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Clinical Significance of the AID Classification in Diabetic Foot Ulcers: Awareness of Arteriopathy, Bacterial Infection, and Foot Deformity

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Abstract

Background

This single-center retrospective study aimed to investigate the impact of our novel AID classification, based on arteriopathy, bacterial infection, and foot deformity, on wound healing in patients with diabetic foot ulcers (DFUs).

Methods

This study included 115 consecutive patients with 129 limbs who were hospitalized for DFU management. The presence of arteriopathy, bacterial infection, and foot deformity was scored as one point each, and wound severity was graded as 1-3. The wound healing rates at 12 months were evaluated. Comprehensive treatment including revascularization, debridement, or offloading was implemented based on the AID concept.

Results

Arteriopathy was observed in 49.6% of patients with DFUs. A total of 82.8% of patients with arteriopathy had DFUs complicated by both bacterial infection and foot deformity; however, 10.9% were complicated by either one. Approximately 14% of patients underwent major amputations. The Kaplan-Meier wound healing curves were significantly ($p=0.002$) different among patients with AID scores of 1, 2, and 3; however, the wound healing rates at 12 months were 89%, 90%, and 88%, respectively.

Conclusions

Diabetic arteriopathy is commonly complicated by bacterial infections of of DFUs and foot deformities. The AID classification effectively stratified the wound healing speed. Furthermore, AID concept-based comprehensive treatment achieved a wound healing rate of approximately 90%.

Key Words: Peripheral artery disease; Diabetes; Wound healing

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Introduction

Diabetes mellitus (DM) is increasing in burden globally, particularly in Asia[1]. DM poses a significant challenge in clinical practice because it changes the nature of peripheral artery disease (PAD) and increases the susceptibility to bacterial infections and foot deformities[2]. Diabetic foot ulcers (DFUs) are an amalgamation of arteriopathy, bacterial infection, and foot deformity[3]. Therefore, a multidisciplinary approach, encompassing vascular and wound management, is indispensable for the treatment of diabetic PAD and DFU.

To date, traditional classification systems have been used in the study of PAD and DFUs, such as Fontaine[4], Rutherford[5], Meggitt-Wagner[6], SINBAD[7], University of Texas[8], Kobe[9], and WIfI[10]. However, the Fontaine and Rutherford systems focus only on the severity of ischemia, while the Meggitt-Wagner, SINBAD, University of Texas, Kobe, and WIfI systems lack a perspective on foot deformities. There is an increasing opportunity to treat patients with DFU in vascular practice. Thus, a simple, easy-to-use, and clinically relevant classification system for DFUs is urgently needed. Given the individual significance of arteriopathy, bacterial infection, and foot deformity in wound management, we recently proposed the Arteriopathy, bacterial Infection and foot Deformity (AID) classification, which has a maximum possible score of 3 points[2]. We aimed to assess the impact of the AID classification on wound healing at 12 months in patients with DFUs.

Methods

This single-center retrospective study included 115 consecutive patients (129 limbs) who were hospitalized for DFU treatment between January 2015 and December 2016. The study protocol was approved by the Medical Ethical Committee of our hospital (No: TGE01275-004; August 9, 2019) and was conducted in accordance with the Declaration of Helsinki. DFU was defined as foot ulcers in patients with DM. Diabetes mellitus was diagnosed based on the American Diabetes Association criteria or the use of antidiabetic agents or insulin[11]. Blood glucose and subsequent fasting blood sugar levels were evaluated at admission. Hyperglycemia was controlled with insulin or an oral hypoglycemic agent, at the discretion of the managing endocrinologist. Wound healing was defined as the complete epithelialization of the wound.

AID classification and scoring

The AID classification comprises three elements: arteriopathy, bacterial infection, and foot deformity. Each component was scored as 0 or 1, and the wound severity was graded with an AID score of 0 (none of the components) to 3 (all components). Representative cases of AID 1, 2, and 3 are shown in Figure 1.

Arteriopathy scoring: To assess the severity of arteriopathy-induced microcirculation disorder, the foot's skin perfusion pressure (SPP) (SensiLase™ PAD3000, Vasamed Inc., Minnesota, USA) was measured. Multiple measurements were obtained for the dorsal and plantar aspects of the affected foot. The lowest values were selected. According to Castronuovo et al[12], an SPP of ≧40 mm Hg at the proximal wound margin is associated with ≧90% likelihood of wound healing in critically ischemic limbs. Thus, arteriopathy was defined as SPP ≧40 mm Hg, scoring 1 point.

Bacterial infection scoring: According to the guidelines of the Infectious Disease Society of America (IDSA)[13] and the International Working Group on the Diabetic Foot (IWGDF)[14], bacterial infection of the wound was defined as the presence of two or more clinical signs (local swelling or induration, erythema >0.5 cm^2 around the wound, local tenderness or pain, increased warmth, and purulent

Figure 1. Representative cases with AID scores of 1, 2, and 3. The simple AID classification can aid in dividing a broad spectrum of diabetic foot ulcers (DFUs) in clinical practice.

discharge) and no other cause for the inflammatory response of the skin (e.g., trauma, gout, acute Charcot's neuro-osteoarthropathy, fracture, thrombosis, or venous stasis). The presence of bacterial infection was scored 1 point.

Foot deformity scoring: According to the guidelines of IWGDF[15], foot deformity was defined as

alterations or deviations from the normal shape or size of the foot, such as hammer, mallet, or claw toes, hallux valgus, prominent metatarsal heads, pes cavus, pes planus, pes equinus, or consequences of Charcot's neuro-osteoarthropathy, trauma, amputations, other foot surgery, and other causes. The presence of foot deformities was scored 1 point.

Comprehensive treatment

A comprehensive treatment was considered based on the AID concept. Medical treatment, including antiplatelet therapy or clinically driven antibiotics, and wound care were essential. The need for invasive treatment was determined by a team consisting of a cardiologist, vascular surgeon, and plastic surgeon based on the risks and benefits of the procedure. Endovascular or open revascularization was considered for arteriopathy. Debridement of the infected wound and offloading (knee-high or ankle-high offloading devices, fitting footwear, or surgical offloading interventions) for the foot deformity were implemented based on the principles of good standard care and at an experienced plastic surgeon's discretion[16].

Statistical analysis

Continuous data of the three groups were compared using one-way analysis of variance (ANOVA) followed by Bonferroni's post-hoc test. Categorical data of the three groups were compared using the chi-square or Fisher's exact tests, as appropriate. Patients with different AID scores in the left and right feet were analyzed using the AID score of the first limb. Wound healing, amputation-free survival, and overall survival rates were calculated using Kaplan-Meier analysis and compared using the log-rank test. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS (version 21; IBM Corp., Armonk, NY, USA).

Results

The patient characteristics are shown in Table 1. All patients scored one or higher on the AID scale. The prevalence of coronary artery disease and hemodialysis differed significantly among the three groups ($p=0.003$). In particular, their prevalence was significantly higher in those with AID 3 than in those with AID 1 and 2.

The foot characteristics are shown in Table 2A. Arteriopathy was observed in 49.6% of DFUs,

Table 1. Patient Characteristics

Variable	Overall, n=115	AID score 1, n=19	AID score 2, n=49	AID score 3, n=47	p value
Age, yrs	65.9±12.5	68.5±14.8	62.6±13.0	68.3±10.3	0.05
Male, n (%)	82 (71.3)	12 (63.2)	32 (65.3)	38 (80.9)	0.168
Hypertension, n (%)	83 (72.2)	15 (78.9)	33 (67.3)	35 (74.5)	0.57
Diabetes mellitus, n (%)	115 (100)	19 (100)	49 (100)	47 (100)	
Random blood glucose (mg/dL)	194±91	173±76	213±100	183±85	0.145
HbA1c (%)	7.4±2.0	7.0±1.5	7.9±2.4	6.9±1.5	0.029
Insulin use, n (%)	56 (48.7)	9 (47.4)	26 (53.1)	21 (44.7)	0.708
Dyslipidemia, n (%)	27 (23.5)	7 (36.8)	8 (16.3)	12 (25.5)	0.183
Smoking history, n (%)	62 (53.9)	10 (52.6)	30 (61.2)	22 (46.8)	0.364
Coronary artery disease, n (%)	34 (29.6)	4 (21.1)	8 (16.3)	22 (46.8)*	0.003
Cerebrovascular disease, n (%)	17 (14.8)	3 (15.8)	4 (8.2)	10 (21.3)	0.193
Hemodiaylsis, n (%)	42 (36.5)	2 (10.5)	15 (30.6)	25 (53.2)	0.003

*$p<0.05$ for AID 2 vs 3.

bacterial infection in 87.6%, and foot deformities in 86.8%. A history of a minor amputation was observed in 15.5% (20/129 limbs) of the limbs overall and in 17.9% (20/112 limbs) of the limbs with a foot deformity. Furthermore, AID 3 and AID 2 accounted for 82.8% and 10.9% of patients with arteriopathy, respectively (Fig. 2). There were significant differences in the wound location ($p=0.003$), ankle-brachial index ($p<0.001$), and SPP ($p<0.001$) among the three groups. There was no significant

Table 2A. Foot characteristics

Variable	Overall, n=129	AID score 1, n=22	AID score 2, n=54	AID score 3, n=53	p value
Right, n (%)	74 (57.4)	14 (63.6)	32 (59.3)	28 (52.8)	0.644
Wound location toe/body/heel/crural/extensive, n (%)	57(44)/38 (30)/ 12 (9)/9 (7)/ 13 (10)	5 (23)/7 (32) /0 (0)/6 (27)/ 4 (18)	27 (50)/15 (28)/ 5 (9)/2 (4)/ 5 (9)*	25 (47)/16 (30) /7 (13)/1 (2)/ 4 (8) †	0.003
Arteriopathy, n (%)	64 (49.6)	4 (18.2)	7 (13.0)	53 (100) † ‡	<0.001
Bacterial infection, n (%)	113 (87.6)	9 (40.9)	51 (94.4)*	53 (100) †	<0.001
Foot deformity, n (%)	112 (86.8)	9 (40.9)	50 (92.6)*	53 (100) †	<0.001
Ankle brachial index	0.85±0.23	0.97±0.22	0.96±0.21	0.74±0.20 † ‡	<0.001
Dorsal skin perfusion pressure, mm Hg	44±23	59±29	60±17	29±13 † ‡	<0.001
Plantar skin perfusion pressure, mm Hg	43±24	65±39	54±17	31±15 † ‡	<0.001

*p<0.05 for AID 1 vs 2, †p<0.05 for AID 1 vs 3, ‡p<0.05 for AID 2 vs 3.

Table 2B. Breakdown of comprehensive treatment

Variable	Overall	AID score 1	AID score 2	AID score 3	p value
Revascularization for arteriopathy, n (%)	45 (70.3)	1 (25)	4 (57.1)	40 (75.5)	0.075
Debridement for bacterial infection, n (%)	113 (100)	9 (100)	47 (92.2)	53 (100)	0.08
Offloading for foot deformity, n (%)	101 (90.2)	9 (100)	47 (94)	45 (84.9)	0.177

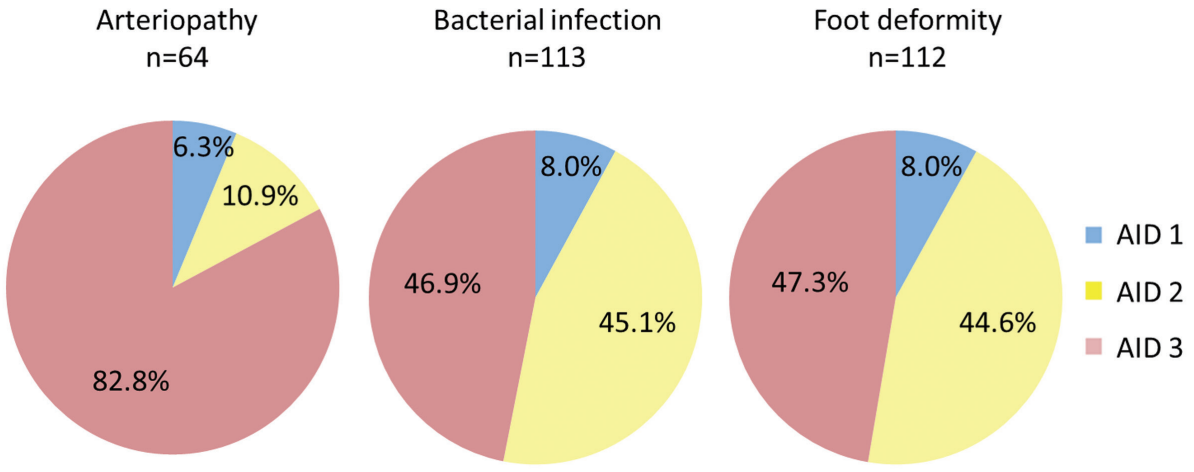
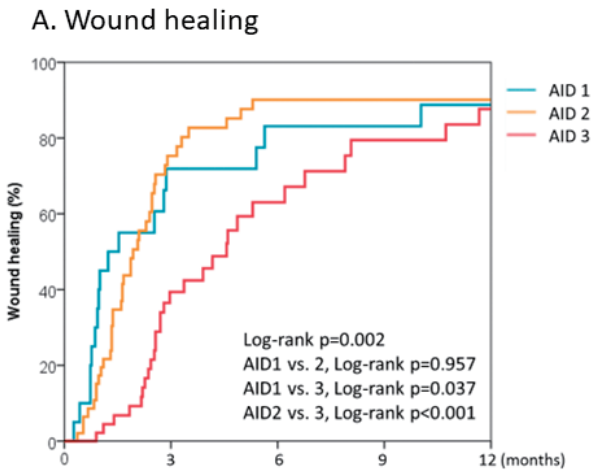
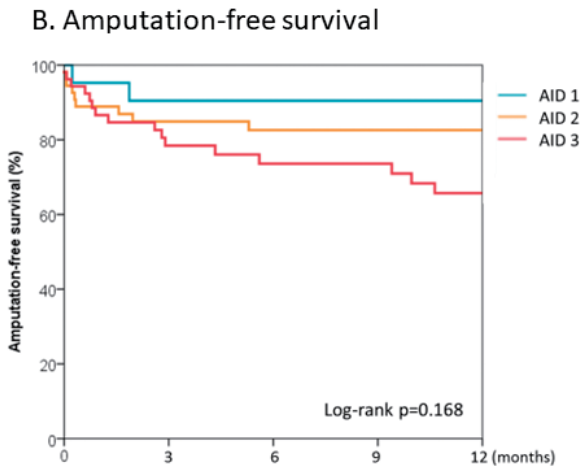


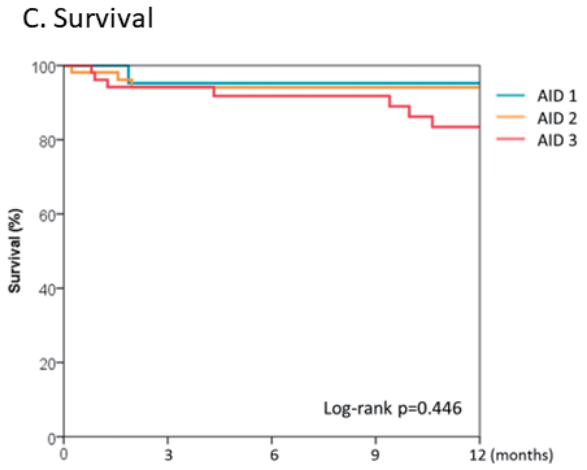
Figure 2. AID scores in arteriopathy, bacterial infection and foot deformity.



	Months	1	3	6	9	12
AID 1	Number at risk	11	5	3	3	2
	Percentage	45%	72%	83%	83%	89%
AID 2	Number at risk	38	10	3	3	2
	Percentage	17%	75%	90%	90%	90%
AID 3	Number at risk	44	21	9	5	3
	Percentage	2%	39%	63%	79%	88%



	Months	1	3	6	9	12
AID 1	Number at risk	20	18	16	16	16
	Percentage	95%	91%	91%	91%	91%
AID 2	Number at risk	46	42	35	33	32
	Percentage	89%	85%	83%	83%	83%
AID 3	Number at risk	45	37	30	28	25
	Percentage	87%	78%	74%	74%	66%



	Months	1	3	6	9	12
AID 1	Number at risk	21	18	16	16	16
	Percentage	95%	95%	95%	95%	95%
AID 2	Number at risk	50	46	40	38	37
	Percentage	98%	94%	94%	94%	94%
AID 3	Number at risk	50	43	35	33	30
	Percentage	96%	94%	92%	92%	83%

Figure 3. Kaplan-Meier estimates of A) wound healing, B) amputation-free survival, and C) overall survival.

difference in the intensity of revascularization (p=0.075), debridement (p=0.08), or offloading (p=0.177) among the three groups (Table 2B). Even in the AID 3 group, revascularization was performed in 75.5% of patients with arteriopathy, debridement in 100% of patients with infected wounds, and offloading in 84.9% of patients with foot deformities.

Seventeen patients (14.8%) died and 18 limbs (14%) were amputated during the study period. According to Kaplan-Meier analysis, wound healing was significantly (p=0.002) different among the AID scores of 1, 2, and 3 (Fig. 3A). Patients with AID 3 exhibited the most delayed wound healing (p=0.037 for AID 1 vs 3, p<0.001 for AID 2 vs 3). With AID-based comprehensive management, wound

healing rates of those with AID scores of 1, 2, and 3 at 12 months were 89%, 90%, and 88%, respectively. The amputation-free survival rate of AID 3 was 66% at 12 months, which was the lowest among the three groups, without being statistically significant (Fig. 3B). The overall survival stratified by the AID score was analyzed using the Kaplan-Meier method. The overall survival rate was 83% at 12 months, which was the lowest for AID 3, without being statistically significant (Fig. 3C).

Discussion

The main findings of this study were as follows: 1) arteriopathy was observed in 49% of DFUs; 2) 10.9% of arteriopathy cases were complicated by bacteria-infected wounds or foot deformities, and 82.8% of arteriopathy cases were complicated by both; 3) the intensity of revascularization for arteriopathy, debridement for infected wounds, and offloading for foot deformities was comparable among the AID score groups; and 4) Kaplan-Meier estimates stratified by AID scores demonstrated that those with AID scores of 3 exhibited the most delayed wound healing, but the wound healing rates at 12 months was comparable (89% in AID 1, 90% in AID 2, and 88% in AID 3) .

Considerable attention should be paid to arteriopathy, even in patients with DFUs. Traditional classifications for the assessment of wound severity, such as Fontaine[4] and Rutherford[5], are based only on arteriopathy. However, multiple disorders including arteriopathy, bacterial infection, neuropathy, foot deformity, and decubitus are associated with DFUs. To date, Meggitt-Wagner[6], SINBAD[7], University of Texas[8], Kobe[9], and WIfI[10] are available for wound assessment, given the importance of several factors in DFUs. The Meggitt-Wagner classification is based on the depth and area of the wound. The University of Texas and WIFI classifications are based on the depth or area of the wound, arteriopathy, and bacterial infection. The Kobe classification focuses on neuropathy, bacterial infection, and arteriopathy. The SINBAD classification is based on neuropathy, wound location, depth or area of the wound, arteriopathy, and bacterial infection. However, these classifications are not frequently utilized in clinical practice because of their complexity. Furthermore, these classifications underappreciate foot deformity, which is affected by neuropathy and a history of amputation[17]. Thus, a simple, easy-to-use, and clinically relevant classification of DFUs is urgently needed in vascular medicine practice. Here, we propose the AID classification based on arteriopathy, bacterial infection, and foot deformity.

In the present study, approximately half of the patients with AID 3 had coronary artery disease and end-stage renal disease requiring hemodialysis. This suggests that those who scored 3 on the AID classification were the most challenging subset of patients in clinical practice. Arteriopathy-induced microcirculation disorder was observed in 49.6% of patients with DFUs. Furthermore, AID 3 and AID 2 accounted for 82.8% and 10.9% of patients with arteriopathy, respectively. These findings suggest that approximately half of the patients with DFUs were affected by diabetic arteriopathy, and >90% coexist with bacterial infections and/or foot deformities. There was no significant difference in the intensity of revascularization for arteriopathy, debridement for bacterial-infected wounds, or offloading for foot deformity among patient with AID scores of 1, 2, and 3 (Table 2B). These findings suggest that the AID concept-guided comprehensive treatment should be practiced in any severity of DFUs.

Studies that have investigated the relationship between wound classification and wound healing are limited. Alexandrescu et al reported a significantly lower incidence of wound healing at 12

months using the Wagner grading; the incidence was 67% for grade 3-4 wounds, and 89% for grade 1-2 wounds[18]. Weaver et al reported that WIfI stage 3/4 wounds had a lower incidence of healing at 12 months than WIfI stage 1/2 wounds (57.2% vs 77.3%) did[19]. According to a study by Ince et al, which used the SINBAD classification, a score of ≧3 was associated with an increase in healing time[7]. In the present study, Kaplan-Meier estimates demonstrated different wound healing speeds among those with AID scores of 1, 2, and 3. Patients with AID 3 exhibited the most delayed wound healing. However, with an AID-based multidisciplinary treatment approach (revascularization in 76%, debridement in 100%, and offloading in 85%), the wound healing rate at 12 months among the three groups was comparable (88%, 89%, and 90%, in those with AID 3, AID 1, and AID 2, respectively). These findings suggest that the AID score can predict wound healing speed and that an AID-based comprehensive treatment could facilitate wound healing in approximately 90% of the most challenging DFUs. Focusing on each component of the AID classification facilitates treatment planning in clinical practice. Arteriopathy requires revascularization, bacterial infection requires debridement, and foot deformity requires offloading. AID concept-guided comprehensive treatment can ensure optimal treatment, which may result in similar wound healing rates for AID 1 and AID 2, and similar amputation-free survival rates for AID 2 and AID 3 at 12 months follow-up.

Our study had several limitations. First, it was retrospective observational study, which may be affected by confounding factors. Second, a relatively small number of patients were enrolled in this study. Third, the indications, timing, and intensity of revascularization, debridement, and offloading might have been heterogeneous. Finally, the AID classification does not consider the DFU complexity, such as the size, depth, or location of wounds, which might be associated with wound healing. The AID classification is intended to expeditiously appreciate the importance of the three essential components in the management of contemporary DFUs. Larger prospective studies are needed to confirm and externally validate the clinical significance of AID classification.

In conclusion, our study showed that diabetic arteriopathy is commonly complicated by both infected wounds (bacterial) and foot deformities in the context of DFUs. The AID classification was clinically relevant for wound healing stratification. Furthermore, AID concept-guided comprehensive treatment could facilitate wound healing in approximately 90% of all patients with DFUs at 12 months.

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All authors have no COI to declare regarding the present study.

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