

Utility of skin perfusion pressure values with the Society for Vascular Surgery Wound, Ischemia, and foot Infection classification system



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ABSTRACT

Objective: The addition of skin perfusion pressure (SPP) might enhance the predictive value of the Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIFI) classification system. The purpose of the present study was to evaluate the SPP for each WIFI classification stage among patients with foot wounds by cross-referencing the results of prospectively monitored limb outcomes and to derive the SPP criteria that could be combined with other measurements to grade ischemia for the WIFI classification.

Methods: From July 2015 to June 2017, patients with foot wounds that met the WIFI classification criteria were prospectively enrolled. We assessed the limbs using the WIFI ischemia grade without measuring the transcutaneous oxygen pressure but measured the SPP. After monitoring for 1 year, the predictability of the WIFI stages was analyzed according to whether the limbs had not healed (unchanged or worsened wounds, minor or major amputation, all-cause death) or had healed (improved or healed wounds) by comparing stages 1 and 2 with stages 3 and 4. We also statistically analyzed the SPP values that could be the boundary values between each ischemia grade and reevaluated the predictability of the WIFI stages with the boundary SPP values.

Results: We enrolled a total of 91 limbs for 76 patients (mean age, 70.5 ± 12.0 years). The mean SPP values stratified by ischemia grade 0 to 3 were 52.1, 41.1, 27.1, and 18.8 mm Hg, respectively (an SPP of <30 mm Hg indicates severe ischemia). After monitoring for 1 year, 19 of 48 limbs in stage 1 and 2 and 35 of 43 in stage 3 and 4 were in the nonhealed group and 29 limbs in stage 1 and 2 and 8 limbs in stage 3 and 4 were in the healed group. The SPP boundary values between each ischemia (I) grade were calculated as 45 mm Hg for I-0/I-1, 35 for I-1/I-2, and 25 for I-2/I-3. When jointly using the boundary SPP values, the ischemia grade changed for 23 limbs, altering the distribution of the WIFI stages and limb outcomes: 11 of 38 limbs in stage 1 and 2 and 43 of 53 in stage 3 and 4 were transferred to the nonhealed group. The sensitivity, efficiency, and negative predictive value of WIFI staging improved when staging with SPP: from 65% to 80%, 70% to 77%, and 60% to 71%, respectively.

Conclusions: The SPP boundary values that could be used with ischemia grade in the WIFI classification were identified as 45, 35, and 25 mm Hg. The addition of SPP could improve the accuracy of the evaluation. (*J Vasc Surg* 2019;70:1308-17.)

Keywords: Amputation; Foot wound; Skin perfusion pressure; SPP; Ischemia; WIFI classification

As the global population ages, patients with peripheral arterial disease and diabetes are increasing in number, and these patients have an increased risk of amputation owing to their greater propensity to develop nonhealing

wounds. Many complicated pathologic factors can threaten these patients' lower limbs, such as ischemia, infection, and delays in wound care for patients with diabetes. These factors must be evaluated comprehensively to accurately assess the severity of the wounds and the associated risk of limb amputation. Traditionally, determining which limbs had a high risk of amputation focused only on the potential for ischemia, signified by pain at rest and the ulcer or necrosis stage using the Fontaine et al¹ and Rutherford et al² classifications and critical limb ischemia criteria as defined in the TransAtlantic Inter-Society Consensus (TASC) document.³ In addition, dermatologists and plastic surgeons who treated many patients with diabetic foot ulcers used the Wagner classification.⁴ The Wagner grade is determined by the depth of a wound or the presence of myelitis or gangrene. The University of Texas classification for diabetic foot includes the wound depth and ischemia or infection among the items evaluated.^{5,6} However, that system does not consider the stage of the infection or ischemia. The Infectious Diseases Society

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of America (IDSA) system evaluates diabetic foot severity according to infection severity without accounting for ischemia.⁷ Because of the problems with comprehensive evaluation, the lower extremity threatened limb (Wound, Ischemia, and foot Infection [WIFI]) classification system was developed by the Society for Vascular Surgery in 2014.⁸ Research in various countries has been conducted of the WIFI classification system to verify the rationality and validity of the assessment tool in actual clinical practice.⁹⁻²⁴ WIFI has been useful for assessing 1-year amputation-free survival, predicting wound healing, and facilitating treatment strategy development.

However, a notable issue exists with using the WIFI classification in Japan because it evaluates ischemia according to the ankle-brachial index (ABI), ankle pressure (AP), toe pressure (TP), and transcutaneous oxygen pressure (TcPO₂). However, the measurement of TcPO₂ was not covered by health insurance in Japan until April 2016. Even after 2016, the use of TcPO₂ measured was not popular because of the many costs, including electroprobe maintenance and the use of disposable rings for probe fixation. Instead of the TcPO₂, the skin perfusion pressure (SPP) has been widely used in Japan. The SPP, similar to the TcPO₂, is a noninvasive microcirculation test that can assess ischemic limbs and wound healing potentials accurately, even for limbs with severely calcified noncompressible arteries,²⁵⁻³⁰ which occur frequently in patients with diabetes and those requiring dialysis. Studied for over 20 years in many countries, an SPP of ≥ 30 to 40 mm Hg has been considered necessary for wound healing²⁷⁻³⁶; the similar TcPO₂ value is ≥ 20 or 30 mm Hg. Moreover, the SPP does not require consumables and has a low maintenance cost, and it is reimbursed at the same medical fee per measurement as for TcPO₂ in Japan. In addition, the SPP has a short measurement time and less variance and might be a more reliable predictor of wound healing than the TcPO₂.^{28,32}

The purpose of the present study was (1) to evaluate the SPP for each WIFI classification stage among patients with foot wounds by cross-referencing the results of prospectively monitored limb outcomes and (2) to derive the SPP criteria that could be combined with other measurements to grade ischemia for the WIFI classification.

METHODS

The present study included patients who had visited the Department of Plastic Surgery at Kawasaki Medical School Hospital and Kawasaki Medical School General Medical Center from July 2015 to June 2017 and had met the set criteria, which were the same as those for the WIFI classification.⁸ The institutional review board of Kawasaki Medical School approved the study (reception no. 2150-4). All the study participants provided written informed consent.

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter, prospective, non-randomized cohort study
- **Key Findings:** Skin perfusion pressure (SPP) values and Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIFI) staging without transcutaneous oxygen pressure in 91 limbs derived the SPP boundary values for ischemia (I) grades I-0/I-1, I-1/I-2, and I-2/I-3. The corresponding values were 45, 35, and 25 mm Hg. Staging with SPP improved the sensitivity, efficiency, and negative predictive value from 65%, 70%, and 60% without SPP to 80%, 77%, and 71%, respectively.
- **Take Home Message:** Our results suggest that SPP could be useful to grade ischemia in the WIFI classification system. The SPP values that set the boundary between WIFI ischemia grades were 45 mm Hg for I-0/I-1, 35 mm Hg for I-1/I-2, and 25 mm Hg for I-2/I-3.

Lower limb evaluation. The limbs were initially evaluated using the WIFI classification,⁸ with the use of only ABI and/or AP and/or TP measurements to assess the ischemia grade. The SPP was also measured in all limbs on the same or different day after 15 minutes at rest. The patients were examined in the supine position with both legs horizontal and at an examination room temperature of $25^{\circ} \pm 2^{\circ}\text{C}$. A laser Doppler probe was placed beneath an 8-cm-wide blood pressure cuff at the dorsal and plantar aspects of the foot. The blood pressure cuff was inflated to 100 to 200 mm Hg to cause local circulatory arrest and gradually deflated. The cuff pressure at the point at which the laser Doppler instrument detected blood flow was recorded as the SPP value.²⁵⁻²⁹ The mean of the dorsal and plantar values was regarded as the SPP value for the limb. The same technician measured all ABI, AP, TP, and SPP values for all the patients in each facility.

The patients were prospectively followed up for 1 year after the evaluation date under a rigorous inpatient or outpatient management protocol that included appropriate wound treatment, internal medicine management, and revascularization, as necessary. If the same limb had multiple wounds, the worst wound was evaluated. For patients with wounds on both limbs, both wounds were evaluated. If a wound had healed, but a separate new wound had developed on the same or opposite limb, that limb was newly evaluated and treated as if it were a new limb on a separate patient. When revascularization changed the ischemia grade, we excluded the previous data, reevaluated the SPP and WIFI classification stage, and followed up the patient for 1 year after surgery. For severely infected wounds requiring early treatment, we performed surgery until the infection had been controlled, reevaluated the SPP and WIFI classification stage, and initiated the follow-up

protocol. The pertinent demographic-type information included the year the follow-up was started, patient sex, smoking history, and comorbidities, including diabetes mellitus, hypertension, hyperlipidemia, renal failure (with dialysis status), coronary artery disease, and cerebrovascular disease. Patients who did not complete 1 year of follow-up were excluded from the sample.

Outcomes after 1 year. At 1 year after the initiation of follow-up, data were obtained on limb amputations (major or minor), wound status (healed, improved, unchanged, worsened), and all-cause death. We defined the outcomes as follows: major amputations, amputations above the ankle; minor amputations, amputations below the ankle; wound healing, completely epithelialized wounds without minor or major amputation; improved wounds, wounds that had decreased in size but had not healed; and worsened wounds, wounds that had increased in size without amputation. Even though minor amputation wound healed, the limbs were not defined as healed but classified as minor amputation. Additionally, when patients who had undergone a minor amputation required a major amputation later or had died, the outcome was shifted to the worse outcome. We calculated the limb amputation rate by combining the minor and major amputations and calculated the wound healing rate by combining the healed and improved groups.

Calculation of SPP that could be jointly used as each ischemia grade. The boundary value of the SPP was analyzed using two methods and the SPP value for each ischemia grade obtained without using the TcPO₂. First, we used the Mahalanobis distance,³⁷ which is used for discriminant analysis between groups in a multivariate space. The formula shown in Table I holds true. Second, a scatter plot of the SPP values for each ischemia grade was created, and the boundary value of the SPP was obtained using an approximate straight line. Using the obtained boundary SPP value, we reevaluated the ischemia grades and Wifl stages and compared the Wifl predictabilities with and without the SPP criteria. The predictive value of the Wifl stages with and without SPP (ie, sensitivity, specificity, efficacy, positive predictive value, negative predictive value) were evaluated between stages 1 and 2 and stages 3 and 4. The outcome was classified as “nonhealed” (including unchanged, worsened, minor or major amputation, and death categories) or “healed” (including healed and improved categories).

Statistical analysis. All continuous variables are presented as the mean ± standard deviation. All statistical analyses were performed with Easy-R (EZR; Saitama Medical Center, Jichi Medical University; available at: <http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmedEN.html>), which is a graphic user interface for R, version 2.13.0 (The R Foundation for Statistical

Table I. Mahalanobis distance calculation formula

$\frac{x(\alpha - \beta) - \mu(\alpha)}{\sigma(\alpha)} = \frac{\mu(\beta) - x(\alpha - \beta)}{\sigma(\beta)}$
$x(\alpha - \beta) = \frac{\sigma(\alpha)\mu(\beta) + \sigma(\beta)\mu(\alpha)}{\sigma(\alpha) + \sigma(\beta)}$
<i>I, Ischemia grade; SPP, skin perfusion pressure; $x(\alpha - \beta)$, SPP boundary value between I-α and I-β; $\mu(\alpha)$, SPP mean value in I-α; $\mu(\beta)$, SPP mean value in I-β [$\mu(\alpha) < \mu(\beta)$]; $\sigma(\alpha)$, SPP standard deviation in I-α. $\sigma(\beta)$, SPP standard deviation in I-β [$\mu(\alpha) < \mu(\beta)$].</i>

Computing, Vienna, Austria). More precisely, it is a modified version of R commander, version 1.6-3, designed to add statistical functions frequently used in biostatistics.³⁸ At the Mahalanobis distance, the 95% confidence intervals for the SPP boundary values for each ischemic grade were obtained using the bootstrap method.³⁹

RESULTS

Initial evaluation. During the entry period, 103 consecutive patients with lower limb ulcers visited our institutions. Of the 103 patients, 76 (91 limbs), who had met the study criteria, participated in the present study (Table II). The mean patient age was 70.5 ± 12.0 years; 55 were men (72%). The comorbidities were diabetes in 63 patients (83%) and dialysis secondary to terminal renal failure for 21 patients (28%). Of the 76 patients, 61 had wounds on only 1 limb, 15 had wounds on both lower limbs, and 3 patients (3 limbs) had new wounds that had developed after a previous wound had healed. These were included as separate patients and separate limbs.

Revascularization was performed in 17 limbs, with obstruction confirmed in five during the observation period. The TP could not be measured in 51 limbs (13 with weak pressure and 38 with toe wounds or previous digital amputations). In limbs with weak TP, the ischemia grade was treated as I-3. In limbs without examinable toes, the ischemia grade was evaluated using only the AP and ABI.

The distribution of limbs according to the Wifl classification system and SPP value at baseline are shown in Table III. The number of limbs in each Wifl classification was 25 in stage 1, 23 in stage 2, 19 in stage 3, and 24 in stage 4. Ischemia (I) grade I-0 was common among limbs with stage 1 or 2, and I-3 was common for limbs with stage 4. No limb had stage foot infection 3 because severe infections had been controlled before our evaluations. The mean SPP values according to ischemia grade 0 to 3 were 52.1, 41.1, 27.1, and 18.8 mm Hg, respectively.

Outcomes after 1 year. The 1-year limb and patient outcomes are shown in Table IV. Of the 91 limbs, nine were amputated despite previous revascularization. Even when the Wifl classification evaluation was performed without using the TcPO₂, the more severe the stage, the greater the incidence of large amputation and mortality.

Table II. Patient demographic data and comorbidities (N = 76 patients)

Characteristic	Value
Age, years	70.5 ± 12.0
Sex	
Male	55 (72)
Female	21 (28)
Smoking status	
Never	29 (38)
Former	28 (37)
Current	19 (25)
Comorbidities	
Diabetes mellitus	63 (83)
Hypertension	56 (74)
Hyperlipidemia	46 (61)
Coronary artery disease	24 (32)
Cerebrovascular disease	21 (28)
Dialysis	21 (28)

Data are presented as mean ± standard deviation for continuous variables and as number (%) for categorical variables.

The limb amputation rate, combining minor and major amputations, stratified by the Wifl stage was 8% (2 of 25 limbs) in stage 1, 22% (5 of 23) in stage 2, 26% (5 of 19) in stage 3, and 42% (10 of 24 limbs) in stage 4. All 11 patients who died had wounds on only one limb. In the lower Wifl stages, more limbs had healed or improved. The wound healing rate, combining healed and improved wounds, was 72% (18 of 25 limbs) in stage 1, 48% (11 of 23) in stage 2, 37% (7 of 19) in stage 3, and 3% (1 of 24 limbs) in stage 4.

Cases with divergence between SPP value and Wifl ischemia grade evaluated without TcPO₂. Among the 65 limbs with ischemia grade 0 to 1, 13 (20%) of 65 patients had an SPP of <35 mm Hg. After 1 year, 7 of these limbs had undergone amputation: 3 had required minor amputations, 1 a major amputation, and 3 patients had died after amputation (Table V). Of these seven patients, six (86%) had had diabetes and dialysis was required for five (71%). Of the seven limbs, three in stage 2 had required amputation (2 minor and 1 major) and all three patients had had diabetes. Additionally, two limbs in stage 3 and four had required a major amputation. All three major amputations were in patients who required dialysis and two patients had died after amputation. Two limbs had an ABI of >1.3. Both patients had required dialysis and had undergone minor amputations (the patient with a TP of 55 mm Hg had died after the minor amputation).

Analysis of boundary value of SPP in each ischemic grade. According to the Mahalanobis distance, the SPP boundary values for each ischemia grade were 45.9 mm Hg for I-0/I-1 (Fig 1, A), 32.9 for I-1/I-2 (Fig 1, B),

and 22.6 for I-2/I-3 (Fig 1, C). The 95% confidence intervals between each of the SPP boundary values were 41.2 to 50.1 mm Hg for I-0/I-1, 25.6 to 38.5 for I-1/I-2, and 19.4 to 26.6 for I-2/I-3. A linear approximation was created from a scatter plot of the SPP values for each ischemia grade. Those values were 45.7 mm Hg for I-0/I-1, 34.8 mm Hg for I-1/I-2, and 23.9 mm Hg for I-2/I-3 (Fig 2).

From these 2 results, we developed an easy-to-use, well-partitioned set of SPP values that corresponded to the boundary between each ischemia grade: 45 mm Hg for I-0/I-1, 35 mm Hg for I-1/I-2, and 25 mm Hg for I-2/I-3. We reevaluated the ischemia grades and Wifl classification clinical stages. A total of 23 limbs shifted to a worse ischemic grade: 6 from I-0 to I-1, 5 from I-0 to I-2, 3 from I-0 to I-3, 3 from I-1 to I-2, 2 from I-1 to I-3, and 4 from I-2 to I-3. These included all the aforementioned 13 limbs with divergence between the ischemia grade (I-0 to I-1) and SPP value (<35 mm Hg). Thus, the number of limbs in clinical stage 1 and 2 decreased and those in stage 3 and 4 increased, and the outcome distribution changed (Table VI).

After reevaluation of the Wifl stage using the SPP criteria, the sensitivity (from 65% to 80%), efficiency (from 70% to 77%), and negative predictive value (from 60% to 71%) had improved compared with Wifl staging without the SPP (Table VII). Although the specificity had been slightly reduced (from 78% to 73%), the positive predictive value remained high (81%).

DISCUSSION

In the present study, we attempted to define the criteria for SPP values that could be used with the Wifl classification scheme for patients with threatened lower limbs from diverse causes, ranging from a diabetic foot to a severe ischemic limb. We prospectively traced the limb outcomes and confirmed the validity of the ischemia stratification using the SPP. We have proposed SPP values of 45, 35, and 25 mm Hg for the boundary values between I-0 and I-1, I-1 and I-2, and I-2 and I-3, respectively. We found that the reevaluated Wifl stages using the SPP boundary values improved the sensitivity, efficiency, and negative predictive value and retained a high positive predictive value. Also, we found that ABI, AP, and TP alone were sometimes insufficient for evaluating the severity of ischemia, especially for patients with diabetes or those requiring dialysis. Our results suggest the possibility of adding SPP values to improve the accuracy of the evaluation.

We first stratified patients according to the Wifl classification system using only the ABI, AP, and TP for the ischemia evaluation. We then evaluated the SPP values for each ischemia grade and each clinical stage. The SPP values were lower when the ischemia grade was more severe, confirming that the SPP value can enable accurate evaluation of ischemic limbs. As the clinical stage progressed, the 1-year outcome and the wound

Table III. Distribution of limbs according to Wound, Ischemia, and foot Infection (WIFI) classification system⁸

Clinical stage	Total limbs	I-0 (n = 50); SPP 52.1 ± 18.1 mm Hg		I-1 (n = 15); SPP 41.1 ± 14.1 mm Hg		I-2 (n = 7); SPP 27.1 ± 9.8 mm Hg		I-3 (n = 19); SPP 18.8 ± 8.2 mm Hg	
		Grade	Limbs	Grade	Limbs	Grade	Limbs	Grade	Limbs
Stage 1	25								
		W0, fl-0	0	W0, fl-0	0				
		W0, fl-1	0	W1, fl-0	2				
		W1, fl-0	18						
		W1, fl-1	5						
Stage 2	23								
		W0, fl-2	0	W0, fl-1	0	W0, fl-0	0	W0, fl-0	0
		W1, fl-2	0	W1, fl-1	2	W0, fl-1	0		
		W2, fl-0	10			W1, fl-0	2		
		W2, fl-1	9						
Stage 3	19								
		W0, fl-3	0	W0, fl-2	0	W0, fl-2	0	W0, fl-1	0
		W1, fl-3	0	W1, fl-2	0	W1, fl-1	1	W0, fl-2	0
		W2, fl-2	5	W-2 fl-0	3	W2, fl-0	1	W1, fl-0	3
		W3, fl-0	0	W2, fl-1	2			W1, fl-1	2
		W3, fl-1	2						
Stage 4	24								
		W2, fl-3	0	W0, fl-3	0	W0, fl-3	0	W0, fl-3	0
		W3, fl-2	1	W1, fl-3	0	W1, fl-2	0	W1, fl-2	0
		W3, fl-3	0	W2, fl-2	3	W1, fl-3	0	W1, fl-3	0
				W2, fl-3	0	W2, fl-1	1	W2, fl-0	3
				W3, fl-0	0	W2, fl-2	1	W2, fl-1	4
				W3, fl-1	2	W2, fl-3	0	W2, fl-2	1
				W3, fl-2	1	W3, fl-0	0	W2, fl-3	0
				W3, fl-3	0	W3, fl-1	0	W3, fl-0	3
						W3, fl-2	1	W3, fl-1	1
						W3, fl-3	0	W3, fl-2	2
								W3, fl-3	0

SPP, Skin perfusion pressure (mean ± standard deviation); fl, foot infection grade; I, ischemia grade; W, wound grade. Data are presented as number of limbs.

Table IV. Wound, Ischemia, and foot Infection (WIFI) classification and limb outcomes after 1-year follow-up

WIFI clinical stage	Limbs (N = 91)	1-Year outcomes						
		Healed	Improved	No change	Worsened	Minor amputation	Major amputation	Death
Stage 1	25	11 (44)	7 (28)	5 (20)	0 (0)	2 (8)	0 (0)	0 (0)
Stage 2	23	6 (26)	5 (22)	6 (26)	0 (0)	5 (22)	0 (0)	1 (4)
Stage 3	19	4 (21)	3 (16)	4 (21)	0 (0)	4 (21)	1 (5)	3 (16)
Stage 4	24	0 (0)	1 (3)	3 (13)	3 (13)	5 (21)	5 (21)	7 (29)

Categorical data are presented as number of limbs (row %).

healing status were both poor. In particular, major amputations and wound worsening were more common with stage 4 than for the other stages. Mills et al¹⁸ reported no significant differences between stage 2 and 3 with

respect to the 1-year amputation-free survival rate according to multiple follow-up studies; the major amputation rates showed little difference between stage 2 and 3, irrespective of whether the SPP had been used

Table V. Cases of amputation with divergence between skin perfusion pressure (SPP) and Wound, Ischemia, and foot Infection (WIFI) ischemia grade

Case No.	Age, years	Sex	ABI	AP, mm Hg	TP, mm Hg	W	I	fi	Wifi stage	1-Year outcome	SPP, mm Hg	DM	HD
1	80	M	0.83	146	NA	2	0	1	2	Major amputation; death	30	Yes	Yes
2	50	M	1.16	188	NA	3	0	1	3	Major amputation	23	Yes	Yes
3	62	M	1.87	213	NA	2	0	1	2	Minor amputation	19	Yes	Yes
4	81	F	0.70	95	NA	1	1	1	2	Minor amputation	34	Yes	No
5	78	M	0.78	109	NA	2	1	2	4	Minor amputation	31	Yes	No
6	77	M	1.03	92	80	3	1	1	4	Major amputation; death	22	No	Yes
7	75	F	1.30	219	55	2	1	0	3	Minor amputation; death	11	Yes	Yes

ABI, Ankle-brachial index; AP, ankle pressure; DM, diabetes mellitus; F, female; fi, foot infection; HD, hemodialysis; I, ischemia; M, male; NA, not available (could not be measured due to the toe wounds); TP, toe pressure; W, wound.

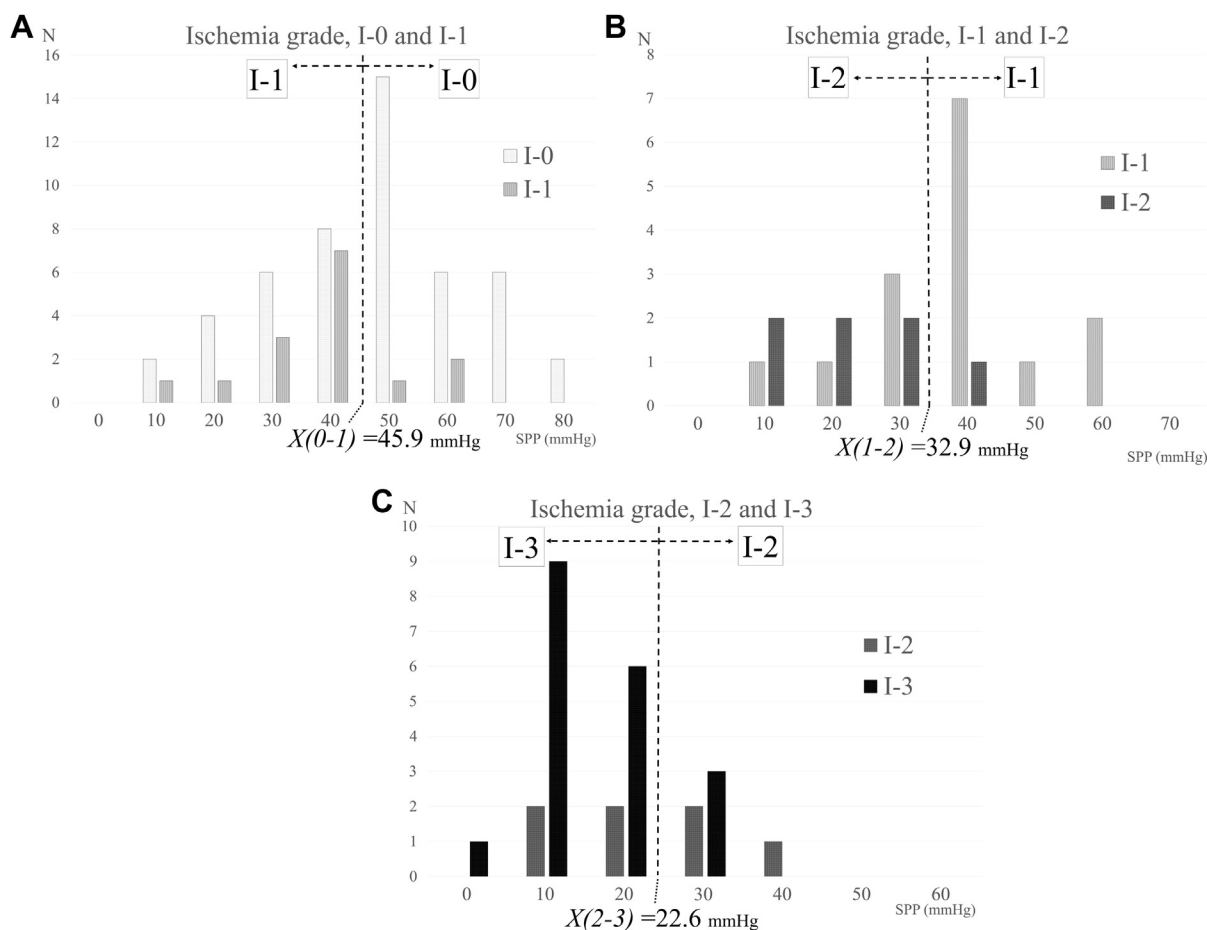


Fig 1. Histogram of skin perfusion pressure (SPP) values according to ischemia (I) grade, I-0/I-1, I-1/I-2, and I-2/I-3. $X(\alpha - \beta)$ indicates the SPP boundary value between I - α and I - β calculated using the Mahalanobis distance $x(\alpha - \beta) = \frac{\sigma(\alpha)\mu(\beta) + \sigma(\beta)\mu(\alpha)}{\sigma(\alpha) + \sigma(\beta)}$. This value represents the boundary value of SPP of I- α and I- β . From this value, the dotted line indicates that the left belongs to I- α and the right belongs to I- β ; $\mu(x)$ indicates the SPP mean value in I-x; $\sigma(x)$, the SPP standard deviation in I-x. **A**, Histogram of SPP values according to ischemia grade 0 and 1: $X(0 - 1) = 45.9$ mm Hg; for I-0, n = 50; $\mu(0) = 52.1$ mm Hg; $\sigma(0) = 18.1$; for I-1, n = 15; $\mu(1) = 41.1$ mm Hg; $\sigma(1) = 14.1$. **B**, Histogram of SPP values according to ischemia grade 1 and 2: $X(1 - 2) = 32.9$ mm Hg; for I-1, n = 15; $\mu(1) = 41.1$ mm Hg; $\sigma(1) = 14.1$; for I-2, n = 7; $\mu(2) = 27.1$ mm Hg; $\sigma(2) = 9.8$. **C**, Histogram of SPP values according to ischemia grade 2 and 3: $X(2 - 3) = 22.6$ mm Hg; for I-2, n = 7; $\mu(2) = 27.1$ mm Hg; $\sigma(2) = 9.8$; for I-3, n = 19; $\mu(3) = 18.8$ mm Hg; $\sigma(3) = 8.2$.

in our study. However, the minor amputation rate was greater in stage 3 than in stage 2 when the SPP was used. Therefore, SPP, because it assesses the

microcirculation, might be more useful for predicting the distal foot prognosis. Nevertheless, our study included only a small number of patients. Future studies

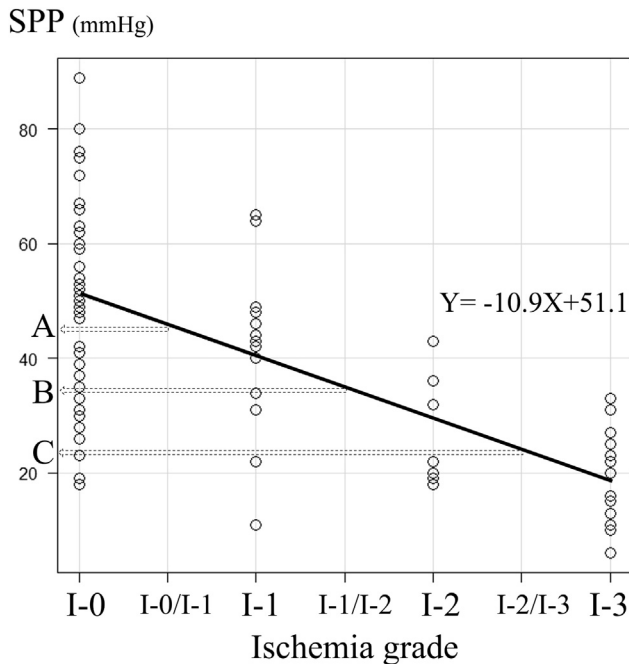


Fig 2. Scatter plot of skin perfusion pressure (SPP) values for each ischemia (I) grade. The intersection of the approximate straight line and the center points of each ischemia grade were taken as the boundary value of the SPP. $SPP = -10.9 \times X + 51.1$. The boundary value of SPP can be obtained by assigning the following values to X: I-0/I-1, 0.5; I-1/I-2, 1.5; I-2/I-3, 2.5. A, Boundary value between I-0 and I-1, 45.7 mm Hg. B, Boundary value between I-1 and I-2, 34.8 mm Hg. C, Boundary value between I-2 and I-3, 23.9 mm Hg.

are needed to determine whether the two stages should remain separated or can be combined into one moderate risk stage.

After confirming that the SPP evaluation was appropriate and determining the criteria for using SPP combined with the ischemia grade in the Wiffl classification, the boundary values obtained from the Mahalanobis distance discriminant analysis and those obtained from the linear approximation in the scatter plot of SPP values were very similar. From these results, we identified easy-to-use, well-partitioned criteria and have proposed the following values: SPP I-0 and I-1, 45 mm Hg; SPP I-1 and I-2, 35 mm Hg; SPP I-2 and I-3, 25 mm Hg (Table VIII). The Mahalanobis distance is a method to find equal distances from 2 groups in multivariate space. To find the boundary between the two groups, we used the Mahalanobis distance to analyze the SPP boundary value in our study. Other analysis methods could be available; however, this method was considered simple and easy to calculate. Because the standard deviation is used as the denominator for the calculation formula, if the number of samples were small, a possibility of error in the result exists, which seems to be the limit of using the Mahalanobis distance. The 95% confidence intervals between each of the SPP boundary values were

calculated as 41.2 to 50.1 mm Hg for I-0/I-1, 25.6 to 38.5 mm Hg for I-1/I-2, and 19.4 to 26.6 mm Hg for I-2/I-3. These results suggested that a boundary value 45, 35, and 25 mm Hg would be reasonable. The ischemia grade I-1 and I-2 boundary SPP value of 35 mm Hg were also in line with the 30- to 40-mm Hg value that was previously reported as the desired SPP for wound healing in threatened lower limbs.²⁷⁻³⁶ According to the TP and SPP correlation values reported by Tsai et al,⁴⁰ a TP of 60 mm Hg will correspond to an SPP of 53.6 mm Hg, a TP of 40 mm Hg to an SPP of 36.9 mm Hg, and a TP of 30 to an SPP of 28.6 mm Hg ($TP [mm Hg] = 1.20 \times SPP [mm Hg] - 4.26$), supporting the validity of the 45, 35, and 25 mm Hg SPP boundary values we have proposed.

Of the 65 limbs assessed as mild (I-0, I-1) in the evaluation of ischemia using only ABI, AP, and TP, 13 limbs (20%) had an SPP value of <35 mm Hg. Many of these limbs had had poor outcomes after 1 year. In particular, all the limbs that had required major amputations were limbs of diabetic patients requiring dialysis. Additionally, one diabetic patient requiring dialysis with a mild low TP underwent a minor amputation and died. These results suggest that the ischemic grades could have been underestimated in patients with noncompressible arteries when only the ABI, AP, and TP were used. Numerous patients currently undergo dialysis in Japan.⁴¹ Most of these patients have diabetic kidneys, and because they survive for a long time after initiating dialysis, many patients have peripheral arterial disease and severely calcified arteries. The Wiffl classification includes an annotation to use the TP and TcPO₂ when the ABI is >1.3 in the evaluation.⁸ However, our results showed that using only the TP measurement without the TcPO₂ can be insufficient for such patients. Although Salaun et al⁴² reported that the TP and TcPO₂ are the best available hemodynamic measurements for critical limb ischemia, the TP measurement is frequently difficult to perform because of toe wounds and digital artery calcification. When we used the SPP criteria we have proposed, the ischemia grades became more severe for 23 limbs, including the 13 limbs that likely had noncompressible arteries and the prognoses were evaluated more accurately. Additionally, the reevaluated Wiffl stages with the SPP boundary values improved in sensitivity (from 65% to 80%), efficiency (from 70% to 77%), and negative predictive value (from 60% to 71%), retaining a high positive predictive value (81%). Therefore, determination of the SPP can be useful for a more accurate evaluation of limb ischemia, including when the TcPO₂ cannot be used.

Japan does not have podiatrists, unlike Europe and the United States. Therefore, the lower extremity threatened limb will be treated by a multidisciplinary medical team, including cardiovascular surgeons, cardiologists, endocrinologists, nephrologists, dermatologists, and plastic surgeons, as was the case for our patients. The Wiffl

Table VI. Wound, Ischemia, and foot Infection (WIFI) classification and 1-year outcomes after correction using skin perfusion pressure (SPP)

WIFI clinical stage	Limbs (N = 91)	1-Year outcomes						
		Healed	Improved	No change	Worsened	Minor amputation	Major amputation	Death
Stage 1	21↓	10↓ (48)	6↓ (29)	3↓ (14)	0 (0)	2 (9)	0 (0)	0 (0)
Stage 2	17↓	6 (35)	5 (29)	4↓ (24)	0 (0)	2↓ (12)	0 (0)	0↓ (0)
Stage 3	22↑	5↑ (22)	3 (14)	7↑ (32)	0 (0)	5↑ (23)	0↓ (0)	2↓ (9)
Stage 4	31↑	0 (0)	2↑ (6)	4↑ (13)	3 (10)	7↑ (23)	6↑ (19)	9↑ (29)

Categorical data are presented as number of limbs (row %); arrows indicate change in number of limbs before and after use of SPP.

Table VII. Limb outcome and predictive values of Wound, Ischemia, and foot Infection (WIFI) stages before and after adding skin perfusion pressure (SPP) criteria

Variable	Without SPP			With SPP		
	Nonhealed	Healed	Total	Nonhealed	Healed	Total
Stage 3-4	35	8	43	43	10	53
Stage 1-2	19	29	48	11	27	38
Total	54	37	91	54	37	91
Sensitivity, %	35/54 = 65			43/54 = 80		
Specificity, %	29/37 = 78			27/37 = 73		
Efficiency, %	64/91 = 70			70/91 = 77		
PPV, %	35/43 = 81			43/53 = 81		
NPV, %	29/48 = 60			27/38 = 71		

NPV, Negative predictive value; PPV, positive predictive value.

Nonhealed group included unchanged, worsened, minor or major amputation, and death; healed group included healed and improved.

Table VIII. Proposed skin perfusion pressure (SPP) criteria for ischemic grades

Grade	ABI	AP, mm Hg	TP, TcPO ₂ , mm Hg	SPP, mm Hg
0	≥0.80	>100	≥60	≥45
1	0.6-0.79	70-100	40-59	35-44
2	0.4-0.59	50-70	30-39	25-34
3	≤0.39	<50	<30	<25

ABI, Ankle-brachial index; AP, ankle pressure; TP, toe pressure; TcPO₂, transcutaneous oxygen pressure.

classification that comprehensively evaluates multiple elements tends to clarify which elements will be problematic in the limbs. This allowed all the staff to share the information on the severity and prognosis of the limbs. This will also be useful for overcoming barriers between different professions and treating the lower extremity threatened limb. We hope that these research results will contribute greatly to enabling the use of SPP to facilitate optimization of the WIFI classification in the evaluation of ischemia, not only in Japan, but also in facilities around the world that use the SPP instead of the TcPO₂.

The present study had several limitations. First, the number of patients was small. In the future, we plan to include more patients and study previous patients retrospectively to verify whether the defined SPP values are valid. We also hope that the SPP criteria we have defined will be validated in more patients and institutions regarding their validity in the WIFI classification system. Second, because

we could not measure the TcPO₂, we could not evaluate the ischemia grades using the conventional WIFI classification. Therefore, some of our results might have been flawed, including the corresponding SPP value calculations. In the future, we hope to analyze the SPP values by directly comparing the ischemia grades using the TcPO₂, clinical stage, and SPP.

CONCLUSIONS

The results from the present study suggest that the SPP could be useful for grading ischemia in the WIFI classification system. The SPP values that set the boundary between WIFI ischemia grades were 45 mmHg for I-0/I-1, 35 mm Hg for I-1/I-2, and 25 mm Hg for I-2/I-3 in the present study. Especially for patients with diabetes or those requiring dialysis, the addition of SPP to the ABI, AP, and TP could improve the accuracy of the ischemia evaluation, even in cases for which the TcPO₂ cannot be used.

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