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Original article

Clinical observation of diabetes mellitus based on thermal sensitivity measurement

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Abstract

***Objective*:** To study the clinical observation of diabetes mellitus based on the determination of meridian thermal sensitivity.
***Methods*:** A total of 1,426 patients who were admitted to Doshisha University Japan, and Chengxintang Clinic in Xi 'an from March 2019 to March 2023 were selected for observation and analysis. Among them, 600 patients with symptoms (18 patients with diabetes) and 826 patients with no symptoms were observed. The sensitivity and specificity of twelve meridians were analyzed and compared according to the test results of thermal sensitivity. The results showed that the values of the sanjiao, heart, liver, bladder, and kidney meridians were useful for diagnosis. By combining these meridians, we were able to improve diagnostic accuracy. In conclusion, this method can be used to diagnose and differentiate diabetes and can guide prescription and acupoints selection. Further studies are needed for investigating the relation between pathogenesis of diabetes and alterations in meridian thermal sensitivity.

***KEY WORDS*:** diabetes, thirsty, sub-cold; sub-heat, well point

Introduction

Acupoints are special parts of human Qi『気』and also for blood『血』transfusion. Physiologically, they are the conduction points of life signals. Pathologically, they are the passageways for the entry and exit of pathogenic diseases, and the reaction points of diseases. At the same time, they are also the stimulation points of acupuncture treatment. "Spiritual Pivot · Nine Needles and Twelve original" says: "What comes out is a well," "Difficult Scriptures · 65 difficult" says: "What comes out is a well, the well is spring in the East, the beginning of all things, so what comes out is a well." It is precisely because the well point is a part of Qi germination and emergence of meridians, it is the place where Yin meridian and Yang meridian meet each other, and it is the beginning and end of Qi and blood flow. Moreover, the well point is at the end of the hands and feet, where the skin is thin, the meridians are shallow, and the strength and weakness of the meridians are most easily detected [1].

The thermal sensitivity measurement method was discovered in 1953 by the Japanese acupuncturist Kobei Akabane. It is a method to measure the deficiency and fullness of the meridian and zang fu organs under the guidance of the meridians theory and the sensitivity of well points to constant temperature [2]. When there are lesions on the meridians of the viscera, the sensitivity of the well points and the back points of the corresponding meridians to the warm stimulation also changes [3]. Therefore, the heat source can be used to stimulate the twelve well points on both sides to determine their sensitivity to temperature, and compare the numerical difference between the left and right sides, so as to analyze the deficiency, and cold heat of each meridian and zang fu organs [4].

Method

The operation method of thermal sensitivity measurement is as follows. The doctor lit thread incense made of carbon (about 7 mm in diameter), placed the tip of the thread at about 5 mm, recorded the time (in seconds) when the subject felt the heat, and inferred the Yin and Yang of the meridians. The general test order is first hand and then foot, on the same well point, first left and then right, in turn [5].

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1. Objects

Clinical data *Table 1*: 826 asymptomatic patients were enrolled in Doshisha University Japan, and Xi'an Chengxintang Clinic, including 296 males and 530 females. Six-hundred patients with symptoms were from Xi'an Chengxintang Clinic, including 215 males and 385 females (18 with diabetes). Thermal sensitivity was measured in 1,426 patients, and sensitivity and specificity were analyzed for each meridian.

2. Indicators:

Sensitivity: Clinical sensitivity can be used to measure the ability of a test to detect disease. Sensitivity is the proportion of people with actual disease who are diagnosed to be positive.

Specificity: Clinical specificity is a measure of the ability of the test to correctly identify disease-free people, and specificity is the proportion of actual disease-free people who are identified as true negative;.

3. Diagnostic criteria for observed cases of diabetes:

TCM diagnosis conforms to:

Main symptoms of Traditional Chinese Medicine (TCM) syndrome differentiation of diabetes mellitus: (1) dry mouth; (2) fatigue; (3) upset; (4) hands and feet or muscle surface fever. Secondary disease: (1) less Qi lazy talk; (2) excessive sweating; (3) tolerance; (4) vertigo; (5) thin loose stool; (6) blurred vision; (7) insomnia; (8) tinnitus; (9) weak pulse, or large and long; (10) light tongue, thin fur, edge tooth marks. With two main symptoms and two secondary symptoms combined with tongue and pulse, diabetes can be diagnosed. This standard combines "Spleen and Stomach" and "Guiding Principles for Clinical Research of New Chinese Medicine (Trial)."

Western medical diagnosis is consistent with:

Developed with reference to the 2020 China Type 2 Diabetes Prevention and Treatment Guidelines. (1) Typical

Table 1-1. Comparison of general information of the three groups

		Group 1 (with diabetes) n = 18 (male 8, female 10)			Group 2 n = 582 (male 208, female 374)				Group 3 n = 826 (male 296, female 530)			
		Mean	95% CI		Mean	95% CI		p Value	Mean	95% CI		p Value
Age (Year)	Total	55.3	51.0	59.7	43.9	42.6	45.4	***	44.1	43.3	45.2	***
	male	54.1	47.8	60.4	45.5	43.9	48.0		44.9	43.1	46.7	
	female	56.3	49.2	63.4	43.9	42.6	45.4	**	43.6	42.5	44.7	**
Height (cm)	Total	164.6	160.4	168.7	161.2	160.8	162.0	***	165.3	164.8	166.6	***
	male	170.6	163.2	177.9	172.1	172.0	173.7		172.9	172.0	173.8	
	female	159.8	157.1	162.5	161.2	160.8	162.0		164.1	158.6	169.7	
Weight (kg)	Total	65.6	60.6	70.6	58.2	57.5	59.5	*	61.7	61.3	63.3	
	male	71.3	60.5	82.2	74.6	73.5	77.1		71.2	69.5	72.8	
	female	61.0	58.7	63.4	58.2	57.5	59.5		56.2	55.3	57.1	
BMI	Total	24.1	22.9	25.4	22.4	22.1	22.8		29.9	19.5	35.9	
	male	24.4	21.7	27.2	25.2	24.7	25.8		23.7	23.2	24.1	
	female	23.9	22.7	25.2	22.4	22.1	22.8		21.5	21.2	21.8	*

Group 1 consisted of 18 patients with diabetes; Group 2 consisted of 582 patients without diabetes, but with an underlying disease or symptoms; Group 3 consisted of 826 healthy subjects with no diabetes. † $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by Dunnett test vs. Group 1. BMI, body mass index; 95% CI, 95% confidential interval.

Table 1-2. Breakdown of diseases and symptoms.

	Group 1 (with diabetes) n = 18			Group 2 n = 582			Group 3 n = 826		
	total	male	female	total	male	female	total	male	female
(Number)	18	8	10	582	208	374	826	296	503
Diabetes	18	8	10	0	0	0	0	0	0
Edema	3	1	2	109	25	84	0	0	0
Constipation	3	1	2	64	14	50	0	0	0
Insomnia	2	1	1	105	41	64	0	0	0
Gastritis	2	1	1	44	19	25	0	0	0
Cardiac disease	5	3	2	322	101	221	0	0	0
Nephropathy	12	3	9	191	81	110	0	0	0

diabetic symptoms (polydipsia, polyuria, weight loss) combined with random blood glucose detection or venous blood glucose ≥11.1 mmol/L; (2) Fasting blood glucose test ≥7.0 mmol/L; (3) Patients with blood glucose detection ≥ 11.1 mmol/L 2 hours after glucose loading and no symptoms of diabetes need to repeat the test on another day.

Inclusion criteria

(1) Meets the above diagnostic criteria; (2) The patient is conscious and in stable condition; (3) The patient and family members gave informed consent and signed an informed letter.

Exclusion criteria

(1) Those who do not meet the above diagnostic criteria for edema in Chinese and Western medicine; (2) Those who suffer from psychiatric or infectious diseases; and (3) Patients who are uncooperative or incapable of cooperating during the testing process.

Thermal sensitivity measurement methods

The test time is 2:00~8:00 p.m., the test environment is fixed in a quiet, bright room, the temperature is 20 °C ± 5 °C, and the humidity is about 60-65 %[5].

During the test, the subject took a sitting position and was calm and quiet. The tester will be made of lit carbon incense (diameter of 7 mm), with the tip of the incense at an approximate distance of about 4 ± 1 mm, so that the incense and nails to maintain a horizontal relationship between the left and right swing at a frequency of 2 times / second, with a stopwatch to record the time to know the degree of heat sensation (seconds), the time detected to 60s to stop the clock. The order of measurement was the hands first and the foot after, the same name meridian starting with the left followed by the right. After the determination of a meridian, the next meridian is measured, the specific order of precedence is as follows: left Shao shang『少商』(LU11), right Shao shang (LU11), left Shang yang『商陽』(LI1), right Shang yang (LI1), left Zhong chong『中衝』(PC9), right Zhong chong (PC9), left Guan chong『関衝』(TE1), right Guan chong (TE1), left Shao chong『少衝』(HT9), right Shao chong (HT9), left Shao ze『少沢』(SI1), right Shao ze (SI1), left Yin bai『隠白』(SP1), right Yin bai (SP1), left Da dun『大敦』(LR1), right Da dun (LR1), left Li dui『厲兌』(ST45), right Li dui (ST45), left Zu qiao yin『足竅陰』(GB44), right Zu qiao yin (GB44), left Zhi yin『至陰』(BL67), right Zhi yin (BL67), left Yong quan『湧泉』(KI1), right Yong quan (KI1).

Precautions

Before the measurement, the patient should be informed of the safety of the measurement process, and should be allowed to rest quietly for at least five min. The patient should not be overly fatigued from hunger and satiety. The patient should be instructed to maintain concentration during the whole measurement process. To avoid the influence of other factors on the results, the environment should be a quiet, constant temperature and humidity; when the weather is cold, the patient should be asked to warm up the limbs first before testing; during the measurement and the patient's limbs should not exert too much force; exclude other physical stimuli, so as not to affect the results of the measurement. If the researcher fails to comply with the above steps and precautions during the measurement, the measurement should be repeated under the specified conditions[6-10].

Conventional Observation indicators

Values of the twelve meridians in terms of the sensibility of Thermal Measurement at the well points: Under normal circumstances, the twelve meridians from the lung meridian to the kidney meridian have the same value on the left and right sides, usually 10 seconds. The detection time varies according to the season and individual differences, so the normal value for the measurement of heat sensation is considered to be 8-12 sec. For further study, 0-7 sec was set as A, considered as Yang bias (sub-heat); 8-12 sec as B, considered as healthy; 12-60 sec as C, considered as Yin bias (sub-cold); and the left and right meridians were counted separately. Numerical results were classified into 9 categories (AA/AB/BA/AC/CA/BB/BC/CB/CC). This study mainly focuses on the classification of two major categories of numerical values of different meridians for healthy people, symptomatic patients and patients with diabetes: hot (AA/AB/BA), cold (BC/CB/CC).

Sensitivity: Clinical sensitivity can be used as a measure of the ability of a test to detect a person with a disease; sensitivity is the proportion of people who are actually sick who have a positive diagnosis.

Specificity: Clinical specificity is a measure of the ability of the test to correctly identify people who are free of disease; specificity is the proportion of people who are actually free of disease who are correctly identified as true negatives;

Statistical methods employed

IBM SPSS 13.0 statistical software was used, in which the count data were expressed as a percentage (%) and the measurement data were expressed as mean ± standard deviation (x ± SD), which were compared using x^2 and t-test respectively. $p < 0.05$ indicated that the difference was statistically significant.

Measurement data conforming to normal distribution were expressed as mean ± standard deviation. Dunnett's test was used for inter-group comparisons, and one way analysis of variance (ANOVA) test was used for intra-group comparisons. $p < 0.05$ was taken as the statistically significant difference. Multi-factor logistic regression analysis was used to analyze the influencing factors; After introducing it into multifactorial logistic regression analysis, the influencing factors were analyzed and the odds ratio and diagnostic accuracy were evaluated.

Ethical Review

When starting this study, subjects were allowed to decide to participate in the program freely, and signed informed consent was obtained from the subjects after explaining that they would not suffer any disadvantages even

if they withdraw from participation due to any circumstances. This research has been approved by the Ethics Review Committee for "Research on Human Subjects" of Doshisha University (Application Number: #14089, #17039).

Results

In Group 1 (diabetic group) when compared with Group 3 (non-diabetic asymptomatic group), the heat detection time was significantly shortened for the left LU, left TE, left HT, left SI, left LR, and bilateral ST meridians, and TSM sensitivity was enhanced (***Table 2***). However, in a comparison between Group 1 (diabetic group) and Group 2 (non-diabetic group with other diseases/symptoms), their heat detection time was significantly prolonged in the right PC, and right TE, and additionally, right HT meridians increased. There was no significant difference in the meridians with enhanced TSM sensitivity when comparing Group 1 and Group 3. Edema, constipation, insomnia, gastritis, heart disease, and nephropathy accompanied with Group 3 affected the TSM of the left LU, left TE, left HT, left SI, left LR, and bilateral ST meridians.

According to ***Table 3***, the sensitivity of 12 meridians in 18 diabetic patients was observed. When 18 patients with type AA diabetes (Group 1) were observed, the sensitivity for positive AA was low, less than 30 % for all meridians, and the most sensitive meridians were TE and SI with a sensitivity of 27.9 %. For Group 3, the specificity was extremely high, being more than 89 % for all meridians when AA was tested negative. For Group 2, the specificity of negative AA was less than 57 % for all meridians. In particular, the specificity of SP, LR, and GB was extremely low, being less than 37 %, and less than 10 % for BL and KT. These meridians were affected by comorbidities and symptoms (edema, constipation, insomnia, gastritis, heart disease, and nephropathy).

Multivariate analysis

Initially, a multivariate analysis was performed on 844 patients, including diabetics in Group 1 and healthy subjects in Group 3 (***Table 4***). The objective variable was the presence or absence of diabetes, and the explanatory variable was the heat detection time (in seconds) of each meridian. When the detection time was short, it meant that the meridian was highly sensitive, and the odds ratio was less than 1. For some meridians, the probability of "diabetes present" may be high when the detection time is long and the sensitivity is low. The odds ratio is then above 1. The meridians with low odds ratios in all variable analyses (odds ratio in parentheses) were

Table 2. TSM detection time in the twelve meridians.

			Group 1 (with diabetes) n = 18			Group 2 n = 582				Group 3 n = 826			
			Mean	95 % CI		Mean	95 % CI		p Value	Mean	95 % CI		p Value
Lung	LU	left	8.9	7.3	10.5	7.7	7.4	8.0		13.4	12.8	14.0	**
		right	10.9	8.3	13.5	7.7	7.3	8.2		14.5	13.7	15.2	
Large Intestine	LI	left	9.4	7.7	11.0	7.3	7.1	7.6		12.5	12.0	13.1	†
		right	10.9	8.1	13.7	7.4	7.0	7.8	†	13.3	12.7	13.9	
Pericardium	PC	left	9.4	8.1	10.8	7.6	7.2	8.0		11.8	11.4	12.2	†
		right	11.1	9.0	13.3	7.4	7.1	7.7	*	13.2	12.7	13.6	
Sanjiao	TE	left	8.3	6.8	9.8	7.2	6.9	7.5		13.5	13.0	14.1	**
		right	10.9	7.7	14.0	7.4	7.1	7.7	*	11.3	10.9	11.8	
Heart	HT	left	8.4	6.7	10.2	7.2	6.9	7.5		11.9	11.4	12.4	*
		right	13.6	6.8	20.3	7.0	6.7	7.3	***	12.3	11.8	12.8	
Small Intestine	SI	left	8.2	6.6	9.8	6.9	6.5	7.2		14.1	13.3	14.8	**
		right	9.4	7.9	10.9	7.1	6.8	7.4		12.3	11.7	13.0	
Spleen	SP	left	12.6	9.4	15.8	10.1	9.6	10.6		14.1	13.6	14.6	
		right	13.3	8.6	18.0	10.2	9.7	10.7		15.9	15.2	16.5	
Liver	LR	left	11.2	8.5	14.0	8.9	8.5	9.2		14.7	14.1	15.2	*
		right	11.2	8.5	13.9	8.5	8.1	8.9	†	12.2	11.7	12.7	
Stomach	ST	left	10.5	8.9	12.1	9.4	8.8	9.9		14.5	13.9	15.0	*
		right	9.4	7.3	11.6	9.1	8.7	9.6		13.6	13.1	14.1	*
Gall-bladder	GB	left	13.4	10.2	16.7	10.4	9.9	11.0		15.3	14.8	15.9	
		right	11.3	9.0	13.7	10.2	9.6	10.7		14.8	14.3	15.4	†
Bladder	BL	left	18.1	12.0	24.2	14.6	13.8	15.4		18.0	17.3	18.7	
		right	16.0	9.7	22.3	14.6	13.7	15.4		17.5	16.8	18.2	
Kidney	KI	left	20.7	14.4	27.0	17.0	16.2	17.9		18.1	17.4	18.7	
		right	19.7	12.0	27.4	16.4	15.6	17.2		16.6	16.0	17.2	

Group 1: 18 patients with diabetes; Group 2: 582 patients without diabetes but with underlying disease or symptoms; Group 3: 826 healthy subjects with no diabetes. † $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by Dunnett test vs. Group 1. TSM, thermal sensitivity measurement; 95 % CI, 95 % confidential interval.

Table 3. Evaluation of three classifications of TSM detection time: Comparison of the presence of diabetes.

Group 1 (with diabetes)		LU	Sensitivity	LI	Sensitivity	PC	Sensitivity	TE	Sensitivity	HT	Sensitivity	SI	Sensitivity
n = 18	AA	4	22.2%	4	22.2%	1	5.6%	5	27.8%	3	16.7%	5	27.8%
	AB	3	16.7%	1	5.6%	2	11.1%	2	11.1%	3	16.7%	3	16.7%
	AC	1	5.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	5.6%
	BA	2	11.1%	0	0.0%	2	11.1%	1	5.6%	1	5.6%	1	5.6%
	BB	3	16.7%	9	50.0%	7	38.9%	5	27.8%	7	38.9%	3	16.7%
	BC	3	16.7%	2	11.1%	4	22.2%	3	16.7%	2	11.1%	3	16.7%
	CA	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	CB	1	5.6%	1	5.6%	1	5.6%	0	0.0%	0	0.0%	1	5.6%
	CC	1	5.6%	1	5.6%	1	5.6%	2	11.1%	2	11.1%	1	5.6%
Group 2 (without diabetes)		LU	Sensitivity	LI	Sensitivity	PC	Sensitivity	TE	Sensitivity	HT	Sensitivity	SI	Sensitivity
n = 582	AA	281	48.3%	311	53.4%	291	50.0%	311	53.4%	313	53.8%	329	56.5%
	AB	63	10.8%	49	8.4%	58	10.0%	66	11.3%	66	11.3%	70	12.0%
	AC	2	0.3%	4	0.7%	1	0.2%	5	0.9%	6	1.0%	5	0.9%
	BA	86	14.8%	80	13.7%	84	14.4%	59	10.1%	83	14.3%	67	11.5%
	BB	93	16.0%	77	13.2%	83	14.3%	92	15.8%	70	12.0%	73	12.5%
	BC	19	3.3%	22	3.8%	20	3.4%	18	3.1%	18	3.1%	16	2.7%
	CA	6	1.0%	6	1.0%	6	1.0%	3	0.5%	7	1.2%	2	0.3%
	CB	15	2.6%	13	2.2%	16	2.7%	10	1.7%	12	2.1%	8	1.4%
	CC	17	2.9%	20	3.4%	23	4.0%	18	3.1%	7	1.2%	12	2.1%
Group 3 (without diabetes and underlying diseases)		LU	Specificity	LI	Specificity	PC	Specificity	TE	Specificity	HT	Specificity	SI	Specificity
n = 826	AA	30	96.37%	58	92.98%	32	96.13%	43	94.79%	61	92.62%	84	89.83%
	AB	50	93.95%	62	92.49%	65	92.13%	30	96.37%	66	92.01%	44	94.67%
	AC	13	98.43%	11	98.67%	20	97.58%	3	99.64%	12	98.55%	6	99.27%
	BA	45	94.55%	47	94.31%	36	95.64%	101	87.77%	50	93.95%	88	89.35%
	BB	240	70.94%	245	70.34%	271	67.19%	233	71.79%	277	66.46%	216	73.85%
	BC	124	84.99%	119	85.59%	146	82.32%	69	91.65%	107	87.05%	47	94.31%
	CA	4	99.52%	6	99.27%	3	99.64%	47	94.31%	14	98.31%	35	95.76%
	CB	107	87.05%	92	88.86%	74	91.04%	139	83.17%	84	89.83%	114	86.20%
	CC	213	74.21%	186	77.48%	179	78.33%	161	80.51%	155	81.23%	192	76.76%

Group 1 (with diabetes)		SP	Sensitivity	LR	Sensitivity	ST	Sensitivity	GB	Sensitivity	BL	Sensitivity	KI	Sensitivity
n = 18	AA	2	11.1%	3	16.7%	3	16.7%	1	5.6%	1	5.6%	0	0.0%
	AB	2	11.1%	2	11.1%	0	0.0%	0	0.0%	1	5.6%	0	0.0%
	AC	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	BA	1	5.6%	1	5.6%	4	22.2%	4	22.2%	1	5.6%	2	11.1%
	BB	3	16.7%	6	33.3%	5	27.8%	4	22.2%	2	11.1%	3	16.7%
	BC	1	5.6%	1	5.6%	1	5.6%	1	5.6%	2	11.1%	1	5.6%
	CA	1	5.6%	0	0.0%	0	0.0%	0	0.0%	1	5.6%	0	0.0%
	CB	4	22.2%	2	11.1%	4	22.2%	3	16.7%	2	11.1%	4	22.2%
	CC	4	22.2%	3	16.7%	1	5.6%	5	27.8%	8	44.4%	8	44.4%
Group 2 (without diabetes)		SP	Sensitivity	LR	Sensitivity	ST	Sensitivity	GB	Sensitivity	BL	Sensitivity	KI	Sensitivity
n = 582	AA	149	25.6%	211	36.3%	200	34.4%	142	24.4%	56	9.6%	35	6.0%
	AB	68	11.7%	52	8.9%	61	10.5%	45	7.7%	29	5.0%	28	4.8%
	AC	2	0.3%	4	0.7%	8	1.4%	7	1.2 %	4	0.7%	17	2.9%
	BA	59	10.1%	93	16.0%	64	11.0%	64	11.0 %	31	5.3%	26	4.5%
	BB	137	23.5%	114	19.6%	123	21.1%	143	24.6%	135	23.2%	72	12.4%
	BC	41	7.0%	24	4.1%	35	6.0%	48	8.2%	52	8.9%	69	11.9%
	CA	9	1.5%	6	1.0%	4	0.7%	8	1.4%	6	1.0%	9	1.5%
	CB	40	6.9%	26	4.5%	40	6.9%	47	8.1%	73	12.5%	67	11.5%
	CC	77	13.2%	52	8.9%	47	8.1%	78	13.4%	196	33.7%	259	44.5%
Group 3 (without diabetes and underlying diseases)		SP	Specificity	LR	Specificity	ST	Specificity	GB	Specificity	BL	Specificity	KI	Specificity
n = 826	AA	32	96.13%	51	93.83%	50	93.95%	46	94.43%	16	98.06%	15	98.18%
	AB	44	94.67%	26	96.85%	27	96.73%	21	97.46%	18	97.82%	25	96.97%
	AC	12	98.55%	1	99.88%	5	99.39%	5	99.39%	7	99.15%	3	99.64%
	BA	21	97.46%	70	91.53%	53	93.58%	24	97.09%	22	97.34%	18	97.82%
	BB	170	79.42%	208	74.82%	190	77.00%	162	80.39%	112	86.44%	106	87.17%
	BC	138	83.29%	41	95.04%	77	90.68%	87	89.47%	93	88.74%	62	92.49%
	CA	3	99.64%	13	98.43%	14	98.31%	9	98.91%	7	99.15%	10	98.79%
	CB	71	91.40%	172	79.18%	122	85.23%	144	82.57%	109	86.80%	128	84.50%
	CC	335	59.44%	244	70.46%	288	65.13%	328	60.29%	442	46.49%	459	44.43%

Group 1: 18 patients with diabetes; Group 2: 582 patients without diabetes but with underlying disease or symptoms; Group 3; 826 healthy subjects with no diabetes. TSM values: A, 0-7 sec; B, 8-12 sec; C, 12-60 sec. AB indicates A on the left side and B on the right side. TSM, thermal sensitivity measurement.

Table 4. Logistic multiple regression analysis of TSM detection time.

		Groups 1 & 3 n = 844								All groups (Groups 1, 2 & 3) n = 1,426			
		Full variate analysis				Stepwise method:Variable reduction				Full variate analysis			
	Variable	Odds	95 % CI		p Value	Odds	95 % CI		p Value	Odds	95 % CI		p Value
Sex	(famale:0, male:1)	0.55	0.12	2.63						0.99	0.36	2.73	
Age	(year)	1.03	0.99	1.07						0.99	0.96	1.02	
LU	left	1.09	1.00	1.19	†					0.84	0.63	1.11	
	right	1.01	0.92	1.10						0.99	0.88	1.12	
LI	left	0.89	0.68	1.16						0.94	0.72	1.21	
	right	0.98	0.88	1.09						1.05	0.92	1.21	
PC	left	0.79	0.59	1.07						1.16	0.94	1.44	
	right	0.90	0.68	1.19						1.07	0.91	1.26	
TE	left	1.04	0.84	1.29						0.71	0.52	0.99	*
	right	1.34	1.16	1.55	***	1.34	1.08	1.30	***	1.15	0.95	1.40	
HT	left	0.72	0.54	0.96	*	0.72	0.48	0.93	*	0.81	0.61	1.08	
	right	1.02	0.94	1.10						1.12	1.01	1.24	*
SI	left	0.79	0.60	1.04	†					0.93	0.73	1.19	
	right	1.01	0.88	1.17						0.96	0.81	1.13	
SP	left	1.21	0.98	1.49	†					1.06	0.93	1.21	
	right	0.99	0.85	1.16						1.05	0.91	1.21	
LR	left	0.69	0.56	0.86	***	0.69	0.59	0.97	*	1.00	0.80	1.25	
	right	1.17	1.05	1.30	**	1.17	0.99	1.22	†	1.02	0.96	1.08	
ST	left	1.04	0.89	1.20						0.94	0.78	1.15	
	right	0.86	0.73	1.02	†					0.77	0.60	0.99	*
GB	left	0.87	0.72	1.06						1.08	0.99	1.16	†
	right	1.02	0.91	1.14						1.01	0.83	1.24	
BL	left	1.06	0.97	1.15						1.00	0.92	1.09	
	right	1.08	1.01	1.16	*	1.08	1.001	1.09	*	0.94	0.84	1.05	
KI	left	1.03	0.91	1.16						1.02	0.95	1.09	
	right	1.11	1.03	1.20	*	1.11	0.99	1.09		0.99	0.92	1.06	
Edema										0.49	0.12	2.05	
Constipation										1.27	0.30	5.34	
Insomnia										0.39	0.07	2.21	
Nephropathy										3.66	1.23	10.87	*
Gastritis										1.63	0.33	8.07	
Cardiac disease										0.69	0.21	2.32	
ROC analysis AUC		0.830	0.754	0.906		0.873	0.817	0.93		0.802	0.701	0.903	

Group 1, 18 patients with diabetes; Group 2, 582 patients with no diabetes but with underlying disease or symptoms; Group 3, 826 healthy subjects with no diabetes. † $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by the binomial logistic regression analysis. TSM, thermal sensitivity measurement; 95% CI, 95% confidential interval; ROC, receiver operating characteristic; AUC, area under the curve.

left HT (0.72), left SI (0.79), left LR (0.69), and right ST (0.86). Since one of the complications of diabetes mellitus is neuropathy, there are cases with peripheral nerve paresthesia. Therefore, the sensitivity when AA was determined to be positive was less than 30 % in all meridians. The meridians with odds ratios above 1 were left LU (1.09), right TE (1.34), left SP (1.21), right LR (1.17), right BL (1.08) and right KI (1.11).

The meridians were selected using a stepwise (decreasing and increasing) method. As a result, the left HT (0.72) and left LR (0.69) were selected as meridians with odds less than 1, and the right TE (1.34), right LR (1.17), right BL (1.08) and right KI (1.11) were selected as meridians with odds greater than 1.

Next, Group 2, which included other diseases and symptoms, was added to the analysis for a total of 1,426 cases. Only the right ST (0.77) remained among the meridians mentioned above due to the influence of concomitant diseases and symptoms. Diseases/symptoms with higher odds ratios and greater impact on diabetes were nephropathy (3.66), gastritis (1.63), and constipation (1.27).

ROC was analyzed for diagnostic accuracy (***Fig. 1***). The ROC AUC in the whole-variate analysis was 0.830, but the ROC AUC (0.873) was increased by using meridians selected by the stepwise (decremental) method. In diseases such as diabetes mellitus, which can cause blunting of

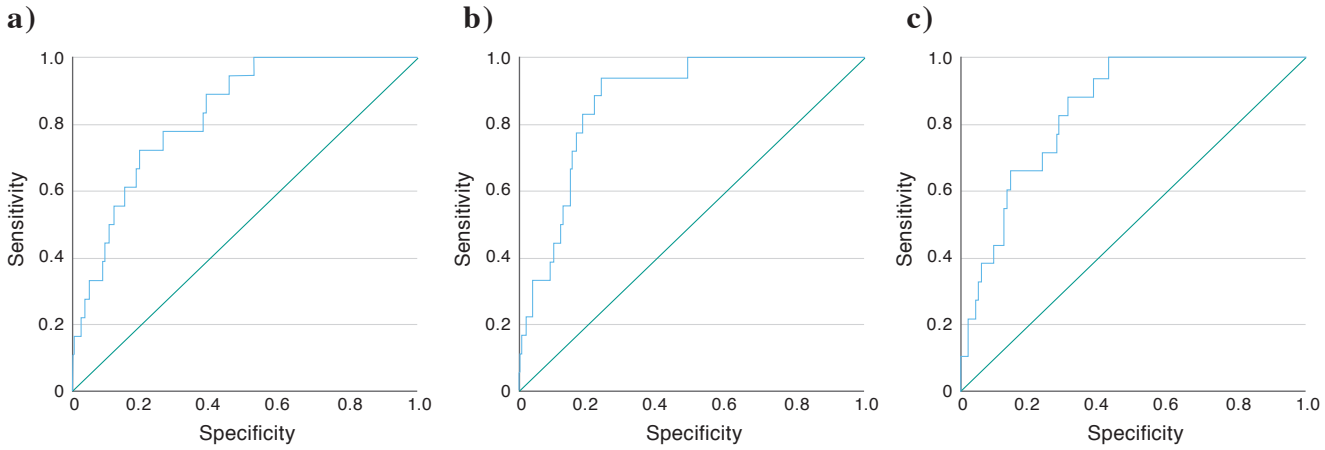

Fig.1. **ROC curve.**

a) Group 1 & Group 3 full variate analysis (n = 844), AUC; 0.830, CP; TPF= 0.722 & FPF = 0.194. **b)** Group diabetes & Group 2; stepwise analysis (n = 600), AUC; 0.873, CP; TPF 0.944 & FPF 0.237. **c)** All groups (n = 1,426), AUC; 0.845, CP; TPF 0.833 & FPF 0.290. Group 1, 18 patients with diabetes; Group 2, 582 patients with no diabetes but with underlying disease or symptoms; Group 3, 826 healthy subjects with no diabetes. CP, closest point from top left corner; BP, basal point; FPF, false positive fraction; TPF, true positive fraction; ROC, receiver operating characteristic.

sensory nerves, there are meridians with increased sensitivity as well as meridians with decreased sensitivity, so limiting the diagnostic criteria to AA positivity would be impractical because it would reduce sensitivity. It was shown that selecting meridians based on the results of multivariate analysis and pairing them appropriately would increase diagnostic accuracy.

Discussion

Multivariate analysis

Multivariate analysis was performed on 844 patients, including diabetic patients in group 1 and healthy controls in group 3. The objective variable was the presence or absence of diabetes, and the explanatory variable was the heat detection time (seconds) for each meridian. A short detection time means that the meridian is highly sensitive, and the odds ratio is less than 1. For some meridians, if the detection time is long and the sensitivity is low, the probability that "diabetes exists" is high. In that case, the odds ratio is greater than 1. The only meridians (odds ratios in parentheses) with low odds ratios (< 0.9) in all variable analyzes were left HT (0.72), left SI (0.79), left LR (0.69), and right ST (0.86). One of the complications of diabetes is neuropathy, which may result in decreased sensation in peripheral nerves. Therefore, the sensitivity for positive AA was less than 30 % for all meridians. The criterion of positive AA is not suitable for the diagnosis of diabetes. Only seven meridians (29 %) showed increased sensitivity (odds ratio less than 0.9), and in the remaining meridians, sensitivity was due to nature (odds ratio near 1) or decreased sensitivity.

Meridians with decreased sensitivity (odds ratio greater than 1.1) were the right TE (1.34), left SP (1.21), right LR (1.17), and right KI (1.11). For improving the diagnostic accuracy of diabetes, it is likely necessary to incorporate meridians for which the sensitivity of the diagnostic criteria has decreased. In order to find meridians useful for diagnosing diabetes, we selected meridians using the stepwise method (decrease method). As a result, the meridians with increased sensitivity (odds ratios in parentheses) were the left HT (0.72) and left LR (0.69), while the selected meridians with decreased sensitivity included the right TE (1.34), right LR (1.17), right BL. (1.08), and right KI (1.11). Under this condition, the ROC AUC was the highest at 0.873, indicating that the diagnosis of diabetes can be optimized by calculating the combination of these meridians.

To examine the influence of concurrent diseases and symptoms, we added Group 2, which included other diseases and symptoms, to the analysis (n = 1,426). Diseases/symptoms that significantly influenced the diagnosis of diabetes (odds ratio 1.2 or higher) were nephropathy (3.66), gastritis (1.63), and constipation (1.27). The contribution rate of co-occurring diseases/symptoms to diabetes diagnosis was 7.3 % of the total. Among these, the contribution ratio of each pathological condition was 38.4 % for nephropathy, 20.7 % for insomnia, and 16.3 % for edema. Only nephropathy had a high odds ratio (odds ratio 3.65) and was extracted as a factor that increases the risk of diabetes.

For the purpose of finding meridians useful for the diagnosis of diabetes, meridians were selected by the stepwise (decreasing) method. ROC AUC was used as an index of diagnostic accuracy. As a result, left HT (0.72) and left LR (0.69) were selected as meridians with increased sensitivity (odds ratio in parentheses), and right TE (1.34), right LR (1.17), right BL (1.08) and right KI (1.11) as meridians with decreased sensitivity. Under this condition, ROC AUC was the highest at 0.873. Therefore, it has been shown that diagnosis of diabetes can be optimized by diagnosis that combines these meridians.

Relationship with diabetes pathology

In multivariate analysis using the stepwise method, ROC AUC could be increased to 0.873 by using the six

extracted meridians as indicators. It is expected that accuracy will be improved by increasing the number of diabetes cases. However, this is only a mathematical analysis and shows a cause-and-effect relationship. A rational explanation is required in relation to the pathology of diabetes.

In diabetic patients, there is a risk of inducing diabetic neuropathy as a complication. The risk is said to be approximately 30~35%[11,12]. In diabetic neuropathy, which damages peripheral nerves, only about 15% of people have subjective symptoms such as pain and numbness, concurrently this occurs in 30 to 40% of people, including those who do not have any symptoms[13]. When nerves (motor nerves, sensory nerves, autonomic nerves) are damaged, and sensory nerves are damaged, people may experience unpleasant pain, or conversely, become less sensitive to pain or cold. Therefore, it is not realistic to diagnose diabetes as positive for AA. It is expected that appropriately combining meridians with increased sensitivity and meridians with decreased sensitivity will lead to improved diagnostic accuracy.

There are many unknown points about the sensory stimulus conduction routes of the extracted meridians. A route different from that of the nervous system, vascular system, and lymphatic system is assumed, and in recent years, the route via fascia has attracted attention. However, the anatomical structure of the fascial pathway remains to be elucidated through future research.

Interpretation according to traditional Chinese medicine

Traditional medicine is a valuable medical technology derived from valuable empirical rules obtained from over 2000 years of accumulated information. How was diabetes considered in Chinese medicine? Which meridians are involved in the presence or absence and degree of diabetes? In search of an answer to this question, we tried to gather information that could serve as a clue.

Kunimatsu Y et al.[14] cited, as important materials for Chinese medicine, Kouteidaikei『黄帝内径 [Huángdì nèijìng]』, Shobyogenkoron 『諸病源候論 [Zhū bìngyuán hòu lùn]』, Bikyusenkinyoho『備急千金要方[Bèi jí qiānjīn yào fāng]』, Saninkyokuitsubyosyohoron 『三因極一病証方論 [Sān yīn jí yī bìng zhèng fāng lùn]』、Shinkyushiseikyo『鍼灸資生経 [Zhēnjiǔ zī shēng jīng]』、Saiseiho『済生方 [Jì shēng fāng]』、Huzaiho『普済方 [Pǔ jì fāng]』、Tankeishinpohuyo『丹溪心法附餘[Danxi Xin Fa fu yu]』、Kokonitotaizen『古今醫統大全[Gǔjīn yītǒng dàquán]』、Shinkyutaisei『鍼灸大成[Zhēnjiǔ dàchéng]』、Shochijyunki『證治準繩 [Zhèng zhì zhǔnshéng]』、Ruikei『類経 [Lèi jīng]』、and Keigakuzensyoyakuchu『景岳全書譯注 [Jǐng yuè quánshū yìzhù]』.

Diabetes has long been referred to as "shokatsu『消渇 [Xiaoke]』",' and is said to be a symptom of dry mouth, excessive drinking, and wasting the rhythmic fluid[15-18]. "Kouteidaikei" says that "the inside of the mouth becomes sweet".

This is called splenic phlegm "hitan『脾癉 [pidan]』", and the fluid stagnates in the spleen[19-21]. The cause is gourmet overeating, which overflows with fever". "Shobyogenkoron" also has a description of shoukatu. "Shinkyushiseikyo" describes 12 acupoints for treating thirst.

Later, in "Tankeishinpohuyo'" and "Kokonitotaizen", the idea of dividing "shokatsu" into three categories based on "proofs『証 [jiao]』" appeared. In the Sui and Tang Dynasties, it was suggested that kidney disease should be treated by Sanjiao. In Song, Jin and Yuan Dynasties, "Danxi Xin Fa fu yu·Xiaoke 46" officially divides Xiaoke into upper, middle and lower three Xiaoke and defines it, that is, "The upper Xiaoke, the lung is also included. Persons who go down also have impaired kidneys, their urine is creamy, their complexion is dark, and their bodies are thin." This method of division and naming has a positive effect on the treatment of diabetes, so it is still used today[22,23]. Accordingly, "Shinkyutaisei'" describes 20 acupoints for treating Xiaoke (***Table 5***). This is not an independent book, but a collection of various Chinese medicine books. Therefore. This book published in each era has different acupoints for treating diabetes.

The sanjiao are classified into the following three based on oroofs.

1. Extinguishment in upper Xiaoke.

Main symptoms: Annoyance, excessive drinking, dry mouth, dry tongue.

Concomitant symptoms: Frequent urination, polyuria, polyphagia.

Acupoints: Feishu (BL13), Yuji (LU10), Xinshu (BL15), Shaofu (HT8), Hegu (LI4).

2. Extinguishment in the middle Xiaoke.

Main symptoms: Eating too much food (being hungry all the time because of eating too much).

Concomitant layer: Fever, excessive sweating, body loss, constipation.

Table 5. Acupoints for diabetes treatment described in "Shinkyutaisei [Zhēnjiǔ dàchéng]".

Acupoints		
Chinese	English	WHO classification
足三里	zusanli	ST36
隱白	yinbai	SP1
太谿	taixi	KI3
水溝	shuigou	GV26
兌端	duiduan	GV27
陽池	yangchi	TE4
然谷	rangu	KI2
照海	zhaohai	KI6
行間	xingjian	LR2
湧泉	yongquan	KI1
太衝	taichong	LR3
承漿	chengjiang	CV24
金津	jinjin	EX-HN12
玉液	yuye	EX-HN13
腎俞	shenshu	BL23
意捨	yishe	BL49
關衝	guanchong	TE1
公孫	gongcun	SP4
脾俞	pishu	BL20
中脘	zhongwan	CV12

Acupoints: Pishu (BL20), Weisyu (BL21), Neiting (ST44), Quchi (LI11), Sanyinjiao (SP6).
3. Extinguishment in lower Xiaoke.
Main symptoms: Frequent urination, polyuria, cloudy urine.
Concomitant symptoms: Dry lips, dizziness, blurred vision, flushed cheeks, feeling hungry but unable to eat, feeling cold, cold extremities, excessive urine output, dark complexion
Acupoints. Shenshu (BL23), Fuliu (KI7), Taichong (LR3), Sanyinjiao (SP6), Ganshu (BL18).

Acupuncture treatment is also being tried for diabetes in Japan[24-27]. In the report by Kinoshita N. et al.[28], treatment was divided into a common treatment that is regularly used for all patients and a targeted treatment that corresponds to specific symptoms. Common treatments include Zhongyuan (CV12), Liangmen (ST21), Guanmen (ST22), and Fuai (SP16) in the abdomen, Ganshu (BL18), Pishu (BL20), and Sanjiaoshu (BL22) in the back, and Zusanli (ST36) of the foot.

In Japanese acupuncture and moxibustion medicine, the acupoints for diabetes (syokatsu [Xiaoke]) are Zhongyuan (CV12), Liangmen (ST21), Fuai (SP16), Ganshu (BL18), Pishu (BL20), Sanjiaoshu (BL22), Quchi (LI11), Zusanli (ST36), Shenshu (BL23), Neiguan (PC6), Dachangshu (BL25), and Fengchi (GB20). The core of the treatment is the BL meridian as an acupoint.

However, when administering acupuncture treatment to diabetic patients, we always try to select acupoints according to Chinese medicine dialectics. It should be understood that there are no set acupoints for treatment.

In the field of Western medicine, there have been reports on the treatment of borderline diabetes[29] and associated complications such as peripheral neuropathy[30, 31], diabetic foot lesions[32, 33], and cognitive dysfunction[34]. There are many unknowns regarding the meridians associated with the diagnosis of diabetes and the acupoints (meridians) used in the treatment of diabetes. Future consideration is required. It is an interesting topic to understand how thermal sensitivity changes in patients who actually receive acupuncture treatment. This will be useful for the future development of acupuncture and moxibustion medicine.

Comparison with diagnosis of edema

The results of TSM in edema cases are being reported in a separate report (accepted)[35]. When the detection time of each meridian was compared between edema (n = 112) and diabetic patients (n = 18), the values were longer for all meridians in diabetic patients (***Table 6***). The meridians with significantly prolonged detection times were bilateral LU, right LI, right C, bilateral TE, right HT, right SI, right SP, and right GB.

Is the phenomenon of prolongation of detection time

Table 6. Comparison of TSM data between the groups with diabetes and edema.

			Group with diabetes n = 18			Group with edema n = 112			
			DT	Odds	CR	DT	Odds	CR	p Value
Lung	LU	left	8.9	1.09	1.8	7.3	1.01	0.9	***
		right	10.9	1.01	2.1	7.3	1.00	0.1	*
Large Intestine	LI	left	9.4	0.89	0.3	**6.7**	**0.87**	**11.6**	†
		right	10.9	0.98	0.7	6.9	1.04	3.5	**
Pericardium	PC	left	9.4	0.79	0.9	6.9	0.99	0.8	
		right	11.1	0.90	0.7	**6.7**	**0.80**	**16.9**	***
Sanjiao	TE	left	8.3	1.04	1.1	**6.8**	**0.86**	**12.5**	***
		right	**10.9**	**1.34**	**8.7**	6.9	1.06	3.9	***
Heart	HT	left	8.4	0.72	4.5	7.0	1.09	6.4	
		right	13.6	1.02	2.8	6.8	1.02	1.9	**
Small Intestine	SI	left	8.2	0.79	4.2	6.7	1.00	0.4	
		right	9.4	1.01	3.6	6.4	0.96	3.5	***
Spleen	SP	left	12.6	1.21	2.5	9.8	1.05	4.2	
		right	13.3	0.99	6.8	9.3	0.98	2.1	*
Liver	LR	left	**11.2**	**0.69**	**11.4**	**8.3**	**0.92**	**7.3**	
		right	**11.2**	**1.17**	**19.2**	8.0	1.04	2.8	
Stomach	ST	left	10.5	1.04	2.5	8.4	0.97	2.4	
		right	9.4	0.86	0.2	8.0	0.94	5.4	
Gall-bladder	GB	left	13.4	0.87	4.4	10.3	1.03	2.9	
		right	11.3	1.02	1.5	9.3	0.97	2.4	*
Bladder	BL	left	18.1	1.06	7.8	13.4	0.99	0.7	
		right	16.0	1.08	0.7	14.2	1.03	3.5	
Kidney	KI	left	20.7	1.03	2.2	15.4	1.00	0.3	
		right	**19.7**	**1.11**	**9.6**	16.2	1.03	3.6	

Group with diabetes, 18 patients with diabetes; Group with edema, 112 patients with edema from Reference 35; † $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by the binomial logistic regression analysis. Bold red text indicates the values of the four meridians in descending order of CR. TSM, thermal sensitivity measurement; DT, detection time; CR, contribution rate.

useful for diabetes diagnosis? To answer this question, we compared the average detection time of all meridians between people with and without diabetes. However, the detection time was 12.0 ± 8.1 seconds with diabetes and 12.2 ± 8.3 seconds without diabetes, with no significant difference. It is a very interesting phenomenon that there is a meridian that increases sensitivity and shortens detection time due to diabetes.

As a result of multivariate analysis, the meridians (odds ratios in parentheses) useful for diagnosing edema included left LU (0.81), right PC (0.81), left TE (0.65), and left LR (0.81); sensitivity was increasing, and right LR (1.19), right BL (1.11), and right KI (1.12); sensitivity was increasing.

The meridians (odds ratios in parentheses) useful for diagnosing diabetes included left HT (0.72), left LR (0.69), right TE (1.34), right LR (1.17), right BL (1.08), right KI (1.11), similarly there was a mixture of low and high sensitivity meridians. Only the right BL and right KI were common between edema and diabetes, however, the overall meridian variation patterns were significantly different.

Next, we compared the contribution rates. For diabetes, the contributing meridians were the right LR (19.2%), left LR (11.4%), right KI (9.6%), and right TE (8.7%). Other than the left LR, the odds ratio was 1 or more, indicating that the meridians had dulled sensation. On the other hand, regarding edema, the contributing factors were the right PC (16.9%), the left TE (12.5%), the left LI (11.6%), and the left LR (7.3%). All odds ratios were less than 1, indicating that the meridians had increased susceptibility. The contribution rate of the left LR was large for both diabetes and edema.

Since the later onset of edema occurs in the lower limbs, we predicted that the meridians measured in the toes (SP, LR, ST, GB, BL, KI) would be more susceptible. All of these meridians had shorter sensing times and increased sensitivity in cases of edema[35]. This result was contrary to expectations. In cases of diabetes, similar trends were observed for LR, ST, and GB.

Conclusion

Through analysis of 1,426 meridian TSM data, we investigated changes in the meridian sensitivity characteristics of diabetic patients (n = 18) and verified whether they could be useful for diabetes diagnosis. As a result of multivariate analysis, the left HT and left LR were identified as meridians with increased sensitivity characteristically to diabetes, and the right TE, right LR, right BL, and right KI were identified as meridians with decreased sensitivity. By combining these meridians, we were able to improve diagnostic accuracy.

Regarding diabetes, there is a meridian theory based on experience and tradition, but it was shown that the extracted meridians do not contradict the traditional theory. The TSM reflects the cold and heat state of diabetes intuitively and concretely in a digital format, enriching the diagnostic method of Chinese medicine. There are still many unknowns regarding the relationship between meridians and the pathology of diabetes. In the future, we hope that by analyzing changes in TSM during acupuncture treatment for diabetes and accumulating information, we will be able to further elucidate the mechanisms that cause changes in meridians.

Conflict of interest statement

The authors claim no conflict of interest in this study.

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