

Hallucal thenar index: A new index to detect peripheral arterial disease using laser speckle flowgraphy

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Abstract

Objectives: Laser speckle flowgraphy is a technology using reflected scattered light for visualization of blood distribution, which can be used to measure relative velocity of blood flow easily without contact with the skin within a short time. It was hypothesized that laser speckle flowgraphy may be able to identify foot ischemia. This study was performed to determine whether laser speckle flowgraphy could distinguish between subjects with and without peripheral arterial disease.

Materials and methods: All subjects were classified based on clinical observations using the Rutherford classification: non-peripheral arterial disease, class 0; peripheral arterial disease group, class 2–5. Rutherford class 6 was one of the exclusion criteria. Laser speckle flowgraphy measured the beat strength of skin perfusion as an indicator of average dynamic cutaneous blood flow change synchronized with the heartbeat. The beat strength of skin perfusion indicates the strength of the heartbeat on the skin, and the heartbeat strength calculator in laser speckle flowgraphy uses the blood flow data to perform a Fourier transform to convert the temporal changes in blood flow to a power spectrum. A total of 33 subjects with peripheral arterial disease and 40 subjects without peripheral arterial disease at a single center were prospectively examined. Laser speckle flowgraphy was used to measure hallucal and thenar cutaneous blood flow, and the measurements were repeated three times. The hallucal and thenar index was defined as the ratio of beat strength of skin perfusion value on hallux/beat strength of skin perfusion value on ipsilateral thenar eminence. The Mann–Whitney *U*-test was used to compare the median values of hallucal and thenar index and ankle brachial index between the two groups. A receiver operating characteristic curve for hallucal and thenar index of beat strength of skin perfusion was plotted, and a cutoff point was set. The correlation between hallucal and thenar index of beat strength of skin perfusion and ankle brachial index was explored in all subjects, the hemodialysis group, and the non-hemodialysis (non-hemodialysis) group.

Results: The median value of the hallucal and thenar index of beat strength of skin perfusion was significantly different between subjects with and without peripheral arterial disease (0.27 vs. 0.87, respectively; $P < 0.001$). The median value of ankle brachial index was significantly different between subjects with and without peripheral arterial disease (0.8 vs. 1.1, respectively; $P < 0.001$). Based on the receiver operating characteristic of hallucal and thenar index, the cutoff was 0.4416 and the sensitivity, specificity, positive predictive value, and negative predictive value were 68.7%, 95%, 91.7%, and 77.6%, respectively. The correlation coefficients of all subjects, the hemodialysis group, and the non-hemodialysis group were 0.486, 0.102, and 0.743, respectively.

Conclusions: Laser speckle flowgraphy is a noninvasive, rapid, and widely applicable method. Laser speckle flowgraphy using hallucal and thenar index would be helpful to determine the differences between subjects with and without peripheral arterial disease. The correlation between hallucal and thenar index of beat strength of skin perfusion and ankle brachial index indicated that this index was especially useful in the non-hemodialysis group.

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Keywords

Mean blur rate, beat strength of skin perfusion, ankle brachial index, hemodialysis

Introduction

Examination of the feet and screening inspection for peripheral arterial disease (PAD) can avoid amputation of the leg in many cases.¹ Accurate evaluation of blood flow in the foot is important to prevent deterioration of PAD. Ankle brachial index (ABI) and/or skin perfusion pressure (SPP) are frequently used in preliminary evaluation of blood flow in the feet.^{2,3} Although these inspections are highly accurate, they also have several problems. ABI was reported to show sensitivity of 80% and specificity of 95% with 0.90 as a cutoff.⁴ It is unclear whether ABI is an indicator of blood flow in the foot because it measures ankle blood pressure. SPP was reported to show sensitivity of 76.1% and specificity of 84.2% with 40 mmHg as a cutoff.⁵ In this method, patients experience strong discomfort and require long rest times with a cuff pressed against the foot.

Laser speckle flowgraphy (LSFG) can be used to determine cutaneous blood flow without making contact with the skin.⁶⁻⁸ There have been several reports of the evaluation of ocular blood flow with LSFG,⁹⁻¹³ but there has been only one report of the use of this method to determine cutaneous blood flow in the leg.⁶

It was hypothesized that LSFG may indicate foot ischemia and the condition of blood flow in the foot could be evaluated using the ratio of values measured at hallux and thenar eminence as a reference based on ABI. This study was performed to examine the applicability of the hallux thenar index (HTI) determined by LSFG to distinguish between subjects with and without PAD.

Materials and methods

Laser speckle flowgraphy

LSFG irradiates the skin with a near-infrared laser (wavelength 830 nm) from a distance of 24 cm, and a CCD camera captures reflected light. The image sensor within the LSFG processes this signal to display a two-dimensional map on the monitor (Figure 1).

The measurement time is 4 s, and the measurement range is 20 × 15 cm. Up to six regions of interest (ROIs) can be set anywhere in the monitor.

The principle of the LSFG is that laser irradiation of the skin forms a random speckled pattern from which

reflected light and light scattered from erythrocytes in the blood interfere with each other. This speckled pattern changes with the movement of erythrocytes, and the velocity of the scattering pattern is correlated with the velocity of erythrocytes in the blood. This is defined as the mean blur rate (MBR). Each pixel on the blood map has a blood flow value. Areas where erythrocytes are moving quickly have a high value, while areas where their movement is slow have a low value. The blood map of the LSFG indicates blood flow velocity in pseudocolor, with red, yellow, pea green, sky blue, blue, and black in descending order of blood flow velocity.

The laser is attenuated in the deeper tissue, so the blood flow in blood vessels in the foreground contributes more to the change in speckled pattern so it is difficult to determine absolute velocity with LSFG.

The beat strength of skin perfusion (BSSP) indicates the strength of the heartbeat to the skin. The LSFG can sense the heartbeat, align the beginning of one or more heartbeats, and choose a similar frequency. The LSFG made the averaged blood map that the heartbeat map creation part in the LSFG could average along the time axis in one heartbeat. LSFG can analyze blood flow changes in one heartbeat to distinguish an arterial sharp rising waveform from a venous dull rising waveform in this averaged blood map. LSFG chooses the arterial sharp rising waveform and produces blood flow data along the time axis in the region of interest. The heartbeat strength calculator uses the blood flow data to perform a Fourier transform to convert the temporal

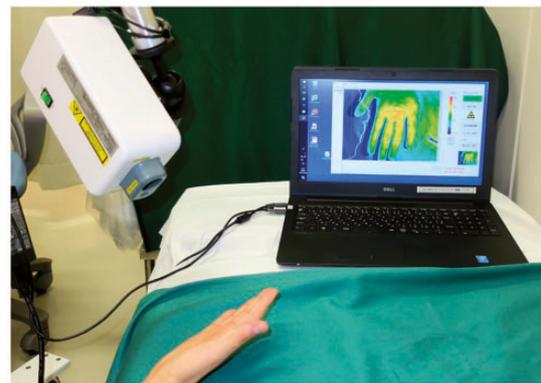


Figure 1. Laser speckle flowgraphy involves irradiation of the right hand with near infrared light and shows blood flow with pseudocolor on the monitor.

changes in blood flow to a power spectrum; this is the BSSP.

Two laser pointers are projected from the camera and are designed to overlap at a distance of 24 cm from target. A measurement is taken for 4 s by clicking the measurement button on the monitor and the process is completed.

Reproducibility was good as the coefficient of variation of optic disc blood vessels and retinal blood vessels was 3%.¹⁴ As near-infrared light cannot pass through black areas, it is not possible to obtain precise measurements in areas with skin pigmentation or nevi.

Subjects. This prospective observational study was approved by the ethics committee of Shinshu University School of Medicine.

Subjects were randomly recruited for inclusion in the study from among patients presenting to Shinshu University Hospital between 2017 and 2019. Subjects with PAD were inpatients who had physical symptoms of foot ischemia and/or $ABI < 0.9$ and were admitted for catheter treatment of the lower limbs at the cardiology department. Subjects without PAD were outpatients and/or inpatients at the plastic surgery and/or nephrology departments without podiatry symptoms.

A total of 39 patients (age 47–93 years) with PAD and who had not undergone endovascular therapy were eligible for inclusion in the study (PAD group). The exclusion criteria included foot amputation, tremor at rest, and foot infection. After application of the exclusion criteria, 33 patients were selected for inclusion in this study. The PAD group consisted of patients in stages 2–5 according to the Rutherford classification. A total of 40 subjects without PAD (age 44–95 years) also participated in this study (non-PAD group).

All subjects provided informed consent to participate in this study.

Measurement. All subjects underwent LSFG examination in the supine position (LSFG-PFI®; Softcare, Fukuoka, Japan). Measurements were performed on the lesion side in the PAD group and on the right

side in the non-PAD group. At the same time, ABI was measured on the ipsilateral side.

The regions of interest (ROIs) were set as the thenar eminence and hallux (Figure 2). As the skin perforators issue from the medial plantar artery to the hallux,¹⁵ and from the superficial and deep palmar arches to the thenar eminence,¹⁶ these areas were considered to be appropriate for assessing the status of perforators from the major limb arteries. Measurements were made on these areas three times for 4 s each time to obtain the average values of the mean blur rate (MBR) and beat strength of skin perfusion (BSSP).

First, ABI, HTI of BSSP, and MBR were compared between the two groups. Second, whether the HTI with LSFG could distinguish between patients with and without PAD by receiver operating characteristic (ROC) curve analysis was examined. In addition, ABI ROC curve analysis was also performed. Third, the study population was divided into the hemodialysis group (HD group) and non-HD group. The correlation coefficients were examined between HTI and ABI in all subjects, the HD group, and the non-HD group. The several degrees of arterial calcification in hemodialysis patients make it difficult to accurately assess lower limb ischemia using ABI. This subgroup was examined to evaluate whether the LSFG was also affected by arterial calcification.

Statistical analysis. Data are presented as the mean \pm standard deviation, median [interquartile range], or number (%) and were compared using the Mann-Whitney *U*-test or chi-square test.

In all analyses, $P < 0.05$ was taken to indicate statistical significance. Statistical analyses were performed using IBM SPSS version 23 (IBM, Chicago, IL).

Results

Characteristics of subjects with and without PAD. The background characteristics of the PAD group and non-PAD group are shown in Table 1. The number of females was significantly lower in the PAD group

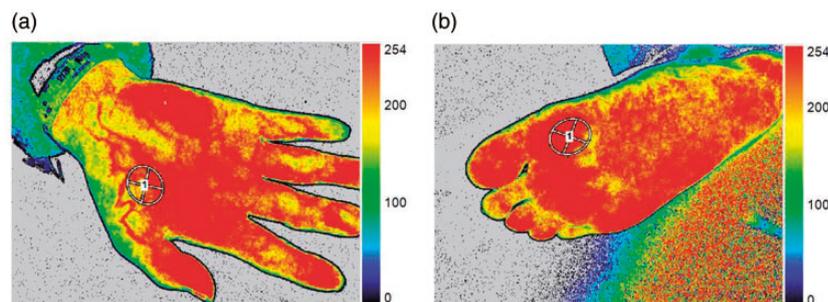


Figure 2. The results are shown as color variations. The regions of interest were set as (a) the thenar eminence and (b) the hallux.

Table 1. Characteristics of all subjects, subjects with PAD, and subjects without PAD.

	All	Subjects with PAD	Subjects without PAD	P
Limbs	73	33	40	
Age	70.6 ± 11.8	71.2 ± 12.2	69.7 ± 12.4	0.365
Female sex	22 (30%)	4 (12%)	18 (45%)	0.002
hypertension	47 (64%)	21 (64%)	27 (68%)	0.709
DM	44 (60%)	24 (73%)	20 (50%)	0.048
HD	35 (48%)	12 (39%)	23 (58%)	0.149
CVD	18 (25%)	10 (30%)	8 (20%)	0.309
IHD	24 (33%)	18 (55%)	6 (15%)	<0.001

PAD: peripheral arterial disease; DM: diabetes mellitus; HD: hemodialysis; CVD: cerebrovascular disease; IHD: ischemic heart disease.

than the non-PAD group. The prevalence rates of diabetes mellitus and ischemic heart disease were significantly higher in the PAD group than the non-PAD group (73% vs. 50%, $P=0.048$ and 55% vs. 15%, $P<0.001$, respectively).

There were no significant differences in age, hypertension, hemodialysis, or cerebrovascular disease between the PAD and non-PAD groups.

The background characteristics of the HD group and non-HD group are shown in Table 2. The prevalence rates of hypertension and cerebrovascular disease were significantly higher in the HD group than the non-HD group (80% vs. 50%, $P=0.007$ and 37% vs. 13%, $P=0.02$, respectively). The ABI was significantly higher in the HD group than the non-HD group (1.05 [0.92–1.19] vs. 0.94 [0.68–1.12], respectively; $P=0.01$), and the number of cases with ABI > 0.9 was much higher in the HD group the non-HD group (77% vs. 55%, respectively; $P=0.05$). There were no significant differences in age, percentage of female patients, diabetes mellitus, peripheral arterial disease, or ischemic heart disease between the HD group and non-HD group.

Results of HTI. The HTI of MBR was significantly lower in the PAD group than the non-PAD group (0.44 [0.31–0.63] vs. 0.63 [0.50–0.82], respectively; $P=0.007$; Figure 3(a)).

The HTI of BSSP was significantly lower in in the PAD group than the non-PAD group (0.27 [0.15–0.53] vs. 0.87 [0.63–1.02]), respectively, $P<0.001$; Figure 3(b)).

The areas under the ROC curves (AUCs) for HTI of BSSP and MBR were 0.873 and 0.686, respectively, in all subjects (Figure 4).

Using an HTI of BSSP value of 0.4416 as a cutoff, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 68.7%, 95%, 91.7%, and 77.6%, respectively (Table 3). The true positive rate, false-positive rate, true negative rate, and false-negative rate were 66.7%, 33.3%, 95%, and 5%, respectively.

Table 2. Characteristics of the HD group and the non-HD group.

	HD group	Non-HD group	P
Limbs	35	38	
Age	68 ± 14.1	73.2 ± 8.5	0.147
Female sex	14 (40%)	8 (21%)	0.08
Hypertension	28 (80%)	19 (50%)	0.007
DM	24 (69%)	19 (50%)	0.10
PAD	12 (34%)	21 (55%)	0.07
CVD	13 (37%)	5 (13%)	0.02
IHD	14 (40%)	10 (26%)	0.21

PAD: peripheral arterial disease; DM: diabetes mellitus; HD: hemodialysis; CVD: cerebrovascular disease; IHD: ischemic heart disease.

Using an HTI of MBR value of 0.54 as a cutoff, the sensitivity was 66.7% and the specificity was 72.5%.

Results of ABI. The ABI was significantly lower in the PAD group than the non-PAD group (0.8 ± 0.21 vs. 1.1 ± 0.15, respectively, $P<0.001$; Figure 3(c)).

The AUC for ABI was 0.890 in all subjects (Figure 4). Using an ABI of 0.938 as a cutoff, the sensitivity, specificity, PPV, and NPV were 78.8%, 95%, 93.8%, and 92.3%, respectively (Table 4). The true positive rate, false-positive rate, true negative rate, and false-negative rate were 90.9%, 9.1%, 95%, and 5%, respectively.

Correlation between HTI and ABI. There was a positive correlation in HTI of BSSP and ABI ($r=0.486$; Figure 5(a)). There was a strong positive correlation in HTI of BSSP and ABI in the non-HD group ($r=0.743$; Figure 5(b)), but no such correlation was seen in the HD group ($r=0.102$; Figure 5(c)).

Discussion

As the LSFSG itself is a new test device, there have been few reports of its use for evaluation of blood flow in the lower limbs. The HTI of BSSP and MBR were

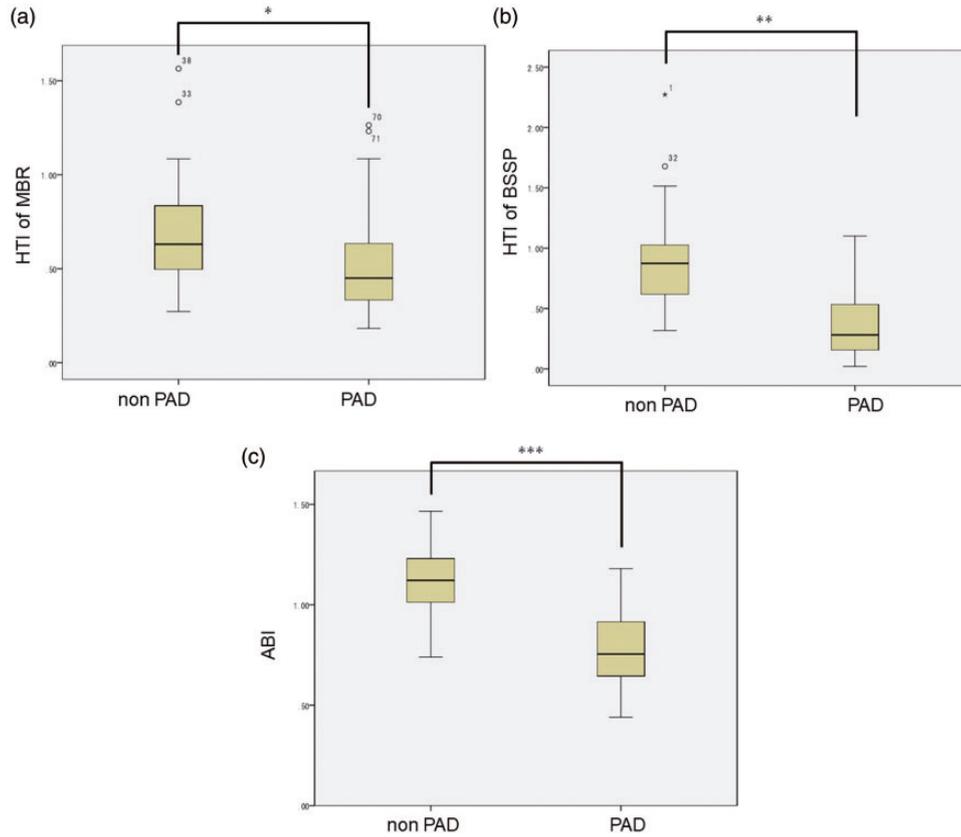


Figure 3. Comparison of HTI of MBR/BSSP between subjects with and without PAD. (a) HTI of MBR on LSFG in subjects with and without PAD. * $P = 0.007$ between the two groups. (b) HTI of BSSP on LSFG in subjects with and without PAD. ** $P < 0.001$ between the two groups. (c) ABI in subjects with and without PAD. *** $P < 0.001$ between the two groups. HTI: hallucal thenar index; BSSP: beat strength of skin perfusion; MBR: mean blur rate; LSFG: laser speckle flowgraphy; PAD: peripheral arterial disease; ABI: ankle brachial index.

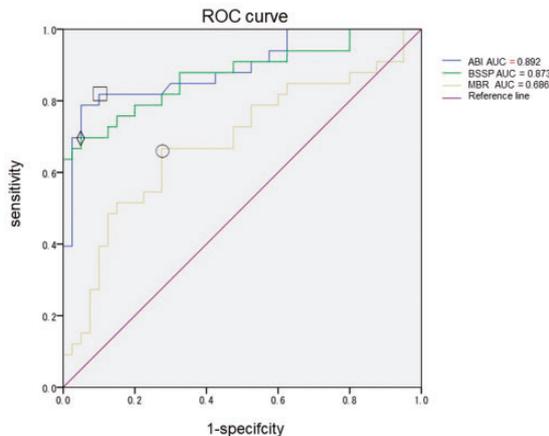


Figure 4. Receiver operating characteristic curve showing ABI, HTI of BSSP, and HTI of MBR (areas under the curves, 0.890 vs. 0.873 vs. 0.686, respectively).
 ◇: HTI of BSSP = 0.4416, Sensitivity: 68.7%, Specificity: 95%.
 ○ HTI of MBR = 0.5400, Sensitivity: 66.7%, Specificity: 72.5%.
 ABI = 0.938, Sensitivity: 78.8%, Specificity: 95%.
 HTI: hallucal thenar index; BSSP: beat strength of skin perfusion;
 MBR: mean blur rate; ABI: ankle brachial index.

significantly lower in patients with PAD than in subjects without PAD in the present study.

Ophthalmologists previously reported evaluation of ocular blood flow with LSFG,^{9–12} and one vascular surgeon reported determination of leg blood flow using this method.⁶ All of these studies used the value itself; the former used the MBR only to monitor individual changes, while the latter used BSSP itself to distinguish between non-PAD controls and PAD patients. Kikuchi⁶ reported that the BSSP value was lower in PAD patients than non-PAD controls, similar to the results of the present study.

As the values of BSSP and MBR itself are relative values, they cannot be compared with between individuals. The HTI may be useful for comparison among individuals because it does not use relative values. The HTI determined using the LSFG was significantly lower in patients with PAD than in subjects without PAD in both BSSP and MBR. This method can be easily adapted to not only the hallux but also other areas of the foot. It was postulated that the HTI may

be useful for distinguishing between subjects with and without PAD.

LSFG indicates two parameters, i.e., MBR and BSSP as skin blood flow. There have been no previous

Table 3. Confusion matrix for HTI of BSSP.

	PAD group	Non-PAD group	Total
HTI < 0.4416	22	2	24
HTI > 0.4416	11	38	49
Total	33	40	72

HTI: hallucal thenar index; BSSP: beat strength of skin perfusion.

Table 4. Confusion matrix for ABI.

	PAD group	Non-PAD group	Total
ABI < 0.938	30	2	32
ABI > 0.938	3	38	41
Total	33	40	73

PAD: peripheral arterial disease; ABI: ankle brachial index.

reports regarding whether using MBR or BSSP is more useful for distinguishing PAD from non-PAD. The results of ROC curve analysis indicated that the HTI of BSSP is a more accurate index than the HTI of MBR to distinguish PAD from non-PAD.

BSSP and SPP showed a moderate correlation coefficient (~ 0.6),⁶ but there have been no previous reports on the correlation between ABI and HTI of BSSP. The correlation between ABI and HTI of BSSP was weak in all subjects in the present study. ABI and HTI of BSSP were not correlated in the HD group, but a strong correlation was seen in the non-HD group.

It had been pointed out that the accuracy of ABI in hemodialysis patients may be reduced due to the effect of vascular calcification. Matsuzawa reported that 42.5% of HD patients with PAD had $ABI > 0.9$.¹⁷ As the ABI may not accurately assess lower limb blood flow in HD patients, this may have resulted in divergence from HTI of BSSP in this study. The HTI showing a strong correlation with ABI could be a useful screening test for likely ABI, especially in non-HD

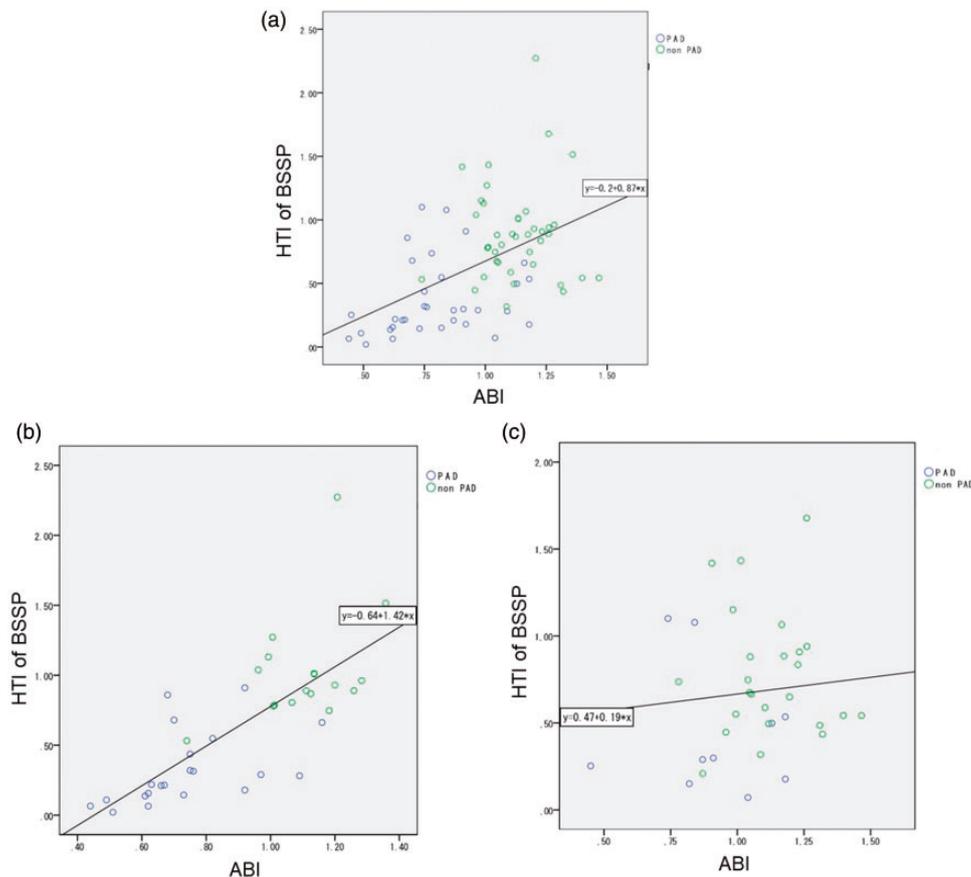


Figure 5. Correlation between HTI of BSSP and ABI. (a) There was a slight correlation between HTI of BSSP and ABI in all subjects. Pearson's correlation coefficient: $r = 0.486$. (b) There was a moderate correlation between HTI of BSSP and ABI in subjects without HD. Pearson's correlation coefficient: $r = 0.743$. (c) There was no correlation between HTI of BSSP and ABI in subjects with HD. Pearson's correlation coefficient: $r = 0.102$.

HTI: hallucal thenar index; BSSP: beat strength of skin perfusion; ABI: ankle brachial index; HD: hemodialysis.

subjects, in whom the effect of arterial calcification is expected to be small. It would be reasonable to determine toe brachial index in HD patients to estimate foot ischemia, but this was not performed in the present study.

Determination of ABI is a very useful and easy method to estimate leg ischemia. This study focused on comparison of HTI of BSSP and ABI. Based on the results of ROC analysis, ABI was superior to HTI of BSSP for distinguishing between subjects with and without PAD. HTI would have low accuracy as a screening test. It was difficult to replace ABI.

The NPV, true negative rate, and false-negative rate of HTI and ABI were similar. Low HTI values may suggest signs of PAD. The main advantages of LSFSG over other methods are that it is a noncontact method with a short inspection time. For patients with pain in their legs or who cannot remain immobile, it is difficult to perform contact-type and time-consuming tests repeatedly because of lack of patient compliance. As LSFSG examination is associated with neither pain nor patient burden, it will be easier to perform more frequently. LSFSG can be measured by simply pressing a button 24 cm away from the target. As the reliability of ABI for evaluation of ischemia is low in hemodialysis patients, LSFSG may be used as in initial noninvasive screening for ischemia at hemodialysis clinics.

Limitations

This study had several limitations. First, the study population consisted only of small numbers of subjects with and without PAD. Second, this study did not show a correlation between healthy subjects and PAD patients using SPP, toe brachial index, or other methods. Third, LSFSG may be unsuitable for subjects with thicker skin and greater body weight because it can obtain measurements only 1–2 mm beneath skin. This study was performed in Japanese subjects and we did not verify the procedure in other races. Thus, our results verified that LSFSG can be used to indicate PAD in limited cases (i.e., lower BMI, Mongolian race, no pigmented skin, and less dense body hair).

LSFSG is currently only used in initial screening. As the focus was on the hallux in this study, there were some aspects that did not take advantage of LSFSG, which could measure over a wide range. In future, it will be necessary to verify the differences in other regions between subjects with and without PAD.

Conclusions

The results of the present study did not show that LSFSG was able to judge limb ischemia as accurately as ABI. HTI results may raise awareness of foot care in

subjects at high risk of PAD and may also help to prevent PAD from becoming more severe.

LSFSG may be a useful tool for determination of lower limb ischemia, but further detailed studies are required in larger cohorts.

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