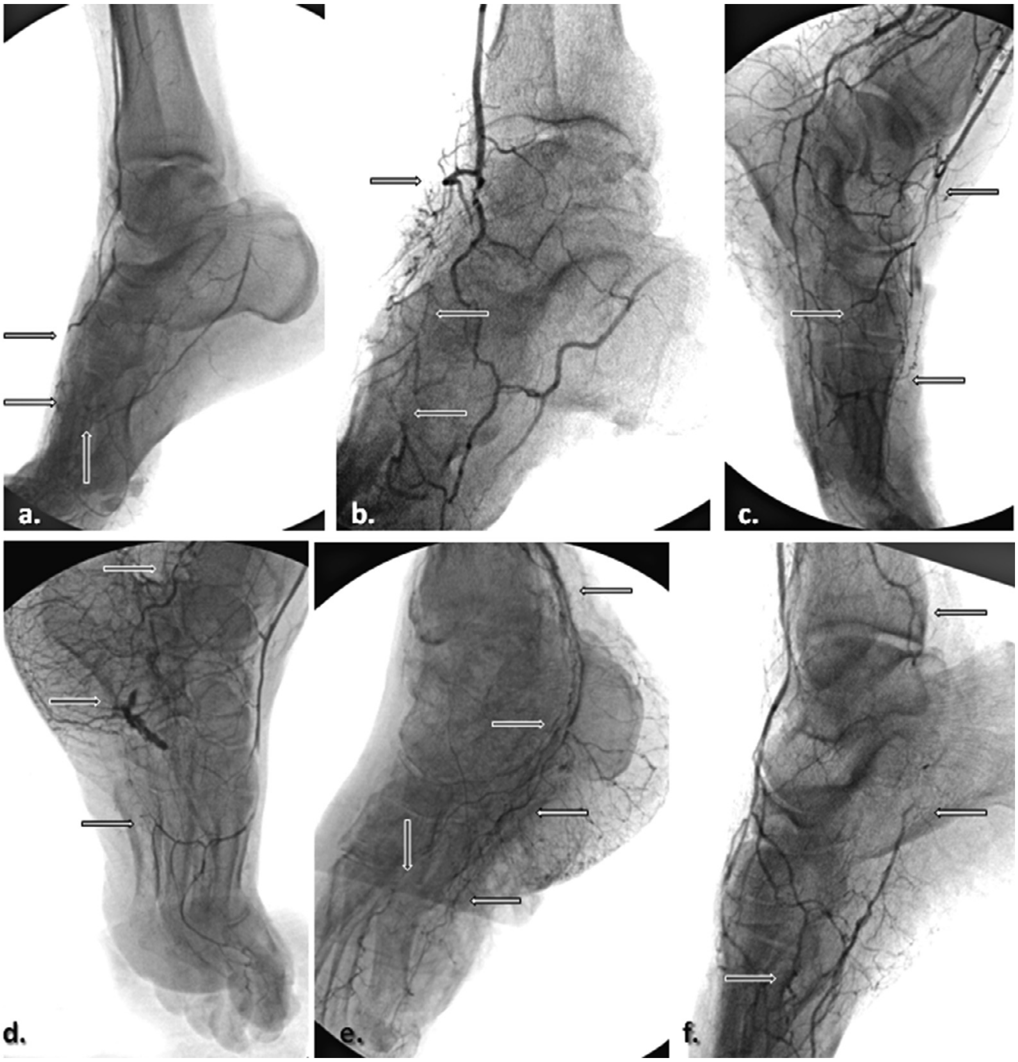

Fig. 7. A few cases showing severe, Grade C lesions:
(A), (B), and (C) Three *TAAP class 3+ LFA class 3 cases.* These Grade C images present > 1/3 length (and >1 cm) DP occlusions, adding >1 cm (1/3-2/3 length) LFA lesions viewed by AT or popliteal injections), (D), (E), and (F) Three *TAAP class 3+ LFA class 2 presentations.* These cases reveal > 2.5 cm and >1/3 length, distal PT and plantar arteries (TAAP) blockages, associating ± 1 cm LFA occlusions. In (B) image (by specific AT angiography), equally in (C) and (F) pictures (by Popliteal injections), only scarce diagonal arteries (partially narrowed) ensure a weak compensation between the dorsal and plantar foot circulation.

each group of patients (diabetic and non-diabetic patients), and to analyze the significance of A-D grades between the two cohorts. All analyses were performed using the Prism (GraphPad) statistics software.

RESULTS

To initially proposed files (n = 439), exclusion criteria were applied, and 369 (84%) limbs were selected for receiving endovascular approaches. Among these limbs, another 33 (9%) cases were excluded, because of technical endovascular failures of concomitant above-the-ankle revascularization. The remnant 336 feet (304 patients) availed appropriate infra-inguinal inflow down to the foot and attained criteria for further BTA analysis.

Multilevel atherosclerotic CLTI disease prevailed in all selected patients. Standard anteroposterior acquisitions were regularly coupled to lateral views in 97% of cases. Two or three concomitant tibial trunk occlusions at different lengths and levels were noted in 210 of 221 (95%) diabetic and 82 of 115 (71%) non-diabetic cases (Table I). Among the whole 336 BTA angioplasties, 134 (40%) targeted the dorsalis pedis and the anterior

Table V. Main diagnostic features observed for Grades A-D.

Grades	Ankle pressure	ABI	$TcPO_2$
Grade A	70-80 mm Hg	0.6-0.7	50-60 mm Hg
Grade B	50-70 mm Hg	0.4-0.6	40-50 mm Hg
Grade C	40-50 mm Hg	0.3-0.4	30-40 mm Hg
Grade D	<40 mm Hg	<0.3	<30 mm Hg

titbial axes, while 165 (49%) focused the plantar arteries and the posterior tibial line of foot flow, attained in concomitant or separate approaches (Table I). Femoropopliteal associated angioplasties were performed in 67 (19%) cases (37 diabetic and 37 non-diabetic feet). All tibial procedures were associated to pedal TAAP concomitant interventions, while 1/3 of femoropopliteal angioplasties were performed before BTK gestures (particularly in renal patients, as to avoid large amounts of contrast use).

According to the GVG-GLASS stratification, of the whole 221 diabetic and 115 non-diabetic limbs, 133 (60%) diabetic and 83 (72%) non-diabetic limbs had dominant P1 lesions, while 88 (39%) diabetic and 32 (28%) non-diabetic limbs showed extended P2, IM/pedal disease.[8]

Lesion stratification

A unified morphological scale was structured, by combining the above data (Table VI) and by defining four resulting anatomical grades that show a crescendo severity of atherosclerotic changes that can be summarized as follows (Table VI):

Grade A. Focal atherosclerotic disease of the TAAP and LFA with spotting stenoses or occlusions, patent arches, and visible large-to-small collateral networks

Anatomy *(Figs. 3-5)*

Isolated TAAP focal stenoses or millimetric occlusions (dominant Class 1 lesions) associated LFA (Class 1-3) presentations and were observed as dominant patterns in these patients. In grades A and B, patent LFA enabled extended TAAP flow beyond their anatomical areas into larger physiological zones of perfusion (the physiological angiosome),[17] owing to the relatively dense collateral background around the wound's territory.[9, 17] Only focal, or short-length atherosclerotic disease (< 1 cm) involved TAAP, LFA, and visible large (1 mm-diameter) collaterals and allowed for correct compensatory flow in these initial ischemic phases. Medium-to-small (< 1mm-diameter) collaterals were also regularly visible in grade A angiographic settings. Only spotting calcifications (category 1) were observed. Since TAAP matched with already described TAP (GLASS classification, GVG),8 a majority of these grade A cases showed specific P0, inframalleolar features.[8] Main angiographic features are assembled in Tables II, III, and VI.

Clinical features

The TAAP and its anatomical and physiological territories were effectively detected by macro-vascular (Doppler, DSA) and complementary micro-vascular assessment ($TcPO_2$ and SPECT-Scan). Intraoperative angiography often revealed "true" [9, 17] and functional inter-angiosomal, arterial-arterial connections.4, 17 Most ischemic ulcers were solitary (Table VIII) and clearly related to one angiosome affectation (22% among all the 336 EVT limbs). Primary EVT (direct or indirect TAAP revascularization) was technically feasible in 95% while direct TAAP and LFA angioplasty was successful in 63% of grade A limbs (Table VIII).

Grade B. Serial stenoses or short TAAP occlusions (<1/3 vessel length) with detectable collateral support (short occlusions in generally permeable arches and present large-to-small collaterals)

Anatomy *(Figs. 3, 6)*

Short length (< 1 cm) TAAP occlusions, adjoining < 1 cm LFA occlusions (Table VI), without eventual obstruction of the opposite foot arch (OFA) were observed. Large-diameter (1 mm) permeable collaterals were also present. Visible medium-to-small collaterals (< 1 mm) were regularly documented. Dominant category 1-2 calcifications were noted, strongly influenced by the age of patients, duration of the metabolic disorders, and by the eventual concomitant renal insufficiency. Most of these grade B presentations (alike grade A) showed contained agiographic disease as to integrate P0 stage (before the more severely diseased P1 stage) of the GLASS and/or IM classification.[8] Main angiographic features are assembled in Tables II, III, and VI.

Clinical features

In these grade B patients, in addition to local sepsis, diabetic neuropathy and pressure injuries, broadened ischemic tissue limits. Ischemic tissue boundaries were strongly conditioned by individual permeability of foot arches [7, 10] and availability of the "true" arterial-arterial communicants.[9, 17]

Similar to that in grade A feet, in grade B presentations, Doppler probe exploration allowed

Table VI. Main angiographic and clinical features for Grades A-D.

Grades Foot Features	A	B	C	D
Foot TAAP	Stenosed or focally diseased	Short occlusion <1 cm, (<1/3 TAAP length)	Occlusions >1 cm, (1/3-2/3 TAAP length)	Subtotal (>2/3), or total TAAP occlusions
Foot LFA	Stenosed or focally diseased	Short occlusion <1 cm, (<1/3 LFA length)	Occlusions >1 cm, (1/3-2/3 LFA length)	Subtotal (>2/3), or total LFA occlusions
Large collaterals (1 mm)	Stenosed or focally diseased	visible	severely deprived	absent
Medium-to-small collaterals (<1 mm)	dense	visible	severely deprived	absent
Calcifications	Category 1	Category 1-2	Category 2-3	Category 3
Associated tibial GLASS grades	3	3-4	4	4
Correspondent GLASS inframalleolar lesions	P0	P0-P1	P1	P2
Detectable boundaries of foot *anatomical* AG	accessible	mitigated	absent	absent
Detectable limits of foot *physiological* AG	accessible	mitigated	absent	absent
Dominant nr. of involved foot AG	1 angiosome	2 angiosomes	3 angiosomes	> 3 angiosomes
$TcPO_2$	accessible 50-60 mm Hg	accessible 40-50 mm Hg	mitigated accessibility 30-40 mm Hg	difficult to apply, or inaccessible
SPECT-Scan	Feasible, strongly connected to angiography	Feasible, strongly connected to angiography	Feasible, fairly connected to angiography	Feasible, poorly connected to angiography
Wounds: Wagner classification	dominant grade 2	dominant grades 2-3	dominant grade 3-4	dominant grades 4
Wounds: UT classification	dominant: solitary Grade 1, Stage D	dominant: often twin Grade 1-2, Stage D	multiple Grades 2-3, Stage D	Foot / generalized Grades 3, Stage D
Correlation: ischemic wounds / AG territory	correct	acceptable	poor	absent
Global EVT feasibility	95%	88%	74%	12%

AG, angiosome(s); LFA, linked foot arches; TAAP, target angiosome artey path.

for an acceptable detection of connections between neighboring angiosomes and for defining much larger “functional angiosomes”,[9, 17] though with a lower propensity in this group (Table V).

The upstream tibial trunks showed concordant GLASS grade 3-4 occlusive disease (Table VI) matching in significant proportions with P0-P1/IM lesions.[8] For such grade B cases, TAAP-related ischemia was correctly documented by coupled macrovascular and microvascular information, proving that not all visible skin defects harbored an equivalent ischemic burden.[7, 10, 16, 18] More challenging EVT procedures for longer CTOs and calcifications (category 1-2) were noted (Table VI). Grade B cases included 46% diabetic and 36% non-diabetic limbs (Table VII). Primary EVT was technically feasible in 88% of grade B limbs (Table VIII).

Table VII. Distribution of Grades A-D (for TAAP, foot arches and collateral disease) in diabetics and non-diabetics.

Patients	Diabetics	Non-Diabetics	*P*	95% CI
GRADES / TAAP + foot Arches & Collaterals	Limbs, $n = 221$	Limbs, $n = 115$		
Grade A.	36 (16%)	37 (32%)	0.010	1.026-1.260
Grade B.	102 (46%)	41 (36%)	0.048	0.823-1.046
Grade C.	68 (31%)	24 (21%)	0.161	0.836-1.021
Grade D.	15 (7%)	13 (11%)	0.218	0.974-1.115

Table VIII. Types of applied treatment per group of occlusive disease.

Grades	A	B	C	D
Total treated limbs $n = 336$	$n = 93$ (28%)	$n = 131$ (39%)	$n = 95$ (28%)	$n = 17$ (5%)
Total successful EVT treatment $n = 278$ (83%)	$n = 89$ (95%)	$n = 116$ (88%)	$n = 71$ (74%)	$n = 2$ (12%)
Direct TAAP & LFA Revasc. $n = 195$ (58%)	$n = 59$ (63%)	$n = 89$ (68%)	$n = 46$ (48%)	$n = 1$ (6%)
Indirect TAAP & LFA Revasc. $n = 83$ (25%)	$n = 30$ (32%)	$n = 27$ (20%)	$n = 25$ (26%)	$n = 1$ (6%)
Secondary bypass $n = 22$ (6%)	$n = 2$ (2%)	$n = 10$ (7%)	$n = 10$ (11%)	$n = 0$
Secondary amputation $n = 25$ (7%)	$n = 2$ (2%)	$n = 3$ (0.7%)	$n = 11$ (12%)	$n = 9$ (53%)
Secondary vein arterialization $n = 11$ (3%)	$n = 0$	$n = 2$ (2%)	$n = 3$ (3%)	$n = 6$ (35%)

Grade C. Extended TAAP occlusions and connected arches (1/3-2/3 vessel length), including a lack of the main foot large collaterals. Only sparse medium-to-small arterial branches were noted

Anatomy *(Fig. 3, 7)*

Longer occlusions (>1 cm) or occlusions that involved 1/3 – 2/3 of TAAP length were associated with >1 cm LFA (± corresponding OFA) occlusive lesions in these grade C ischemic feet. At this stage, only scarce large collaterals or "true" arterial-arterial communicants [9, 17] were detectable. No "functional angiosome" 17 via "true," [17] or "twin-caliber" inter-angiosomal branches was proved by clinical assessment. Merely spotted groups of medium-to-small collaterals [7, 10] with, or mainly without topographic orientation were identified. Extended arterial calcifications (category 2-3) were encountered in these grade C cases. Scattered "surviving" small arterial branches (<1 mm) appearing mostly as "dormant" collaterals and were detected only via selective distal tibial contrast injections. These "hidden" branches to current femoral angiography [7, 12] allowed for direct or indirect TAAP reperfusion in selected presentations.[7, 10] Main angiographic features are assembled in Tables II, III, and VI. Grade C, BTA arterial disease was constantly associated with severe GLASS grade 4 (Table VI) tibial occlusive disease [8] and matched with equivalent P1 (GLASS) 8 rank of foot vascular disease.[8]

Clinical features

In this study, grade C presentations were observed in 31% of diabetic and 21% of non-diabetic limbs (Table VII). In all grade C cases, the main arterial perfusion of the foot was severely compromised. Disparate bulks of infra-millimetric surviving collaterals allowed rather indirect TAAP irrigation (26% feasibility, Table VIII), usually without possible topographic orientation towards the ischemic wounds.[7] Wounds showed confluent necrosis, often affecting three adjacent angiosomes (28% of all 336 EVT limbs). By

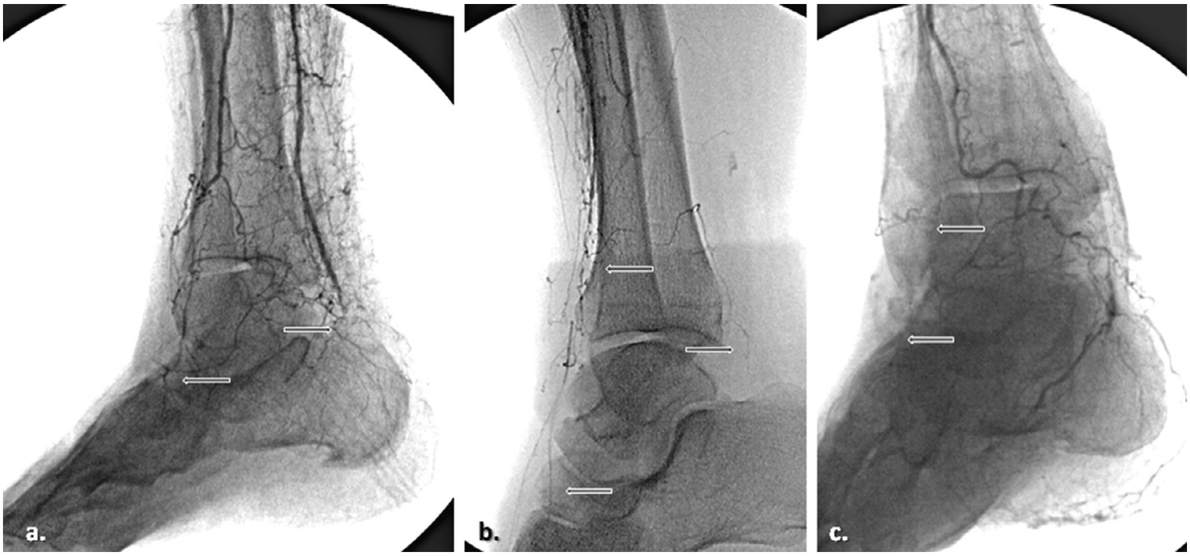

Fig. 8. Three *TAAP class 4+ LFA class 4 cases,* featuring three Grade D subtotal, or total foot arteries occlusions.
A complete absence of the DP as TAAP adding > 2/3, or total LFA occlusions are observed in all images. Both foot arches are occluded in all instances (arrows). Only tiny posterior Peroneal communicants are present in the (A) and (C) images, that partially fill in (C) scattered portions of the plantar arteries. All large and medium-sized collaterals are lost following serial, infra-popliteal injections.

involving neighboring angiosomes with analogous collateral decay, the angiographic "end-artery occlusive disease" (EAOD) aspect,[15] or the "strand perfusion" phenomenon [10, 16] were seemingly described in literature, and particularly concerning the forefoot and the hind foot territories.[10, 16] These grade C cases availed poor (or absent) correlation between the amount of tissue necrosis and the "classical" anatomical angiosome partition.[10, 16, 18] Repeated tissue evaluations performed before and after regional debridement provided however, useful information for ischemic tissue mapping.[10, 16] Primary EVT was feasible in only 74% while direct TAAP and LFA reperfusion was initiated just in 48% of grade C (P1) limbs (Table VIII).

Grade D. Extended TAAP and LFA occlusion (>2/3 vessel length), including a lack of main groups of foot collaterals. None of the main angiosomal foot arteries or linked arches and collaterals were detected

Anatomy *(Fig. 3, 8)*

Subtotal (> 2/3 vessel's length) or total TAAP and LFA occlusions were noted, without any topographic distribution of the surviving collaterals (Fig. 8). Bulky and extensive category 3 calcifications were commonly detected in these limbs. Grade D angiographic lesions were often designated as "desert foot" presentations.[6, 7, 10-12]

Clinical features included extended tissue loss, associating GLASS stage III CLTI presentations.[8] Grade D was currently characterized by the hemodynamic collapse of more than three neighboring angiosomes (5% of all 336 EVT treated limbs, Table VIII), by concomitant occlusion of both foot arches, and the majority of the foot collaterals.

This grade could be matched with equivalent GLASS/P2 rank of IM vascular disease.[8] The angiosome anatomy becomes unrecognizable at this level of foot vascular decay (Tables V and VI).

Very few therapeutic options were applicable for these patients. Exceptional venous arterializations [21] or more reasonable primary amputations could be applied, as per a multidisciplinary consensus.[8] Primary EVT found poor indication in this context. In our experience it was technically feasible in only 12% of cases, while direct TAAP and LFA angioplasty was deceivingly feasible in merely 1 (6%) of these specific grade D (P2) limbs (Tables VI, VIII, and IX).

Although standardized in severity for IM foot arterial perfusion, these four TAAP and LFA anatomical grades were also corresponding with regard to related inflow arterial supply.

Treatment results

PTA was successfully applied in 336 inframalleolar cases [7, 16]. Among the 336 studied limbs that were treated with the primary endovascular techniques, technical success was noted in 278 (83%) cases, of which 181 (65%) were diabetics. TAAP/LFA intentional topographic revascularization was

Table IX. Correspondences between the present study's Grades (A-D) and GVG infra-malleolar patterns of atherosclerotic disease (P0-P2).

Present study Grades	A+B	C	D
Infra-malleolar patterns of disease (GVG)	P0	P1	P2
Foot TAAP	Focal (<1 cm), noticeable atherosclerotic disease	Extended >1 cm, TAP / TAAP severe atherosclerotic disease	Subtotal (>2/3), or total TAP / TAAP occlusions
Foot LFA	Focal (<1 cm), noticeable atherosclerotic disease	Extended >1 cm, TAP / LFA severe atherosclerotic disease	Subtotal (>2/3), or total TAP / LFA occlusions
Large collaterals (1 mm-diameter)	visible	severely deprived	absent
Medium-to-small collaterals (<1 mm diameter)	visible	severely deprived	absent

LFA, linked foot arches; TAAP, target angiosome artey path; TAP, target artery path.

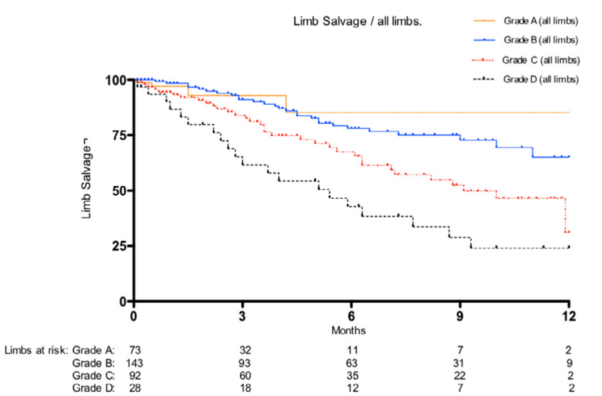

Fig. 9. Limb salvage rates for Grades A-D in all diabetic and non-diabetic treated limbs.

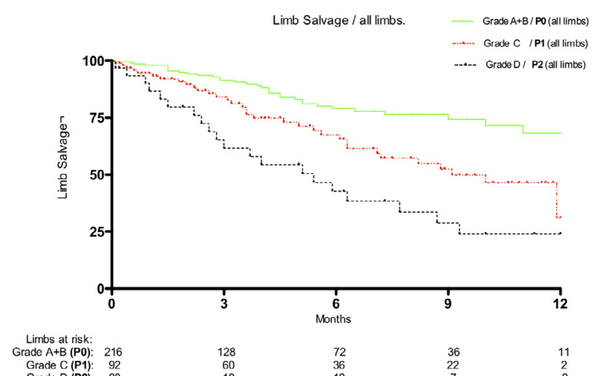

Fig. 10. Since Grade A versus B comparison showed no statistical significance, limb salvage rates were illustrated in correlation with P0-P2 (GVG) stratification: Grades A+B expressed as P0, Grade C as P1, and D (P2) in all diabetic and non-diabetic treated limbs.

achieved in 195 (58%) cases, while compulsory indirect reperfusion was applied in 83 (25%) of all EVT cases (Table VIII). For the remaining 58 (17%) limbs (67% diabetics), 22 secondary distal bypasses, 11 compassionate deep calf or foot vein arterializations, and 25 unavoidable amputations were performed (Table VIII).

Event analysis in grades A-D patients

Limb salvage was evaluated for all anatomical grades (A-D) in diabetic and non-diabetic foot CLTI lesions treated with primary EVT (Figs. 9, 10). In all cases, limb preservation reflected a multidisciplinary consensus about the best treatment to be applied for each individual presentation. This approach was consistently applied in this study for patient selection, in the treatment methods, and for regular follow-up.

Additional subgroup analysis of techniques (EVT vs. bypass, or concerning specific endovascular techniques), and analysis including consequent interventional indicators (primary and secondary patency, major adverse limb events, and survival of patients) were not performed at this stage of the study, since the main analysis endpoint was the anatomical stratification of the emergent foot atherosclerotic disease.

In all cases one straight arterial femoro-pedal flow line to the foot was targeted and analyzed.

The following limb salvage rates were observed in the whole diabetic and non-diabetic patients at six and 12 months: 85% (95% CI 73 – 97%) and 85% (95% CI 73 – 97%), respectively, for grade A, 78% (95% CI 70 – 96%) and 65% (95% CI 52 – 78%), respectively, for grade B, 67% (95% CI 56 – 78%) and 31% (95% CI 17 – 45%), respectively, for grade C, and 42% (95% CI 24 – 60%) and 24% (95% CI 7 – 41%), respectively, for grade D (Fig. 9).

Limb salvage data were compared among grade A-D groups using the log-rank (Mantel-Cox) test. For diabetic limbs, the comparison of grade A versus grade B groups showed no statistically significant differences (P= 0.322), while grade C versus D appeared meaningful ($P = 0.048$). Further significant deviations appeared for diabetic grade A versus C and grade A versus D (P= 0.045 and P= 0.027, respectively), as well as grade B versus C and B versus D groups (P= 0.009 and P= 0.006, respectively). Concerning non-diabetic limbs, no statistical differences were found for grade A versus B (P= 0.226), while C versus D appeared significant (P= 0.034). Significant differences were also revealed between grade A versus C and grade A versus D (P= 0.046 and P= 0.030, respectively), and for grade B versus C, and grade B versus grade D groups (P= 0.038 and P= ~~0.052~~, 0.042 respectively).

Interestingly, no significant disparities were observed when diabetic and non-diabetic patients of the same IM anatomical grades were compared. Additionally, comparison between grade A diabetic vs. grade A non-diabetic (P= 0.322) patients, and further grades B, C, and D diabetic limbs versus B, C, and D non-diabetic limbs revealed no statistical dissimilarities (P= 0.455, P= 0.818, P= 0.998, and P= 0.820, respectively). Following the same complementarity with the GVG document (Table IX), a statistical comparison of grades A+B (assigned as P0) versus grade C (P1), and D (P2), showed significant differences (P= 0.009 and P< 0.0001), respectively (Fig. 10).

In the majority of all diabetic and non-diabetic grade A and B clinical presentations (64%) a reliable correlation between ulcer location and correspondent angiosome ischemic involvement was noted (Table VI), while only poor correspondences were found for grades C and D cases.

DISCUSSION

The present study proposes a complementary analysis of previous data concerning IM foot arterial atherosclerotic disease and AM applications. This study adds information to previously reported data [8, 22-27] that focus (partially or entirely) on BTA vascular anatomical lesions related to CLTI (notwithstanding inherent variations in these observational protocols).[22-29] This study offers clinical premises in better evaluation and understanding of staged atherosclerotic disease in BTA arteries and collaterals from an anatomical (angiographic) point of view, adding important correlations in CLTI basic appraisal and treatment; it also casts original hypothesis and indications for endovascular revascularization specifically oriented by grades of pedal arteries, foot arches and collaterals occlusive disease for future studies.

The present paper puts forward an anatomical differentiation of main pedal angiosomal arteries and collaterals atherosclerotic disease, that appears complementary (Fig. 10, Table IX) to the recent GVG infrapopliteal arterial and run-off status classification.[8]

As per our knowledge, due to the restricted number of cases and the lack of larger, multicenter clinical studies, the four anatomical grades of TAAP and LFA proposed in the current study cannot be correlated as yet with the corresponding hemodynamic stages (similar to the LBP assessment in GVG recommendations).8 The four-class classification of the TAAP, LFA, and the connected visible collaterals proposed in this study comprehensively includes two main categories of previous clinical history. First, the anatomical and physiological foot angiosome features [4, 9, 17] that were analyzed and placed parallel to the second category of graded angiographic atherosclerotic changes (Table II-IV, VI) in the pedal arteries.[7, 8, 10, 29] For each studied TAAP (Table II) and appended LFA plus collaterals class (Table III), four emerging grades were further structured (Table IV and VI). Unlike those for the tibial atherosclerotic affectation, documentation and scoring systems for BTA occlusive disease have been scarce.[8, 26, 30]

The SVS standards reports published in 1997 [26] previously pointed out the importance of pedal arch integrity in limb preservation.[26] Succeeding technical developments in materials permitted new advances in BTK and BTA foot flow apprehension in CLTI. Such publications include the updated TASC II document [22] enlarged in 2015 for BTK arteries,[23] the Bollinger's angiographic scoring system,[24] or Graziani's femoropopliteal and tibial seven-class categorization scale in diabetic CLI.[25] However, the usefulness of these analyses is limited with reference to CLTI IM foot perfusion, as they mention only a few, or none of the associated BTA patterns of disease.[7, 8, 22, 24] Parallel contemporary publications focus on the foot's main pedal arteries, paired arches, and the regional collateral framework, affording valuable information in CLTI understanding with or without topographic angiosomal specificity. In this setting, the pioneering evaluation of the critical ischemic foot vessel's run-off, angiosomal distribution, and collateral connections described by Attinger et al.[4] was further sustained by Varela et al.,[5] Zheng et al.,[6] Spillerova et al.,[27] Iida et al.,[28] and also by the previous work of our team.[1, 7, 10] Parallel reports concerning BTK occlusive disease tibial grading were published by Toursarkissian et al.,[29] in addition to a pertaining work by Mustapha et al. [30] that adds via standardized injection protocols practical hemodynamic features. However, none of these publications was intended to provide a specific BTA classification scale for pedal trunks, foot arches, and appended collaterals during CLTI atherosclerotic aggression.

A notable contribution in this domain was made by Kawarada et al.;[31] their study includes a more detailed stratification of the angiographic anatomy of the pedal arches (Types 1, 2A, 2B, and 3). However, this stratification lacks specific hemodynamic also regional delineation in the ischemic foot. In this context, the present study's morphological grading scale converges with previous BTA published information.[8, 26, 30, 31] It appears to match the SVS standards and expands the distal run-off appraisal in the CLTI foot.[26] It adds to the Kawarada arches stages 2-3 [31] and completes more in detail the GVG P0-P2 grade scoring, in accordance with the original infrainguinal TAP designation.[8]

Although the angiosomal direct revascularization for limb salvage still remains controversial in current CLTI practice,[5-8, 31-35] uniform and standardized macrocirculatory and microcirculatory diagnostic, definition, classification, and therapeutic protocols using AM are still needed.[10, 31-37] The recent GVG consensus document provides a concise (three levels) BTA morphological classification (from P0 to P2, equivalent to intact or slightly diseased, severely diseased, and absent foot arches), and adds a brief dichotomous appraisal of calcification.[8, 16] Several correlations can be stipulated between this study's anatomic scale and previous GVG/IM stratification, that are summarized in Table IX and Fig. 10. Based on angiographic and clinical similarities and following our limb salvage comparison data (lack of significance between A and B groups), a direct analogy of grades A and B with the P0, and of grades C and D with the P1 and P2 stages,8 can be observed.

Previous clinical experience including our published research revealed that specific foot vascular territories with ischemic wounds may address different stages of atherosclerotic occlusive lesions of "source arteries" and appended collaterals,[7, 34-39] and belongs to a larger ongoing investigation regarding the anatomical and hemodynamic aspects of BTA vasculature in CLTI.

Though doubts about the real clinical benefit of WDR for both bypass and EVT have been raised in contemporary literature,[1-8, 10, 19-21, 32, 37] using modern microcirculatory diagnostic methods with valuable topographic information.[10, 19, 40, 42] While some authors have found the assessment of anatomical [6, 10, 16, 28] and physiological [16, 40, 41] angiosomal flow by MRI oximetry,[40] trans-cutaneous laser Doppler,[16, 28] or peripheral SPECT-Scan perfusion [10, 41-43] useful, others have questioned the utility of topographic reperfusion using white-light tissue spectrophotometry,[44] and low-frequency oscillations analyzed by diffuse speckle contrast analysis.[45] The clinical value of all these studies that support or refute specific postoperative angiosomal microcirculatory changes is indisputable. However, several recognized physiological phases for tissue reperfusion [10, 16, 46, 47] such as the gradual opening of the wider physiological angiosome [17] containing its "active" or "dormant" collaterals,[10, 16, 17, 30, 38] and the existence of the postoperative delay-phenomenon in tissue flow redistribution,[17, 48, 49] all add novel and valuable information about delayed increment and the opening of compensatory inter-angiosomal collaterals.[4, 9, 49, 50] This observation needs to be considered in parallel with the arteriogenesis and the angiogenesis processes[10, 16, 47, 51]

The concomitant anatomical grades of CLTI lesions [7, 10, 51, 52] associate local physiological changes at the foot level in a unique morpho-functional pattern that is specific for each individual. The graded anatomical scale presented in this study represents an initial observation that needs larger clinical validation. However, our study reveals that not all reported postoperative microcirculatory patterns and measurements [40-45, 47, 51] are performed in equivalent anatomical degrees of CLTI disease,[10, 43] and in the corresponding pre- or post-reperfusion physiological phases.[10, 45-51] It also suggests that probably not all previously published studies compare limbs that share similar anatomical and functional collateral indexes, densities of ramifications, and calibers of communicants, and thus do not have equivalent peripheral arterial resistances [8, 16, 53] that follow distinct territories of angiosomal reperfusion.[10, 17, 49]

Therefore, it appears that a "correct" postoperative angiographic foot flow cannot always be equivalent to appropriate regional tissue oxygenation, particularly in severe neuropathic diabetic limbs (that may exhibit a cutaneous "steal" phenomenon).[15, 16, 52] Postoperative TAAP flow needs to be further studied in sequential phases of tissue reperfusion.[43-47, 52] When comparing EVT to bypass [1, 5, 8, 33] or solely for bypass performed with angiosomal direct versus indirect revascularization,[5, 33, 54-56] results will probably show different outcomes since addressing dissimilar complexity of the diseased TAAP, foot arches, and related collaterals like in our grades A and B vs. that in grades C and D comparison. The research data provided by this paper needs to be further examined in a larger series by comparing similar, updated revascularization techniques in equivalent risk-patients, wounds, anatomical grades, and physiological phases of BTK and BTA reperfusion.

Finally, in a recent study published by Ferraresi et al. 57 an applied 3-degree severity scoring-system for foot small arteries disease is presented and acts in this mostly uncharted vascular territory, as a complementary perspective to the present study, yet away from eventual topographic orientation.[57] Finally, knowing that specific tissue perfusion is the ultimate goal for BTK and BTA angioplasties,30-39 further TAAP-related LFA collateral evaluation may represent an important an step forward in better appraisal of pre- and post-revascularization regional perfusion in the future.

LIMITATIONS

The present analysis is limited by the retrospective nature of the study design. The consequent association between morphological classes of arterial disease and limb salvage should be relativized because of the multifactorial profile of this indicator. It is known that limb salvage can be eventually influenced by other simultaneous factors beyond progressive degrees of arterial atherosclerotic occlusive disease.[7, 8, 16, 28] The number and caliber of upstream tibial trunks, the type of techniques, the type of ischemic wounds, and other individual systemic factors can also affect limb preservation rates and could not be additionally detailed in this observational anatomic paper. The authors are also aware about the apparent complexity of this BTA staging system at a first sight. However, for current research use, the multifaceted aspects of BTA atherosclerotic arterial disease appears difficult to be emphasized without having a detailed morphological analysis. Table VI was therefore conceived to uniformize main anatomical features in a much simpler perspective for the interventionist, in accordance with recent GVG recommendations.[12] The patient enrollment period extended over eight years in this paper. Therefore, the diagnostic and treatment methods might have been influenced by the inherent evolving technology and skills of the local interventional team. The inherent limitations in the standard 2D DSA interpretation should also be mentioned. This imaging equipment displays specific hindrances in distal foot collateral evaluation,[12] particularly in collateral deprived CLTI subjects.[1, 8, 12, 16] For grades C and D exhibiting scattered “dormant” or “latent” foot collaterals and long and highly calcific tibial occlusions, 2D DSA by femoral way, may allow suboptimal interpretation.[12, 51] Future 3D imaging by perfusion angiography could offer new perspectives in better TAAP and LFA regional mapping.

CONCLUSION

BTA angiosomal source arteries, the connected foot arches, and the main groups of collaterals present progressive and assessable atherosclerotic occlusive changes in CLTI that can be scored on a graded morphological scale. The present TAAP grading system proposes a useful correlation between the severity of BTA angiosomal arteries, foot arches, and collaterals disease and limb salvage, complementary with the P0-P2 GVG severity score.

By its original four-grades morphological scale, this analysis also points the limits of EVT probably to be avoided in grade D, even in the absence of significant differences between patients associating or not diabetes mellitus.(Table V, Table VI, Table VII, Table VIII, Table IX)

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