

Original Article

Lower ankle-brachial index is associated with poor sleep quality in patients with essential hypertension

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Abstract: Background: The ankle-brachial index (ABI), ratio of leg blood pressure to arm blood pressure is used extensively as a screening test for stratification of cardiovascular risk. The problems in sleep disturbed nocturnal fall in blood pressure and may relate to development of hypertension. However, the role of sleep quality on ankle-brachial index remains unclear. Methods and Results: This study examined 101 patients with essential hypertension. We analyzed the association with ABI on age, sex, body height, body weight, body mass index, waist circumference, blood pressure, HDL-cholesterol, LDL-cholesterol, HbA_{1c}, sleep quality evaluated by Pittsburgh Sleep Quality Index (PSQI), smoking habits, alcohol habits. The ABI is associated with the following seven parameters; body height ($r = 0.36, p < 0.001$), body weight ($r = 0.30, p < 0.005$), systolic BP ($r = -0.23, p < 0.05$), HbA_{1c} ($r = -0.24, p < 0.05$), PSQI score ($\rho = -0.31, p < 0.005$), alcohol intake ($\rho = 0.23, p < 0.05$) and sex ($F = 6.65, p < 0.05$). By a multiple linear regression analysis with ABI as the dependent variable after forcing the seven parameters above into the model, body height, HbA_{1c} and PSQI score were significantly associated with ABI (R^2 for the model = 25%, $p < 0.001$). Conclusion: Poor sleep quality was independently associated with lower ABI in patients with essential hypertension. The results may provide new insight related to the interaction between sleep quality and blood pressure.

Keywords: Hypertension, ankle-brachial index, sleep quality

Introduction

The ankle-brachial index (ABI), the ratio of leg blood pressure to arm blood pressure, is an indicator of peripheral vascular disease, and is associated with the risk of coronary artery disease or stroke [1-3]. In symptomatic adults, the ABI is a reliable screening test for peripheral vascular disease, and is sometimes used as a tool for cardiovascular disease risk reclassification. Recently, the ABI has come to be used extensively as a screening test for cardiovascular risk estimation in population of asymptomatic subjects.

Sleep modulates blood pressure [4]. Short sleep period at night might increase sympathetic nervous system activity on the following day [5], leading to increased blood pressure [6]. Results of recent studies showed that problems in sleep disturb the nocturnal fall in blood pressure and might be related with the development of hypertension [7]. Cappuccio et al [8] reported that short sleep (≤ 5 hour per night) is

associated with a higher risk of hypertension. In elderly people, not only sleep time but also sleep quality is frequently disturbed. However, the relation of sleep quality to ABI remains unclear. This study examines potent modifications of sleep quality on ABI in asymptomatic patients with essential hypertension. The association between ABI and poor sleep quality may be a key to the understanding of cardiovascular risk estimation by ABI.

Materials and methods

This study examined 101 patients with essential hypertension, according to the following criteria: (1) patient age > 20 years, (2) onset of hypertension occurred at < 60 years of age, (3) established hypertension defined either as long-term treatment of the disease, or in those previously untreated as systolic/diastolic blood pressures $> 140/90$ mmHg on two consecutive visits, and (4) absence of secondary forms of hypertension as determined through extensive workup. All subjects were in sinus rhythm. None

had a history and/or evidence of coronary heart disease, congestive heart failure, cerebrovascular disease, or renal insufficiency. Patients were enrolled between 1 December 2013 and 28 February 2014 at Takahata Public Hospital, Takahata, Japan and at Tendo Hospital, Tendo, Japan. This study was approved by the Ethics Committee of Yamagata Prefectural University of Health Sciences. Written informed consent was obtained from all patients.

Measurements

Body weight and height

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Waist circumference was measured to the nearest 0.1 cm at the level of the iliac crest while the subject was at minimal respiration [9].

Blood pressure (BP) and ankle-brachial index (ABI)

Blood pressure (BP) and ABI were measured using an automatic waveform analyzer (BP-203RPE; Colin Corp., Komaki, Japan) [10] at Takahata Public Hospital and Tendo Hospital. Measurements were taken from patients lying in a supine position after 5 min of rest. Occlusion and monitoring cuffs were placed snugly around their upper and lower extremities. Pressure waveforms from the brachial and tibial arteries were then recorded simultaneously using an oscillometric method. The ABI value was calculated as $ABI = \text{ankle systolic BP} / \text{brachial systolic BP}$. Mean ABI represents a mean value of measurements from both extremities.

Blood samples

Blood samples were obtained after a minimum 8-h fast for the measurement of serum HDL cholesterol, LDL cholesterol, and HbA_{1c} . The serum levels of low-density lipoprotein (LDL) cholesterol, HDL-C were measured using a biochemical autoanalyzer (Toshiba TBA 120FR; Toshiba Medical Systems Corp., Tokyo, Japan in Takahata Public Hospital, and Hitachi 7180, Hitachi High-Technologies Corp., Tokyo, Japan in Tendo Hospital). The HbA_{1c} levels were measured in the morning under fasting using high-performance liquid chromatography (HLC-723-G8; Tosho Co., Tokyo, Japan) at Takahata Public Hospital and Tendo Hospital.

Medications and complication

Use of medication of diabetes mellitus and hyperlipidemia was defined from medical records. When patients received medication of an anti-diabetic agent, we regarded the medication as that of diabetes mellitus. Furthermore, when patients received medication of a cholesterol-lowering agent, we regarded it as medication of hyperlipidemia. Complication of sleep apnea syndrome was assessed by the standard criteria for obstructive sleep apnea syndrome [11].

Health behaviors

Health behaviors (e.g., alcohol intake, smoking) were assessed by questionnaire. Alcohol consumption was graded as 0 (0 drink/week) to 7 (7 or more drinks/week). Subjects were considered current smokers if they smoked at the time of the interview. They were regarded as previous smokers if they were not current smokers but had smoked 100 cigarettes of tobacco in their entire life. They were considered non-smokers if they had smoked less than those amounts.

The Pittsburgh sleep quality index

The Pittsburgh Sleep Quality Index (PSQI) is a standardized self-rated questionnaire developed to assist in measuring sleep quality [12, 13]. The 24-item questionnaire generates seven component scores, with subscale scores 0 to 3: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. The addition of these seven components yields a global score of subjective sleep quality. The global score is 0 to 21: a higher score is indicative of poorer subjective sleep quality.

Statistical analyses

Data were expressed as mean \pm SD. We analyzed the relation with mean ABI on the following parameters; 1) age (years old), 2) sex (male, female), 3) body height (cm), 4) body weight (kg), 5) BMI (kg/m^2), 6) waist circumference (cm), 7) systolic BP (mmHg), 8) diastolic BP (mmHg), 9) mean BP (mmHg), 10) HDL-cholesterol (mg/dl), 11) LDL-cholesterol (mg/dl), 12) HbA_{1c} (%), 13) global score of PSQI, 14) smoking habit (nonsmoker, previous smoker, current smoker) 15) alcohol habit (drinks/

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Table 1. Univariate analysis with mean ABI as the dependent variable

analysis	variable	statistics	<i>p</i>
Pearson's linear regression			
		<i>r</i> value	
	body height	0.36	< 0.001
	body weight	0.30	< 0.005
	HbA _{1c}	-0.24	< 0.05
	systolic BP	-0.23	< 0.05
	mean BP	-0.19	ns
	diastolic BP	-0.14	ns
	HDL cholesterol	0.12	ns
	LDL cholesterol	0.03	ns
	waist circumference	-0.02	ns
	BMI	-0.01	ns
Spearman's regression			
		<i>rho</i> value	
	global PSQI score	-0.31	< 0.005
	alcohol habit	0.23	< 0.05
	age	-0.18	ns
one-way ANOVA			
		<i>F</i> value	
	male/female	6.65	< 0.05
	smoking habit	1.37	ns
	diabetes mellitus	1.32	ns
	sleep apnea syndrome	1.18	ns
	hypercholesterolemia	1.01	ns

Abbreviations: ABI, ankle-brachial pressure index; BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; BMI, body mass index; PSQI, the Pittsburgh Sleep Quality Index; ANOVA, analysis of variance; ns, not significant.

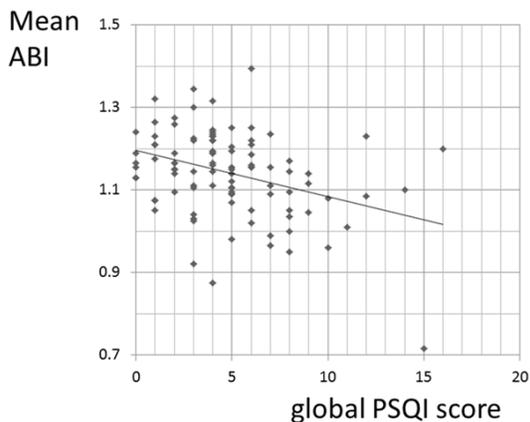


Figure 1. Correlations between global PSQI score and mean ABI. Lower ABI is associated with poor global PSQI ($\rho = -0.31$, $p < 0.005$). PSQI, the Pittsburgh Sleep Quality Index; ABI, ankle-brachial pressure index.

week), 16) medication of diabetes mellitus (yes/no), 17) medication of hyperlipidemia (yes/no), and 18) diagnosis of sleep apnea syndrome (yes/no).

Univariate analysis of the effects of each potential factor on ABI was performed with Pearson's linear regression analysis for continuous variables (body height; body weight; BMI; waist circumference; systolic BP; diastolic BP; mean BP; HDL-cholesterol, LDL-cholesterol, HbA_{1c}), with Spearman's regression analysis for discrete variables (age, PSQI, alcohol habit) and with one-way ANOVA (analysis of variance) for categorical variables (sex, smoking habit, medication of diabetes mellitus, medication of hyperlipidemia, diagnosis of sleep apnea syndrome). Interaction among factors was examined using multiple stepwise regression analysis with mean ABI as the dependent variable after forcing parameters univariately significant into the model. When performing multiple stepwise regression analysis, the enter criterion used was .05 of the *p* value; the removal criterion used was .10 of the *p* value. Statistical analyses were performed using SPSS software version 19.0 (SPSS Inc, Chicago, IL). Statistical significance was inferred for $p < .05$.

Results

The sample of 101 subjects had a mean age of 70.0 ± 10.1 and included 47 (46.5%) women. A mean value of ABIs measured from both extremities for the sample (mean ABI) was 1.14 ± 0.12 . Two subjects (2.0%) had mean ABI < 0.9, suggesting peripheral artery disease. The global PSQI score for the sample was 4.8 ± 3.2 (median 4). Thirty-four subjects (33.6%) had global PSQI scores > 5, indicating poor sleep quality.

Table 1 presents univariate analysis for estimating the effects of each factor on mean ABI. Analysis of the effects was performed with Pearson's linear regression analysis for continuous variables (body height, body weight, BMI, waist circumference, systolic BP, diastolic BP, mean BP, HDL-cholesterol, LDL-cholesterol, HbA_{1c}), with Spearman's rank regression analysis for discrete variables (age, global PSQI score, alcohol habit) and with one-way ANOVA

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Table 2. Multiple stepwise regression with mean ABI as the dependent variable after forcing body height, body weight, systolic BP, HbA_{1c}, global PQSI score, alcohol habit, and sex into the model

model included variable	model summary				regression coefficients		
	<i>R</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	<i>beta</i>	<i>t</i> value	<i>p</i>
1. model including global PSQI score							
body height	.36	.13	14.8	< .001	.28	3.0	< .005
+ global PSQI score	.46	.22	10.4	< .002	-.29	-3.2	< .005
+ HbA _{1c}	.50	.25	4.6	< .05	-.19	2.2	< .05
2. model without global PSQI score							
body height	.36	.13	17.8	< .001	.33	3.5	< .005
+ HbA _{1c}	.42	.17	4.9	< .05	-.21	-2.2	< .05

Abbreviations: ABI; ankle-brachial pressure index, BP; blood pressure, PSQI; the Pittsburgh Sleep Quality Index.

for categorical variables (sex, smoking habit). Among 18 analyzed parameters, seven parameters were found to be significantly related with ABI: body height, body weight, systolic BP, HbA_{1c}, global PSQI score, alcohol habit or sex. Actually, lower ABI is associated with lower body height ($r = 0.36$, $p < 0.001$), lower body weight ($r = 0.30$, $p < 0.005$), greater systolic BP ($r = -0.23$, $p < 0.05$), greater HbA_{1c} ($r = -0.24$, $p < 0.05$), poor global PSQI ($\rho = -0.31$, $p < 0.005$, **Figure 1**), alcohol intake ($\rho = 0.23$, $p < 0.05$) or female sex ($F = 6.65$, $p < 0.05$).

Next, the interaction among factors was examined using multiple stepwise regression analysis with mean ABI as the dependent variable after forcing body height, body weight, systolic BP, HbA_{1c}, global PQSI score, alcohol habit and sex into the model (model 1, **Table 2**). The results indicated that body height, global PSQI score and HbA_{1c} are significant parameters affecting ABI (R^2 for the model = 25%, $p < 0.001$). Lower body height, poor glycemic control and poor sleep quality were independently correlated with decreased ABI. The additional analysis excluding global PQSI score (model 2, **Table 2**) showed that body height and HbA_{1c} were still significant. However for this model, R^2 was limited ($R^2 = 0.17$). Other parameters such as body weight, systolic BP, alcohol habit and sex were not significant.

Discussion

This study is the first demonstrating that the poor sleep quality was associated with lower ABI in patients with essential hypertension. This association was independent of the previously known risk factors or individual body size. The results may provide new information and

insights related to interaction between sleep quality and blood pressure.

Sleep quality and leg blood pressure

Short sleep duration is known to modulate blood pressure [14]. Disturbed sleep acutely increases blood pressure. Prolonged short sleep duration lead to hypertension through extended exposure to raised blood pressure and increased salt retention.

Recently, relations between poor sleep quality and hypertension were investigated by use of the Pittsburgh Sleep Quality Index (PSQI). Results show that poor sleep quality is significantly associated with resistance to treatment, especially in hypertensive women [15]. The PSQI is a self-rating questionnaire resulting in a global score between 0 and 21. The PSQI is a widespread tool to measure sleep quality in various types of subjects groups, such as sleep disorders [13], various somatic disease [16], nursing home residents [17], and healthy elder subjects [18]. In Japanese version of the PSQI (PSQI-J), Doi et al. confirmed the utility of the PSQI-J as a reliable and valid measure for subjective sleep quality in clinical practice and research [19]. The global PSQI score was inversely correlated with The SF-36 mental component summary (MCS) and physical component summary (PCS) [20].

Using this index, the present observations suggest that poor sleep quality is associated with the lower leg blood pressure in patients with essential. The ABI is considered to be a reliable sign of peripheral arterial disease when it is lower than 0.90. However, the cardiovascular risk increases gradually in subjects with ABI

higher than 0.9 [21]. Poor sleep quality might be related with lower ABI, and may be a potent risk factor of cardiovascular events.

Body height and leg blood pressure

This study demonstrated that lower leg blood pressure was associated with body height or HbA_{1c} level as well as sleep quality. Body height has been regarded as a determinant of leg blood pressure [22]. London et al. [22] measured ABIs in 223 subjects including 55 patients with hypertension, and exhibited the relations between ABIs and body heights. They explained the mechanism of association with body height as distance of pulse wave propagation: taller body height, i.e. longer distance of pulse wave propagation increased artery non-uniformity with decreased extensibility of peripheral artery. Therefore, central-to-peripheral blood pressure in tall persons may increase. In their study, they also found a sex difference: high ABI in male and low ABI in female. However, they concluded that the differences were dependent of body height differences. Concordantly, we observed similar tendencies: higher ABI was seen in men, people with heavy body weight, and tall people. After multivariate analysis, sex and body-weight differences in ABIs were attributed to body height differences. These lines of analysis indicate that body height is a major determinant of ABI. The effects on ABIs should be carefully evaluated in a clinical case.

The HbA_{1c} level is also an established determinant of ABI [23, 24]. Poor glycemic control is associated with an increased risk of peripheral artery disease, resulting in low ABIs, as several reports [24] and the present study suggested.

Clinical implication and limitation

This study revealed that lower leg pressure is associated with poor sleep quality, as well as body height or HbA_{1c} level. This might be a key to the elucidating of the relation with sleep disorder to cardiovascular disease. Sleep quality is affected by overall health and endogenous and exogenous factors. Impairments in multiple systems or organs may be accumulated in elderly person and cause comorbid insomnia. With consideration of these relations, more attention should be devoted to poor sleep quality. Criticisms in this study are its study size and

population. The study sample size was relatively small. Additional research should be conducted with a large study size and in other pathological conditions associated with poor sleep quality.

Disclosure of conflict of interest

The authors have no relationship with any industry.

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