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Factor Structure of Indices of the Second Derivative of the Finger Photoplethysmogram with Metabolic Components and Other Cardiovascular Risk Indicators

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Background: The second derivative of the finger photoplethysmogram (SDPTG) is an indicator of arterial stiffness. The present study was conducted to clarify the factor structure of indices of the SDPTG in combination with components of the metabolic syndrome (MetS), to elucidate the significance of the SDPTG among various cardiovascular risk factors.
Methods: The SDPTG was determined in the second forefinger of the left hand in 1,055 male workers (mean age, 44.2±6.4 years). Among 4 waves of SDPTG components, the ratios of the height of the "a" wave to that of the "b" and "d" waves were expressed as b/a and d/a, and used as SDPTG indices for the analysis.
Results: Principal axis factoring analysis was conducted using age, SDPTG indices, components of MetS, and the serum levels of C-reactive protein (CRP) and uric acid. Three factors were extracted, and the SDPTG indices were categorized in combination with age as the third factor. Metabolic components and the SDPTG indices were independently categorized. These three factors explained 44.4% of the total variation. Multiple logistic regression analysis revealed age, d/a, serum uric acid, serum CRP, and regular exercise as independent determinants of the risk of MetS. The odds ratios (95% confidence intervals) were 1.08 (1.04 to 1.11), 0.10 (0.01 to 0.73), 1.24 (1.06 to 1.44), 3.59 (2.37 to 5.42), and 0.48 (0.28 to 0.82), respectively.
Conclusion: The SDPTG indices were categorized in combination with age, and they differed in characteristics from components of MetS or inflammatory markers. In addition, this cross-sectional study also revealed decrease of the d/a as a risk factor for the development of MetS.

Keywords: Cardiovascular risk; Factor analysis; Finger photoplethysmogram; Metabolic syndrome; Occupational study

INTRODUCTION

Measurement of the arterial stiffness is important in various clinical and epidemiological settings, because increased arterial stiffness is well-known to be associated with an increase in the risk of cardiovascular disease (CVD) [1-4]. Determination of the second derivative of the finger photoplethysmogram (SDPTG) is based on double differentiation of the finger photoplethysmogram (PTG), and is a noninvasive method for pulse wave analysis [5,6]. Several previous studies have shown associations of the SDPTG indices with aging, blood pressure (BP), and development/progression of atherosclerosis [7-10]. However, there is no information on the factor structure of the SDPTG indices in combination with the components of the metabolic syndrome (MetS). Moreover, there are few reports on the association between MetS and the SDPTG indices, including inflammation and lifestyle factors.

The main purpose of this study was to clarify the factor structure of the SDPTG indices in combination with various risk factors for CVD, and also the probability of the risk of

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MetS by the SDPTG indices in middle-aged Japanese men.

METHODS

Study population

This study was undertaken during an annual health examination conducted at a company in Kanagawa, Japan. All employees (n=1,155), aged 35 to 63 years, were engaged in daytime, desk work. Among them, 85 females were excluded from this analysis, because of the small size of the sample. Subjects with serum C-reactive protein (CRP) ≥10.0 mg/L (n=15) were also excluded, because of the possible presence of a confounding infection or inflammation. Finally, 1,055 subjects were included in the analysis in the present study. The study protocol was approved by the Ethics Committee of Nippon Medical School, and written informed consent was obtained from all the participants.

Biochemical and physical measurements

All anthropometric and hemodynamic measurements and blood samplings were conducted before noon. Blood samples were obtained from the antecubital vein after the subjects had fasted overnight. Standard enzymatic methods were used to measure the serum triglycerides (TG) and plasma glucose in an automated analyzer (Model 7170; Hitachi High-Technologies, Tokyo, Japan). The serum high density lipoprotein cholesterol (HDL-C) was measured using the direct method. The serum CRP level was measured using a latex turbidimetric immunoassay kit (LPIA CRP-H; Mitsubishi Kagaku Iatron, Tokyo, Japan) in an automated analyzer (Model 7170). The detection limit of this assay was 0.1 mg/L. The intra-assay coefficient of variation was under 3.4% [11]. The systolic and diastolic BP were measured twice in the right arm of the subjects in the seated position using a mercury sphygmomanometer, after the subjects had rested for at least 5 minutes.

Definition of MetS

The 2001 National Cholesterol Education Program Adult Treatment Panel III (ATP III) report defined ATP III-MetS as the presence of three or more of the following criteria: central obesity as assessed by a waist circumference of ≥85 cm, modified for Japanese men; hypertriglyceridemia (serum TG ≥150 mg per 100 mL [1.7 $mmolL^{-1}$]) and/or low level of HDL-C (serum HDL <40 mg per 100 mL [1.03 $mmolL^{-1}$] in men); high BP (systolic BP ≥130 mm Hg and/or diastolic BP ≥85 mm Hg, or current history of use of antihypertensive drugs; high fasting glucose (≥100 mg per 100 mL [5.6 $mmolL^{-1}$]). The cut-off point for plasma fasting glucose was based on the modified ATP III criteria [12].

Lifestyle factors

Lifestyle factors were categorized in a binary manner. Namely, desirable lifestyle was categorized as 1. In contrast, current smoking, alcohol intake over 5 days a week, exercise less than 2 days a week, and average sleeping time under 6 hours per day were categorized as 0.

SDPTG measurement

The SDPTG was recorded in the sitting position using an SDP-100 instrument (Fukuda Denshi, Tokyo, Japan), after the subject had rested for at least 5 minutes after the BP measurement. The details of this procedure are described elsewhere [8]. Namely, the SDPTG consists of 4 waves in systole ("a," "b," "c," and "d" waves) and 1 wave in diastole ("e" wave). The "a" and "b" waves exist in the early systolic phase of the PTG, and the "c" and "d" waves exist in the late systolic phase. The height of each wave from the baseline was measured and the ratios of the height of the "a" wave to that of the "b" and "d" waves, expressed as b/a and d/a, were calculated and used as the SDPTG indices in the present study.

Statistical analysis

Since the serum values of CRP and TG were skewed to the left, the data were log-transformed for this analysis. Principal axis factoring analysis with Varimax rotation was conducted using age, b/a and d/a of the SDPTG, with each MetS component including the log-transformed values of TG and CRP with an initial eigenvalue of over 1 as the cutoff point. Furthermore, age, b/a and d/a of the SDPTG, serum uric acid, log-transformed values of CRP, and smoking, drinking and regular exercise histories were used as explanatory variables in multiple logistic regression analysis to determine the existence of MetS. The SPSS version 16.0J for Windows (SPSS Japan Inc., Tokyo, Japan) was used for the analyses.

RESULTS

The characteristics of the study subjects are shown in Table 1. The prevalence of MetS was 14.1% (148/1,052).

Means (standard deviations) of associated parameters and

Table 1. Characteristics of subjects

Variable	Value
Age, yr	44.2±6.4
Waist circumference, cm	82.4±7.9
SBP, mm Hg	120.3±13.5
DBP, mm Hg	76.9±9.9
TG, mg/dL	96.2 (1.8)
HDL-C, mg/dL	56.1±13.3
Plasma glucose, mg/dL	92.0±12.5
CRP, mg/L	0.34 (2.7)
Uric acid, mg/dL	6.0±1.2
Not current smoking	743/1,053 (70.6)
Not habitual drinking	796/1,054 (75.5)
Regular exercise	224/1,054 (21.3)
Sleeping time ≥6 hr	308/1,052 (29.3)
SDPTG index	
b/a	-0.63±0.12
d/a	-0.26±0.12
MetS	148/1,052 (14.1)

Values are presented as mean±standard deviation or case/total number (%).The values of TG and CRP are expressed as geometric mean (geometric standard deviation).
SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CRP, C-reactive protein; SDPTG, second derivative of a finger photoplethysmogram; MetS, metabolic syndrome.

prevalence MetS by classifying subjects into quartiles according to d/a SDPTG index were presented (Table 2). Dunnett's multiple comparison by setting highest quartile as control presented that waist circumference, TG, plasma glucose, CRP and MetS of subjects in lowest quartile of d/a SDPTG index showed statistical higher values compared with those in highest quartile of d/a SDPTG index. Age and BP also presented lower values as the quartile of d/a SDPTG index increased.

A correlation matrix for several variables was presented in Table 3. Although significant relationship between SDPTG indices and the other variables were observed, correlation coefficient higher than 0.3 was recognized between d/a SDPTG index and BP except age.

Principal axis factoring analysis was conducted using age, the SDPTG indices, components of MetS, serum CRP, and serum uric acid. Factor loadings of over 0.35 were tentatively selected. Four factors were extracted, and factor 1 consisted of two items related to the BP, accounting for 15.4% of the total variation. Factor 2 consisted of four items related to waist circumference, the lipid profile and markers of inflammation, accounting for 14.5% of the total variation. Factor 3 consisted of three items related to age and the SDPTG indices, accounting for 14.5% of the total variation. These four factors together accounted for 44.4% of the total variation (Table 4).

The results of multiple logistic regression analysis revealed

Table 2. Means±standard deviations or percentage of variables stratified by quartile of d/a SDPTG index

Item	1st	2nd	3rd	4th
Age	48.2±6.7[c]	45.2±6.0[c]	42.5±5.6[a]	41.2±5.1
Waist	83.6±7.4[b]	82.2±7.5	82.5±8.2	81.4±8.5
Circumference				
SBP	126.8±14.2[c]	120.7±13.5[b]	116.8±11.8	116.9±11.9
DBP	81.9±10.5[c]	77.3±10.3[c]	74.8±8.5	74.0±8.2
TG	103.3 (1.7[b])	97.6 (1.8)	96.5 (1.9)	88.4 (1.7)
HDL-C	56.8±14.9	57.0±12.9	54.0±12.5	56.5±12.9
Plasma glucose	94.8±16.8[b]	91.7±10.6	90.5±8.6	91.1±12.4
CRP	0.40 (2.9[a])	0.34 (2.5)	0.33 (2.7)	0.32 (2.8)
Uric acid	6.1±1.3	6.0±1.2	6.0±1.3	5.8±1.2
MetS	59/253 (23.3)[c]	33/275 (12.0)	33/255 (12.9)	23/268 (8.6)

Values are presented as mean±standard deviation or case/total number (%). The values of TG and CRP are expressed as geometric geometric mean (geometric standard deviation). Multiple comparison by Dunnett's method was selected by setting highest quartile of d/a SDPTG index as control.
SDPTG, second derivative of a finger photoplethysmogram; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CRP, C-reactive protein; MetS, metabolic syndrome.
[a]$P<0.05$, [b]$P<0.01$, [c]$P<0.001$.

Table 3. A correlation matrix with Pearson's moment corelation coefficient for 11 related variables

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10
V2	0.111[c]									
V3	0.262[c]	0.361[c]								
V4	0.222[c]	0.343[c]	0.770[c]							
V5	0.106[b]	0.380[c]	0.170[c]	0.218[c]						
V6	0.000	-0.339[c]	-0.004	-0.029	-0.487[c]					
V7	0.226[c]	0.195[c]	0.253[c]	0.230[c]	0.174[c]	-0.059				
V8	0.047	0.364[c]	0.125[c]	0.152[c]	0.280[c]	-0.251[c]	0.099[b]			
V9	0.013	0.235[c]	0.164[b]	0.198[b]	0.285[b]	-0.103[b]	-0.018	0.197[c]		
V10	0.450[c]	0.028	0.146[c]	0.132[c]	0.075[a]	-0.027	0.120[c]	0.056	0.028	
V11	-0.446[c]	-0.094[b]	-0.315[c]	-0.322[c]	-0.107[c]	-0.018	-0.126[c]	-0.094[b]	-0.078[a]	-0.596[c]

V1, age; V2, waist circumference; V3, systolic blood pressure; V4, diastolic blood pressure; V5, triglyceride (log); V6, high density lipoprotein cholesterol; V7, plasma glucose; V8, C-reactive protein (log); V9, Uric acid; V10, b_a second derivative of a finger photoplethysmogram index; V11, d_a second derivative of a finger photoplethysmogram index.
[a]$P<0.05$, [b]$P<0.01$, [c]$P<0.001$.

Table 4. Varimax rotated principal factor loadings of variables

Item	Factor 1	Factor 2	Factor 3	Communality
Age	0.149	0.036	0.561[a]	0.400
SDPTG index				
b/a	-0.005	0.037	0.784[a]	0.618
d/a	-0.221	-0.044	-0.758[a]	0.628
Waist circumference	0.318	0.569[a]	0.011	0.435
SBP	0.862[a]	0.109	0.173	0.804
DBP	0.820[a]	0.163	0.166	0.729
TG (log)	0.086	0.699[a]	0.079	0.508
HDL-C	0.104	-0.633[a]	0.022	0.423
Plasma glucose	0.199	0.137	0.135	0.240
CRP (log)	0.103	0.453[a]	0.049	0.219
Uric acid	0.190	0.341	0.033	0.222
Eigenvalue	1.692	1.597	1.591	
% of variance	15.4	14.5	14.5	

SDPTG, second derivative of a finger photoplethysmogram; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; CRP, C-reactive protein.
[a]Factor loadings over 0.4 are marked.

Table 5. Multiple logistic regression analysis to reflect metabolic syndrome

Variable	B	SE	OR	95% CI	Sig.
Age (1 yr increase)	0.07	0.02	1.08	1.04-1.11	$P<0.001$
SDPTG index					
b/a	-1.20	1.03	0.30	0.04-2.30	NS
d/a	-2.29	1.01	0.10	0.01-0.73	$P<0.05$
Uric acid	0.21	0.08	1.24	1.06-1.44	$P<0.01$
Common logarithm of	1.28	0.21	3.59	2.37-5.42	$P<0.001$
CRP					
Not current smoking	-0.01	0.21	0.99	0.66-1.49	NS
Not habitual drinking	0.18	0.23	1.20	0.76-1.88	NS
Regular exercise	-0.74	0.28	0.48	0.28-0.82	$P<0.01$
Sleeping time ≥6 hr	-0.17	0.22	0.84	0.55-1.28	NS

B, nonstandardized regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; Sig., significance; NS, not significant; SDPTG, second derivative of a finger photoplethysmogram; CRP, C-reactive protein.

age, d/a of the SDPTG serum uric acid, serum CRP and regular exercise as being significantly associated with the risk of MetS (Table 5). The odds ratio and 95% confidence intervals (CI) indicated within parentheses were 1.08 (1.04 to 1.11), 0.10 (0.01 to 0.73), 1.24 (1.06 to 1.44), 3.59 (2.37 to 5.42), and 0.48 (0.28 to 0.82), respectively. Multiple logistic regression analysis was also conducted to know the risk for components of MetS, and d/a significantly associated with the risk of hypertension; the odds ratio and 95% CI were 0.012 and 0.003 to 0.058, respectively.

DISCUSSION

The main purpose of this study was to clarify the factor structure of the SDPTG indices in combination with several MetS components, because there have been no previous reports of

factor analysis using these parameters. The b/a and d/a were used as the SDPTG indices in the present study. The d wave is included in the late systolic phase of the PTG, and is enhanced by the backward wave from the periphery. The d/a is significantly correlated with the central augmentation index [5]. Augmentation index is a predictor of cardiovascular events, and high values of the augmentation index have been reported to be associated with target organ damage [13]. Although augmentation index and central BP represent different aspects of arterial stiffness, it has been reported that a significant relationship exists between the augmentation index and central BP [14]. In our study, two SDPTG indices were categorized with age. Although the SDPTG indices are considered to be markers of arterial stiffness, BP and lipid variables were not included in the same category in this study. However, consistent with past reports of a significant association between the SDPTG and age [5,7-10], the present study showed that the SDPTG indices were related to age, although the principal factor analysis revealed that this factor (factor 3) accounted for 14.5% of the total variance.

In addition, multiple logistic regression analysis was also performed to identify the association between the risk of MetS and the SDPTG indices. As a result, d/a was selected as a significant variable in combination with age, serum uric acid, serum CRP, and habitual exercise. Elevated BP is thought to increase arterial stiffness [6,15], and the authors previously reported that hypertension appears to have a greater impact on the d/a than on the b/a [8]. There is a report that b/a is correlated with distensibility of the carotid artery [16], and this indicator might reflect large arterial stiffness. Although BP and the SDPTG indices were not be categorized together by factor analysis, the d/a was significantly associated with the risk of MetS and hypertension.

This study is a cross-sectional design, and cause-effect relationship cannot be determined. Follow-up study is needed to determine the association between the d/a and BP with causality.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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