Assessing the efficacy of a tongue image analyzing system (TIAS) for the objective diagnosis of static blood: An observational, retrospective, single-center study of Japanese Kampo medicine

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ABSTRACT

Aim: Static blood (SB) is an important pathological concept of Kampo medicine. Although tongue findings are very useful in the diagnosis of SB, the relation between the severity of SB and tongue color (TC) is unclear. The purpose of this study was to evaluate the relation between the severity of SB and TC obtained by the use of a Tongue image analyzing system (TIAS).

Methods: We analyzed data from 227 new patients (age 20–85) who visited the Kyushu University Hospital Kampo Clinic between 2013 and 2018. The SB score was calculated based on the diagnostic criteria by Terasawa et al. and classified into three groups: non-static blood (NSB) ≤20 points, SB 20.5 to 39.5 points, severe static blood (SSB) ≥40 points. TC was measured by the device-independent international commission on Illumination 1976L*a*b* color space standards at four points: (i) edge; (ii) posterior; (iii) middle; and (iv) apex.

Results: SB and SSB occurred significantly more frequently in women and patients were of younger age than in the NSB group (P < 0.05). Analysis of TC found 1L* and 4L* to be significantly lower (P < 0.05), and 1a*, 2a*, 3a*, and 4a* significantly higher in SSB than in NSB (P < 0.05). The cutoff value of 2a* and the combination of 1L* + 1a* for SSB prediction obtained from the ROC curve were 2a*, 25.78 (Se: 43%, Sp: 85%, AUC: 0.65), 1L* + 1a*: 1L*, 61.31 and 1a*, 26.16 (Se: 51%, Sp: 82%, AUC: 0.65).

Conclusion: TC diagnosis with TIAS would be a useful screening tool for judging the severity of SB.

KEY WORDS: Kampo medicine, static blood, TIAS, tongue color, tongue imaging analyzing system

INTRODUCTION

It is said that “the tongue reflects the general condition” [1]. Tongue diagnosis is one of the most important diagnostic methods of Kampo medical practice, in which doctors observe tongue color, gloss, shape, and tongue coating in their diagnosis of a patient’s health status [2]. Moreover, it gives important clues to the constitution and medical condition of a patient, including the disease [3].

“Static Blood (SB)” is an important pathological concept of Kampo medicine that is used to decide the sho, which is a Kampo medicine diagnosis. SB is a stagnant state in which the flow of “blood” that nourishes each organ around the whole body becomes poor [4]. It includes subjective symptoms, mental symptoms such as insomnia and restlessness, autonomic symptoms such as headache, excessive sweating, coldness and hot flashes, and menstrual disorders. The SB state can be evaluated by the criteria presented by Terasawa et al. [5], and the diagnostic criteria are popularly called the SB score (Table 1). Recent studies have demonstrated that...
SB is correlated with a deterioration of erythrocyte deformability [6], an elevation in blood viscosity [7], acceleration of erythrocyte aggregation [8], blood fluidity [9–11], autonomic nervous activity changes [12], and microcirculatory dysfunction [13]. In this way, the pathological conditions of SB have been clarified scientifically. On the other hand, in clinical practice, although tongue findings are very useful in the diagnosis of SB, there are insufficient reports to support the accuracy of associations between the severity of SB and tongue diagnosis. Furthermore, it is known that tongue diagnosis is affected by subjective factors such as a doctor’s experience and knowledge, color sensation, and environmental factors such as light, room temperature, and light source. In addition, because the description of tongue findings in various books describing tongue diagnosis are diverse and inconsistent, studies about unifying the diagnosis description have been conducted [14], and attempts to standardize tongue diagnosis are being made. It has been reported that it takes more than 10 years of Kampo diagnosis practice to be able to make an accurate diagnosis without being affected by subjective factors such as age and color discrimination ability [15], and it is not easy for doctors with little experience to judge the findings. In order to obtain accurate SB findings on the tongue, quantitative indicators that support diagnosis and systems that can be used in education are necessary. However, no such indicators or support systems have as yet been reported.

Recently, we constructed a tongue imaging analyzing system (TIAS) that can be used for computer-aided tongue diagnosis based on tongue color [16,17]. The key characteristic of the tongue imaging method in TIAS is the exclusion of the influence of external light by use of an integrating sphere to achieve an evenly distributed light intensity with a halogen light source. Further, TIAS can remove the gloss of the tongue surface from its images in order to stabilize the color of the tongue surface and the coating of the tongue. Quantification of tongue color by TIAS would be a useful tool for diagnostic methods based on the tongue, observing medical conditions over time, and for doctors in educational settings. Previously, a study using TIAS reported a relation between tongue color and upper gastrointestinal tract disease, suggesting that it would be a useful non-invasive tool for the screening of gastroesophageal diseases [18,19].

To improve the accuracy of tongue diagnosis and make it available to clinicians who practice general medicine including Kampo medicine and who may or may not be Kampo specialists, this study was done to evaluate the relation between the severity of SB and tongue color obtained by the use of TIAS.

### METHODS

#### Patient enrollment

Retrospective analysis was done of the pre-treatment data of 515 new patients (≥20 years) who visited the Kampo Medicine Clinic of Kyushu University Hospital from August 2013 to February 2018. The exclusion criteria included patients taking Kampo medicines, patients for whom electronic medical records were not available, patients under 20 years of age, and patients with outliers in tongue color. Outliers were defined as values lower than “1st quartile + 1.5 × inter-quartile range (IQR)” or higher than “3rd quartile + 1.5 × IQR” in the IQR. Age, sex, height, weight, BMI, body temperature, and Kampo medical findings taken at the first visit were collected from electronic medical records. Using the collected information, a score was calculated based on the diagnostic criteria for SB by Terasawa et al. [5] (Table 1). In all cases, the score was assigned to a trial in which the findings were clearly observed, and findings that were mild were divided by 2. A score of 20 points or less was classified as non-static blood (NSB), 20.5 points to 39.5 points as SB and 40 points or higher as severe static blood.

### Table 1 | Static blood score

| Symptom                           | Score | Male | Female |
|-----------------------------------|-------|------|--------|
| Dark-rimmed eyes                  | 10    | 10   |        |
| Areas of dark pigmentation of facial skin | 2     | 2    |        |
| Rough skin                        | 2     | 5    |        |
| Livid lips                        | 2     | 2    |        |
| Livid gingiva                     | 10    | 5    |        |
| Livid tongue                      | 10    | 10   |        |
| Telangiectasis/vascular spiders   | 5     | 5    |        |
| Subcutaneous hemorrhage           | 2     | 10   |        |
| Palmar erythema                   | 2     | 5    |        |
| Resistance and tenderness on pressure of the left para-umbilical region | 5 | 5 | |
| Resistance and tenderness on pressure of the right para-umbilical region | 10 | 10 | |
| Resistance and tenderness on pressure of the umbilical region | 5 | 5 | |
| Resistance and tenderness on pressure of the ileocecal region | 5 | 2 | |
| Resistance and tenderness on pressure of the sigmoid region | 5 | 5 | |
| Resistance and tenderness on pressure of the subcostal region | 5 | 5 | |
| Hemorrhoids                       | 10    | 5    |        |
| Dysmenorrhea                      | —     | 10   |        |

Patients with a total score of less than 21 were classified as non-static blood (NSB), with a total score of 21 to 39 as static blood (SB), and larger than or equal to 40 were classified as severe static blood (SSB).
All of these Kampo medical diagnoses were made by specialists of the Japanese Society of Oriental Medicine who are familiar with Kampo medicine. This study was carried out after obtaining approval from the Ethics Committee of Kyushu University hospital (approval number: 28–130).

**Analysis of tongue color by TIAS**

At first visit the tongue was photographed with TIAS, a tongue image analyzing system that has been validated in previous studies [16,17]. Pictures were taken in a shade-controlled room with the subject’s face fixed with chin and forehead rests. Because the mouth cannot be opened after both the chin and forehead are fixed, first the chin is placed on the chin rest and, after swallowing saliva, the mouth is opened and the tongue extended, following which the forehead is placed against the forehead rest. Each tongue extension is for 20 s, and images are taken every 100 ms, for a total of 200 images. After that the operator visually confirms the tongue color. Tongue color was measured by the device-independent international commission on Illumination (CIE) 1976L*a*b* color space standards (L* indicates the brightness component, a* the red component, and b* the blue component) at four points: (i) tongue edge; (ii) tongue posterior; (iii) tongue middle; and (iv) tongue apex [18]. Because coating does not grow on the edge of the tongue, the color of the edge can be considered the color of the tongue body. In contrast, the color at the other three points is a mixture of the coating and the body of the tongue. By calculating the ratio to the tongue’s edge (<1.0), we can confirm that the color of the tongue reflects the body of the tongue, not the coating.

**Statistical analysis**

The Wilcoxon rank sum test was used for comparison of age and BMI, and the $\chi^2$ test was used for comparison of the male:female ratio. The tongue color obtained by TIAS is expressed as mean value ± standard deviation. Logistic regression analysis was used to compare the tongue color value with the NSB group, and the odds ratio (OR), its 95% confidence interval (95% CI), and $P$-value were calculated. Furthermore, receiver operating characteristic (ROC) analysis was performed for items for which a significant difference was obtained by logistic regression analysis, and the cutoff value, sensitivity (Se), specificity (Sp), and area under the curve (AUC) were calculated. All statistical analyses were performed using JMP (Ver. 13, SAS Institute Japan Ltd., Tokyo, Japan), and $P < 0.05$ represents a significant difference.

**RESULTS**

**Enrollment**

Of the initial 515 patients, 288 were excluded, leaving the data of 227 available for analysis (Fig. 1). These were divided into three groups: NSB 39 (19 males, 20 females), SB 139 (34 males, 105 females), and SSB 49 (6 males, 43 females). There were significantly more women in SB and SSB than in NSB. The age of patients in SB and SSB was significantly younger than in NSB (NSB 64.7 years, SB: 54.3 years, SSB: 47.6 years). There was no difference in BMI or body temperature among the three groups (Table 2).

**The correlation of SB and tongue color**

The correlation between tongue color and SB is shown in Table 3. 1L* and 4L* were significantly lower in SSB than in...
Mean ± SD. *P < 0.05 vs NSB, chi-squared test. † P < 0.05 vs NSB, Wilcoxon rank sum test.
BT, body temperature; NSB, non-static blood; SB, static blood; SB score, Terasawa’s diagnostic criteria for static blood; SB, severe static blood.

NSB (1L*: NSB 64.38 ± 6.95, SB: 60.05 ± 8.69; 4L*: NSB 63.11 ± 7.14, SB 59.63 ± 8.50). In addition, 1a*, 2a*, 3a*, and 4a* were significantly higher in SB (1a*: NSB 28.54 ± 9.34, SB 33.09 ± 10.74; 2a*: NSB 19.32 ± 7.57, SB 24.74 ± 10.67; 3a*: NSB 27.22 ± 7.92, SB 31.76 ± 8.62; 4a*: NSB 35.62 ± 10.31, SB 41.34 ± 10.59).

### Table 2 | Clinical characteristics of the subjects

|                | NSB (n = 39) | SB (n = 139) | SSB (n = 49) |
|----------------|--------------|--------------|--------------|
| Sex (M/F)      | 19/20        | 34/105†      | 6/43†        |
| Age (years)    | 64.7 ± 13.3  | 54.3 ± 15.1* | 47.6 ± 15.5* |
| BMI (kg/m²)    | 22.1 ± 3.4   | 22.4 ± 4.4   | 22.8 ± 4.0   |
| BT (°C)        | 36.3 ± 0.4   | 36.5 ± 0.5   | 36.6 ± 0.4   |
| SB score       | 14.0 ± 4.3   | 30.7 ± 5.4*  | 49.0 ± 7.1*  |

### Table 3 | The association between the SB score to the tongue color

|                | NSB (n = 39) | SB (n = 139) | SSB (n = 49) |
|----------------|--------------|--------------|--------------|
| 1L*            | 64.38 ± 6.95 | 61.62 ± 8.73 | 60.05 ± 8.69*|
| 1a*            | 28.54 ± 9.34 | 31.26 ± 9.61 | 33.09 ± 10.74*|
| 1b*            | 6.73 ± 3.94  | 7.20 ± 4.34  | 8.11 ± 4.63  |
| 2L*            | 58.21 ± 9.47 | 57.75 ± 10.67| 58.14 ± 10.66|
| 2a*            | 19.32 ± 7.57 | 22.15 ± 9.89 | 24.74 ± 10.67*|
| 2b*            | 7.80 ± 5.32  | 7.50 ± 5.29  | 8.32 ± 5.83  |
| 3L*            | 64.75 ± 6.93 | 62.98 ± 7.84 | 62.18 ± 7.82 |
| 3a*            | 27.22 ± 7.92 | 29.48 ± 8.83 | 31.76 ± 8.62*|
| 3b*            | 5.86 ± 3.93  | 5.97 ± 3.55  | 6.28 ± 2.95  |
| 4L*            | 63.11 ± 7.14 | 60.95 ± 7.90 | 59.63 ± 8.50*|
| 4a*            | 35.62 ± 10.31| 38.51 ± 11.25| 41.34 ± 10.59*|
| 4b*            | 7.96 ± 5.83  | 8.70 ± 5.57  | 9.89 ± 5.51  |
| 2L*/1L*        | 0.91 ± 0.14  | 0.94 ± 0.14  | 0.97 ± 0.13  |
| 2a*/1a*        | 0.68 ± 0.19  | 0.70 ± 0.19  | 0.74 ± 0.17  |
| 2b*/1b*        | 1.33 ± 0.84  | 1.05 ± 1.19  | 1.06 ± 0.51  |
| 3L*/1L*        | 1.01 ± 0.07  | 1.03 ± 0.09  | 1.04 ± 0.09  |
| 3a*/1a*        | 0.97 ± 0.14  | 0.95 ± 0.14  | 0.98 ± 0.15  |
| 3b*/1b*        | 0.81 ± 0.62  | 0.87 ± 0.43  | 0.85 ± 0.31  |
| 4L*/1L*        | 0.98 ± 0.07  | 0.99 ± 0.09  | 1.00 ± 0.08  |
| 4a*/1a*        | 1.27 ± 0.22  | 1.25 ± 0.21  | 1.29 ± 0.22  |
| 4b*/1b*        | 1.06 ± 0.66  | 1.16 ± 0.83  | 1.15 ± 0.56  |

Mean ± SD. *P < 0.05 vs NSB, Wilcoxon rank sum test.

### Table 4 | Predictors for SB and SSB with tongue color using TIAs

|                | OR    | 95% CI | P-value |
|----------------|-------|--------|---------|
| 1L*            | 0.96  | 0.91–1.00 | 0.062  |
| 1a*            | 1.03  | 0.99–1.08 | 0.102  |
| 1b*            | 1.03  | 0.94–1.12 | 0.53   |
| 2L*            | 1     | 0.96–1.03 | 0.809  |
| 2a*            | 1.04  | 0.99–1.08 | 0.087  |
| 2b*            | 0.99  | 0.93–1.06 | 0.756  |
| 3L*            | 0.97  | 0.92–1.02 | 0.194  |
| 3a*            | 1.03  | 0.99–1.08 | 0.137  |
| 3b*            | 1.01  | 0.91–1.11 | 0.878  |
| 4L*            | 0.96  | 0.91–1.01 | 0.115  |
| 4a*            | 1.03  | 0.99–1.06 | 0.139  |
| 4b*            | 1.02  | 0.96–1.09 | 0.464  |
| 4L*/1L*        | 4.55  | 4.01–50.77| 0.224  |
| 2L*/1L*        | 1.57  | 1.23–10.74| 0.645  |
| 3L*/1L*        | 0.74  | 0.49–1.11 | 0.125  |
| 4L*/1L*        | 24.27 | 23.02–2535| 0.164  |
| 3a*/1a*        | 0.4   | 0.03–4.74 | 0.466  |
| 3b*/1b*        | 1.29  | 0.62–2.69 | 0.5    |
| 4L*/1L*        | 6.57  | 5.07–586.40| 0.4    |
| 4a*/1a*        | 0.58  | 0.11–3.12 | 0.523  |
| 4b*/1b*        | 1.18  | 0.73–1.89 | 0.492  |

*P < 0.05 vs NSB, Logistic regression analysis. 95% CI, confidence interval; OR, odds ratio.

**Analysis of positive predictors of SB and SSB**

The tongue color in patients with SB and SSB was compared with that of NSB patients using logistic regression analysis. 1L* and 4L* were significantly lower and 1a*, 2a*, 3a*, 4a*, 2L*/1L*, and 3L*/1L* were significantly higher in SB (Table 4).

**The discrimination of SSB by ROC curve**

The cutoff values for SSB prediction obtained from the ROC curves are 1L*: 61.82 (Se: 53%, Sp: 79%, AUC: 0.65); 4L*: 61.89 (Se: 55%, Sp: 69%, AUC: 0.62); 1a*: 26.42 (Se: 65%, Sp: 59%, AUC: 0.63); 2a*: 25.78 (Se: 43%, Sp: 85%, AUC: 0.65); 3a*: 26.51 (Se: 69%, Sp: 62%, AUC: 0.68); 4a*: 36.48 (Se: 59%, Sp: 74%, AUC: 0.68). Furthermore, the cutoff values for the prediction of SSB obtained from the ROC curve were 1L*: 61.31, 1a*: 26.16 (Se: 51%, Sp: 82%, AUC: 0.65) for combination of 1L + 1a and with 4L* + 4a*, was 4L*: 62.97, 4a*: 34.95 (Se: 67%, Sp: 67%, AUC: 0.68) (Fig. 2).
Figure 2 | The discrimination of SSB by ROC curve. The cutoff value for SSB prediction obtained from the ROC curve is 1 L*: 61.82 (Se: 53%, Sp: 79%, AUC: 0.65); 4 L*: 61.89 (Se: 55%, Sp: 69%, AUC: 0.62); 1a*: 26.42 (Se: 65%, Sp: 59%, AUC: 0.63); 2a*: 25.78 (Se: 43%, Sp: 85%, AUC: 0.65); 3a*: 26.51 (Se: 69%, Sp: 62%, AUC: 0.68); 4a*: 36.48 (Se: 59%, Sp: 74%, AUC: 0.68) (A). Furthermore, the cutoff values for the prediction of SSB obtained from the ROC curve were 1 L*: 61.31, 1a*: 26.16 (Se: 65%, Sp: 82%, AUC: 0.65) for combination of 1 L* + 1a*. With a combination of 4 L* + 4a*, they were 4 L*: 62.97, 4a*: 34.95 (Se: 67%, Sp: 67%, AUC: 0.68). Se, sensitivity; Sp, specificity; AUC, area under the curve.
DISCUSSION

This is the first report to demonstrate the usefulness of the TIAS tongue diagnosis support system for the diagnosis of the severity of SB.

Automated tongue diagnosis has advantages in that it can be visually judged and expressed easily, it can be diagnosed from images that can be shared with the findings, and it can be used to observe the medical condition through images recorded over time. A number of tongue diagnosis support systems have been developed [20,21]. However, there are no reports that have objectively evaluated their ability to accurately diagnose SB. To address this problem, we examined the relation between the severity of SB and the tongue color obtained by TIAS.

In this study, 227 patients were categorized into NSB, SB and SSB based on the SB score. The patients in SB and SSB were significantly younger and significantly more were female than those in NSB. SB is said to be closely associated with gynecological disorders such as menstrual disorders and climacteric syndrome [22,23], and the fact that more women were observed in SB and SSB is consistent with our expectations. A possible reason that younger female patients were categorized into SB and SSB is that many of the younger participants in this study might have had menstrual disturbance.

Compared with NSB, SB was characterized by significantly lower brightness (1L*), 4L*), and significantly higher redness (1a*-4a*) of the tongue. In contrast, no significant difference was observed in 4L*/1L*, 2a*/1a*, 3a*/1a*, or 4a*/1a*, which represent the effects of the coating of the tongue. From these results, our data confirm that the color of the tongue reflects the body of the tongue, not the coating. Previous studies have reported that SB is a pathology in which blood viscosity increases due to increased red blood cell aggregation and decreased red blood cell deformability [6–8]. It has also been shown that SB patients have reduced blood fluidity compared to NSB patients [24]. From the pathology, it is considered that red blood cells are stagnant in the tongue of SB patients, thus the tongue of a SB patient becomes darkened.

Because we considered the combination of L* and a* to be nearer the actual findings of the dark red color of the tongue’s body, further analysis was done by measuring points with a combination of L* and a*, and both L* and a* had a positive correlation with SSB in logistic regression analysis. 2a* and the combination of 1L*+1a* was predictive of SSB. Even though the sensitivity was not high, the specificity was. As a practical application, if specificity exceeds the cutoff value, it can be considered highly likely to be SSB. In clinical practice, we usually judge the tongue color on the tongue’s edge, because there is no coating there. Furthermore, a tongue color combination of 1L*+1a* is closer to a dark red tongue than is 2a* only. Therefore, we think that a cutoff value using the combination of 1L*+1a* might be useful for diagnosis of the severity of SB.

This study has some limitations. First, there were many outliers in the tongue color obtained by TIAS, with 55 patients excluded for that. This is a problem for clinical use, and it will be necessary to improve the imaging technology and analysis method of TIAS. Second, the examination was conducted at only one facility. In order for TIAS use to become more widespread, an effective diagnostic index is required that can be used regardless of the shooting location, time, and photographer. It will be necessary to conduct research at multiple facilities and to compare their results with the results of our study to validate the indicators. Third, we did not compare SB score pre and post taking Kampo. Further studies including a post-treatment analysis must be done to provide more detailed information on the usefulness of tongue diagnosis of SB by TIAS.

Conclusion

TIAS might be a useful screening tool for tongue color diagnosis of the severity of SB.

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Author contributions are as follows: CM, AM, TN analyzed the data. MK wrote the paper. TK, DK, TN and TS assisted in the interpretation of the data. All authors contributed to the design and methodology of the study. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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