267
Yoshimura K[1], Shimizu Y[1], Kanematsu A[2], Ogawa O[1], Sekine A[3], Nakayama T[3]
1. Kyoto University Graduate School of Medicine, 2. Hyogo College of Medicine, 3. Kyoto University School of Public Health

CORRELATES OF NOCTURNAL VOIDING IN WOMEN: CARDIOVASCULAR AND METABOLIC FACTORS

Hypothesis / aims of study
Previous epidemiological studies have shown several correlates of nocturnal voiding, such as hypertension, diabetes, stroke, body mass index, snoring, arrhythmia, and sleeplessness. Several of these factors have associations with metabolic syndrome and abnormalities of the cardiovascular system. Some studies have shown a relationship between lower urinary tract symptoms including nocturnal voiding and cardiovascular/metabolic factors. (1, 2) In this study, we investigated the relationship between nocturnal voiding in women and objective parameters related to cardiovascular and metabolic parameters.

Study design, materials and methods
The Nagahama study was composed of a questionnaire survey, anthropometric, physiological, and biochemical measures from blood samples, and we obtained genomic information as well. A total of 5,980 women, aged 35 to 70 years, were enrolled in this study. Among the variables assessed, we selected 32 parameters (12 derived from the questionnaire, 9 from anthropometric or physiological measures, and 11 from biochemical measures) to be evaluated as correlates of nocturnal voiding. These parameters included the cardio-ankle vascular index (CAVI) and augmentation index (AI), which represent the stiffness of the arteries, and the ankle-brachial index (ABI), which represents the degree of stricture of the arteries. Statistical analyses were performed in 3 steps. First, univariate analysis was performed to confirm the basic relationship between 1 variable and nocturnal voiding, and if $p<0.25$, the variable was applied to the next step. In step 2, multivariate logistic regression analysis was performed using the parameters included in the same category; for example, diabetic history, blood sugar, hemoglobin A1c, and serum insulin levels in the category of diabetes, to remove confounding factors. The types of categories are shown in the Table. Using the variables with $p<0.05$ in step 2, the final multivariate logistic regression analysis was performed.

Results
Age, length of sleep, sleeplessness, urgency, waist circumference, menopause, history of hypertension, hypersensitive C-reactive protein (hsCRP), LDL cholesterol, and serum B-type natriuretic peptide (BNP) were independently associated with one or more nocturnal voiding per night. Age, length of sleep, sleeplessness, urgency, serum BNP, waist circumference, body mass index, and hsCRP were independently associated with two or more nocturnal voiding per night. (Table)

Interpretation of results
Most variable assessed had an association with nocturnal voiding in univariate analyses. However, the important correlates of nocturnal voiding were age, quality and quantity of sleep, waist circumference, serum BNP, and hsCRP. Although the objective parameters, which represent the stiffness or degree of stricture of the arteries, had no association, the progressing atherosclerosis, which was represented by hsCRP, had an independent association with nocturnal voiding

Concluding message
Inflammation inducing arteriosclerosis, which is represented by hsCRP, has an independent association with nocturnal voiding in women. Cardiac loading, which is represented by serum BNP, is an important correlate with nocturnal voiding as well

Category	Factor		Nocturnal Frequency≥1		Nocturnal Frequency≥2	
			p-value	OR (95% CI)	p-value	OR (95% CI)
Age	Age		<0.001	1.052 (1.042-1.061)	<0.001	1.063 (1.049-1.078)
Hormonal status	Menopause	(yes/no)	0.008	1.326 (1.075-1.635)	0.06	
Urgency	Urgency	(yes/no)	<0.001	1.545 (1.430-1.669)	<0.001	1.525 (1.413-1.645)
Sleep	Time in bed	(hrs.)	<0.001	1.333 (1.256-1.414)	<0.001	1.197 (1.099-1.303)
	Sleeplessness	(yes/no)	<0.001	2.519 (2.141-2.968)	<0.001	2.825 (2.336-3.413)
	Snoring	(yes/no)	NA		NA	
	Daytime sleepness	(yes/no)	0.27		0.56	
Obesity	BMI	(kg/m/m)	0.82		0.005	0.932 (0.897-0.979)
	Waist circumference	(cm)	0.002	1.011 (1.004-1.018)	<0.001	1.036 (1.018-1.054)
Hypertension	History	(yes/no)	0.008	1.271 (1.066-1.516)	0.06	
	Systolic pressure	(mmHg)	0.10		Con	
	Diastolic pressure	(mmHg)	0.56		0.49	
	Central systolic pressure	(mmHg)	0.16		0.60	
Diabetes	History	(yes/no)	Con		Con	
	Blood sugar	(mg/dl)	0.55		0.25	
	Hemoglobin A1c	(%)	0.69		0.70	
	Insulin	(μU/ml)	NA		NA	
Dyslipidemia	History	(yes/no)	0.79		0.84	
	Triglycelide	(mg/dl)	0.35		0.12	
	LDL-cholesterol	(mg/dl)	0.011	0.997 (0.995-0.999)	0.06	
	HDL-cholesterol	(mg/dl)	Con		Con	
Cerebrovascular disease	History	(yes/no)	0.46		0.40	
Cardiac functions	History of cardiovascular disease	(yes/no)	0.81		0.25	
	Heart rate	(/min)	0.11		0.53	
	Augmentation index	(%)	0.06		0.62	
	B-type natriuretic peptide	(pg/ml)	0.028	1.005 (1.001-1.009)	<0.001	1.007 (1.003-1.011)
Arterioscrelosis	Hypersensitive C-reactive protein	(mg/dl)	0.010	1.003 (1.001-1.006)	0.025	1.003 (1.001-1.005)
	Cardio-ankle vascular index		0.95		0.16	
	Ankle brachial index		0.96		0.46	
Renal functions	Serum creatinine	(mg/dl)	0.27		0.90	
	Estimated glomerular filtration rate	(ml/min)	0.26		0.06	
Hepatic function	Serum cholinesterase	(IU/L)	0.29		0.82	

NA: not analysed in step 2 because of a lack of association in step 1; Con: removed from final analysis because of confounding in step 2.

References
1. Ponholzer A. The association between vascular risk factors and lower urinary tract symptoms in both sexes. Eur Urol, 50; 581-586
2. Kim S. Association between lower urinary tract symptoms and vascular risk factors in aging men: The Hallym aging study. KJU, 51; 477-482, 2010

Specify source of funding or grant	**Takeda Scinence Foundation**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Kyoto University medical institutional review board**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**