Association between subclinical hypothyroidism and *Sasang* constitution in a Korean population

SE-YOUNG AHN*, SUNG-HWAN PARK*, SU-RYUN HAN, YOUNG-MIN AHN and BYUNG-CHEOL LEE

Department of Internal Medicine, College of Oriental Medicine, Kyung Hee University, Seoul 130-702, Republic of Korea

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Abstract. Serum thyroid-stimulating hormone screening of asymptomatic individuals to diagnose subclinical hypothyroidism remains controversial. We evaluated the potential role of *Sasang* constitutional discrimination and ryodoraku testing as an alternative and complementary diagnostic tool for subclinical hypothyroidism. Among 1,105 potential subjects, 1,073 were included in this study. Of these, 134 subjects had subclinical hypothyroidism (SCH) and 939 were healthy (euthyroid; EU) control subjects. Blood parameters, including serum thyroid hormone levels, were measured. We classified the participants into the four *Sasang* constitutional types, Taeyang-type individuals, Taeeum-type individuals, Soyang-type individuals and Soeum-type individuals, and measured their ryodoraku scores (RS). The mean levels of free thyroxine (FT4), glucose, red blood cells and hematocrit in the SCH group were significantly lower compared to those in the EU group ($p<0.0183$, $p=0.0006$, $p=0.0162$ and $p=0.0224$, respectively). The mean FT4 level of the Soeum-type SCH patients was significantly lower compared to the Soeum-type EU patients ($p=0.0423$). The total RS was significantly higher in the Taeeum-type SCH patients ($p=0.0253$) and lower in the Soeum-type SCH patients ($p=0.0094$) compared to controls. Ryodoraku testing and *Sasang* constitutional discrimination have the potential to serve as alternative and complementary diagnostic tools for subclinical hypothyroidism.

Introduction

Subclinical hypothyroidism is defined as serum thyroid-stimulating hormone (TSH) level above the upper limit of normal, despite normal levels of free thyroxine (FT4). The prevalence of this condition in different population studies varies from 5.9 to 16% (1). The most frequent cause of subclinical hypothyroidism is chronic autoimmune thyroiditis, and stress can be an environmental factor for thyroid autoimmunity (2).

Ryodoraku testing is a basic diagnostic tool for meridian or internal organ diseases. Because of its safety, non-invasive nature and cost-effectiveness, such testing is widely used in Asian countries, including Korea and Japan. Ryodoraku score (RS) changes according to sympathetic nervous system activity or human mood (3).

Sasang constitutional medicine, a construct of traditional Korean medicine, classifies people into four constitutional types, Taeyang-type individuals (Greater yang individuals), Taeeum-type individuals (Greater yin individuals), Soyang-type individuals (Lesser yang individuals) and Soeum-type individuals (Lesser yin individuals), according to individual psychological and physical traits. This theory holds that individual differences in disease susceptibility and drug response depend on constitution (4). Several studies have reported significant differences in stress response according to *Sasang* constitution, and certain constitutional types may be related to hypothyroidism (5).

TSH screening is prone to producing inaccurate results when endogenous interfering antibodies are present (6). The onset and course of subclinical hypothyroidism are often insidious, and patients do not become symptomatic until they develop overt hypothyroidism or goiters (2). Accordingly, screening healthy people is generally not recommended. *Sasang* constitutional discrimination and ryodoraku testing have the potential to serve as complementary diagnostic screening tools for subclinical hypothyroidism. This is the first study to investigate possible associations between subclinical hypothyroidism, *Sasang* constitution and RS.

Patients and methods

Study sample. From March 2010 and April 2011, a total of 1,105 subjects >19 years of age (range 19-85) who were living in Korea were screened at the Kyung Hee University Medical Center. Pregnant women, subjects with personal histories of thyroid disease or taking medication affecting thyroid function, such as thyroxine or antithyroid drugs, and those who were recently diagnosed with hypothyroidism or hyperthyroidism were excluded. Ultimately, 1,073 participants aged 25-81 years were enrolled, and completed physical examinations and blood sample measurements were carried out.

Correspondence to: Dr Byung-Cheol Lee, Department of Internal Medicine, College of Oriental Medicine, Kyung Hee University, 1 Hoegi-dong, Dongdaemun-Ku, Seoul 130-702, Republic of Korea
E-mail: hydrolee@korea.com

*Contributed equally

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Subclinical hypothyroidism was defined as an elevated level of TSH (TSH >4.5 μU/ml; Kyung Hee University Medical Center) with normal T3 (80-200 ng/dl) and FT4 (0.77-1.94 ng/dl). This study was approved by the Institutional Review Board of the Kyung Hee University Medical Center (KOMC IRB 2009-16).

Determination of Sasang constitution. All subjects were classified into the four constitutional types using the Questionnaire for *Sasang* Constitution Classification II$^+$ (QSCC II$^+$; Neomyth, Seoul, Korea) and an interview with a *Sasang* constitution specialist. Classification of the *Sasang* constitution was considered to be acceptable only if the primary result using QSCC II$^+$ and secondary result from SCM specialists agreed with each other.

The questionnaire was divided into four sections: the first dealt with general mental and behavioral characteristics, the second with personal business and social life, the third with physical characteristics and the last with some general questions on health. The QSCC II$^+$ is a survey method that only makes use of 54 questions among all QSCC II questions that have been standardized by international criteria, providing accurate results according to diagnostic clinical data (7). Since the QSCC II$^+$ has fewer questions than the QSCC II, completing the QSCC II$^+$ usually requires a shorter time, encouraging patients to provide better answers. The subjects were interviewed by a *Sasang* constitution medical specialist.

Ryodoraku testing. Ryodoraku testing was performed using the Medira Skin Resistance Checker SME 5800N (Neomyth). The testers applied probes vertically to points with the same pressure (60 g) and same duration (2 sec) for all subjects. The measuring points were LU9 of the Lung Meridian, PC7 of the Heart Constrictor Meridian, HT7 of the Heart Meridian, SI5 of the Small Intestine Meridian, TE4 of the Triple Heater Meridian, LI5 of Large Intestine Meridian, SP3 of the Spleen Meridian, LR3 of the Liver Meridian, KI5 of the Kidney Meridian, BL65 of the Bladder Meridian, GB40 of the Gall Bladder Meridian and ST42 of the Stomach Meridian. All 24 points were assessed by registered expert checkers.

Statistical analysis. Quantitative variables are presented as the means ± standard deviation and qualitative variables as percentages. Relationships between anthropometric and biochemical parameters between subclinical hypothyroidism patients and controls and among *Sasang* constitution types were examined by Student's t-test or the Mann-Whitney rank test. Two-sided p-values <0.05 were considered significant. Statistical analyses were performed with SPSS for Windows (version 17.0; SPSS Inc., Chicago, IL, USA).

Results

A total of 1,073 people were enrolled in this study, including 134 subclinical hypothyroidism (SCH) patients and 939 healthy euthyroid (EU) subjects. SCH and EU subjects differed in both age and gender, as well as serum levels of FT4, TSH, glucose, red blood cells (RBC) and hematocrit (p=0.0109, p<0.0001, p=0.0183, p<0.0001, p=0.0006, p=0.0162 and p=0.0224, respectively). The distribution of *Sasang* constitutions in the SCH group was Taeeum-type individuals 36.30%, Soeum-type individuals 24.44%, Soyang-type individuals 39.26% and Taeyang-type individuals 0%. EU subjects were similar, with a constitutional distribution of Taeeum-type individuals 40.06%, Soeum-type individuals 21.61%, Soyang-type individuals 37.75% and Taeyang-type individuals 0.58% (Table I).

In the sub-analyses of *Sasang* constitutions, the proportion of Taeeum-type individuals was greater in SCH women than in EU women (p=0.0012). There were no gender-specific differences in the proportion of Soeum-type between SCH and EU subjects, in contrast to the other constitution types. The mean FT4 level of SCH patients with Soeum-type was significantly lower than that in corresponding EU subjects (p=0.0423). The mean TSH levels for Taeeum-type individuals, Soeum-type individuals and Soyang-type individuals were higher in SCH patients than in EU subjects (p<0.0001; Table II).

To determine whether *Sasang* constitution was associated with RS, we measured the RS of all 1,105 participants. The total RS in Taeeum-type SCH patients was significantly higher than the total RS in corresponding EU subjects (p=0.0253), and the total RS in Soeum-type SCH patients was significantly lower than the total RS in corresponding EU subjects (p=0.0094). Total RS was not different in SCH and EU Soyang-type subjects (Table II).

Discussion

The most frequent cause of subclinical hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's thyroiditis), which is usually detected using the positive anti-thyroperoxidase (TPO) antibody. Although most evidence that stress contributes to the onset and course of autoimmune disease is circumstantial and the underlying mechanisms are not fully understood, many studies have shown that stress can be an environmental factor in thyroid autoimmunity (2).

The immunoassay technology used to measure serum TSH is more prone to producing inaccurate results when endogenous interfering antibodies are present. Recently, Zazove *et al* considered thyroid function screening to be a high-effort intervention given the cost of screening the elderly. Accordingly, they did not support routine thyroid screening as a preventive health care recommendation, even for elderly women. In support, they cited a relatively low point prevalence of overt disease and uncertainty over the benefits of detecting subclinical hypothyroidism (6). An ideal diagnostic test for screening would have to be highly sensitive, reliable and cost-effective. Considering these restrictions, TSH screening is far from ideal.

Ryodoraku testing is a useful parameter for evaluating the activity of the sympathetic nervous system. The mechanism may be explained by the viscero-skin sympathetic nerve reflex. The impulse from the viscerum radiates to the spinal cord and to reflexed zones on the skin via the efferent sympathetic nerve, as demonstrated by lines of connected reactive electropermeable points. The physiological range of the RS is within 40-80, with a core less than 40 representing a hypo-functional state (3).

When *Sasang* constitutions were not included in the analysis, there were no significant differences in total RS

Table I. Characteristics of the SCH and EU participants and group differences.

	SCH (n=134)	EU (n=939)	p-value
Age (years)	51.10±12.01	48.41±11.61	0.0109
Gender (M:F)	45:89	528:411	<0.0001
Constitutions, n (%)			
Taeeum-type individuals	49 (36.30)	278 (40.06)	0.4133
Soeum-type individuals	32 (24.44)	150 (21.61)	0.4681
Soyang-type individuals	53 (39.26)	262 (37.75)	0.7413
Taeyang-type individuals	0 (0)	4 (0.58)	1.0000
BMI (kg/m^2)	24.02±3.51	24.08±3.40	0.8563
T3 (ng/dl)	138.76±14.36	140.11±15.67	0.3806
FT4 (ng/dl)	1.17±0.22	1.22±0.23	0.0183
TSH (μU/ml)	6.30±3.03	2.29±0.89	<0.0001
AST (U/l)	25.31±9.54	26.34±22.80	0.6872
ALT (U/l)	24.59±17.43	27.29±48.16	0.5201
GGT (U/l)	29.96±21.25	41.48±13.37	0.1421
BUN (mg/dl)	13.75±3.71	13.78±3.70	0.9231
Creatinine (mg/dl)	0.71±0.17	0.73±0.17	0.2658
Ca (mg/dl)	8.51±1.16	8.75±0.57	0.2364
Phosphorus (mg/dl)	3.64±0.73	3.51±1.87	0.4330
Total cholesterol (mg/dl)	188.57±42.65	193.08±37.98	0.2097
Triglyceride (mg/dl)	123.80±84.68	128.99±96.45	0.5564
LDL-cholesterol (mg/dl)	115.10±34.03	116.79±33.80	0.5909
HDL-cholesterol (mg/dl)	57.57±15.88	55.69±15.83	0.2004
Glucose (mg/dl)	86.09±23.16	93.11±21.90	0.0006
RBC ($10^6/\mu$l)	4.61±0.56	4.73±0.53	0.0162
Hemoglobin (g/dl)	15.10±11.44	14.36±2.49	0.0946
Hematocrit (%)	41.76±4.47	42.72±4.50	0.0224
MCV (fL)	90.14±5.02	90.53±5.82	0.4609
MCH (pg)	30.56±5.50	30.34±2.64	0.4537
MCHC (%)	33.37±1.54	33.39±1.46	0.8759
Platelet ($10^3/\mu$l)	256.58±60.66	255.75±64.29	0.8885
Total RS	41.44±21.98	41.83±35.62	0.8628

SCH, subclinical hypothyroidism group; EU, euthyroidism group; BMI, body mass index; T3, triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; AST, aspartate transaminase; ALT, alanine transaminase; GGT, γ-glutamyl transaminase; BUN, blood urea nitrogen; LDL, low-density lipoprotein; HDL, high-density lipoprotein; RBC, red blood cells; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RS, ryodoraku score.

between SCH and EU subjects. In sub-analyses according to *Sasang* constitution, however, the total RS was significantly higher in Taeeum-type SCH subjects and lower in Soeum-type SCH subjects than in the controls. According to the theory of *Sasang* constitution medicine outlined in Dong-Yi-Soo-Se-Bo-Won, Taeeum-type and Soeum-type individuals possess contrasting pathological reactions to stress (8). Lee *et al* reported that Taeeum-type individuals show significantly higher sympathetic activation and emotional changes in response to stress than other constitutional types (9). By contrast, Soeum-type individuals exhibit considerable emotional instability and a decreased stress response, which corresponds to poorer health status, as the degree of perceived stress is higher (10). Our findings were in agreement with these observations.

This is the first study to investigate possible associations between subclinical hypothyroidism, *Sasang* constitutions and ryodoraku score. Taeeum-type and Soeum-type individuals are vulnerable to subclinical hypothyroidism, and we demonstrated their opposite pathological reactions by comparing the ryodoraku score. We conclude that the combination of ryodoraku testing and *Sasang* constitutional discrimination has potential as an alternative and complementary diagnostic tool for subclinical hypothyroidism.

Table II. Group differences in age, gender, BMI, blood tests and RS according to *Sasang* constitution.

	Taeeum-type individuals			Soeum-type individuals			Soyang-type individuals		
	SCH (n=49)	EU (n=278)	p-value	SCH (n=32)	EU (n=150)	p-value	SCH (n=53)	EU (n=262)	p-value
Age (years)	50.84±12.76	48.17±11.01	0.1394	50.88±14.04	48.37±11.54	0.3751	51.49±10.05	49.85±12.00	0.1204
Gender (M:F)	19:30	171:107	0.0012	6:26	55:95	0.0595	20:33	159:103	0.0003
BMI (kg/m^2)	22.55±2.97	23.93±3.24	0.0038	25.36±3.76	24.01±3.35	0.0688	24.58±3.38	24.29±3.63	0.7263
T3 (ng/dl)	141.31±15.29	140.28±14.88	0.6481	137.59±13.38	137.63±16.42	0.5818	137.11±13.96	140.96±15.58	0.0894
FT4 (ng/dl)	1.17±0.19	1.21±0.21	0.3937	1.12±0.25	1.22±0.22	0.0423	1.19±0.24	1.21±0.21	0.4503
TSH (μU/ml)	7.17±4.47	2.34±0.89	<0.0001	5.82±1.03	2.32±0.85	<0.0001	5.78±1.81	2.24±0.87	<0.0001
Total cholesterol (mg/dl)	185.55±58.05	191.76±39.30	0.7255	200.84±42.95	190.91±34.92	0.2809	186.40±38.26	195.69±38.37	0.3308
Triglyceride (mg/dl)	123.96±76.16	132.68±106.83	0.8635	147.56±42.95	117.09±67.52	0.3010	115.98±62.92	131.84±95.94	0.3667
LDL-cholesterol (mg/dl)	114.65±40.26	116.93±36.41	0.4495	120.41±38.00	114.22±29.51	0.5894	114.47±33.58	118.43±33.07	0.5803
HDL-cholesterol (mg/dl)	60.41±15.79	55.40±15.83	0.0315	56.03±14.06	56.23±16.27	0.8082	57.91±15.95	55.56±16.39	0.3582
RBC ($10^6/\mu$l)	4.56±0.59	4.72±0.48	0.0746	4.56±0.50	4.61±0.59	0.5367	4.56±0.45	4.77±0.46	0.0035
Hemoglobin (g/dl)	14.16±1.29	14.30±1.57	0.3134	13.72±1.44	14.61±5.06	0.0899	14.32±4.39	14.36±1.57	0.0184
Hematocrit (%)	42.32±3.76	42.90±4.46	0.2411	40.76±3.88	42.15±5.14	0.0508	41.33±4.46	43.02±4.21	0.0220
Glucose (mg/dl)	92.20±17.49	93.75±26.30	0.8890	89.94±18.69	93.93±19.29	0.6239	90.11±18.30	93.14±22.44	0.2198
Total RS	49.89±22.30	42.95±34.29	0.0253	25.71±8.14	39.98±34.04	0.0094	43.11±22.69	44.22±39.38	0.9190
H1	60.84±29.31	50.05±29.48	0.0009	31.67±17.12	49.93±36.48	0.0001	52.40±34.26	51.14±34.78	0.7354
H2	45.19±28.69	37.65±25.39	0.0085	22.92±12.23	34.59±27.94	0.0012	37.47±26.23	38.10±28.17	0.8324
H3	37.34±31.75	30.68±25.40	0.0228	17.53±9.40	28.96±25.36	0.0005	29.71±25.26	29.69±24.44	0.9953
H4	45.53±33.22	37.73±31.06	0.0244	22.19±12.26	33.73±29.29	0.0022	33.87±24.13	36.90±32.02	0.3575
H5	51.17±32.99	53.18±40.76	0.6455	33.88±22.94	52.53±42.52	0.0008	56.02±39.01	59.39±68.47	0.6238
H6	56.77±35.80	46.93±55.80	0.0934	30.78±23.56	43.27±37.67	0.0117	47.79±38.37	48.52±38.7	0.8599
F1	61.90±36.01	50.74±32.03	0.0020	29.20±14.33	46.21±35.26	0.0002	56.30±37.58	50.48±31.81	0.0986
F2	51.59±29.97	47.48±30.83	0.2247	36.59±26.13	42.49±33.37	0.1877	43.82±34.74	48.60±32.74	0.1775
F3	48.01±32.83	40.71±29.87	0.0293	22.59±14.58	38.31±32.59	0.0002	42.37±29.67	42.70±45.28	0.9431
F4	51.22±32.07	43.89±31.15	0.0336	24.80±16.66	41.71±34.20	0.0001	46.34±31.09	46.56±40.11	0.9579
F5	38.20±25.55	32.55±27.22	0.0572	15.03±10.45	28.87±26.40	<0.0001	30.68±26.61	33.46±29.73	0.3737
F6	50.86±32.55	43.80±32.87	0.0512	21.39±13.13	39.20±34.58	<0.0001	40.55±29.20	45.08±37.67	0.2438

SCH, subclinical hypothyroidism group; EU, euthyroidism; T3, triiodothyronine; BMI, body mass index; RS, ryodoraku score; T3, triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; LDL, low-density lipoprotein; HDL, high-density lipoprotein; RBC, red blood cells; H1, lung; H2, pericardium; H3, heart; H4, small intestine; H5, triple energizer; H6, large intestine; F1, spleen; F2, liver; F3, kidney; F4, urinary bladder; F5, gallbladder; F6, stomach.

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